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Clinical and behavioral correlates in adult methamphetamine users with childhood exposure to household drug and alcohol use

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Abstract

Aims: To describe and compare methamphetamine (MA) users with and without a family history of alcohol or drug (FAOD) use in the household.

Design: A total of 1,144 Thai-speaking MA users in Thailand were recruited for a cohort study. Cross-sectional baseline data were analyzed according to their exposure to FAOD use (FAOD+/FAOD-). The Semi-Structured Assessment for Drug Dependence and Alcoholism (SSADDA) was utilized to collect baseline socio-demographic information and variables known to be associated with the impact of FAOD use.

Findings: FAOD+ participants had lower average years of education ($p < 0.01$), fewer average months of employment in the past year ($p < 0.01$) and reported higher rates of self-harm experience ($p < 0.001$), gambling ($p = 0.018$) and antisocial personality disorder ($p = 0.015$). FAOD+ participants had more severe clinical, adverse consequences. FAOD+ significantly predicted episodes of lifetime MA use ($R^2 = 0.004$, $p = 0.032$), the largest number of drinks ever had in a 24-hour period (MAXDRINKS) ($R^2 = 0.01$, $p = 0.001$), paranoid experiences (OR = 1.090, $p = 0.004$), alcohol dependence (OR = 1.112, $p = 0.001$) and antisocial personality disorder (OR = 1.139, $p = 0.015$). FAOD+ participants who were exposed to alcohol only were more likely to report a significantly higher MAXDRINKS ($p < 0.005$). Similarly, FAOD+ participants who were exposed to MA use only were significantly more likely to report more frequent use of MA ($p < 0.005$).

Conclusions: FAOD+ participants were characterized by a generally more severe clinical presentation than FAOD- participants. Moreover, we show that the specificity of drug type mattered, with family exposure of alcohol and MA associated with greater subsequent use of the respective drugs.

Introduction

In 2016, an estimated 3.4% of the Thai population aged 12–65 years used methamphetamine (MA), one of the highest national prevalence rates in the world (Saengow et al., 2016). MA has spread rapidly from initial use among students and laborers (e.g., truck drivers, shift workers) to the general population, in part due to its low cost and ready availability. The relative importance of the role of genetic and environmental factors in the vulnerability to psychostimulant, including MA, dependence remains an important focus of human substance use disorder (SUD) research (Gelernter & Polimanti, 2021; Koob & Volkow, 2016). For example, environmental factors appear to play a stronger role in exposure to and therefore the initiation of use of a specific drug, whereas genetic factors are apparently more important in the transition from initial use to the development of addiction (Heilig et al., 2021; Pasman et al., 2021). In this context, it is important to understand the relationships between specific environmental factors and their impact and specificity for the development of an SUD (Palmer et al., 2015).

Individuals who grow up in families with access to psychoactive drugs are at significantly greater risk of developing an SUD (Matson et al., 2021). For example, a family history of exposure to household drug or alcohol use is associated with earlier initiation of substance use among adolescents (Freisthler et al., 2014). A range of subsequent substance use problems and outcomes, including increased addiction severity, more unsuccessful quit attempts, and a greater likelihood of dependence, were also observed among

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individuals in families with a history of drug or alcohol use (Ewing et al., 2015). Several studies have shown that parental SUDs predicted increased risk for SUDs in the offspring (Mellentin et al., 2016; Timko et al., 2021).

Although part of this risk is attributable to genetic factors, environmental contributions are also at play. For example, drug or alcohol use is not only associated with greater access to drugs through their parents and primary parenting inadequacies, such as poor supervision, increased inappropriate punishment, and poor parental skills, but also other secondary dysfunctional outcomes (Freisthler et al., 2014; Mellentin et al., 2016) such as a greater likelihood of job and/or home loss, all of which can create an environment of insecurity and stress for the child (Kendler et al., 2019b; Khemiri et al., 2020). The impact of such effects is also supported by the higher rates of impaired personality function, cognitive deficits (Parolin et al., 2016), mental disorders, suicide, and self-injury in individuals growing up in such drug-influenced environments (Smith & Wilson, 2016).

