

# Serial Progression from Attention-Deficit/Hyperactivity Disorder to Alcohol Use Disorder: Serial Multiple Mediated Effects of Externalizing Disorders and Depression

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**Objective:** Externalizing disorders such as attention-deficit/hyperactivity disorder (ADHD), conduct disorder and anti-social personality disorder, as well as depression are common comorbidities in alcohol use disorder (AUD). The current study focused on the temporal relationship between the onsets of these disorders and AUD, and investigated the serial multiple mediator model of externalizing disorders (e.g., ADHD) and depression on AUD.

**Methods:** We analyzed the mediated effects of the Adult ADHD Self-Report Scale (ASRS), the Barratt Impulsiveness Scale motor (BIS\_M) and the Beck Depression Inventory (BDI) on Korean version of the Alcohol Dependence Scale (ADS\_K) using the multiple-step multiple mediation procedure regression analysis. In addition, we comparatively analyzed different clinical characteristics in relation to conduct problems.

**Results:** The multiple-step multiple mediation procedure found the serial multiple mediated effects of the BIS\_M and the BDI on the relationship between the ASRS and the ADS\_K. Also, the group with conduct problem was significantly high in ADHD symptoms, depression, anxiety, impulsivity, legal problems and alcohol-related problems, compared to the group without conduct problems.

**Conclusion:** To sum up, the results of this study show that ADHD symptoms in childhood could exert significant effects on the severity of AUD in adulthood, and both disorders might be mediated by the externalizing disorders characterized by the core feature of motor impulsivity, and depression serially. Thus, the treatment of preceding disorders in accordance with developmental stages is an overarching clinical component for preventing the subsequent development of AUD and for its treatment.

**KEY WORDS:** Attention deficit disorder with hyperactivity; Depression; Externalizing disorder; Alcohol use disorder; Impulsive behavior; Conduct disorder.

## INTRODUCTION

Alcohol use disorder (AUD) is one of the most common substance use disorders (SUD) with its lifetime prevalence in adults up to 20%.<sup>1)</sup> It is well-documented that AUD shows high co-occurrence rates with other psychiatric disorders, such as affective disorders including depression and mania, externalizing disorders including attention-deficit/hyperactivity disorder (ADHD), conduct dis-

order (CD) and antisocial personality disorder (ASPD), and diverse anxiety disorders.<sup>2,3)</sup> Therefore, it is very important to clarify the relationships between the foregoing comorbidities and AUD for further understanding and treatment of AUD. Among other comorbidities, the current study focused on depression and the externalizing disorders such as ADHD, CD and ASPD which is highly associated with AUD.

First, many previous studies have shown that ADHD was significantly associated with AUD. Approximately 33% of AUD patients were diagnosed with a comorbid ADHD.<sup>3)</sup> In addition, about 40% of adult ADHD patients had comorbid SUD such as AUD.<sup>4)</sup> As widely known, while ADHD is a neurodevelopmental disorder presenting itself in young children, AUD in late adolescents or early adults. According to the previous study focused on

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the time of onset, the childhood-onset ADHD group showed high incidence of AUD in adolescence and adulthood. This suggests that ADHD could be considered as a predisposing factor in the onset of AUD.<sup>5)</sup>

Externalizing disorders encompass childhood-onset ADHD, adolescence-onset oppositional defiant disorder (ODD) and CD, and adult-onset ASPD.<sup>6,7)</sup>

These are known to be closely associated with each other. Specifically, the conduct problems in teens are known to mediate between the hyperactive/impulsive symptoms in children and the externalizing behavior including criminality or antisocial behavior in adults.<sup>8)</sup> Also, the presence of comorbid CD in ADHD is known to increase the risk of adulthood-onset antisocial behavior.<sup>9)</sup> Notably, the externalizing disorders are reported to be closely associated with AUD in many studies. For example, ADHD and CD are highly related to AUD to the extent that both are considered the independent predictors of AUD,<sup>10)</sup> while CD and antisocial behavior have genetic correlation with AUD.<sup>11,12)</sup>

