ORIGINAL RESEARCH

Mediating Effect of Emotional Symptoms on the Association Between Alexithymia and Substance Dependence in Patients with Substance Use Disorder: The Protective Role of Family Support and Self-Efficacy

Dian-Jeng Li [ID][1,2], Hung-Chi Wu[1,3,4]

[1]Department of Addiction Science, Kaohsiung Municipal Kai-Syuan Psychiatric Hospital, Kaohsiung, Taiwan; [2]Department of Nursing, Meiho University, Pingtung, Taiwan; [3]Department of Nursing, Fooyin University, Kaohsiung, Taiwan; [4]College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

Correspondence: Dian-Jeng Li, Department of Addiction Science, Kaohsiung Municipal Kai-Syuan Psychiatric Hospital, 130, Kai-Syuan 2nd Road, Ling-Ya District, Kaohsiung, 802, Taiwan, Tel +886-7-751-3171 ext. 2317, Fax +886-7-16-1843, Email edcrfvm45@hotmail.com

Background: The etiology of the association between alexithymia and substance use is complex, and there is an urgent need to explore the related factors. The aims of this study were to develop a conceptual model to verify the mediating effect of emotional symptoms and moderating effect of family support and self-efficacy on the association between alexithymia and substance dependence.

Methods: A total of 117 participants (103 males and 14 females; age at 35.29 ± 8.72 years) with substance use disorder were analyzed. Outcome measures included demographic characteristics, severity of dependence, symptoms of alexithymia, emotional symptoms (depression, anxiety, and somatic symptoms), level of family support, and self-efficacy. The PROCESS macro in SPSS was used to estimate path coefficients and adequacy of the moderated mediation model, which was adjusted for demographic characteristics.

Results: Most of the participants had amphetamine use disorder (n = 42, 35.9%). After controlling for the effects of demographic characteristics, the moderated mediation model showed that the association between alexithymia and substance dependence was mediated by emotional symptoms and moderated by family support and self-efficacy. A higher level of family support reduced the effect of alexithymia on emotional symptoms, and a higher level of self-efficacy reduced the effect of emotional symptoms on substance dependence.

Conclusion: Family support and self-efficacy have a protective effect on the association between alexithymia and substance dependence in patients with substance use disorder. Early interventions to enhance these protective factors may be beneficial.

Keywords: alexithymia, emotional symptom, family support, self-efficacy, substance use

Introduction

Characteristics of Alexithymia

Alexithymia is defined as the inability or difficulty to identify and verbalize emotions.[1] The term "alexithymia" is derived from Greek, and translates to "a lack of words for emotion". It was first proposed by Nemiah et al, who comprehensively investigated patients suffering from psychosomatic problems such as gastrointestinal symptoms, and used the term to describe observations about their patients' characteristics, including difficulties in describing subjective emotions, poor fantasy, and pragmatic cognitive style.[2] A previous study further described that a lack of imagination and positive emotions, and a high prevalence of negative emotions were characteristics of alexithymia.[3] In other words, alexithymia is

considered to reflect deficits or alterations in emotional processing,[4] which is associated with deficits in the regulation of emotion.[5] Moreover, alexithymia is also considered to be a personality trait within the general population.[6] A well-known conceptual model of alexithymia classified the four key factors of alexithymia as: difficulties in describing and recognizing emotions; difficulties in differentiating between feelings and emotion-related bodily sensations; limited imagination; and an externally oriented cognitive style.[7] Another study conceptualized the components of alexithymia as difficulties in the attentional and appraisal stages of emotion processing.[8] Alexithymia is associated with several mental disorders, including depression, anxiety disorders, and eating disorders.[9,10] A meta-analysis also found that approximately half of patients with autistic spectrum disorder also had alexithymia, and further identified shared symptoms between them.[11]

Association Between Alexithymia, Substance Use, and Other Factors

As alexithymia is commonly comorbid with a number of mental disorders, we were interested in the association between alexithymia and substance use. Substance use has become a predominant public health concern affecting many people worldwide. It is diagnosed as a condition in which there is uncontrolled use of a substance despite harmful consequences and impaired social-economic function.[12] According to the World Drug Report in 2021,[13] about 275 million people used substances globally in 2020 with a prevalence of 0.55%, which was an increase of 22% from 2010. Regarding the association between substance use and alexithymia, a high prevalence of alexithymia (40–50%) among patients diagnosed with alcohol abuse or dependence was reported in an earlier study.[14] In addition, a recent meta-analysis reported a significant association between substance use and alexithymia.[15] It reported that substance users had substantially higher alexithymia than nonusers, and alexithymic individuals had significantly higher levels of substance use than non-alexithymic ones. Furthermore, alexithymia may have an undesirable impact on the outcomes of substance use disorder (SUD) treatment, such as shorter engagement in the treatment course and earlier relapse.[16] Many factors may be involved in the intertwined relationship between substance use and alexithymia. For example, the association between alexithymia and severity of alcohol use has been associated with a number of psychological factors including mood and emotional dysregulation, attachment, trauma, and cognitive function.[17] Taken together, this evidence highlights the need to understand the complicated etiologies of the association between alexithymia and substance use.

The complicated interaction between alexithymia and emotional problems may result from the nature of emotional disabilities for alexithymia. Etiologically, several studies for emotional processing deficits in alexithymia have been proposed including emotional avoidance,[18] poor interoceptive awareness[19], and impaired perceptual abilities.[20,21] On the other hand, substance use is also significantly correlated with emotional features, such as depression and anxiety.[22] Taking together, we suppose that alexithymia and substance use share etiological overlap with emotional functions.

Regarding other factors, family support may also involve the above association. Previous research highlighted the relationship between alexithymia and addiction (problematic online gambling), and it highlighted the moderation role of family cohesion.[23] Another study shows that a lack of family support is associated with alexithymia in patients with alcohol use disorder.[24] On the other hand, self-efficacy is reported to be beneficial in substance abstinence by reducing the negative affect scores.[25] In summary, these factors deserve further investigation to explore their role in the association between alexithymia and substance use.