Only a few studies have attempted to examine the role of childhood environmental (i.e., household) exposure to drug and alcohol use in person who use MA. Thus, we sought to describe and compare a group with a history of exposure to drug and alcohol use in the household with a group without exposure. We hypothesized that the two groups would differ in their clinical characteristics (e.g., age of onset, severity and pattern of drug and alcohol use, other comorbid substance use and/or mental disorders). We further hypothesized that the impact of the type of household substance exposure (e.g., MA vs. alcohol) would be associated with substance-specific patterns of adult drug/alcohol use in MA-using adults. Subjects were participants in a genetic study of MA dependence and other SUDs in Bangkok, Thailand.

Method

Participants

The study cohort consisted of 1,144 Thai-speaking individuals who used MA, aged 18 years or older, who were receiving either outpatient or inpatient treatment for drug use between 2015 and 2018 at the Princess Mother National Institute on Drug Abuse Treatment (PMNIDAT) of the Ministry of Public Health, Thailand. The study is part of a genetic study of MA dependence that sought to enroll severe MA cases (i.e., individuals meeting at least 6 out of 7 criteria for MA dependence) per the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition. Patients with primary psychotic disorders or neurological disease (e.g., cerebrovascular disease, epilepsy) were excluded. The study was approved by the Ethics Committees of the Faculty of Medicine, Chulalongkorn University, the PMNIDAT, and the Yale University School of Medicine IRB. Each subject signed an informed consent form prior to their research participation and was compensated (500 Thai baht, or roughly USD15).

Assessments

Demographic, diagnostic, substance use, and environmental data were obtained by using the Thai version of the Semi-Structured Assessment for Drug Dependence and Alcoholism (SSADDA; Kalayasiri et al., 2014; Malison et al., 2011). The SSADDA is a comprehensive, semi-structured interview based on DSM-IV criteria for genetic studies of SUDs and related phenotypes. The Thai version was translated, back translated, and validated in genetic studies of opioid dependence in Northern Thailand, where it was shown to have high inter-rater/inter-instrument reliability for opioid dependence. Standard SSADDA training and quality control algorithms were applied (except audiotaping), including completion of 10 practice interviews required for interviewer certification, and ongoing quality control procedures including international weekly teleconference calls with collaborators having expert knowledge of the SSADDA (Kalayasiri et al., 2010; Pierucci-Lagha et al., 2005) in the US and Thailand. Thai SSADDA interviewers were trained by certified interviewers, initially with established training expertise in the English version of the SSADDA in the US, and more recently with specific expertise in the Thai version of the instrument.

Household exposure to substance use was assessed using the following SSADDA instrument item: “Now I'm going to ask about use of drugs or alcohol in the household where you grew up, by the time you were 13 years old. Were you ever aware of adults in your household drinking enough to get drunk, or using drugs or alcohol, by the time you were 13?” Those individuals responding ‘‘yes’’ to this item were identified as having a family history of alcohol or drugs use or “FAOD+”. They were then probed by substance type, including by “Were you aware of adults in your household, or your older siblings, drinking enough to get drunk by the time you were 13?” for household alcohol intoxication (“yes”: “FAOD+ Alc”; “no”: “FAOD- Alc”) and “Were you aware of adults in your household, or your older siblings, using MA by the time you were 13?” for household MA exposure (“yes”: “FAOD+ MA”; “no”: “FAOD-MA”). The question, “Did this happen more than 10 times?” was used as a measure of severity of household alcohol/MA use exposure. For alcohol the categories were: “FAOD+ Alc > 10”; “FAOD+ Alc≤10”; and “FAOD- Alc”, and for MA: “FAOD+ MA > 10”; “FAOD+ MA≤10” and “FAOD- MA”.