Lastly, we hypothesized that depression would serve as an important mediator in the correlation between the externalizing disorders and AUD. In a group difference analysis, the AUD group with comorbid ADHD showed higher depressive symptoms compared to the AUD group without comorbid ADHD.<sup>13)</sup> According to a meta-analysis of the longitudinal outcomes of ADHD and CD, the incidence rates of depression and AUD were significantly high in both ADHD and CD.<sup>14)</sup>

Since, the mechanism or pathophysiology of AUD has not been fully established, and thus relevant treatment programs are far from complete. Although comorbidities or preceding disorders of AUD have been well-documented, relevant facets need further clarification. As the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) shows, it is important to understand the associations among the disorders with dimensional perspective. Therefore, we focused on the motor impulsivity, which is the core trait of externalizing disorders. Longitudinal research on externalizing behavior found the hyperactive/impulsive trait of ADHD predicted the externalizing behavior in teens and young adults.<sup>8)</sup> Another study mentioned the impulsivity, or behavioral impulsivity in particular, was the core symptom of the externalizing spectrum.<sup>15)</sup> After all, as the core trait of externalizing disorders, the motor impulsivity was closely associated with

addictive problems, including AUD.<sup>16,17)</sup>

The current study assumed the close relationships among AUD, externalizing disorders (ADHD, CD and ASPD) and depression. According to these assumptions, the mediated effects of these disorders in relation to the time of onset across developmental stages were analyzed. In addition, we investigated relevant clinical characteristics depending on the presence or absence of conduct problems, which represent the externalizing behaviors in teens.

## METHODS

### Subjects

The current study recruited 62 adult male AUD patients hospitalized in Keyo Mental Hospital Addiction Center. The subjects were diagnosed with AUD using the Structured Clinical Interview for DSM-5 administered by a psychiatrist. Patients with or with history of major psychiatric disorders (e.g., schizophrenia and bipolar disorder), and comorbid neurologic diseases including cerebral hemorrhage and cerebral infarction were excluded. In addition, those with comorbid neurocognitive and neurodevelopmental disorders were excluded. Prior to their participation in the study, the subjects had at least one-week abstinence of the last drinking to avoid the influence of withdrawal symptoms. Those who remained abstinent for over a week but had withdrawal symptoms or alcohol-induced symptoms were excluded as well. The current study was approved by the Institutional Review Board of Hanyang University Hospital (approval No. HYUH 2013-11-018-002). The participants were given a proper explanation of the purpose and detailed progress of the research at separate meeting room and signed the consent form.

### Measurements

We surveyed the subjects for their demographic variables (e.g., age, education and marital state) using semi-structured questionnaire. Also, we conducted the standardized rating scales, including the Adult ADHD Self-Report Scale-V1.1 (ASRS), the Barratt Impulsiveness Scale 11th edition (BIS), the Beck Depression Inventory (BDI) and the Korean version of the Alcohol Dependence Scale (ADS\_K). In case of incomplete responses in the questionnaire and/or the scales, the author interviewed the respondents

in person for the reliability of the data.

First, we screened the adult ADHD using the ASRS translated into Korean.<sup>18)</sup> The ASRS reflecting the severity of diverse symptoms of adult ADHD consists of A and B parts. Here, the A part known as the best part to rate the adult ADHD evaluated the presence or absence of ADHD symptoms. We did not conduct the final interview to diagnose the ADHD. Therefore, we used the term 'ADHD symptoms' as we did in previous studies.<sup>19)</sup>

Second, to rate the impulsiveness, we used the BIS translated into Korean. The BIS consists of three subscales, i.e. nonplanning impulsiveness (BIS\_NP), cognitive impulsiveness (BIS\_C) and motor impulsiveness (BIS\_M). We calculated each sub-scale score and the total score.