Aim of the Study

The aim of this study was to develop a conceptual model to investigate the associations between alexithymia, emotional symptoms, and substance dependence. We developed the model with reference to previous studies which partially investigated the associations between alexithymia, depression/emotion, and substance use.[26,27] As studies exploring potential protective factors in these associations are lacking, we further aimed to investigate these factors. We hypothesized that the association between alexithymia and substance dependence may be mediated by emotional symptoms. If a mediation model could be identified, we further hypothesized that the mediating effect may be moderated by protective factors such as family support or self-efficacy against illicit substance use.

Methods

Participants and Procedures

The current study derived data from the "Establish an integrated medical demonstration center for drug addiction: a pilot program (EIMDCDA)" project, the details of which have been published previously.[28] In brief, EIMDCDA is a multicenter intervention in Taiwan which aims to develop multi-dimensional strategies for the treatment of patients with SUD, including case management, clinical treatment at outpatient departments, and psychological interventions (neurofeedback or mindfulness-based relapse prevention group therapy). The inclusion criteria for the participants in EIMDCDA were: 1) age at least 20 years; 2) meeting the DSM-5 criteria for SUD as diagnosed by a psychiatrist; 3) ability to understand the objectives and processes of the project; and 4) willingness to sign informed consent before treatment. The exclusion criteria were participants: 1) aged below 20 years or above 65 years; and 2) who were unable to cooperate with the treatment programs and assessments.

In the current study, we only included initial assessment data from the EIMDCDA database from March 2020 to May 2024 as a cross-sectional survey. We included data from the initial assessments because the participants may have had sufficiently severe symptoms (substance dependence and emotional symptoms) for analysis before treatment. The current study was approved by the Institutional Review Board of Kai-Syuan Psychiatric Hospital (KSPH-2019-23), and was conducted in accordance with the current revision of the Declaration of Helsinki and national legal requirements (Human Subjects Research Act, Taiwan). Informed consent was obtained from all participants at the time of recruitment.

Outcome Measures

The Severity of Dependence Scale (SDS)

We used the Severity of Dependence Scale (SDS) to assess the severity of illicit substance dependence. The SDS is composed of five self-reported items scored with a four-point Likert scale. A higher total SDS score indicates higher severity of substance dependence. The Chinese version of the SDS has been verified to have good internal consistency (Cronbach's alpha: 0.75) and test-retest reliability (0.88).[29]

Toronto Alexithymia Scale (TAS)

The Toronto Alexithymia Scale (TAS) is a 20-item self-administered questionnaire which is to estimate the severity of alexithymia, with each item being rated on a five-point Likert scale.[6] Five of the items are negatively keyed, and the other 15 items are positively keyed. The TAS consists of three categories, namely difficulty identifying feelings and distinguishing them from the bodily sensations of emotions, difficulty describing feelings to others, and the externally oriented cognitive style of thinking. A higher total TAS score indicates a higher degree of alexithymia. The Chinese version of the TAS has been shown to have good reliability and validity.[30,31]

Chinese Health Questionnaire (CHQ)

The Chinese Health Questionnaire (CHQ) is a 12-item self-reported scale, developed to assess emotional problems and psychosomatic symptoms.[32] The CHQ is based on the General Health Questionnaire, which is used to estimate the severity of somatic symptoms, anxiety, insomnia, social dysfunction and depression.[33] The CHQ is scored using a four-point Likert scale ranging from 0 (not at all) to 3 (much more common than usual), and it has been validated in previous studies.[32] It consists of three dimensions, namely emotional distress, somatic symptoms, and interpersonal difficulties. In the current study, we used the total CHQ score to estimate the severity of emotional problems, with a higher score representing a higher degree of emotional problems.

Family Adaptation, Partnership, Growth, Affection, Resolve Index (APGAR)

We used the Chinese version of the five-item self-administered APGAR Index to estimate the participants' satisfaction with family support during their childhood and adolescence. The Chinese version of the APGAR Index has been shown to have good reliability and validity.[34,35] Each item is rated on a four-point Likert scale from 0 (never) to 3 (all the time). The total score ranges from 0 to 15, with a higher score indicating a higher level of family support.

Drug Avoidance Self-Efficacy Scale (DASES)

The DASES is a 16-item self-reported questionnaire which was designed to estimate the self-efficacy of illicit substance abstinence for those at high risk.[36] Participants are asked to imagine being in a specific environment or situation and to rate their level of ability (self-efficacy) to resist substance use using a seven-point Likert scale (1 = certainly no, to 7 = certainly yes). A higher score indicates higher self-efficacy of illicit substance abstinence. The internal consistency and validity of the DASES have been shown to be acceptable.[37]

Further analysis of these measures was conducted to ensure their reliability and validity in the current study, as discussed in the Statistical analysis section below.

Demographic Information

Demographic data were collected from the EIMDCDA database, including sex, employment status, marital status, psychiatric comorbidities, age, and educational level.

Statistical Analysis

Initially, descriptive statistics were conducted to summarize the clinical characteristics at the initial assessment. To assess the reliability and construct validity of the SDS, TAS, CHQ, APGAR and DASES in the current study, internal consistency (Cronbach's alpha) and experimental factor analysis (EFA) were applied. A Cronbach's alpha value > 0.6 was considered to indicate acceptable reliability.[38] The Kaiser–Meyer–Olkin (KMO) measure of sampling adequacy and Bartlett's test of sphericity were used to estimate the suitability of EFA. A KMO value of > 0.6 and a statistically significant Bartlett's test (P < 0.05) were considered to indicate that the data were suitable for EFA.[39] Moreover, total variance explained in EFA was further analyzed to estimate the construct validity. It is common to consider a solution that accounts for 60% of the total variance as an acceptable threshold in social science.[40]

Before developing the conceptual model, bivariate associations of variables were assessed with Pearson correlation analysis. If there was a significant association between variables (alexithymia, emotional symptoms, substance dependence, family support, and self-efficacy), we further used the conceptual model to identify the interactions between them. In the conceptual model, we hypothesized that the association between "alexithymia" and "substance dependence" may be mediated by "emotional symptoms" (Supplemental Figure 1). If an indirect effect (mediation) was confirmed, we further tested the moderation effect with "family support" (Supplemental Figure 2) or "self-efficacy against substance use" (Supplemental Figure 3).

