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Persistence and Subtype Stability of ADHD Among Substance Use Disorder Treatment Seekers

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Abstract

Objective—To examine ADHD symptom persistence and subtype stability among substance use disorder (SUD) treatment seekers.

Method—In all, 1,276 adult SUD treatment seekers were assessed for childhood and adult ADHD using Conners' Adult ADHD Diagnostic Interview for *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*; CAADID). A total of 290 (22.7%) participants met CAADID criteria for childhood ADHD and comprise the current study sample.

Results—Childhood ADHD persisted into adulthood in 72.8% (n = 211) of cases. ADHD persistence was significantly associated with a family history of ADHD, and the presence of conduct disorder and antisocial personality disorder. The combined subtype was the most stable into adulthood (78.6%) and this stability was significantly associated with conduct disorder and past treatment of ADHD.

Conclusion—ADHD is highly prevalent and persistent among SUD treatment seekers and is associated with the more severe phenotype that is also less likely to remit. Routine screening and follow-up assessment for ADHD is indicated to enhance treatment management and outcomes.

Keywords

ADHD; subtypes; persistence; substance related disorders

Introduction

ADHD is characterized by inattention, hyperactivity, and/or impulsivity. Symptoms have historically been labeled as *predominantly inattentive, predominantly hyperactive-impulsive*, or *combined* "subtypes" of ADHD, although the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*; American Psychiatric Association [APA], 2013) replaced the term "subtypes" with "presentations" to reflect the observation that symptoms can manifest differently over time. As individuals with ADHD become older, symptoms can decrease in severity, with inattentive symptoms generally being more persistent than hyperactive-impulsive symptoms (Turgay et al., 2012; Wilens et al., 2009).

Although ADHD is often described as a childhood disorder, and can remit over time, ADHD symptoms persist into adulthood in about two thirds of cases, with associated impairment across multiple domains (Biederman, Petty, Evans, Small, & Faraone, 2010; Faraone, Biederman, & Mick, 2006; Turgay et al., 2012). Previous research has identified several risk factors for the persistence of childhood ADHD into adulthood: a family history of ADHD (Biederman et al., 1996; Biederman et al., 2010; Biederman, Petty, O'Connor, Hyder, & Faraone, 2012), ADHD symptom severity and associated impairment (Biederman, Petty, Clarke, Lomedico, & Faraone, 2011; Kessler et al., 2005; Lara et al., 2009), and comorbidity

with conduct, oppositional defiant, mood, and anxiety disorders (Biederman et al., 1996; Biederman et al., 2011; Biederman et al., 2010; Biederman et al., 2012; Lara et al., 2009). Early psychosocial adversity, exposure to family conflict and parental psychopathology in particular, has also been shown to predict ADHD persistence (Biederman et al., 1996; Biederman et al., 2011; Biederman et al., 2012; Lara et al., 2009). Although the diagnosis of adult ADHD is based on clinical presentation and history, there is evidence to suggest that persistent ADHD can also be differentiated from remitted ADHD at the neurobiological level, including the presence of structural and functional brain differences between those with persistent and remitted ADHD (Mattfeld et al., 2014; Shaw et al., 2015).

Childhood ADHD is a well-documented, independent risk factor for the development of substance use disorders (SUDs) in adolescence and adulthood (Charach, Yeung, Climans, & Lillie, 2011; Lee, Humphreys, Flory, Liu, & Glass, 2011; Wilens et al., 2011) and is consistently overrepresented among SUD populations (van Emmerik-van Oortmerssen et al., 2012). Moreover, ADHD is associated with an earlier onset, greater severity, and increased chronicity of problematic substance use (Arias et al., 2008; Sullivan & Rudnik-Levin, 2001; Wilens et al., 2011).

The persistence of ADHD symptoms beyond childhood further increases the likelihood of comorbid SUDs, with SUDs far more common among people with adult ADHD than among those with remitted childhood ADHD (Biederman et al., 2010; Molina & Pelham, 2003; Sullivan & Rudnik-Levin, 2001; Wilens et al., 2011). Increased risk of SUDs has also been reported in adults with subthreshold symptoms of ADHD (Faraone et al., 2007).

The risk of those with ADHD developing subsequent SUDs is not only increased among those with persistent ADHD symptoms, but also among those with particular symptom types, that is, with the hyperactive-impulsive (Chang, Lichtenstein, & Larsson, 2012; Elkins, McGue, & Iacono, 2007) or combined (Nogueira et al., 2014; Obermeit et al., 2013; Sprafkin, Gadow, Weiss, Schneider, & Nolan, 2007; Tamm, Adinoff, Nakonezny, Winhusen, & Riggs, 2012; Wilens et al., 2009) subtypes of ADHD. To date, however, factors associated with the persistence and presentation of ADHD symptoms among people with SUDs have received scant attention. Moreover, whether SUD trajectories differ between those whose ADHD symptoms remit versus persist, and between those with different ADHD subtypes, remains unclear. The current study examines (a) the persistence of ADHD symptoms into adulthood among people seeking treatment for SUDs, (b) correlates and childhood predictors of persistent ADHD, and (c) the stability of ADHD subtypes between childhood and adulthood.

Method

Data for this study were collected as part of the International ADHD in Substance Use Disorders Prevalence (IASP) study (van de Glind et al., 2013), a multi-site, cross-sectional study of ADHD among SUD treatment seekers conducted by the International Collaboration on ADHD and Substance Abuse (ICASA). The IASP study had approval from relevant ethics committees in each site and comprised two phases—a screening phase and a full

assessment phase. For further details of the methodology of the IASP study, see van de Glind et al. (2013).