To rate the severity of depression symptoms, we used the BDI standardized in Korea by Hahn *et al.*<sup>20)</sup> The BDI is a useful scale to rate the severity of depression and often used for depression screening tests. The BDI consists of 21 question items in total with the score ranging from 0 to 63 as maximum.

To rate the severity of AUD, we used the ADS\_K. Statistically, the ADS\_K is significantly correlated with alcohol-induced dysfunction, and widely used to evaluate the withdrawal symptoms caused by problem drinking and the compulsive alcohol use. This scale has been standardized by Lee *et al.*<sup>21)</sup> in Korea.

To rate the conduct problems, we screened the subjects using the structured questionnaire first. Then, a psychiatrist confirmed whether the selected subjects had persistent conduct problems in adolescence. Conduct problem was defined as a person's history of violation of rules including school violence, unauthorized absence and run-away from home in the school years, and antisocial behavior as a history of imprisonment in detention center or police station.

### Statistical Analysis

We conducted the descriptive statistical analysis and the frequency analysis of ASRS, BIS, BDI and ADS\_K as well as the demographic variables. Using the part A of ASRS, we screened the patients with ADHD symptoms, and assigned them to the ASRS screening positive group.

Next, in order to determine any associations between ASRS, BIS, BIS sub-scales, BDI and ADS\_K, we performed the correlation analysis based on Pearson's correlation coefficients.

Using the SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, USA) with Multiple Step Multiple Mediation Procedure (MEDTHREE), we analyzed the serial multiple mediated effects of the ASRS, BIS\_M, BDI and ADS\_K, and conducted 10,000 times of bootstrapping. We analyzed the direct effects of the independent variable ASRS on the dependent variable ADS\_K, the indirect effects of BIS\_M and BDI mediating between the ASRS and ADS\_K, and finally the total effects (direct effect plus indirect effects). We selected ASRS, BDI and ADS\_K as the variables that could rate the severities of ADHD, depression and AUD symptoms, respectively, and rated the severity of externalizing disorders using the BIS\_M<sup>15)</sup> scale, which is considered the core trait of externalizing disorders. Finally, we analyzed group difference of the clinical facets in relation to conduct problems using the *t*-test.

## RESULTS

### Subjects' Descriptive Statistics and Analysis of Frequency

Subjects' mean age was 52.44 years old. Low social economic status was accounted for the highest percentage (72.6%) in the frequency analysis. The divorced was accounted for the highest percentage (45.2%), while the married was the lowest percentage (25.8%) of the subjects in terms of the marital state. High school graduates were accounted for the highest percentage (50.0%), followed by middle school graduates or lower. The selected positive group of ADHD was 21.0% (n=13) of all subjects. The BIS, BDI and ADS-K scores averaged 53.81, 20.00 and 23.11, respectively (Table 1).

### Correlation Analysis of ASRS, ADS\_K, BDI, BIS and BIS Subscales

ASRS showed statistically significant correlations with all analyzed variables. Notably, ASRS had the highest correlation with BIS\_M ( $r=0.64$ ). ADS\_K had significant correlations with all variables except BIS\_C. In particular, ADS-K had the highest correlation with the BDI ( $r=0.56$ ). BDI had significant correlations with all variables except BIS\_C. Most of all, BDI had high correlations with ADS\_K and BIS\_M (Table 2).

**Table 1.** Demographics and scales (n=62)

Variable	Data
Social economic status	
High	0 (0)
Middle	17 (27.4)
Low	45 (72.6)
Marital state	
Never-married	18 (29.0)
Married	16 (25.8)
Divorced	28 (45.2)
Education	
Below middle school	23 (37.1)
High school	31 (50.0)
Above college	8 (12.9)
ASRS screening positive	13 (21.0)
BIS_NP	22.16±4.56
BIS_M	15.53±3.53
BIS_C	16.11±2.53
BIS_Sum	53.81±9.14
BDI	20.00±11.00
ADS_K	23.11±11.79

Values are presented as number (%) or mean±standard deviation. ASRS, Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale-V1.1; BIS, Barratt Impulsiveness Scale; NP, nonplanning; M, motor; C, cognitive; BDI, Beck Depression Inventory; ADS\_K, Korean version of Alcohol Dependence Scale.