To test the indirect and moderated indirect effects, we developed a moderated mediation model using PROCESS macro version 3.4 in SPSS.[41,42] In PROCESS, different numbers are used to identify different preset complex models. The mediation effect was verified by Model 4 (Supplemental Figure 1). Model 7 was used for the moderated mediations in the conceptual model shown in Supplemental Figure 2, and model 14 was applied for the conceptual model of moderated mediation in Supplemental Figure 3. PROCESS performs ordinary least square regression to estimate the moderated indirect effect. To prevent the confounding effect of demographic characteristics, the ordinary least square regression was adjusted for sex, age, employment status, educational level, marital status, and psychiatric comorbidities.

In the above models, the quantitative variables were centered,[43] and 95% bootstrap confidence intervals (CIs) with 5000 bootstrapping resamples were calculated to ameliorate the impact of non-normality of the study sample. The standardized indirect effect with 95% CI was used to verify the mediation effect of emotional symptoms. The mediation effect was considered to be statistically significant if the 95% CI did not include zero. The index of moderated mediation and its 95% CI were used to identify the statistical significance of the moderated mediation effect.[41] If the 95% CI did not include zero, the moderated mediation effect was considered to be statistically significant. If the moderated mediation effect was statistically significant, the conditional indirect effects of alexithymia on substance dependence (through emotional symptoms) were evaluated at three different levels of family support or self-efficacy, corresponding to the values of mean plus SD, medium, and mean minus SD. All analyses were performed using SPSS version 23.0 for Windows (IBM Inc., Armonk, NY).

Results

A total of 117 of participants (103 males and 14 females) were included, with a mean age of 35.29 years. Most of the participants had amphetamine use disorder (n = 42, 35.9%). The demographic characteristics of the participants are listed in Table 1, and details of substance use, psychiatric comorbidities, and marital status are listed in Supplementary Table 1. The correlation matrix with significance is shown in Table 2. Positive associations between the TAS, CHQ, and SDS were identified, and they were negatively associated with APGAR and DAES. The results of reliability and construct validity of all measurements are presented in Supplementary Table 2. In brief, the Cronbach's alpha of all measurements was > 0.6, indicating acceptable reliability. The results of KMO and Bartlett's test demonstrated the adequacy of EFA,

Table 1 Distribution of Demographic Characteristics (N = 117)

Variables	Mean (SD)
Age	35.29 (8.72)
Educational level (years)	13.62 (3.86)
SDS	6.55 (3.51)
TAS	36.52 (12.35)
CHQ	4.19 (3.38)
APGAR	4.12 (3.52)
DASES	72.02 (13.5)

Variables	Counts (%)
Sex	
Male	103 (88)
Female	14 (12)
Employment	
On job	89 (76.1)
Jobless	28 (23.9)
Marital status	
With partner	22 (18.8)
Without partner	95 (81.2)
Psychiatric comorbidities	
No	70 (59.8)
Yes	47 (40.2)

Abbreviations: SD, Standard deviation; SDS, Severity of dependence scale; TAS, Toronto Alexithymia Scale-20; CHQ, Chinese Health Questionnaire; DASES, Drug avoidance self-efficacy scale; APGAR, Family Adaptation, Partnership, Growth, Affection, Resolve Index.

**Table 2** The Correlation Matrix of Observed Variables

	SDS	TAS	CHQ	APGAR	DASES
SDS	–	0.418**	0.494**	−0.281**	−0.436**
TAS		–	0.444**	−0.557**	−0.485**
CHQ			–	−0.371**	−0.294**
APGAR				–	0.409**
DASES					–

Note: **: p < 0.001.
Abbreviations: SDS, Severity of dependence scale; TAS, Toronto Alexithymia Scale-20; CHQ, Chinese Health Questionnaire; DASES, Drug avoidance self-efficacy scale; APGAR, Family Adaptation, Partnership, Growth, Affection, Resolve Index.

where the KMO values were all above 0.6 with statistical significance of Bartlett's test (p<0.05). Moreover, the total variances explained were all > 0.5, indicating the adequacy of construct validity.