Participants

All individuals referred to recruiting drug and alcohol treatment centers during the study period (July 2008–November 2011) were invited to participate. Exclusion criteria were the inability to complete the screening questionnaire (e.g., due to limited literacy and/or cognitive impairment), severe physical or psychiatric problems, the inability to participate due to substance intoxication, and unwillingness to sign informed consent.

A total of 3,558 adults (aged 18–65 years) attending 47 drug and alcohol treatment centers in 10 countries (Australia, Belgium, France, Hungary, Norway, Spain, Sweden, Switzerland, Netherlands, and the United States) were screened for the presence of ADHD (screening phase). Screening interviews were conducted upon treatment intake. With the exception of those screened in Australia, Belgium, and the United States (n = 963), all screened participants were invited to participate in a further comprehensive psychiatric interview that took place 1 to 2 weeks after screening (full assessment phase), allowing for a period of patient stabilization in treatment.

Of the 3,558 participants screened, 1,276 completed the full assessment, during which they were evaluated for the presence of SUDs, childhood and current (adult) ADHD, and other comorbid psychiatric disorders. Detailed information on sample characteristics and ADHD prevalence can be found in van de Glind et al. (2014; van de Glind et al., 2013). A previous investigation indicated that there were no significant differences in terms of sociodemographic and clinical characteristics between the 1,276 participants completing the full assessment and the 1,319 participants who dropped out of the study after the screening phase (van de Glind et al., 2013).

Of those participants completing the full assessment, 290 (22.7%) met criteria for a *DSM-5* diagnosis of childhood ADHD and thus comprise the current study sample.

Measures

During the screening phase, a brief structured interview assessing demographics, past and current drug use, and details of current treatment episode was administered. Drug use history was ascertained by asking about the age of first use, years of regular use, and recent (30 days preceding treatment entry) use of alcohol, tobacco, heroin, methadone, opioids other than heroin or methadone, amphetamines, cocaine, ecstasy, benzodiazepines, and cannabis. Participants were also asked to specify their primary drug of current concern.

Diagnoses of ADHD were ascertained using Conners' Adult ADHD Diagnostic Interview for *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*; APA, 1994; CAADID; Epstein, Johnson, & Conners, 2001). Part I of the CAADID was self-administered and obtains information on obstetric complications (e.g., maternal substance use during pregnancy, premature birth, low birth weight), temperamental characteristics (e.g., impulsivity, hyperactivity), developmental milestones, environmental circumstances (e.g., trauma, neglect, family violence), medical history, and familial psychiatric problems to

assess early risk factors for ADHD. Past and current social, academic, and occupational functioning is also assessed.

Given the high rates of childhood trauma among SUD populations (Conroy, Degenhardt, Mattick, & Nelson, 2009; Farrugia et al., 2011), the current study employed the CAADID to examine childhood adversity (i.e., physical, emotional, and sexual abuse; parental neglect; family violence; and other childhood trauma) as a potential risk factor for the persistence of ADHD. Self-reported familial risk factors (i.e., family history of diagnosed ADHD) and in utero substance (i.e., nicotine, alcohol, illicit drug) exposure, as measured by the CAADID, were also investigated as predictors of ADHD persistence.

Part II of the CAADID, administered by trained health professionals, is a semi-structured interview, assessing the five *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev.; *DSM-IV-TR*; APA, 2000) criteria for childhood and adult ADHD: (a) number of symptoms, (b) age of onset, (c) symptom pervasiveness, (d) level of impairment, and (e) whether or not the symptoms can be better explained by another psychiatric disorder. To obtain *DSM-5* diagnoses of ADHD, the age of onset threshold was increased from <7 years to <12 years and the number of symptoms required for an adult diagnosis reduced from six out of nine symptoms of inattention and/or hyperactivity-impulsivity to five out of nine symptoms (APA, 2013). A diagnosis of adult ADHD was contingent on a retrospectively obtained diagnosis of childhood ADHD meeting all five criteria, including the presence of six or more symptoms in childhood. This procedure results in conservative estimates of adult ADHD prevalence, as it is stricter than the *DSM* criteria for adult ADHD, which only require that “several” symptoms must be present before the age of 12.

An additional measure of adult ADHD was provided by the ADHD module of the Mini International Neuropsychiatric Interview (MINI-Plus; Sheehan et al., 1998). The MINI-Plus was also used to assess prior and current episodes of mood disorders (i.e., major depression, bipolar disorder) and antisocial personality disorder (ASPD). Conduct disorder (CD) was retrospectively assessed using the ASPD module of the MINI-Plus, which establishes evidence of CD symptoms with an onset before the age of 15. The borderline personality disorder module of the Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders (SCID II; Williams et al., 1992) was also used. For details of the nature and level of comorbidity in this sample, see van Emmerik-van Oortmerssen et al. (2014).

Data Analysis

Initially, univariable analyses were conducted to identify statistically significant associations between demographic, drug use, and clinical variables and ADHD persistence. For continuous variables, *t* tests were employed. For dichotomous categorical variables, unadjusted odds ratios (OR) and 95% confidence intervals (CI) were reported. All primary statistical tests were determined significant at an alpha level of $p < .05$. Where multiple comparisons were conducted, Holm–Bonferroni corrections were performed to control the familywise error rate at $p < .05$.

