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Attention-Deficit/Hyperactivity Disorder Among Chronic Methamphetamine Users: Frequency, Persistence, and Adverse Effects on Everyday Functioning

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Abstract

Aims—Attention-Deficit/Hyperactivity Disorder (ADHD) is widely regarded as a common comorbidity of methamphetamine (MA) dependence, but the frequency, persistence, and real-world impact of ADHD among MA users is not known.

Methods—Four hundred individuals with MA use disorders within 18 months of evaluation and 355 non-MA using comparison subjects completed a comprehensive neuropsychiatric research battery, including self-report measures of everyday functioning.

Results—In logistic regression models adjusting for potential confounds, lifetime diagnoses of ADHD as determined by a structured clinical interview were significantly more prevalent among the MA participants (21%) versus comparison subjects (6%), particularly the hyperactive and combined subtypes. MA use was also associated with an increased persistence of combined subtype of ADHD into adulthood. Among the MA users, lifetime ADHD diagnoses were uniquely associated with greater concurrent risk of declines in instrumental activities of daily living, elevated cognitive symptoms in day-to-day life, and unemployment.

Conclusions—Findings indicate that ADHD is prevalent among chronic MA users, who are at increased risk for persistence of childhood diagnoses of ADHD into their adult years. ADHD also

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Contributors

Authors Woods, Morgan, Atkinson, and Grant designed the study and wrote the protocol. Authors Obermeit, Cattie, Bolden, Marquine, and Morgan managed the literature search. Authors Woods and Obermeit undertook the statistical analysis. Authors Obermeit, Cattie, Bolden, and Marquine wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of Interest

All authors declare that they have no conflicts of interest.

appears to play an important role in MA-associated disability, indicating that targeted ADHD screening and treatment may help to improve real-world outcomes for individuals with MA use disorders.

Keywords

Substance Abuse; Developmental Disorder; Comorbidity; Functioning; Disability; Neuropsychiatry

1. Introduction

Methamphetamine (MA) is used by over 400,000 Americans every year (SAMHSA, 2011), and can have serious neuropsychiatric and psychosocial consequences (e.g., Scott et al., 2007) that often lead to disability. Specifically, chronic MA users exhibit difficulties handling finances, arranging transportation, adhering to prescribed medications, and maintaining employment (Henry et al., 2010; Moore et al., 2012; Weber et al., 2012). Clinical factors driving MA-associated disability include recency and route of MA use (e.g., Weber et al., 2012) and neurocognitive impairment (e.g., Henry et al., 2010). One potentially important predictor of disability that is commonly comorbid with MA use is Attention-Deficit/Hyperactivity Disorder (ADHD), which is itself associated with functional disability across the lifespan (e.g., Barkley et al., 1996). Therefore, the aim of the current study is to determine the independent influence of ADHD on MA-related disability, including unemployment, declines in instrumental activities of daily living, and self-reported neurocognitive symptoms in daily life.

2. Material & Methods

2.1 Participants

This retrospective study included 755 participants enrolled in MA and human immunodeficiency virus (HIV) infection cohort studies at the University of California San Diego (UCSD), who were recruited primarily through local HIV and drug treatment clinics. Demographic and clinical characteristics of the study groups are displayed in Table 1. Participants were required to be fluent in English, provide a negative urine toxicology screen for illicit substances (excluding marijuana) on the day of testing, have no history of major neurological (e.g., seizure disorder) or psychotic (e.g., schizophrenia) conditions, and not meet diagnostic criteria for alcohol or substance abuse (other than MA or marijuana) within the past year, or dependence within the past five years, as determined by the Composite International Diagnostic Interview (CIDI 2.1; WHO, 1997). Participants with a diagnosis of MA dependence in their lifetime, as well as a recent diagnosis of MA use disorder (abuse or dependence) within 18 months of the evaluation, received a classification of MA+. A semi-structured timeline follow-back interview was also administered to assess participants' patterns of MA use (Rippeth et al., 2004). Diagnoses of ADHD were determined using the Diagnostic Interview Schedule for DSM-IV (DIS-IV; Robins et al., 1995). Current ADHD was defined as meeting full criteria within the past year, and lifetime ADHD was defined as meeting full criteria at any point during the lifetime. In both cases, the presence of childhood symptoms (i.e., between the ages of 6-10) was confirmed per DSM-IV criteria.