The results confirmed the mediation effect of emotional symptoms (Supplementary Table 3 and Figure 1). The ordinary least square regression showed that alexithymia was positively associated with the severity of emotional symptoms (a pathway of Model 4 with β coefficient = 0.12, P < 0.001). The severity of emotional symptoms was also positively associated with the severity of substance dependence (b pathway of Model 4 with β = 0.42, P < 0.001). The standardized indirect effect was estimated to be 0.181 with a 95% CI of 0.0097 to 0.271, demonstrating a significantly positive mediation effect. The results of ordinary least square regression demonstrated that alexithymia was positively associated with the severity of emotional symptoms (a pathway of Model 7 with β = 0.11, P < 0.001) (Figure 2 and Table 3). The severity of emotional symptoms was also positively associated with the severity of substance dependence (b pathway of Model 7 with β = 0.42, P < 0.001). The index of moderated mediation with family support was estimated to be −0.005 with a 95% CI of −0.0012 to −0.0005, indicating a significantly negative moderation effect. Taken together, these results supported the positive indirect effect of alexithymia on substance dependence through the positive mediating effect of emotional symptoms. A higher level of family support was shown to decrease the effect of alexithymia, thus revealing a negative moderating effect. In the moderated mediation model with self-efficacy (Table 4 and Figure 3), the severity of alexithymia was positively associated with the severity of emotional symptoms (a pathway of Model 14 with β = 0.12, P < 0.001). The severity of emotional symptoms was also positively associated with the severity of substance dependence (b pathway of Model 14 with β = 0.32, P < 0.001). The index of moderated mediation with family support was estimated to be −0.003 with a 95% CI of −0.0045 to −0.001, indicating a significantly negative moderation effect.
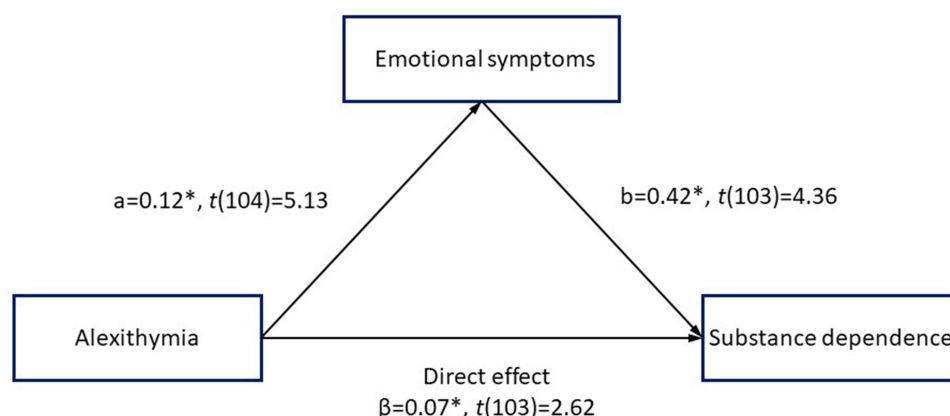
Figure 1 The model of mediation effect with emotional symptoms. (**a**): a pathway of Model 4, p<0.001. (**b**): b pathway of Model 4, p<0.001. Direct effect: p=0.01. *: p<0.05.
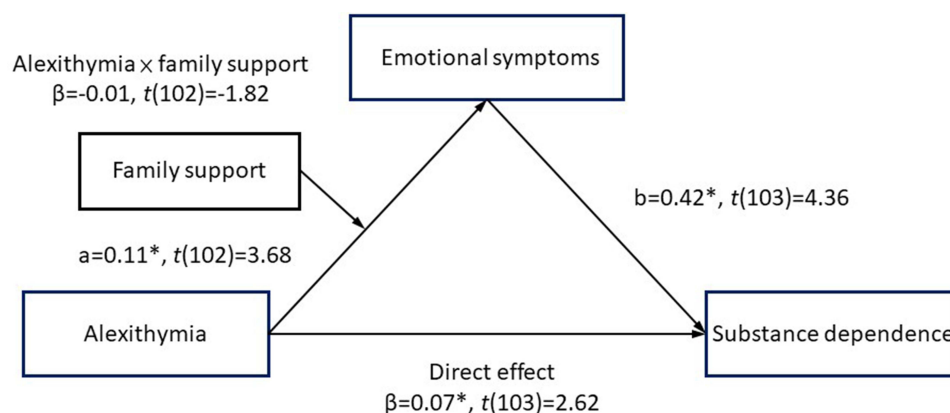
Figure 2 Final model showing the co-efficient estimates and statistical significance for the moderating effect of family support. (**a**): a pathway of Model 7, p<0.001. (**b**): b pathway of Model 7, p<0.001. Direct effect: p=0.01. *: p<0.05.

Table 3 Moderated Indirect Effect of Family Support on the Association Between Alexithymia, Emotional Symptoms, and Substance Dependence with Multiple Adjustment[a]

| Outcome variable: emotional symptoms[b]					
Predictors	β	SE	p	LLCI	ULCI
Alexithymia	0.108	0.029	<0.001	0.05	0.166
Family support	−0.228	0.104	0.03	−0.434	−0.023
Alexithymia ×Family support	−0.013	0.104	0.07	−0.026	0.001
Outcome variable: substance dependence[c]					
Predictors	β	SE	p	LLCI	ULCI
Alexithymia	0.068	0.026	0.01	0.017	0.12
Emotional symptoms	0.417	0.096	<0.001	0.227	0.607
Index of moderated mediation	β	SE	p	LLCI	ULCI
Family support	−0.005	0.003	–	−0.0012	−0.0005

Notes: LLCI: lower limit of 95% confidence interval. ULCI: upper limit of 95% confidence interval. β: regression coefficient. SE: standard error. [a]: Adjusted by sex, age, employment status, educational level, marital status, and psychiatric comorbidities. [b]: Model $F_{(5, 102)}$ = 7.39; $p < 0.001$. [c]: Model $F_{(4, 103)}$ = 11.51; $p < 0.001$.

Table 4 Moderated Indirect Effect of Self-Efficacy on the Association Between Alexithymia, Emotional Symptoms, and Substance Dependence with Multiple Adjustment[a]

Outcome variable: emotional symptoms[b]					
Predictors	β	SE	p	LLCI	ULCI
Alexithymia	0.123	0.024	<0.001	0.075	0.17
Outcome variable: substance dependence[c]					
Predictors	β	SE	p	LLCI	ULCI
Alexithymia	0.039	0.027	0.146	−0.014	0.091
Emotional symptoms	0.324	0.09	<0.001	0.146	0.502
Self-efficacy	−0.096	0.023	<0.001	−0.142	−0.051
Depression × Self-efficacy	−0.021	0.007	0.002	−0.033	−0.008
Index of moderated mediation	β	SE	p	LLCI	ULCI
Self-efficacy	−0.003	0.001	–	−0.0045	−0.001

Notes: LLCI: lower limit of 95% confidence interval. ULCI: upper limit of 95% confidence interval. β: regression coefficient. SE: standard error. [a]: Adjusted by sex, age, employment status, educational level, marital status, and psychiatric comorbidities. [b]: Model $F_{(3, 104)}$ = 9.44; $p < 0.001$. [c]: Model $F_{(6, 101)}$ = 12.98; $p < 0.001$.