To identify factors independently associated with persistence of ADHD symptoms and stability of ADHD subtypes, multivariable logistic regression analyses were conducted. Due

to the hierarchical structure of the data, where participants were nested within sites (i.e., treatment centers), potential clustering by site was taken into account. Intracluster (or intraclass) correlation coefficients (ICCs), which provide a measure of the proportion of outcome variance attributable to between-cluster variance, with values close to 0 indicating negligible within-site clustering, were calculated for outcome variables of interest. Although the ICCs for the primary outcomes of ADHD persistence and subtype stability were less than .1 ($\rho = .05$ and $\rho = .06$, respectively), we took a conservative approach and used the SPSS Complex Samples module, which adjusts for clustering. All regression models were adjusted at the participant level for age, gender, ethnicity (Caucasian = yes/no), level of education (graduated high school = yes/no), CD symptoms (yes/no), and past treatment of ADHD with stimulant medication (yes/no). All analyses were conducted using IBM SPSS Statistics 22 (IBM Corp, 2013).

Results

Persistence of ADHD

Of the 290 participants meeting childhood criteria for ADHD, 211 also met criteria for adult ADHD, representing a persistence rate of 72.8%, and thus comprised the “persistent ADHD” group. The remaining 79 who did not meet criteria for adult ADHD comprised the “remitted ADHD” group.

There was no significant association between the age of the participant and the likelihood of full syndrome ADHD persistence (OR = 0.99, 95% CI = [0.97, 1.02], $p = .703$). Likewise, age was not associated with the persistence of ≥5 symptoms from either the inattentive (OR = 0.99, 95% CI [0.97, 1.01], $p = .374$) or hyperactive-impulsive (OR = 0.98, 95% CI = [0.96, 1.01], $p = .152$) domains.

Correlates of ADHD Persistence

Sociodemographic and treatment characteristics—As shown in Table 1, there were no significant sociodemographic differences or differences in the type of treatment setting (i.e., inpatient vs. outpatient) between the persistent ADHD and remitted ADHD groups.

Substance use history—In 60% of cases, illicit drugs, most commonly cannabis (17%), amphetamines (15%), and heroin (11%), were nominated as the primary drug of concern upon entry to treatment. Of the 40% who nominated alcohol as their primary drug of concern, however, one third (33.6%) had also used illicit drugs in the month preceding treatment.

Both the persistent and remitted ADHD groups reported initiating nicotine, alcohol, and illicit drug use from an average age of 14 onwards (Table 2), at least 2 years after the onset of ADHD symptoms in childhood. Those with persistent ADHD reported an earlier initiation of amphetamine use, a longer duration of regular cocaine use, and more days of cocaine use in the month prior to treatment entry than the remitted ADHD group. The persistent ADHD group were more likely to report illicit drugs (vs. alcohol) -amphetamine and cocaine in particular - as their primary substance of concern; however, these differences,

together with those in substance use initiation, duration, and frequency, did not remain significant after Holm–Bonferroni correction (Table 2).

The majority of participants (83.1%) were lifetime polydrug users, with almost half (48.3%) engaging in polydrug use in the month prior to treatment. Following correction for multiple comparisons, there were no significant between group differences in the extent of either lifetime or recent (i.e., month preceding treatment entry) polydrug use (Table 2).

Past ADHD diagnosis and treatment—Less than a quarter (21.9%) of those meeting criteria for childhood ADHD had received a diagnosis of ADHD before study entry and an even smaller proportion had been treated with stimulant medication (14.5%). There were no significant differences between the persistent and remitted ADHD groups with respect to the prevalence of past diagnosis and treatment of ADHD (Table 1).

Psychiatric comorbidity—Those with persistent ADHD were significantly more likely to meet criteria for ASPD (56.7% vs. 34.7%, OR = 2.46, 95% CI = [1.40, 4.33], $p = .002$) and this association remained significant after Holm–Bonferroni correction (corrected $p < .008$) and after adjusting for potential sociodemographic confounders (i.e., age, gender, ethnicity, level of education) and past stimulant medication treatment ($OR_{adj} = 2.31$, 95% CI = [1.48, 3.59], $p = .001$). As ASPD is difficult to disentangle from the behaviors inherent to an illicit drug-using lifestyle (e.g., lying, stealing, financial irresponsibility; Darke, Kaye, & Finlay-Jones, 1998; Kaye, Darke, & Finlay-Jones, 1998), further regression analysis controlling for an illicit SUD was conducted, following which ASPD remained independently associated with ADHD persistence ($OR_{adj} = 1.84$, 95% CI = [1.09, 3.10], $p = .026$).

Although ASPD was associated with the overall persistence of ADHD, this relationship was different for adult ADHD subtypes. After adjusting for the aforementioned confounders, comorbid ASPD was more likely among those with the combined subtype ($OR_{adj} = 2.37$, 95% CI = [1.54, 3.63], $p = .001$) and less likely among those with the inattentive subtype ($OR_{adj} = 0.33$, 95% CI = [0.12, 0.90], $p = .033$). There was no significant association between ASPD and the hyperactive-impulsive subtype ($OR_{adj} = 1.36$, 95% CI = [0.36, 5.15], $p = .633$).

Predictors of ADHD Symptom Persistence

Childhood ADHD subtype—Although there were no significant differences in proportions with the inattentive subtype in childhood, the persistent ADHD group was more likely to meet criteria for the combined subtype and less likely to meet criteria for the hyperactive-impulsive subtype than the remitted ADHD group (Table 3). After Holm–Bonferroni correction, however, these differences were no longer significant.

Familial, environmental, and psychopathological risk factors—Approximately one third (30.8%) of the sample had a relative who had been diagnosed with ADHD. A family history of ADHD more than doubled the odds of persistent ADHD (Table 3).