**Table 2.** Correlations between ASRS, ADS\_K, BDI and BIS (n=62)

	ASRS	ADS_K	BDI	BIS_NP	BIS_M	BIS_C	BIS_Sum
ASRS	-						
ADS_K	0.47**	-					
BDI	0.36**	0.56**	-				
BIS_NP	0.48**	0.33**	0.59**	-			
BIS_M	0.64**	0.55**	0.57**	0.69**	-		
BIS_C	0.26*	0.01	0.21	0.59**	0.46**	-	
BIS_Sum	0.56**	0.38**	0.57**	0.93**	0.86**	0.75**	-

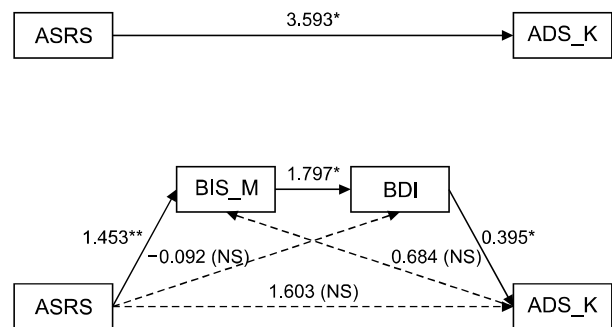
ASRS, Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale-V1.1; ADS\_K, Korean version of Alcohol Dependence Scale; BDI, Beck Depression Inventory; BIS, Barratt Impulsiveness Scale; NP, nonplanning; M, motor; C, cognitive.

\* $p < 0.05$ , \*\* $p < 0.01$ .

### Analysis of Serial Multiple Mediated Effects of ASRS, BIS\_M, BDI and ADS\_K

The total effects of the independent variable ASRS on the dependent variable ADS\_K were 3.593, which was statistically significant.

In the analysis of each model path, the effect of ASRS on BIS\_M was statistically significant, where the B value was 1.453. Both effects of BIS\_M on BDI and BDI on ADS\_K were statistically significant, where B values were 1.797 and 0.395, respectively. The other paths indicated no sig-



**Fig. 1.** Model path analysis of Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale-V1.1 (ASRS), Barratt Impulsiveness Scale motor (BIS\_M), Beck Depression Inventory (BDI) on Korean version of Alcohol Dependence Scale (ADS\_K) in alcohol use disorder patients (n=62). \* $p < 0.01$ , \*\* $p < 0.001$ ; NS, not significant.

**Table 3.** The bootstrap results for individual Indirect effects (n=62)

Path	B	SE	Percentile 95% CI
Total	1.990	0.744	0.722-3.672
ASRS→BIS_M→ADS_K	0.995	0.726	-0.326-2.593
ASRS→BDI→ADS_K	-0.036	0.447	-1.051-0.790
ASRS→BIS_M→BDI→ADS_K	1.032	0.479	0.315-2.164

SE, standard error; CI, confidence interval; ASRS, Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale-V1.1; BIS, Barratt Impulsiveness Scale; M, motor; BDI, Beck Depression Inventory; ADS\_K, Korean version of Alcohol Dependence Scale. Bootstrapping=10,000.

nificant effects. Likewise, the direct effects (B=1.603) of ASRS on ADS\_K were statistically insignificant (Fig. 1).

For the indirect effects of the model path designed in this study, the total indirect effect (B=1.990) was statistically significant. The analysis of each path's indirect effect indicated the significant effects of the ASRS→BIS\_M→BDI→ADS\_K path only (B=1.032) (Table 3).