To better understand the moderating effect of family support and self-efficacy, bootstrap indirect effects were estimated for the mediating effect of the severity of emotional symptoms at three different levels of family support and self-efficacy (mean + SD, mean, and mean - SD). For all levels of family support, none of the 95% CIs of the model in Figure 2 contained zero (Supplementary Table 4). The 95% CIs of the model in Figure 3 showed that the two highest values of self-efficacy did not contain zero, while the lowest two values did (Supplementary Table 5). The results are illustrated in Supplementary Figures 4 and 5.
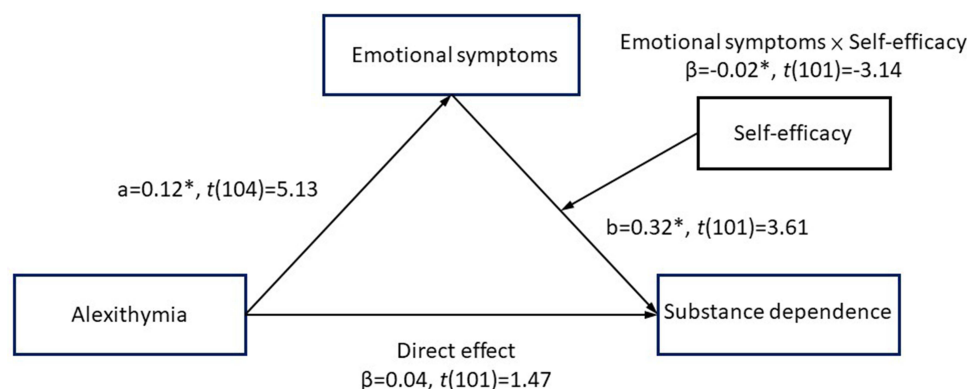
Figure 3 Final model showing the co-efficient estimates and statistical significance for the moderating effect of self-efficacy. (**a**): a pathway of Model 14, p<0.001. (**b**): b pathway of Model 14, p<0.001. Direct effect: p=0.146. *: p<0.05.

To estimate the appropriate sample size in the moderated mediation as a post-hoc analysis, the G-Power software was applied.[44] The alpha value was set at 0.05, the effect size was set at medium level, and the estimating power for the analysis was set at 0.8 to 0.9. The mode of "linear multiple regression, fixed model" was applied. One regression included two predictors (emotional problems and alexithymia in the main mediation model), and another regression included three predictors in the moderation model. With the power at 0.8 to 0.9, the appropriate sample size was estimated at 145 to 187, respectively.

Discussion
Main Findings of the Current Study
All measurements in the current study were shown to be reliable and valid. The significant correlations between variables supported our hypothesis to develop the conceptual models. In summary, the moderating effects of family support and self-efficacy were confirmed. In addition, the mediating effect of emotional symptoms in the association between alexithymia and substance dependence was weaker at higher levels of family support or self-efficacy. This indicated the undesirable impact of emotional symptoms on substance dependence among individuals with alexithymia. Furthermore, we also identified the protective effects of family support and self-efficacy in the conceptual model.

Mediating Effect of Emotional Symptoms
We identified positive associations between alexithymia, emotional symptoms, and substance dependence in the model. A previous study reported a positive association between alexithymia and mood symptoms such as depression and anxiety.[45] Moreover, the association between emotional symptoms and substance use has also been discussed. A comprehensive meta-analysis reported a strong association between substance use and mood disorders including major depressive disorder and anxiety disorder.[46] Another study reported that a self-medication model, overlapping neurological pathways, and shared genetic factors contributed to the association between substance use and mood disorders.[47] In addition, some studies have discussed a conceptual model of mediation similar to our hypothesis in the current study. One study reported that difficulty in identifying feelings in teenagers with alexithymia was positively correlated with depression and SUD in young adulthood, while depression and SUD were also correlated with each other.[27] Another study identified indirect effects of negative mood and alcohol craving on the association between alexithymia and the severity of alcohol dependence.[48] Our results are consistent with the findings of these studies, in that we confirmed the indirect effect of emotional symptoms on the association between alexithymia and substance dependence.

Moderating Effects of Family Support and Self-Efficacy

We also found that a higher level of family support could be a protective factor against the effect of alexithymia on emotional symptoms. Previous studies have discussed the impact of parenting style or social support on alexithymia, and a lack of warmth perceived in the relationship with their father has been associated with alexithymia in patients with alcohol use disorder.[24] Another study found that alexithymia was positively correlated with a higher level of maladaptive parenting style and lower level of social as well as family support.[49] Alexithymia has also been associated with lower perceived social support and maladaptive coping skills among patients with diabetes[50] and fibromyalgia.[51] Regarding the etiologies, it is possible that individuals with alexithymia have difficulties utilizing or approaching social support due to their low emotional and social skills and inability to form close relationships.[52]

Another noticeable finding in the current study was the protective effect of self-efficacy against illicit substance use on emotional symptoms, which ameliorated the severity of substance dependence. Self-efficacy in substance abstinence has been shown to be able to significantly predict lower negative affect scores among patients with SUD.[25] Another study reported that higher self-efficacy was correlated with lower levels of depression and anxiety among patients receiving rehabilitation for spinal cord injuries.[53] On the other hand, increased self-efficacy has been reported to be able to predict subsequent abstinence from substance use in adolescents treated with cognitive behavioral therapy and psychoeducation.[54] Taken together, these findings demonstrate the benefits of self-efficacy for patients with emotional problems or SUD, which is further supported by our findings.