Baseline socio-demographic characteristics as well as variables previously shown to be associated with the impact of family household alcohol and drug use (Berg et al., 2016; Hines et al., 2015) were selected for analysis. Specifically, we included five socio-demographic variables, including “sex,” “age,” “level of education,” “marital status (single, divorced, separated or married)” and “months employed over the last year”. We included eight clinical comorbidity variables as well (nicotine dependence, cannabis dependence, sedative use, period of heaviest gambling [coded in months], major depressive disorder (MDD), antisocial personality disorder (ASPD), history of suicide attempt, and history of self-harm. Diagnoses were based on DSM-IV criteria. Our review of the relevant literature led to the inclusion of 10 additional variables of interest including

"episodes of lifetime MA use," "age of onset of first MA use," "MA combined with other substances," "MA intoxicated all day experience," "MA injection," "paranoid experience," "desire to stop MA," "harm experience from using MA," "being arrested by the police due to MA," and "MA overdose." These are summarized in supplementary Table S.1 in Supplementary Material.

Data Analysis

Individuals with a childhood history of exposure to household drug or alcohol use (FAOD+) and without (FAOD-) were first compared for potential differences in socio-demographic, drug use, and diagnostic comorbidity variables using unpaired *t*-tests for continuous variables (if normal distribution was present). Non-normally distributed variables were log transformed, and if still non-normal, categorized as non-continuous variables. Chi-square ($\chi 2$) testing was used for categorical variables.

Second, to determine whether a history of household drug or alcohol use exposure predicted clinical outcomes, variables that differed significantly ($p < 0.05$) between the FAOD+ and FAOD- groups in the prior analyses were then analyzed using separate regressions. Logistic regression was employed for binary variables ("harm experience from using MA", "paranoid experience", "alcohol dependence", "antisocial personality disorder", "using MA together with one or more other drugs", "self-harm"), and linear regression was used for normally distributed continuous variables ("episodes of lifetime MA use", "the largest number of drinks ever had in a 24-hour period (MAXDRINKS; i.e., 1 standard drink = 1 glass of wine or 1 can [12 oz.] of beer and "period of heaviest gambling [coded in months]"). The regression analyses controlled for the variables as indicated in Table 3 below.

Finally, we used an analysis of variance (ANOVA) to analyze alcohol and MA use (e.g., "episodes of lifetime MA use", "MAXDRINKS", etc.) by others in the household with respect to each of three defined groups for household frequency of exposure: more than 10 times, 10 times or less, and never experienced. All statistical hypotheses were evaluated as two-tailed. SPSS, version 22.0 for Mac was used for all the analyses.

Results

Socio-demographic and clinical comorbidity data are presented in Table 1. Of the 1,144 persons who used MA, 639 (55.8%) experienced household MA use or alcohol intoxication before age 13 years. In the FAOD+ group, 481 (75.2%) experienced household alcohol intoxication only, 52 (8.1%) experienced household MA use only and 106 (16.5%) both household MA use and household alcohol intoxication. FAOD+ status was more common in females. FAOD+ and FAOD- adults did not differ with respect to current marital status. However, FAOD+ individuals had fewer average years of education and fewer average months of employment in the past year. Moreover, FAOD+ individuals reported higher rates of self-harm and gambling and had higher rates of antisocial personality disorder.

Table 1

Socio-Demographic and Clinical Comorbidity Data of Individuals With a Childhood History of Exposure to Household Alcohol or Drug Use (FAOD+) and Without (FAOD-)