Hence, BIS\_M and BDI exerted serial multiple mediated effects via the ASRS→BIS\_M→BDI→ADS\_K path. Also, the insignificant direct effect of ASRS on ADS\_K corroborated the complete mediated effect.

### Analysis of Clinical Facets in Connection with Conduct Problems

The *t*-test of conduct problems highlighted a wider range of comorbidities in the conduct problem positive group. First, in terms of the alcohol-related variables, the conduct problem positive group showed statistically significant early onsets of drinking and pathologic drinking with high ADS\_K scores.

Likewise, the conduct problem positive group scored

**Table 4.** Comparison of demographics, alcohol-related variables and scales between conduct problem positive and negative (n=62)

Variable	Conduct problem positive (n=17)	Conduct problem negative (n=45)	Statistic	p value
Social economic status				
High	0 (0)	0 (0)	0.549 <sup>†</sup>	0.355
Middle	3 (17.6)	14 (31.1)		
Low	14 (82.4)	31 (68.9)		
Marital status				
Unmarried	7 (41.2)	11 (24.4)	2.949 <sup>†</sup>	0.238
Married	2 (11.8)	14 (31.1)		
Divorced	8 (47.1)	20 (44.4)		
Education (yr)	10.88±2.76	11.09±2.42	t=-0.289	0.774
Onset of drinking (yr)	15.71±2.34	18.87±4.17	t=2.945	0.005*
Onset of pathologic drinking (yr)	32.76±8.66	40.07±9.88	t=2.679	0.010*
Abstinence period (mo)	9.24±11.00	16.18±27.27	t=1.015	0.314
Legal problem				
Detention center	12 (70.6)	12 (26.7)	χ <sup>2</sup> =8.267	0.002*
Police station	16 (94.1)	28 (62.2)	4.643 <sup>†</sup>	0.014*
Other substance use (except alcohol)	3 (17.6)	1 (2.2)	2.644 <sup>†</sup>	0.059
BPRS total	35.06±15.58	26.42±15.92	t=-1.916	0.060
Thought disturbance	3.18±2.46	2.64±2.50	t=-0.752	0.455
Withdrawal/retardation	5.47±3.73	4.29±3.18	t=-1.245	0.218
Anxiety/depression	9.18±3.64	6.27±2.93	t=-3.256	0.002*
Hostility/paranoia	5.65±3.46	3.89±3.02	t=-1.962	0.054*
Agitation/arousal	4.24±2.33	3.09±2.30	t=-1.742	0.087
ADS-K	28.00±10.48	21.27±11.84	t=-2.058	0.044*
BDI	26.76±10.55	17.44±10.15	t=-3.191	0.002*
BAI	21.12±10.36	12.93±8.85	t=-3.099	0.003*
BIS				
BIS-NP	24.47±3.81	21.29±4.55	t=-2.562	0.013*
BIS-M	17.82±2.51	14.67±3.49	t=-3.405	0.001*
BIS-C	16.76±2.80	15.87±2.41	t=-1.253	0.215
BIS-total	59.06±7.11	51.82±9.10	t=-2.950	0.005*
ASRS score	3.00±1.58	1.69±1.40	t=-3.183	0.002*
ASRS screening positive	7 (41.2)	6 (13.3)	4.214 <sup>†</sup>	0.032*

Values are presented as number (%) or mean±standard deviation.

ASRS, Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale-V1.1; BPRS, Brief Psychiatric Rating Scale; ADS\_K, Korean version of Alcohol Dependence Scale; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; BIS, Barratt Impulsiveness Scale; NP, nonplanning; M, motor; C, cognitive.

\* $p < 0.05$ ; <sup>†</sup>Fisher's exact test.

higher in the variables of externalizing disorders. The ASRS score, the percentage of ASRS screening positive group, and the percentage of patient whom experienced legal problems were significantly higher in the conduct problem positive group.