Childhood adversity was highly prevalent among participants meeting criteria for childhood ADHD. Of those who completed the section on childhood risk factors for ADHD in Part I of the CAADID (n = 246), 83.3% reported having experienced some form of childhood trauma. Almost two thirds (65.0%) reported experiencing some type of abuse (i.e., sexual, physical, or emotional) in childhood, with emotional abuse the most commonly reported form (53.7%). Other types of childhood trauma, including loss of a loved one, physical trauma, and witnessing traumatic events, were reported by nearly three quarters of participants (71.6%) and over one third had experienced violence within the family (40.7%) and parental neglect (36.7%). The persistent ADHD group was more likely to report trauma other than abuse, as well as parental neglect, although these differences were no longer statistically significant after Holm–Bonferroni correction (Table 3).

Comorbid CD symptoms were prevalent, regardless of ADHD persistence. The odds of CD symptoms among the persistent ADHD group, however, were double that among the remitted ADHD group (Table 3).

After adjustment for possible confounding, both family history of ADHD (OR_{adj} = 2.28, 95% CI = [1.12, 4.63], p = .026) and the presence of CD symptoms (OR_{adj} = 2.59, 95% CI = [1.02, 6.61], p = .047) remained significant independent predictors of ADHD persistence.

Stability of ADHD Subtypes

Of the 211 participants diagnosed with adult (i.e., persistent) ADHD, the most common childhood subtype was “combined” (55.4%), followed by the “inattentive” (24.6%) and “hyperactive-impulsive” (19.9%) subtypes.

Overall, childhood subtypes were stable into adulthood in 66.8% (n = 141) of the cases. The combined subtype was the most stable, with the majority of those with the combined subtype in childhood meeting criteria for the combined subtype in adulthood (78.6%; Figure 1). The inattentive subtype was the least stable, with less than half (48.1%) retaining this symptom presentation in adulthood and the remainder transitioning to the combined subtype.

Of those 70 cases where a transition between childhood and adult subtypes occurred, the most common pathway of transition was from the inattentive subtype in childhood to the combined subtype in adulthood (38.6%), followed by combined to hyperactive-impulsive (21.4%), hyperactive-impulsive to combined (20.0%), combined to inattentive (14.3%), and hyperactive-impulsive to inattentive (5.7%). There were no transitions from the inattentive to hyperactive-impulsive subtypes.

Factors Associated With Childhood Subtype Stability

Those whose ADHD subtype in childhood remained stable into adulthood did not differ from those who transitioned to a different subtype in terms of age, gender, family history of ADHD, CD symptoms, or past treatment with stimulant medication (Table 4). Subtype stability was significantly less likely among those with the inattentive childhood subtype and more likely among those with the combined childhood subtype, with these differences remaining significant after Holm–Bonferroni correction.

Multivariable analysis of subtype stability between childhood and adulthood revealed that, after adjustment for potential confounding, having the combined subtype in childhood was the only significant independent predictor of overall subtype stability (OR_{adj} = 3.21, 95% CI = [1.25, 8.26], p = .018).

The stability of specific childhood subtypes was also explored. Stability of the hyperactive-impulsive subtype was associated with greater odds of a family history of ADHD (OR_{adj} = 7.10, 95% CI = [1.85, 27.26]) and stability of the combined subtype was more likely among those with symptoms of CD (OR_{adj} = 4.70, 95% CI = [1.82, 12.11], p = .003) and past stimulant treatment for ADHD (OR_{adj} = 3.62, 95% CI = [1.87, 7.02], p = .001). There were no significant independent predictors of stability of the inattentive subtype and further analysis of transitions from each childhood subtype to a different subtype in adulthood did not yield any significant findings.

Discussion

To our knowledge, this study provides the first cross-national data on the persistence of ADHD into adulthood among a treatment seeking SUD population. ADHD in childhood and adolescence was highly prevalent (22.7%) and persistent: 72.8% of those meeting *DSM-5* criteria for childhood ADHD also met criteria for adult ADHD. ADHD persistence was predicted by a family history of ADHD and childhood CD symptoms, and independently associated with comorbid ASPD.

The high prevalence of ADHD in the current sample is consistent with previous research (van Emmerik-van Oortmerssen et al., 2012), as are the low rates of previously established formal ADHD diagnosis and treatment (Bernardi et al., 2012; Faraone, Spencer, Montano, & Biederman, 2004; Kaye, Darke, & Torok, 2013; McAweeney, Rogers, Huddleston, Moore, & Gentile, 2010). Moreover, we found a full syndrome ADHD persistence rate in adulthood that is two- to fivefold that observed in outcome studies of childhood ADHD among non-SUD, clinically referred samples of ADHD patients. While two thirds of those with childhood ADHD may continue to have symptoms as adults to some extent, studies of ADHD persistence have typically found that only 15% to 35% of childhood cases of ADHD meet full diagnostic criteria for ADHD by adulthood (Biederman et al., 2011; Faraone et al., 2006).

In contrast to the decline in persistence associated with increasing age found among longitudinal studies of children with ADHD (Biederman, Mick, & Faraone, 2000; Biederman et al., 2010; Faraone et al., 2006), the current study found no association between age and the persistence of symptoms, even for hyperactive-symptoms, which are typically more likely to remit with increasing age. This finding may reflect the developmental course of ADHD, such that the decline in symptom persistence may be steeper up until early adulthood than beyond. As suggested by prospective and retrospective studies of adult ADHD that have also found no effect of age on persistence (Karam et al., 2015; Kessler et al., 2005), once ADHD has persisted into adulthood, age-related remission may be less likely. Importantly, the higher persistence rates than among other populations observed here

may also reflect a greater severity and chronicity of ADHD among those seeking treatment for SUDs.