	FAOD+ n = 639		FAOD- n = 505		*p*-Value
	n	**%**	**n**	**%**	
Male sex	266	41.6	279	55.2	<0.001***
Marital status: Single	548	85.7	425	84.1	0.451
Nicotine dependence	399	62.4	307	60.7	0.584
Marijuana dependence	100	15.6	81	16.0	0.874
Major depressive disorder	8	1.2	2	0.3	0.202
Antisocial Personality Disorder	73	11.4	36	7.1	0.020*
Suicide attempt	81	12.6	49	9.7	0.130
Self-harm	207	32.3	97	19.2	<0.001***
	M	***SD***	***M***	***SD***	
Age (years)	31.22	7.74	31.72	8.01	0.291
Number of months employed in the last year	5.65	4.05	6.70	4.13	<0.01**
Level of education (years)	8.33	3.06	8.97	3.04	<0.01**
Sedative use	1.10	5.03	0.93	4.69	0.553
Period of heaviest gambling (months)	1.33	0.47	1.20	0.40	0.020*

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Table 2 depicts results from analyses of clinical patterns of MA and alcohol use. FAOD+ individuals were more likely to have comorbid alcohol dependence and to report a higher largest number of drinks ever had in a 24-hour period compared to FAOD- individuals. Statistically significant differences between groups were also observed for episodes of lifetime MA use, using MA together with one or more other drugs, and having been harmed (e.g., from an accidental injury) from using MA, all of which were greater in FAOD+ vs. FAOD- individuals. FAOD+ adults also more commonly endorsed the experience of MA paranoia than the FAOD- group.

Table 2

Clinical Pattern of Methamphetamine and Alcohol Use of Individuals With a Childhood History of Exposure to Household Alcohol or Drug Use (FAOD+) and Without (FAOD-)

	FAOD+ n = 639		FAOD- n = 505		*p*-Value
	n	%	n	%	
Alcohol dependence	436	68.2	295	58.4	0.001***
Age onset of first MA use (<18 years)	449	70.3	331	65.5	0.059
MA combined with other substances	254	39.7	168	33.2	0.026*
MA intoxicated all day experience	401	62.7	326	64.5	0.537
MA injection	26	4.1	13	2.5	0.191
Paranoid experience	320	50.4	210	41.5	0.004**
Desire to stop MA	529	82.7	410	81.1	0.487
Harm experience from using MA	542	84.8	371	73.4	<0.001***
Being arrested by the police due to MA	525	82.1	414	81.9	0.937
MA overdose	126	19.7	80	15.8	0.104
	M	***SD***	***M***	***SD***	
The largest number of drinks ever had in a 24-hour periods (MAXDRINKS)	25.91	27.91	20.72	22.24	0.001***
Episodes of lifetime MA use	5147.84	3918.68	4655.00	3740.71	0.030*

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; MA = methamphetamine

Variables differing significantly between groups as described above were next entered into regression analyses. FAOD+ status remained a significant risk factor for all of these same variables following regression analysis, including for harmful MA experiences, MA paranoia experience, alcohol dependence, ASPD, MA combined with other substances, self-harm, episodes of lifetime MA use, the largest number of drinks ever had in a 24-hour periods and duration of heaviest gambling (see Table 3).

Table 3

Effects of Having a Childhood History of Exposure to Household Alcohol or Drug Use (FAOD+) vs No History (FAOD-) on Clinical Diagnoses and Alcohol or MA Use

	FAOD+ vs FAOD-				
Outcome variables	***B***	***SE***	***p*-Value**	***OR***	***95% CI***
Harm experience from using MA ℘, a	0.18	0.04	<0.001	1.192	1.108-1.282
Paranoid experience ℘, b	0.86	0.03	0.004	1.090	1.027-1.156
Alcohol dependence ℘, c	0.11	0.03	0.001	1.112	1.046-1.182
Antisocial personality disorder ℘, c	0.13	0.05	0.015	1.139	1.026-1.264
MA combined with other substances ℘, d	0.07	0.03	0.024	2.073	1.009-1.140
Self-harm ℘, e	0.18	0.04	<0.001	1.191	1.112-1.277
	B	***SE***	***p*-Value**	***R***	***R^2***
Episodes of lifetime MA use ϒ	123.07	57.17	0.032	0.064	0.004
The largest number of drinks ever had in a 24-hour period ϒ	0.008	0.002	0.001	0.100	0.010
Period of heaviest gambling ϒ	0.993	0.224	<0.001	0.130	0.017