In addition, the conduct problem positive group scored significantly higher in the BDI, Beck Anxiety Inventory and Brief Psychiatric Rating Scale's anxiety/depression and hostility/paranoia subgroups.

Finally, the conduct problem positive group's BIS\_total, BIS\_NP and BIS\_M scores were significantly higher (Table 4).

## DISCUSSION

The current study focused on the close associations between AUD and externalizing disorders including the well-known comorbid ADHD in AUD and depression, and in particular took note of the disorders could present themselves in a serial order in accordance with developmental stages. The serial multiple mediated effects of the ADHD in childhood—the externalizing disorders (CD, ODD, ASPD) in adolescence and young adulthood—depression—AUD suggest not only the correlation between these disorders but also the importance of the prevention

of each preceding disorder from prevention and treatment of AUD. It is generally believed, out of the general population of children, ADHD prevalence rate is approximate 5% while CD's is between 2% and 10%.<sup>22)</sup> Such numbers are not low percentages at all, and a considerable number of the children tend to advance to AUD. It is therefore considered that the importance of treatment and prevention of disorders in children and adolescents should be emphasized.

According to previous studies on AUD patients with impulsivity traits, the less severe the ADHD symptoms, the longer the abstinence period. This finding suggests that ADHD symptoms have moderating effects on the severity of AUD and that the treatment of ADHD is very important for the treatment of comorbid AUD.<sup>17)</sup> This finding is supported by a longitudinal study which reported that the medical treatment of ADHD has lowered the risks of adulthood-onset SUD.<sup>23)</sup> Also, children with ADHD symptoms showed high risks of adulthood-onset antisocial behavior and SUD including AUD, and particularly the comorbid ADHD and CD group showed a relatively high risk of SUD including AUD.<sup>24)</sup> These findings support the present finding that externalizing disorders such as CD and antisocial behavior mediate between childhood-onset ADHD and adult-onset AUD, and agree with Kuperman, who hypothesized the onsets of childhood ADHD—adolescent CD—adulthood AUD were in line with developmental stages.<sup>25)</sup>

As previously mentioned, a range of externalizing disorders manifesting in childhood and adolescence and the increasing risk of adulthood-onset AUD are closely correlated in many ways. First, these disorders are known to share common genetic liabilities. Above all, most of genes reported to be associated with AUD were related to ADHD as well.<sup>26,27)</sup> Also, genetics had significant effects on the comorbid CD in SUD including AUD, nicotine use disorder and cannabis use disorder.<sup>28)</sup> Interestingly, a twin study found common genetic and environmental effects on both childhood ADHD symptoms and conduct problems.<sup>29)</sup>

As suggested by Beauchaine *et al.*,<sup>30)</sup> the impulsivity trait is an important factor that explained the heterotypic continuity of a wide externalizing spectrum from childhood to adulthood. From childhood ADHD to ODD, CD, antisocial behavior and AUD, impulsivity plays a pivotal role in each externalizing disorder present in each devel-

opmental stage, which is significantly influenced by genetic factors.<sup>31)</sup> Particularly, among the diverse facets of impulsivity, behavioral impulsivity symptoms drew attention as the key component of the externalizing spectrum.<sup>15)</sup> Based on the foregoing findings, the current study rated the externalizing disorders using the BIS\_M as a variable. In addition, we explored three facets of BIS, i.e. BIS\_M, BIS\_NP and BIS\_C, would influence the externalizing disorders using the regression analysis, and found that BIS\_M exerted influence on three dependent variables, i.e. ADHD symptoms, conduct problems, and severity of AUD. Many other studies confirmed impulsivity served as the key trait in externalizing disorders. Also, among ADHD symptoms, hyperactive/impulsive symptoms are known to predict the externalizing behavior in teens and adults, while inattention has not.<sup>8)</sup> Another study reported the increase in impulsivity could add to the risks of ADHD in childhood and AUD in adulthood, indicating the impulsivity was a factor underlying the correlation between AUD and externalizing disorders including ADHD.<sup>32)</sup>

The current study built on previous findings on the correlation between externalizing disorders and AUD and focused on the mediated effects of depression on the serial onsets of externalizing disorders and AUD.