Consistent with previous research among non-SUD populations (Biederman et al., 1996; Biederman et al., 2000; Biederman et al., 2011; Biederman et al., 2010; Hart, Lahey, Loeber, Applegate, & Frick, 1995), a family history of ADHD was the strongest predictor of the persistence of childhood ADHD into adulthood. The familiality and heritability of ADHD is well-documented. ADHD is a highly heritable disorder, with data from twin studies indicating that approximately 70% to 80% of the phenotypic variability is due to genetic influences (Faraone et al., 2005; Franke et al., 2012; Todd et al., 2001) and that heritability of clinically diagnosed ADHD remains high across the life span (Larsson, Chang, D'Onofrio, & Lichtenstein, 2014). Moreover, the developmental course of ADHD appears to have a strong genetic underpinning, with evidence for a primary role of genetic factors in ADHD symptom trajectories from childhood into adolescence (Pingault et al., 2015) and a higher familial risk for persistent ADHD than for ADHD that remits by adulthood (Franke et al., 2012).

As SUDs also have substantial heritability (≈0.5; Urbanoski & Kelly, 2012), it has been hypothesized that ADHD-SUD comorbidity reflects a shared genetic liability to both disorders (Biederman et al., 2008; Carpentier et al., 2013; Derks, Vink, Willemsen, van den Brink, & Boomsma, 2014) and to externalizing pathology more broadly, including ASPD (Carragher et al., 2014). The association between familial ADHD and persistence of childhood ADHD in the current study suggests that this form of comorbidity in adulthood reflects a more severe phenotype of ADHD with a greater genetic loading. As all of the participants in the current study were seeking SUD treatment, the relative contribution of a genetic liability to persistent ADHD to the development and maintenance of SUD is unclear.

The presence of childhood CD symptoms also significantly predicted ADHD persistence. Moreover, ADHD continued to be associated with ASPD in adulthood, even after controlling for antisocial behavior associated with illicit drug use. These findings support those of earlier work in clinical SUD samples showing higher rates of ASPD among those with comorbid adult ADHD (Carpentier, van Gogh, Knapen, Buitelaar, & De Jong, 2011).

ADHD is generally associated with an earlier onset and more severe course of SUDs. The present study, however, did not find any significant differences in SUD trajectories according to ADHD persistence or symptom presentation. This may reflect the nature of the current sample in that SUDs among a treatment seeking sample are likely to be at the more severe end of the spectrum (J. T. Young et al., 2015), regardless of whether ADHD has persisted or remitted. It is also possible that differences in SUD trajectories were obscured by the use of a categorical, rather than dimensional, approach to the measurement of ADHD. Previous research has found that when ADHD is measured on a continuum, increased symptom levels, even if below the diagnostic threshold, are associated with increased odds of SUD and that such approaches may be more sensitive in identifying clinically important variations in SUD risk (Ameringer & Leventhal, 2013; Elkins et al., 2007).

Although earlier onset and greater extent of illicit stimulant (i.e., cocaine, amphetamine) use among the persistent ADHD group was not significant after multiple comparison correction, the direction of the findings are consistent with some studies showing that, among treatment and community SUD samples, adult ADHD symptoms are associated with a preference for stimulants over other drug classes (Bihlar Muld, Jokinen, Bolte, & Hirvikoski, 2013; Ginsberg, Hirvikoski, & Lindefors, 2010), higher rates of stimulant dependence, and a greater frequency and chronicity of stimulant use (Kaye et al., 2013; Wilens et al., 2007; J. T. Young et al., 2015). As stimulants are considered effective first-line pharmacotherapy for ADHD, illicit stimulant use among those with ADHD is often speculated to be a form of "self-medication" of undiagnosed or untreated ADHD (Wilens et al., 2007; S. Young & Sedgwick, 2015). Other studies, however, have not found a preference for stimulants among those with ADHD (van Emmerik-van Oortmerssen et al., 2012), possibly reflecting the high levels of polydrug use that are typical among illicit drug users (Darke & Hall, 1995; van Emmerik-van Oortmerssen et al., 2012). Although a preference for stimulants associated with adult ADHD has not been unequivocally demonstrated, the persistence of ADHD may make longer term, higher frequency, and, consequently, problematic use of stimulants for their reinforcing and possibly "medicating" effects more likely.

Childhood maltreatment (e.g., physical/sexual abuse, neglect) has been associated with childhood and adult ADHD (Briscoe-Smith & Hinshaw, 2006; Fuller-Thomson & Lewis, 2015; Ouyang, Fang, Mercy, Perou, & Grosse, 2008), while psychosocial childhood adversity more broadly has been shown to predict ADHD in childhood (Biederman et al., 1995; Kessler et al., 2005) and the persistence of ADHD into late adolescence (Biederman et al., 1996). In the current study, however, childhood adversity was not independently associated with ADHD persistence. Previous studies that have specifically examined the role of childhood adversity in predicting the persistence of ADHD into adulthood have likewise failed to demonstrate such an association (Kessler et al., 2005; Lara et al., 2009; McLaughlin et al., 2010). Childhood adversity is a well-documented antecedent to problematic substance use (Darke, 2013). Its potential moderating effect on ADHD persistence among those with SUDs, however, is not borne out by the current study, perhaps due to the high prevalence of childhood trauma in both the persistent and remitted ADHD groups, and has yet to be determined. Further studies may help to elucidate this relationship.