Clinical Implications of the Current Study

Based on our findings regarding the mediating role of emotional symptoms, the clinical implication of the current study is that timely interventions for emotional symptoms may be beneficial for patients with alexithymia and SUD. Psychopharmacotherapy and psychotherapy for emotional problems should be considered for patients with SUD. Moreover, our findings also highlight the importance of family support and self-efficacy due to their protective effect on the associations between alexithymia, emotional symptoms, and substance dependence. Family interventions such as systemic or behavioral family therapy could be integrated into the treatment course of SUD.[55] We suggest that such interventions could be beneficial to empower the families of patients with SUD, further resulting in enhanced family support. In addition, we also identified the role of self-efficacy. Developing and enhancing self-efficacy may be a beneficial clinical intervention for patients with SUD, such as coping skills training, motivation interviewing, and the 12-step program of Alcoholics Anonymous.[56] Clinicians may consider these interventions to treat emotional symptoms and enhance family support as well as self-efficacy in clinical practice for patients with SUD, especially for those with alexithymia.

Limitations

There are several limitations to the present study. First, the limited number of participants may have compromised the interpretation and applicability of the results. From the post-hoc power analysis, we suggest that 145 to 187 participants can be a more adequately-powered sample size to the current moderated mediation model if other researchers want to replicate this model in the future. Moreover, the sample size may be better more than 198 cases if advanced moderation model is tested, such as model 21 of PROCESS macro. Increased statistical power will make our result more applicable to other studies and more powerful interpretation. For instance, the interaction of Alexithymia × Family support may reach statistical significance, and the index of moderated mediation may increase with adequate-powered sample. Second, the cross-sectional design of this study limited our ability to identify relationships among the variables examined within the moderated mediation model. A longitudinal study is beneficial to identify the interaction and time effect among change of severity on alexithymia, emotional symptoms, self-efficacy, and substance dependence. Third, although we had adjusted for many variables in the moderated mediation, it may exist other unadjusted variables to confound our results. For instance, medical comorbidities were unadjusted because that it was not unrecorded in the database. Chronic medical comorbidities are reported to be associated with risk of substance use[57] and mood disorder.[58] Therefore, it may interfere the interaction between the association of alexithymia, emotional symptoms and substance use. Fourth,

participants with different type of substance use are group together into the analysis due to the limited numbers of participants. Further research with larger sample size can be helpful to identify the effect of different substance use, such as psychostimulants, sedatives or hallucinogens. Moreover, we suppose that different type of substance use may have different impact on alexithymia, which is also considered to be a personality trait.[6] Individuals who reported using psychostimulant compared to the rest, obtained a significantly higher level of aggressive-hostility personality.[59] Another study revealed that patients with opioid dependence demonstrated higher scores of harm-avoidance features in personality than healthy controls.[60] Taking together, we suppose that subgroup analysis of different substance may exhibit different impact on the mediation or moderated mediation model that we built. Fifth, the gender imbalance and self-reported measurements may also limit the interpretation of our results. Clinical-rated instruments can be applied in the future studies to verify our results.

Conclusions

The findings of the current study suggested the mediating effect of emotional symptoms and moderating effect of family support and self-efficacy on the association between alexithymia and substance dependence. Clinicians should be aware of the symptoms of alexithymia in patients with SUD. We also suggest that timely interventions to treat emotional symptoms and enhance family support and self-efficacy may be beneficial to patients comorbid with alexithymia and SUD. Further longitudinal studies with longer follow-up are warranted to extend the applicability of the current study.

Data Sharing Statement

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request to Dian-Jeng Li (edcrfvm45@hotmail.com).

Ethics Approval

This study was approved by the Institutional Review Board of Kai-Syuan Psychiatric Hospital (KSPH-2019-23). The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

Informed Consent

All of the participants have signed the informed consent prior to the initiation of the study.

Acknowledgments

Funding

Disclosure

All authors declare that they have no conflicts of interest.

References

1. Sifneos PE. The prevalence of 'alexithymic' characteristics in psychosomatic patients. *Psychother Psychosom*. 1973;22(2):255–262. doi:10.1159/000286529

2. Nemiah JC. Psychology and psychosomatic illness: reflections on theory and research methodology. *Psychother Psychosom*. 1973;22(2–6):106–111. doi:10.1159/000286478

3. Luminet O, Bagby RM, Taylor GJ. *Alexithymia: Advances in Research, Theory, and Clinical Practice*. Cambridge University Press; 2018.

4. Luminet O, Nielson KA, Ridout N. Cognitive-emotional processing in alexithymia: an integrative review. *Cognit Emotion*. 2021;35(3):449–487. doi:10.1080/02699931.2021.1908231

5. Taylor GJ, Bagby RM, Parker JD. *Disorders of Affect Regulation: Alexithymia in Medical and Psychiatric Illness*. Cambridge University Press; 1999.

6. Bagby RM, Parker JD, Taylor GJ. The twenty-item Toronto alexithymia scale-I. Item selection and cross-validation of the factor structure. *J Psychosom Res.* 1994;38(1):23–32. doi:10.1016/0022-3999(94)90005-1

7. Taylor GJ, Bagby RM, Parker JD. The alexithymia construct: a potential paradigm for psychosomatic medicine. *Psychosomatics.* 1991;32 (2):153–164. doi:10.1016/S0033-3182(91)72086-0

8. Preece D, Becerra R, Allan A, Robinson K, Dandy J. Establishing the theoretical components of alexithymia via factor analysis: introduction and validation of the attention-appraisal model of alexithymia. *Pers Individ Dif.* 2017;119:341–352. doi:10.1016/j.paid.2017.08.003

9. Leweke F, Leichsenring F, Kruse J, Hermes S. Is alexithymia associated with specific mental disorders. *Psychopathology.* 2011;45(1):22–28.