As a common comorbidity in ADHD patients, depression was assumed to manifest itself as facet of adjustment disorders involving enduring social and learning dysfunction resulting from non-adaptive symptoms of ADHD.<sup>33,34)</sup> Other studies shed light on the genetic risks common to ADHD and depression shared via familial links.<sup>35,36)</sup> Meta-analysis of the long-term outcomes of ADHD and CD highlighted a high risk of comorbid depression in not only ADHD but also CD.<sup>14)</sup> Also, depression symptoms increased with the CD symptoms and callous-unemotional traits.<sup>37)</sup> Interestingly, the latest theoretical models predict that depression shares a common potential endophenotype, or reward dysfunction, with the impulsivity-based disorders including substance abuse, which is substantiated by accumulating physiological grounds.<sup>38-41)</sup> Also, a large-scale twin study reported that the genetic covariation between depression and AUD could be explained by negative emotionality and behavioral control.<sup>42)</sup> In other studies, it was demonstrated that insulin-like growth factor-1 (IGF-1) was significantly higher in patients with AUD accompanied with depressive symptoms

than ones without the symptoms, which shows IGF-1 would be a biomarker of AUD accompanied with depression.<sup>43)</sup> To sum up, the foregoing findings support the present findings, i.e. the correlation between depression and AUD and the mediated effect of depression between impulsivity-based externalizing disorders and AUD. Other studies reported externalizing behaviors and substance use has increased emotional instability, which was associated with declining cortisol reactivity. Also, depression or externalizing disorders (CD and ODD) were found to be risk factors increasing the onset of SUD.<sup>44)</sup>

The current study conducted a cross-sectional analysis of different clinical facets in conjunction with the presence of adolescent CD problems, and found the group with CD problems had more severe impulsivity, ADHD symptoms, antisocial behavior, depression, anxiety, and alcohol problems. This finding underpins the serial multiple mediated effects of the 'ADHD-externalizing disorders (CD and ASPD)-depression-AUD' and suggests these disorders may present themselves not only as serial onsets but also as comorbidities.

However, this study has several limitations. First, the sample size is relatively small. In addition, we recruited only men due to the lack of women patients with AUD. These points limit the generalizability of the findings. Also, this study was conducted only with inpatients of a hospital, and did not include any clinical aspects of outpatients with mild-moderate AUD. And another limitation is that a single hospital was only chosen as a place of the research, so that multicenter study has not been carried out. Second, a self-report inventory was used to screen ADHD symptoms, resulting in the increased false-positive of ADHD symptoms. Moreover, information on ADHD in childhood was not fully investigated; therefore there have been difficulties to make a definitive diagnosis for ADHD. As a result, future studies should take into account with an additional interview. Third, this study adopted a cross-sectional design, indicating that the causality between variables might be suggestive. Finally, using BIS\_M that measures motor impulsivity, externalizing disorders were assessed. Although motor impulsivity is a core feature of externalizing disorders, it still has limits to measure them by itself. Thus, we excluded patients with other psychiatric disorders except for AUD to minimize confounding effect of other variables related to externalizing disorders.

AUD is a chronic disorder causing severe dysfunctions

at an individual level, while adding enormous burdens at social and national levels. Currently, however, AUD is very hard to treat, and in spite of many fierce studies, few effective medications were developed. Thus, it is very important to early detect and treat the disorders preceding the onset of AUD, which is the first and foremost preventive measure to reduce the onset of AUD. That is, understanding the correlation between externalizing disorders, e.g. ADHD, CD, ODD and ASPD, and depression, as well as the early detection and aggressive treatment of such disorders, will be conducive to the prevention and treatment of AUD.

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