℘ Logistic regression model; ϒ Linear regression model; MA = methamphetamine

Models were adjusted by gender, antisocial personality disorder, self-harm, duration of heaviest gambling and by:

[a]MA paranoia experience, alcohol dependence, MA combined with other substances, episodes of lifetime MA use

[b]harmful MA experiences, alcohol dependence, MA combined with other substances, episodes of lifetime MA use

[c]harmful MA experiences, MA paranoia experience, MA combined with other substances, episodes of lifetime MA use

[d]harmful MA experiences, MA paranoia experience

[e]harmful MA experiences, MA paranoia experience, MA combined with other substances, episodes of lifetime MA use

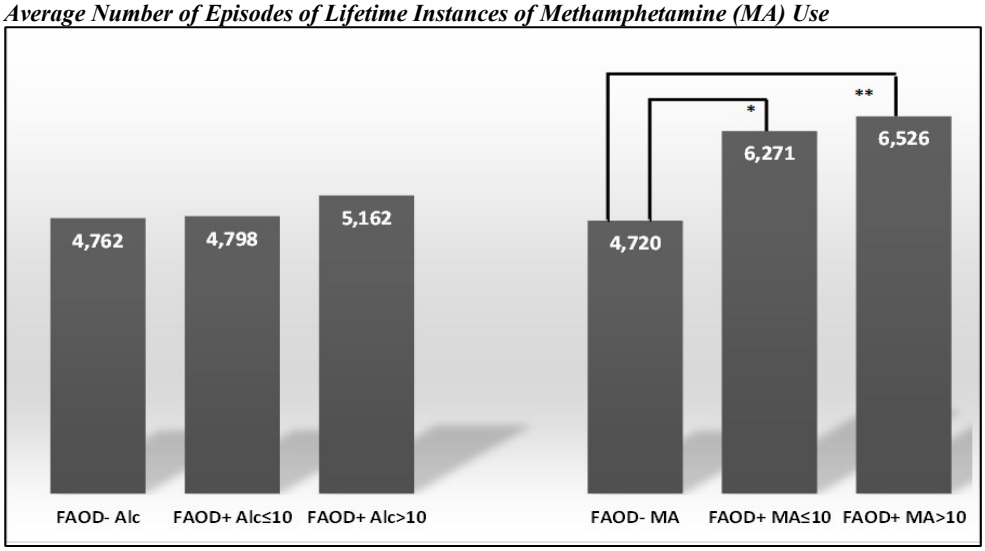
Figure 1 depicts the number of lifetime episodes of MA use in the FAOD+ group as a function of the type of childhood drug exposure (alcohol vs. MA) and the frequency of exposure (more than 10 times, 10 times or less, or never). Episodes of lifetime MA use were significantly higher in children with higher vs. no household exposure and intermediate levels compared to no household exposure to MA use. There were no significant differences between children with higher vs. intermediate levels of household MA use. In contrast, episodes of MA use did not differ by

group as a function of childhood household alcohol exposure.

Figure 2 shows similar relationships between levels of adult drinking (measured by the largest number of drinks ever had in a 24-hour period) and level of childhood exposure. In brief, FAOD+ MA individuals with high levels of exposure (> 10 times) to family member intoxication had significantly higher total maximum drinks in 24 hours than individuals lacking such exposure. There was no significant difference between children with 10 times or less instances of FAOD+ to family member intoxication compared to those with no household exposure. Conversely, the maximum lifetime number of drinks in any 24-hour period, did not differ by group as a function of childhood household MA exposure.