10. Nowakowski ME, McFarlane T, Cassin S. Alexithymia and eating disorders: a critical review of the literature. *J Eat Disord.* 2013;1:1–14. doi:10.1186/2050-2974-1-21

11. Kinnaird E, Stewart C, Tchanturia K. Investigating alexithymia in autism: a systematic review and meta-analysis. *Eur Psychiatry.* 2019;55:80–89. doi:10.1016/j.eurpsy.2018.09.004

12. Livne O, Shmulewitz D, Stohl M, et al. Agreement between DSM-5 and DSM-IV measures of substance use disorders in a sample of adult substance users. *Drug Alcohol Depend.* 2021;227:108958. doi:10.1016/j.drugalcdep.2021.108958

13. United Nations Office on Drugs and Crime. World drug report 2021: United Nations. 2021. Available from: https://www.unodc.org/unodc/en/data-and-analysis/wdr2021.html. Accessed August 15, 2021.

14. Thorberg FA, Young RM, Sullivan KA, Lyvers M. Alexithymia and alcohol use disorders: a critical review. *Addict Behav.* 2009;34(3):237–245. doi:10.1016/j.addbeh.2008.10.016

15. Kun B, Alpay P, Bodo V, et al. Differences in the associations between psychoactive substance use and alexithymia: a series of meta-analyses. *Clin Psychol Rev.* 2023;103:102297. doi:10.1016/j.cpr.2023.102297

16. Palma-Alvarez RF, Ros-Cucurull E, Daigre C, et al. Is alexithymia related to retention and relapses in patients with substance use disorders?: a one year follow-up study. *Addict Behav.* 2021;113:106681. doi:10.1016/j.addbeh.2020.106681

17. Cruise KE, Becerra R. Alexithymia and problematic alcohol use: a critical update. *Addict Behav.* 2018;77:232–246. doi:10.1016/j.addbeh.2017.09.025

18. Panayiotou G, Leonidou C, Constantinou E, et al. Do alexithymic individuals avoid their feelings? Experiential avoidance mediates the association between alexithymia, psychosomatic, and depressive symptoms in a community and a clinical sample. *Compr Psychiatry.* 2015;56:206–216. doi:10.1016/j.comppsych.2014.09.006

19. Murphy J, Brewer R, Hobson H, Catmur C, Bird G. Is alexithymia characterised by impaired interoception? Further evidence, the importance of control variables, and the problems with the heartbeat counting task. *Biol Psychol.* 2018;136:189–197. doi:10.1016/j.biopsycho.2018.05.010

20. Lane RD, Hsu CH, Locke DE, Ritenbaugh C, Stonnington CM. Role of theory of mind in emotional awareness and alexithymia: implications for conceptualization and measurement. *Conscious Cogn.* 2015;33:398–405. doi:10.1016/j.concog.2015.02.004

21. Pollatos O, Werner NS, Duschek S, et al. Differential effects of alexithymia subscales on autonomic reactivity and anxiety during social stress. *J Psychosom Res.* 2011;70(6):525–533. doi:10.1016/j.jpsychores.2010.12.003

22. Gobbi G, Atkin T, Zytynski T, et al. Association of cannabis use in adolescence and risk of depression, anxiety, and suicidality in young adulthood: a systematic review and meta-analysis. *JAMA Psychiatry.* 2019;76(4):426–434. doi:10.1001/jamapsychiatry.2018.4500

23. Topino E, Gori A, Cacioppo M. Alexithymia, dissociation, and family functioning in a sample of online gamblers: a moderated mediation study. *Int J Environ Res Public Health.* 2021;18(24):13291. doi:10.3390/ijerph182413291

24. De Rick A, Vanheule S. The relationship between perceived parenting, adult attachment style and alexithymia in alcoholic inpatients. *Addict Behav.* 2006;31(7):1265–1270. doi:10.1016/j.addbeh.2005.08.010

25. May EM, Hunter BA, Ferrari J, Noel N, Jason LA. Hope and abstinence self-efficacy: positive predictors of negative affect in substance abuse recovery. *Community Ment Health J.* 2015;51(6):695–700. doi:10.1007/s10597-015-9888-y

26. Bonnet A, Brejard V, Pedinielli JL. Emotional dispositions and substance use: mediating effect of alexithymia. *Psychol Rep.* 2013;112(1):289–302. doi:10.2466/18.09.20.PR0.112.1.289-302

27. Patwardhan I, Mason WA, Chmelka MB, et al. Prospective relations between alexithymia, substance use and depression: findings from a National Birth Cohort. *Nord J Psychiatry.* 2019;73(6):340–348. doi:10.1080/08039488.2019.1634758

28. Chiu C-H, Chou FH-C, Wu H-C, et al. Factors associated with neurofeedback and mindfulness-based combination therapy for patients with substance use disorder: a multicenter study. *Eur J Psych.* 2024;38(2):100245. doi:10.1016/j.ejpsy.2023.100245

29. Chen VC-H, Chen H, Lin T-Y, et al. Severity of heroin dependence in Taiwan: reliability and validity of the Chinese version of the Severity of Dependence Scale (SDS [Ch]). *Addict Behav.* 2008;33(12):1590–1593. doi:10.1016/j.addbeh.2008.06.001

30. Lin Y, Chan C. A factor analysis of the Taiwan version of the Toronto Alexithymia Scale-20. *Taiwan J Psychiatry.* 2003;17(4):276–282.

31. Zhu X, Yi J, Yao S, et al. Cross-cultural validation of a Chinese translation of the 20-item Toronto Alexithymia Scale. *Compr Psychiatry.* 2007;48 (5):489–496. doi:10.1016/j.comppsych.2007.04.007

32. Cheng TA, Williams P. The design and development of a screening questionnaire (CHQ) for use in community studies of mental disorders in Taiwan. *Psychol Med.* 1986;16(2):415–422. doi:10.1017/S0033291700009247

33. Goldberg DP, Hillier VF. A scaled version of the General Health Questionnaire. *Psychol Med.* 1979;9(1):139–145. doi:10.1017/S0033291700021644

34. Chen YC, Hsu CC, Hsu SH, Lin CC. A preliminary study of family apgar index. *Acta Paediatrica Sin.* 1980;21(3):210–217.