2.2 Materials and Procedures

This study was approved by UCSD's Human Research Protections Program. Participants completed a comprehensive neuropsychological, psychiatric, and medical assessment battery as part of a larger ongoing study (for details regarding these measures, see Rippeth et al., 2004 and Blackstone et al., in press). Participants also completed two self-report

measures of everyday functioning to assess instrumental activities of daily living, neurocognitive symptoms and employment. On the Heaton et al. (2004) modification of the Lawton and Brody (1969) Activities of Daily Living Scale (ADL), “current” ADL scores (range 0-11) were of primary interest, where higher scores represent greater levels of dependence (Blackstone et al., in press). Neurocognitive symptoms in daily life were assessed using the Patient's Assessment of Own Functioning Inventory (PAOFI; Chelune et al., 1986). PAOFI total scores were derived by summing the number of items with scores 3 (range 0-31), with higher total scores indicating more severe cognitive symptoms (Blackstone et al., 2012). The PAOFI was also used to determine participants' employment status (employment was categorized as either full or part time).

3. Results

Figure 1 shows that the MA+ group had significantly higher rates of ADHD than the MA– group; specifically, rates of Combined (lifetime [OR=1.92] and current [OR=1.79], $p<.001$) and Hyperactive (lifetime [OR=5.27] and current [OR=4.26], $p<.05$), but not Inattentive ($p>.10$) subtypes were higher in the MA+ group. A logistic regression confirmed that MA status was independently associated with higher rates of ADHD ($p<.05$; OR=1.86) while accounting for key variables that differed across the MA+/- groups (see Table 1). Moreover, Figure 1 shows that MA+ participants were significantly less likely to experience a resolution of childhood ADHD diagnoses in adulthood ($p=.005$, OR=10.5) for the Combined, but not Inattentive or Hyperactive subtypes ($p>.10$).

A planned series of multivariable regressions were then conducted separately in the MA+ and MA– groups to determine whether ADHD (any lifetime diagnosis) was an independent predictor of cognitive symptoms (PAOFI total), IADL dependence, and employment status while controlling for cognitive reserve (i.e., education and oral word reading), age, major depressive disorder, global neurocognitive impairment, and lifetime history of alcohol or other substance use disorders. In the MA+ group, all of the individual regression models predicting functional outcomes were significant ($p<.05$), with ADHD emerging as an independent predictor of cognitive symptoms ($\beta=0.17$; $p<.001$), IADL dependence ($\beta=0.14$; $p=.002$), and unemployment ($\chi^2=17.5$; $p=.025$). In contrast, lifetime ADHD did not significantly predict any functional outcome in the non-MA using cohort ($p<.10$).

4. Discussion

It has been widely observed that MA use and ADHD are highly comorbid (Jaffe et al., 2005). This comorbidity may be due to shared neural substrates and accompanying behavioral profiles that may both promote and maintain MA abuse disorders in individuals diagnosed with ADHD in childhood. The present study extended the literature by demonstrating this relationship in a large, well-categorized outpatient sample of individuals with histories of MA dependence, among whom a substantially elevated prevalence of lifetime ADHD was observed (20.8%) relative to non-MA users in our study (6.2%) and general population estimates (de Graaf et al., 2008). Importantly, a number of factors that may influence the detection of this relationship were controlled (e.g., rigorous assessment methods to establish DSM-IV MA dependence and ADHD diagnoses, and inclusion of a substantial range of MA use severity). Our findings revealed that lifetime and current ADHD was between 2 and 6 times more common in MA users versus non-MA users, which varied by subtype (with combined being most common, followed by hyperactive and inattentive). In addition, we observed robust effects of ADHD on all functional outcomes examined (i.e., activities of daily living, neurocognitive symptoms in daily life, and employment status) in MA-dependent individuals, even in the context of several other known contributors to impaired everyday functioning in this group (e.g., verbal IQ,

demographics, history of depression and other substance use disorders). These findings underscore the frequent comorbidity of ADHD among MA users, as well as the potentially wide-ranging disruption in real-world functioning associated with this comorbid diagnosis.