In accordance with previous research demonstrating an association between the combined subtype of ADHD and SUDs (Nogueira et al., 2014; Obermeit et al., 2013; Sprafkin et al., 2007; Tamm et al., 2012; Wilens et al., 2009), the combined subtype was the most common symptom presentation in both childhood and adult ADHD in this sample. Moreover, the combined subtype was the most stable presentation between childhood and adulthood, and this stability was significantly associated with a history of CD symptoms and past stimulant medication treatment of ADHD. ADHD symptoms causing sufficient impairment to require stimulant medication treatment and comorbid symptoms of CD indicate a greater severity of childhood ADHD. As such, a more severe adult symptom presentation with persistence of both inattentive and hyperactive-impulsive symptoms is not surprising and highlights the need to improve identification and management of adult ADHD among those with SUDs.

These findings, along with the similarity in prevalence of the hyperactive-impulsive and inattentive subtypes throughout childhood and adulthood, suggest that SUDs may be associated with a different clinical manifestation and trajectory of ADHD than that typically seen in non-SUD populations. Among clinical and community samples, the inattentive subtype predominates (Wilens et al., 2009; Willcutt, 2012) and hyperactive-impulsive symptoms in childhood are more likely to remit by adulthood or become less impairing as people learn to channel their hyperactivity-impulsivity into careers and hobbies that will accommodate these tendencies. It would thus be reasonable to expect a transition from the combined subtype in childhood to the inattentive subtype in adulthood in a greater proportion of cases than we observed. Only one in seven transitioned from the combined to the inattentive subtype, whereas almost half of those with the inattentive and hyperactive-impulsive subtypes in childhood transitioned to a combined subtype in adulthood. Although we were unable to identify any factors significantly associated with transitioning to the combined subtype, the developmental trajectories of ADHD symptoms in this group, and greater persistence of hyperactive-impulsive symptoms in particular, warrant further investigation to illuminate the likely mechanisms involved. It is possible that persistent impulsivity increases the likelihood of developing SUDs, but it is also plausible that chronic drug use, in and of itself, impairs prefrontal inhibitory function, via reduced dopamine transmission, resulting in greater impulsivity and hyperactivity (Volkow, Fowler, Wang, Baler, & Telang, 2009).

There are a number of methodological limitations to be acknowledged. First, the representativeness of the sample of SUD treatment seekers in this study should be considered. Although the potential for selection bias cannot be discounted, there were no significant differences in the demographic and SUD profiles between those who participated in the study and those who dropped out prior to the full assessment phase (van de Glind et al., 2013). Therefore, potential bias due to study attrition is likely to be non-differential. Second, this was a predominantly male, Caucasian sample. As such, the findings may not be generalizable to populations with greater gender and ethnic diversity. It should be noted, however, that the gender distribution in our sample is consistent with that found in other SUD treatment seeking samples (European Monitoring Centre for Drugs and Drug Addiction, 2011). Third, the findings were based on retrospective self-report. With regard to the assessment of substance use history, carefully collected self-report data have been found to be a sufficiently reliable and valid measure for drug use patterns and associated problems (Darke, 1998; Ledgerwood, Goldberger, Risk, Lewis, & Price, 2008). In cases where family networks were fractured, obtaining collateral information to support recall of childhood events was difficult. As such, information pertaining to familial and environmental risk factors may be subject to recall bias. Due to the likelihood that many participants would not have had access to informants willing or able to provide information confirming the presence of ADHD symptoms in childhood, collateral report was not a requirement for the diagnostic assessment of ADHD, nor was the lack of collateral information a criterion for exclusion from the study. Although the use of retrospective self-report may potentially lead to an underreporting of the presence and severity of symptoms of ADHD (Barkley, Fischer, Smallish, & Fletcher, 2002), most adults have been found to accurately report their own symptoms of childhood and adult ADHD (Murphy & Schachar, 2000). Moreover, studies

have shown that, among those with a clinical diagnosis of adult ADHD, retrospective informant reports of childhood symptoms do not improve diagnostic accuracy over self-report and may be even less reliable than the patient's own recall (Breda et al., 2015; Sandra Kooij et al., 2008). Finally, due to the cross-sectional study design, inferences regarding causal associations cannot be made. Although the predictors of persistence identified in the current study are consistent with the known risk factors for childhood ADHD (Banerjee, Middleton, & Faraone, 2007; Froehlich et al., 2011; Warikoo & Faraone, 2013) per se, it is possible that they are also associated with a greater severity of childhood ADHD which, in turn, is more likely to persist.

Although ADHD is prevalent and persistent among SUD treatment seekers and is associated with a more severe phenotype that is less likely to remit, it typically remains undiagnosed and untreated. Routine screening and follow-up assessment for ADHD and other externalizing disorders at treatment intake, to identify and manage this complex comorbidity, is critical to improving treatment outcomes. Moreover, given the neurobiological and clinical differences between persistent and remitted ADHD, there is a need for follow-up studies of those diagnosed in adulthood. In particular, studies investigating the clinical outcomes of treatment for comorbid adult ADHD and SUD and randomized controlled trials evaluating the sequence and effect of different treatment strategies are warranted.