Figure 1

Average Number of Episodes of Lifetime Instances of Methamphetamine (MA) Use

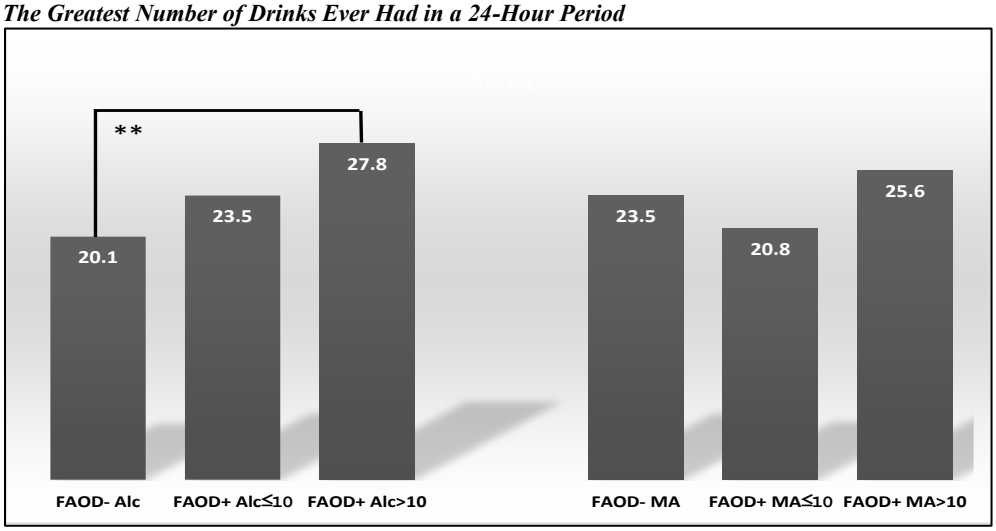


*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

Note: FAOD- Alc = groups who never experienced others in the household using alcohol; FAOD+ Alc≤10 = groups who experienced others in the household using alcohol 10 times or less; FAOD+ Alc>10 = groups who experienced others in the household using alcohol more than 10 times; FAOD- MA = groups who never experienced others in the household using MA; FAOD+ MA≤10 = groups who experienced others in the household using MA 10 times or less; FAOD+ MA>10 = groups who experienced others in the household using MA more than 10 times.

Figure 2

The Greatest Number of Drinks Ever Had in a 24-Hour Period



*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

Note: FAOD- Alc = groups who never experienced others in the household using alcohol; FAOD+ Alc≤10 = groups who experienced others in the household using alcohol 10 times or less; FAOD+ Alc>10 = groups who experienced others in the household using alcohol more than 10 times; FAOD- MA = groups who never experienced others in the household using MA; FAOD+ MA≤10 = groups who experienced others in the household using MA 10 times or less; FAOD+ MA>10 = groups who experienced others in the household using MA more than 10 times.

Discussion

We examined socio-demographic and clinical correlates of a childhood history of household drug or alcohol exposure in a treatment sample of adults who were "severely dependent" on MA in Thailand. In brief, our report is consistent with findings from previous studies, which showed comparable prevalence of a childhood history of household drug or alcohol exposure rates among affected individuals (i.e., in more than half of persons who used MA) (Kendler et al., 2019a, 2019b). Similarly, we replicate prior findings that a childhood history of household drug or alcohol exposure in persons who used MA is associated with lower educational attainment and lower of levels of employment in the past year (Kuppens et al., 2020; Lander et al., 2013; Pihkala et al., 2017).