Our results demonstrated a substantial impact of ADHD status on both subjective and objective measures of everyday functioning across a broad spectrum of MA use severity. More specifically, MA users who had met DSM-IV criteria for ADHD were less likely to be employed, evidenced more dependence in critical aspects of everyday living, and reported higher perceived levels of everyday functioning difficulties. These results are particularly compelling given that the robust effect of ADHD was consistently observed despite accounting for several other documented determinants of everyday functioning (verbal IQ, demographic factors, and history of depression and other substance use disorders). Notably, ADHD was the only factor that was significantly predictive of all functional outcomes included in this investigation. This finding raises several questions regarding the nature of ADHD-related risk for everyday functioning difficulties. That is, specific symptoms, features, or subtypes of ADHD may be driving its observed impacts on everyday functioning. Therefore, it may be informative to explore the specific mechanisms (for instance, neurocognitive mechanisms) by which this relationship may occur. For example, it has been proposed that working memory deficits may amplify risky decision-making in MA users with ADHD (Duarte et al., 2012), potentially increasing the likelihood of vocational difficulties, engagement in HIV transmission risk behaviors, or financial mismanagement. These types of deficits might also be partially responsible for the everyday functioning disruptions observed in the present study. Alternatively, it is possible that observed deficits in executive functions (organization, planning, and complex problem solving) and impaired monitoring/inhibition in individuals with ADHD may be compounded by chronic MA use, thereby increasing the likelihood that ADHD symptoms will persist into adulthood and exacerbate everyday functioning impairments in dual-risk individuals.

Among MA-dependent individuals with ADHD, the elevated risks for everyday functioning problems suggest that ADHD may also impede successful substance use treatment. For example, prior work shows that those diagnosed with ADHD in drug treatment facilities experienced more severe psychiatric symptomatology, stronger associations with the positive psychological effects of substances, more severe substance abuse and drug related problems, reported more drug cravings and had a harder time resisting use than those who did not endorse ADHD symptoms (Faraone et al., 2007; Jaffe et al., 2005; Horner & Scheibe, 1997). Additionally, individuals with comorbid MA dependence histories and ADHD were more likely to leave treatment prematurely and had greater difficulty with medication adherence (Jaffe et al., 2005). Moreover, there is evidence to suggest that ADHD treatment positively impacts substance treatment outcomes by reducing both cravings and relapse. Lower rates of substance use disorder onset are also associated with early ADHD treatment (Wilens et al., 2003). This evidence, combined with the current findings, strongly suggests that efforts aimed at identification and treatment of ADHD among individuals with comorbid MA use disorders could enhance overall health outcomes.

The clinical importance of considering ADHD comorbidity in the management of MA users is further underscored by the prevalence of the comorbidity (especially hyperactive and combined subtypes) and the potential role of MA in the persistence of ADHD. One possible explanation for this relationship is increased susceptibility of individuals with ADHD to MA use disorders later in life, which may be driven by psychosocial, cognitive, and/or neural factors. For example, ADHD is associated with risky decision-making and impulsivity, which may disrupt consideration of future outcomes and impair choices in everyday life (Sonuga-Barke & Fairchild, 2012), including those pertaining to MA (Paulus et al., 2005). It is also reasonable to posit that initiation of MA use following the onset of ADHD

symptomatology may be a form of self-medication, especially considering the benefits associated with stimulants in controlling ADHD symptomatology (Arnsten, 2006).

A few limitations of this study deserve consideration in interpreting its findings. Our measurement of functional outcomes was predominately via self-report, which may be subject to bias. As such, future studies might include objective, performance-based measures of real-world functioning (see Blackstone et al., 2012). Although the high prevalence of MA + and ADHD comorbidity was confirmed in the present study, the directionality of this relationship was not definitively determined. Specifically, it remains unclear ADHD+ individuals are predisposed to initiate (potentially more severe) MA use, or whether the high frequency of ADHD among MA users relates to the persistence of early use, particularly among persons expressing the hyperactive subtype. Additionally, there was no available information regarding participants' MA or ADHD treatment histories, which may be an important mediator of the impact of these conditions on real-world outcomes. In addition, we were not able to include HCV (which differed by MA status) in the statistical models due to missing data across both cohorts; nevertheless, HCV was not associated with ADHD diagnoses in the subset with serostatus available. Certainly, the relatively high prevalence of infectious disease in these cohorts limits the external validity of the study findings. Finally, the disproportionate number of male participants in both the MA- (76.1%) and MA+ (86.5%) groups may hinder generalizability given gender differences in the presentation of ADHD, diagnosis of ADHD and ADHD subtypes, comorbidity of substance abuse, using patterns of those with ADHD, and treatment outcomes (Biederman et al., 2002; Disney et al., 1999; Hser et al., 2005).