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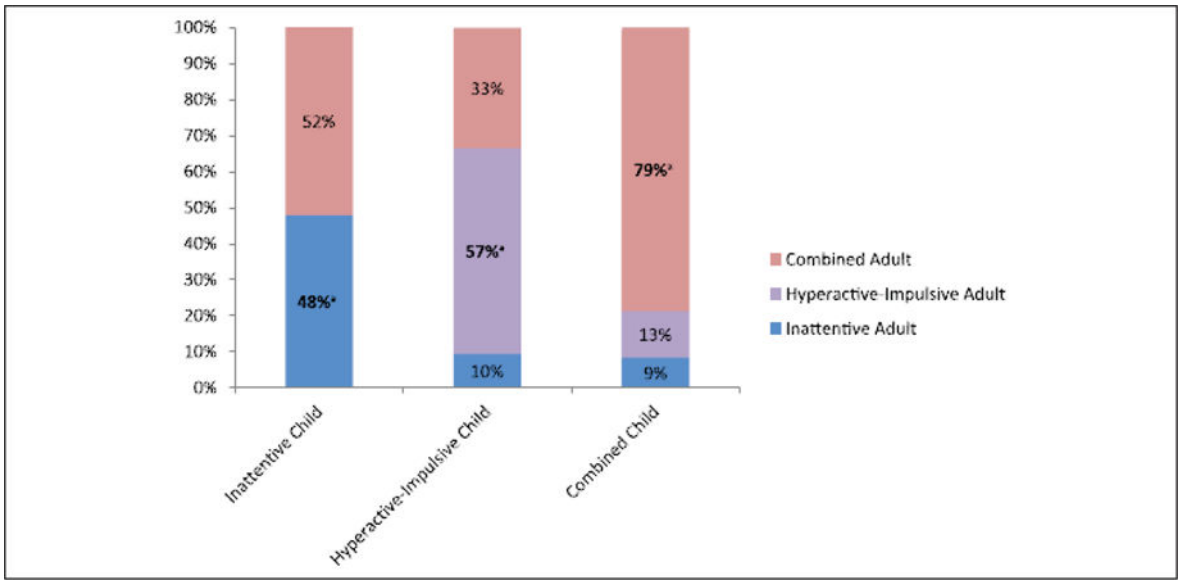

Figure 1.

Stability of childhood ADHD subtypes among those with persistent ADHD.

[a]Indicates subtype stability (i.e., child subtype = adult subtype).

Table 1

Sample Characteristics According to Persistence or Remission of Childhood ADHD Into Adulthood.

	Persistent ADHD (*n* = 211)	**Remitted ADHD (*n* = 79)**	**Unadjusted OR (95% CI) or *t*-statistic**	**Uncorrected *p* values**
Mean age (*SD*)	35.6 (9.6)	36.1 (10.4)	$t_{287} = -0.38$	$p = .704$
Range	18–63	18–60		
% Male	76.8	79.7	OR 1.19 [0.63, 2.25]	$p = .590$
% Caucasian	95.8	93.0	OR 1.74 [0.55, 5.52]	$p = .345$
% Graduated high school[a]	47.6	40.3	OR 1.35 [0.76, 2.39]	$p = .310$
% Unemployed[b]	72.8	74.4	OR 0.92 [0.51, 1.67]	$p = .788$
% Married/de facto relationship[c]	10.3	17.2	OR 0.55 [0.25, 1.24]	$p = .151$
% Inpatient SUD treatment setting[d]	31.6	41.8	OR 0.64 [0.38, 1.10]	$p = .105$
% Diagnosed with ADHD prior to study entry[d]	21.1	24.1	OR 0.84 [0.46, 1.56]	$p = .583$
% Past stimulant medication treatment for ADHD[e]	16.1	10.3	OR 1.68 [0.74, 3.81]	$p = .216$
% Current stimulant medication treatment for ADHD[f]	8.6	5.7	OR 1.56 [0.32, 7.46]	$p = .580$

Note. OR = odds ratios; CI = confidence intervals; SUD = substance use disorder.

[a] $n = 235$.

[b] $n = 280$.

[c] $n = 248$.

[d] $n = 288$.

[e] $n = 283$.

[f] $n = 151$.

Table 2

Drug Use Correlates of ADHD Persistence.

	Persistent ADHD (n = 211)	Remitted ADHD (n = 79)	Unadjusted OR (95% CI) or t-statistic	Uncorrected p values
Primary substance of concern (%)[a]				
Alcohol	35.1	51.9	OR 0.50 [0.29, 0.85]	$p = .010^{\dagger}$
Illicit drugs	64.9	48.1	OR 2.00 [1.18, 3.40]	$p = .010^{\dagger}$
Heroin	12.0	9.1	OR 1.37 [0.57, 3.30]	$p = .488$
Amphetamine	17.8	6.5	OR 3.12 [1.18, 8.25]	$p = .022^{\dagger}$
Cocaine	12.0	2.6	OR 5.12 [1.18, 22.17]	$p = .029^{\dagger}$
Cannabis	15.4	22.1	OR 0.64 [0.33, 1.24]	$p = .186$
Benzodiazepines	3.8	5.2	OR 0.73 [0.21, 2.50]	$p = .616$
Age of first use (mean)				
Nicotine	14.3	14.4	$t_{143} = -0.17$	$p = .867$
Alcohol (<5 glasses)	14.7	15.2	$t_{182} = -0.56$	$p = .579$
Alcohol (>5 glasses)	16.7	18.7	$t_{83} = -1.72$	$p = .089$
Heroin	22.3	20.1	$t_{69} = 1.45$	$p = .150$
Methadone	28.4	32.4	$t_{39} = -0.91$	$p = .368$
Cocaine	21.5	21.0	$t_{132} = 0.45$	$p = .653$
Amphetamines	18.9	21.2	$t_{135} = -2.11$	$p = .037^{\dagger\dagger}$
Cannabis	15.9	16.4	$t_{189} = -0.75$	$p = .454$
Benzodiazepines	22.8	24.3	$t_{114} = -0.84$	$p = .403$
Regular use (mean years)				
Nicotine	20.3	19.1	$t_{137} = 0.63$	$p = .531$
Alcohol (>5 glasses)	13.4	14.0	$t_{196} = -0.37$	$p = .711$
Heroin	7.7	7.4	$t_{61} = 0.12$	$p = .906$
Methadone	3.8	3.7	$t_{37} = 0.08$	$p = .936$
Cocaine	5.8	3.3	$t_{69} = 2.56$	$p = .013^{\dagger\dagger}$
Amphetamines	8.7	6.3	$t_{123} = 1.21$	$p = .227$
Cannabis	12.0	12.2	$t_{172} = -0.10$	$p = .917$
Benzodiazepines	7.2	5.5	$t_{104} = 1.13$	$p = .260$
Days used past month (mean)				
Nicotine	28.1	26.3	$t_{53} = 1.04$	$p = .302$
Alcohol (>5 glasses)	10.3	13.5	$t_{202} = -1.63$	$p = .105$
Heroin	3.2	1.1	$t_{62} = 0.94$	$p = .351$
Methadone	11.7	16.0	$t_{39} = -0.68$	$p = .502$
Cocaine	3.6	1.1	$t_{70} = 2.10$	$p = .040^{\dagger\dagger}$
Amphetamines	3.9	3.3	$t_{118} = 0.28$	$p = .784$
Cannabis	9.5	11.9	$t_{172} = -1.09$	$p = .277$