35. Smilkstein G. The family APGAR: a proposal for a family function test and its use by physicians. *J Fam Pract.* 1978;6(6):1231–1239.

36. Martin GW, Wilkinson DA, Poulos CX. The drug avoidance self-efficacy scale. *J Subst Abuse.* 1995;7(2):151–163. doi:10.1016/0899-3289(95)90001-2

37. Norozi E, Miri MR, Soltani R, et al. Drug Avoidance Self Efficacy Scale (DASES): a cultural adaptation and validation study. *J Subst Use.* 2016;21 (5):449–454. doi:10.3109/14659891.2015.1056851

38. Hinton PR, McMurray I, Brownlow C. *SPSS Explained.* Routledge; 2014.

39. Tabachnick BG, Fidell LS. *Using Multivariate Statistics.* 5th ed. New York, NY: Allyn and Bacon; 2007.

40. Beavers AS, Lounsbury JW, Richards JK, et al. Practical considerations for using exploratory factor analysis in educational research. *Pract Assess Res Eval.* 2013;18:1–13.

41. Hayes AF. An index and test of linear moderated mediation. *Multivar Behav Res.* 2015;50(1):1–22. doi:10.1080/00273171.2014.962683

42. Hayes AF. *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach*. 2nd ed. New York: Guilford Press; 2018.

43. Hayes AF, Matthes J. Computational procedures for probing interactions in OLS and logistic regression: SPSS and SAS implementations. *Behav Res Methods*. 2009;41(3):924–936. doi:10.3758/BRM.41.3.924

44. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods*. 2007;39(2):175–191. doi:10.3758/BF03193146

45. Morie KP, Jackson S, Zhai ZW, Potenza MN, Dritschel B. Mood disorders in high-functioning autism: the importance of alexithymia and emotional regulation. *J Autism Dev Disord*. 2019;49(7):2935–2945. doi:10.1007/s10803-019-04020-1

46. Lai HM, Cleary M, Sitharthan T, Hunt GE. Prevalence of comorbid substance use, anxiety and mood disorders in epidemiological surveys, 1990–2014: a systematic review and meta-analysis. *Drug Alcohol Depend*. 2015;154:1–13. doi:10.1016/j.drugalcdep.2015.05.031

47. Quello SB, Brady KT, Sonne SC. Mood disorders and substance use disorder: a complex comorbidity. *Sci Pract Perspect*. 2005;3(1):13–21. doi:10.1151/spp053113

48. Thorberg FA, Young RM, Hasking P, et al. Alexithymia and alcohol dependence: the roles of negative mood and alcohol craving. *Subst Use Misuse*. 2019;54(14):2380–2386. doi:10.1080/10826084.2019.1650773

49. Karukivi M, Joukamaa M, Hautala L, et al. Does perceived social support and parental attitude relate to alexithymia? A study in Finnish late adolescents. *Psychiatry Res*. 2011;187(1–2):254–260. doi:10.1016/j.psychres.2010.11.028

50. Celik S, Taskin Yilmaz F, Yurtsever Celik S, Anataca G, Bulbul E. Alexithymia in diabetes patients: its relationship with perceived social support and glycaemic control. *J Clin Nurs*. 2022;31(17–18):2612–2620. doi:10.1111/jocn.16088

51. Di Tella M, Tesio V, Ghiggia A, et al. Coping strategies and perceived social support in fibromyalgia syndrome: relationship with alexithymia. *Scand J Psychol*. 2018;59(2):167–176. doi:10.1111/sjop.12405

52. Kojima M, Senda Y, Nagaya T, Tokudome S, Furukawa TA. Alexithymia, depression and social support among Japanese workers. *Psychother Psychosom*. 2003;72(6):307–314. doi:10.1159/000073027

53. van Diemen T, Tran Y, Stolwijk-Swuste JM, et al. Trajectories of self-efficacy, depressed mood, and anxiety from admission to spinal cord injury rehabilitation to 1 year after discharge. *Arch Phys Med Rehabil*. 2021;102(10):1939–1946. doi:10.1016/j.apmr.2021.04.018

54. Burleson JA, Kaminer Y. Self-efficacy as a predictor of treatment outcome in adolescent substance use disorders. *Addict Behav*. 2005;30(9):1751–1764. doi:10.1016/j.addbeh.2005.07.006

55. Hogue A, Schumm JA, MacLean A, Bobek M. Couple and family therapy for substance use disorders: evidence-based update 2010–2019. *J Marital Fam Ther*. 2022;48(1):178–203. doi:10.1111/jmft.12546

56. Kadden RM, Litt MD. The role of self-efficacy in the treatment of substance use disorders. *Addict Behav*. 2011;36(12):1120–1126. doi:10.1016/j.addbeh.2011.07.032

57. Hadland SE, Walker LR. Medical comorbidity and complications. *Child Adolesc Psychiatr Clin N Am*. 2016;25(3):533–548. doi:10.1016/j.chc.2016.02.006

58. Thom R, Silbersweig DA, Boland RJ. Major depressive disorder in medical illness: a review of assessment, prevalence, and treatment options. *Psychosom Med*. 2019;81(3):246–255. doi:10.1097/PSY.0000000000000678

59. Bucher JT, Vu DM, Hojat M. Psychostimulant drug abuse and personality factors in medical students. *Med Teach*. 2013;35(1):53–57. doi:10.3109/0142159X.2012.731099

60. Zaaijer ER, Bruijel J, Blanken P, et al. Personality as a risk factor for illicit opioid use and a protective factor for illicit opioid dependence. *Drug Alcohol Depend*. 2014;145:101–105. doi:10.1016/j.drugalcdep.2014.09.783