Growing up in a household where family members misuse drugs or alcohol is associated with poorer cognitive and executive functioning (Kuppens et al., 2020). Poor parental nurturing in such families might be a risk factor for the poor cognitive control associated with substance use disorders (Khemiri et al., 2020; Kuppens et al., 2020; Mellentin et al., 2016). Consistent with this hypothesis, persons who used MA in the exposure group reported more severe patterns of MA use, including greater numbers of episodes of lifetime MA use and more frequent use of MA with other substances. Such findings are consistent with prior research showing that a family history of drug misuse was found to increase the risk of MA use (Kuppens et al., 2020; Russell et al., 2008). Prior twin studies of substance use disorders are consistent with a substantial role for environmental risk factors in SUD etiology. Perhaps one of the most interesting findings of the current study relates to the apparent specificity of childhood exposure for drug type. Specifically, childhood exposure to alcohol was associated in a dose dependent fashion with adult alcohol drinking (but not MA use) behaviors in our MA users. Conversely, childhood exposure to MA use only appeared to impact patterns of MA, but not alcohol use (again, in a dose dependent way). Both results are consistent with the hypothesis that childhood environment can impact the risk for adult drug and alcohol exposure during adulthood in a drug-specific fashion. However, these results are also consistent with genetic liability reflected similarly in parents and offspring.

Individuals in the exposure group also reported more paranoid symptoms associated with their MA use. This observation is consistent with results obtained in other research that the concurrent use of alcohol or drugs and/or a family history of drug use is associated with increased risk for the phenotype in persons who used MA (Chang et al., 2018). Similar to prior research (De Genna & Cornelius, 2015; Lander et al., 2013), we found that individuals in the exposure group reported higher rates of being hurt or having accidental injuries when using MA. As reported in prior literature, our results are consistent with the notion that substance related household dysfunction may broadly impact an individual's coping skills, resulting in behavioral problems and violence through the life span (Ewing et al., 2015; Kuppens et al., 2020). It is potentially useful in understanding who is most at risk from harm in further studies. Our findings are also consistent with genetic influences on severity of the effect on the individual. Consistent with either possibility are observations that those positive for childhood exposure manifested broad evidence of non-substance related phenotypes, including higher rates of antisocial personality disorder, more self-harm, and higher levels of gambling. Such phenotypes reflect a more severe MA phenotype. This is perhaps not surprising, as childhood exposure to drug/alcohol use may well have broad and non-specific effects as a risk factor on other related and unrelated phenotypes and confounding patterns of MA use resulting in more severe consequences of MA use (Chang et al., 2018; Kendler et al., 2019b). Similarly, family studies have shown that genetic liability to SUDs is associated with liability to other psychiatric traits and behaviors as well (Chang et al., 2018; Polimanti et al., 2017). While several studies show a strong relationship between positive family history of drug use and elevated depression symptoms (Bradshaw et al., 2010; Lander et al., 2013), our findings did not support those results. The inconsistent outcome may be explained by the very low prevalence of diagnosed depressive disorders in our sample.

Among our study's strengths is its large sample size, the largest study, to our knowledge, of an Asian MA-use cohort. Even with its strengths, we note several limitations. First, our study focused on a severely dependent population of MA users; as such, our findings, may not generalize to other less severely affected MA cohorts. Second, and perhaps the foremost limitation of the current study, is the fact that the primary "environmental" risk factor studied, namely childhood exposure is strongly correlated with genetic risk factors. Specifically, higher levels of household exposure may well be the result of greater genetic severity in first degree relatives (e.g., parents), which in turn, could predispose affected children to a greater biological risk for the disorder. Our study design cannot distinguish environmental from genetic risk; and therefore, our results reflect correlation with genetic factors, and we make no claims regarding causation. Furthermore, the questions for childhood exposure to drug and alcohol use in households were asked of adults, so recall bias may have affected the results. In fact, this study is part of an ongoing study on a MA genome in Thailand. A major long-term goal of our work is to better understand these genetic factors, which will in turn clarify the role of the environment on SUD risk.

Conclusion

In conclusion, our results contribute to a literature suggesting the association of environmental factors in general, and the role of childhood family exposure more specifically, in the clinical features observed in MA-using adults. Specifically, we show that persons who used MA with a positive family history of childhood exposure are characterized by a generally more severe clinical presentation than individuals without such exposure. Moreover, we show the specificity of drug type for such childhood exposure effects. Future studies are required to investigate the extent to which such effects are mediated by environmental vs. genetic risk factors for MA use disorder.

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