	Persistent ADHD (*n* = 211)	Remitted ADHD (*n* = 79)	Unadjusted OR (95% CI) or *t*-statistic	Uncorrected *p* values
Benzodiazepines	11.8	14.8	$t_{106} = -1.04$	$p = .301$
Polydrug use (mean no. drug classes)				
Lifetime	4.0	3.4	$t_{259} = 2.05$	$p = .041$ †††
Recent	1.8	1.6	$t_{259} = 0.96$	$p = .336$

Note. OR = odds ratios; CI = confidence intervals.

[a] $n = 285$.

† *p* value not significant after correcting for multiple comparisons (corrected $p < .007$).

†† *p* value not significant after correcting for multiple comparisons (corrected $p < .006$).

††† *p* value not significant after correcting for multiple comparisons (corrected $p < .025$).

Table 3

Early Predictors of ADHD Persistence.

	Persistent ADHD (*n* = 211)	Remitted ADHD (*n* = 79)	Unadjusted OR (95% CI)	Uncorrected *p* values
% ADHD childhood subtype				
Inattentive	24.6	25.3	OR 0.96 [0.53, 1.75]	$p = .906$
Hyperactive-impulsive	19.9	32.9	OR 0.51 [0.28, 0.90]	$p = .021^{\dagger}$
Combined	55.5	41.8	OR 1.74 [1.03, 2.93]	$p = .039^{\dagger}$
% Family history of ADHD[a]	38.7	21.5	OR 2.30 [1.17, 4.55]	$p = .016^{*}$
% In utero exposure[b]				
Nicotine	37.8	40.8	OR 0.88 [0.50, 1.55]	$p = .657$
Alcohol	15.6	18.6	OR 0.81 [0.39, 1.68]	$p = .573$
Illicit drugs	1.2	2.9	OR 0.40 [0.05, 2.88]	$p = .361$
% Childhood adversity[c]				
Trauma				
Sexual abuse	23.4	18.3	OR 1.37 [0.68, 2.74]	$p = .381$
Physical abuse	40.6	47.9	OR 0.74 [0.43, 1.29]	$p = .294$
Emotional abuse	55.4	49.3	OR 1.28 [0.74, 2.22]	$p = .383$
Other trauma	76.3	60.0	OR 2.15 [1.19, 3.88]	$p = .012^{\dagger\dagger}$
Any trauma	84.0	81.7	OR 1.18 [0.57, 2.43]	$p = .660$
Family violence	40.6	40.8	OR 0.99 [0.56, 1.73]	$p = .968$
Neglect	41.4	25.4	OR 2.08 [1.12, 3.84]	$p = .020^{\dagger\dagger}$
% Conduct disorder symptoms[d]	69.0	51.4	OR 2.10 [1.21, 3.67]	$p = .009^{*}$

Note. OR = odds ratios; CI = confidence intervals.

[a] $n = 172$.

[b] $n = 243$.

[c] $n = 246$.

[d] $n = 259$.

$^{\dagger}p$ value not significant after correcting for multiple comparisons (corrected $p < .017$).

$^{\dagger\dagger}p$ value not significant after correcting for multiple comparisons (corrected $p < .008$).

$^{*}p$ value significant at $p < .05$.

Table 4

Factors Associated With Childhood Subtype Stability.

	Stable childhood subtype (*n* = 141)	Unstable childhood subtype (*n* = 70)	Unadjusted OR (95% CI)	Uncorrected *p* values
Mean age	35.5	35.8	$t_{208} = -0.18$	$p = .860$
% Male	78.0	74.3	OR 0.81 [0.42, 1.59]	$p = .546$
% Family history of ADHD	37.3	42.3	OR 0.81 [0.32, 2.04]	$p = .657$
% Conduct disorder symptoms	73.3	61.2	OR 1.74 [0.92, 3.30]	$p = .087$
% Past stimulant medication treatment for ADHD	16.8	14.7	OR 1.17 [0.52, 2.62]	$p = .703$
% Childhood subtype				
Inattentive	17.7	38.6	OR 0.34 [0.18, 0.66]	$p = .001$ *
Hyperactive-impulsive	17.0	25.7	OR 0.59 [0.30, 1.18]	$p = .139$
Combined	65.2	35.7	OR 3.38 [1.86, 6.15]	$p < .001$ *

Note. OR = odds ratios; CI = confidence intervals.

* *p* value significant after correcting for multiple comparisons (corrected $p < .017$).