5. Conclusions

Findings indicate that ADHD is prevalent among chronic MA users, who are at increased risk for persistence of childhood diagnoses of ADHD into their adult years. ADHD also appears to play an important role in MA-associated disability, including declines in everyday living, self-reported neurocognitive symptoms, and unemployment. Targeted ADHD screening and treatment may help to improve real-world outcomes for individuals with MA use disorders.

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Highlights

- ADHD is prevalent among chronic methamphetamine (MA) users.
- Chronic MA users are at increased risk for persistence of ADHD symptoms.
- In MA users, ADHD diagnoses were associated with unemployment, cognitive symptoms, and declines in everyday living.
- ADHD appears to play an important role in MA-associated disability.

* $p < .05$. ** $p < .01$.

Only individuals meeting criteria for lifetime ADHD could be assigned with current ADHD diagnoses, per DSM-IV criteria.

Resolved subtypes: Inattentive $n = 28$; Hyperactive $n = 33$; Combined $n = 44$.

Figure 1.

Prevalence and Resolution of ADHD in the MA+ and MA- Groups.

Table 1

Demographic, Psychiatric, and Substance Use Characteristics of Participants by MA Group (N = 755) and by ADHD group within MA+ group (n = 400).

Variable	MA-(n = 355)	MA+		
		Entire MA+ (n = 400)	MA+/No ADHD (n = 317)	MA+/Lifetime ADHD (n = 83)
Demographic Characteristics				
Age (years)	39.8 (11.3)	38.6 (8.3)	39.0 (8.2)	36.9 (8.2)
Education (years) ^{I**, 2*}	13.3 (2.2)	12.1 (2.3)	12.3 (2.3)	11.6 (2.2)
Sex (% men) ^{I**}	76.1	86.5	87.1	84.3
Ethnicity (% Caucasian) ^{I*}	63.1	71.5	71.0	73.5
WRAT-3 Reading (SS) ^{I**, 2**}	100.9 (11.2)	97.0 (10.6)	100.0 (92.0-107.0)	96.0 (88.0-103.0)
HCV (% seropositive) ^{a, I**}	15.9	26.5	25.4	32.1
HIV Infection (% seropositive)	42.3	44.0	42.6	49.4
Psychiatric Characteristics (%)				
Major Depressive Disorder				
Current ^{b, I*, 2*}	10.2	15.8	11.3	24.8
Lifetime ^{c, 2*}	35.9	44.4	37.2	60.0
ASPD ^{d, I**, 2**}	6.2	23.8	18.7	43.4
Methamphetamine Use Characteristics ^e				
Last use (days)	--	91.3 (37-201)	91.3 (36-202)	91.3 (38-203)
Cumulative duration of use (days)	--	3022 (1370-5160)	2896.0 (1309-5209)	3360.0 (1503-5084)
Cumulative quantity of use (gram)	--	2148.63 (647-5375)	1892.8 (619-5017)	2750.7 (808-6102)
Age at first use (years)	--	21.0 (17-27)	21.0 (17-28)	19.0 (16-27)
Injection use (%)	--	23	39.8	37.4
Lifetime Substance Use Disorders (%)				
Alcohol ^{I**, 2*}	31.6	68.8	66.3	78.3
Other substances ^{f, I**, 2*}	29.6	72.8	70.4	81.9
Marijuana ^{I**}	22.0	52.5	50.5	60.2
Cocaine ^{I**}	7.6	39.3	37.9	44.6
Opioids ^{I**}	3.4	11.0	10.7	12.1
Inhalants ^{I**, 2**}	0.3	3.75	2.2	9.6

Note. HCV = Hepatitis C Infection; WRAT = Wide Range Achievement Test 3; ASPD = antisocial personality disorder; HIV = human immunodeficiency virus; SS = Standard Score.

Significance between MA groups (n = 755)

Significance between ADHD groups within MA+ group (n = 400)

^a total n = 655; MA+ n = 328.

^b total n = 752; MA+ = 398.

^ctotal $n = 753$; MA+ $n = 399$; includes current major depressive disorder.

^dMA+ $n = 399$.

^eMedian and interquartile range reported for all but injection use.

^fExcluding MA and alcohol.

I^*
 $p < .05$.

I^{**}
 $p < .01$

2^*
 $p < .05$.

2^{**}
 $p < .01$