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ORIGINAL ARTICLE

Adult attention-deficit/hyperactivity disorder and its association with substance use and substance use disorders in young men

N. Estévez[1]*, M. Dey[1], D. Eich-Höchli[2], S. Foster[1], G. Gmel[3] and M. Mohler-Kuo[1]

[1] *Epidemiology, Biostatistics and Prevention Institute, Zurich, Switzerland*
[2] *Psychiatric University Hospital Zurich, Zurich, Switzerland*
[3] *Alcohol Treatment Centre, Lausanne University Hospital CHUV, Lausanne, Switzerland*

Background. Functional and mental health impairments that adults with attention-deficit/hyperactivity disorder (ADHD) experience may be exacerbated by regular substance use and co-morbidity with substance use disorders (SUD). This may be especially true during young adulthood, which represents a critical stage of life associated with increased substance use and associated problems. However, previous studies investigating the association between ADHD and substance use and SUD have demonstrated inconsistent results, probably due to methodological limitations (e.g., small and non-representative samples). Thus, the relationship of ADHD with substance use and related disorders remains unclear. The aim of the present study was to examine the association between ADHD and both the use of licit and illicit substances and the presence of SUD in a large, representative sample of young men.

Method. The sample included 5677 Swiss men (mean age 20 ± 1.23 years) who participated in the Cohort Study on Substance Use Risk Factors (C-SURF). ADHD was assessed using the adult ADHD Self Report Screener (ASRS). The association between ADHD and substance use and SUD was assessed for alcohol, nicotine, cannabis and other illicit drugs, while controlling for socio-demographic variables and co-morbid psychiatric disorders (i.e., major depression (MD) and anti-social personality disorder (ASPD)).

Results. Men with ADHD were more likely to report having used nicotine, cannabis and other illicit drugs at some time in their life, but not alcohol. ADHD was positively associated with early initiation of alcohol, nicotine and cannabis use, the risky use of these substances, and the presence of alcohol use disorders, and nicotine and cannabis dependence. Additionally, our analyses revealed that these patterns are also highly associated with ASPD. After adjusting for this disorder, the association between ADHD and licit and illicit substance use and the presence of SUDs was reduced, but remained significant.

Conclusions. Our findings suggest that adult ADHD is significantly associated with a propensity to experiment with licit and illicit substances, especially at earlier ages, to exhibit risky substance use patterns, and to subsequently develop SUDs. Preventive strategies that include early intervention and addressing co-morbidity with ASPD may be crucial to reducing substance use and the development of pathological substance use patterns in young men affected by ADHD and, thus, helping to prevent further illness burden later in life.

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Key words: Adult attention-deficit/hyperactivity disorder, alcohol, cannabis, nicotine, substance use, substance use disorder.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neuropsychiatric disorders in childhood (average prevalence: 5.2%; 6.1% in boys and 3.3% in girls) (Steinhausen *et al.* 1998) and often persists into adulthood (Faraone *et al.* 2000; Ebejer *et al.* 2012). Recent studies estimated the prevalence in adults at about 4.0% (Estévez *et al.* 2014; Fayyad *et al.* 2007). ADHD can significantly affect mental health and functioning in many life domains over one's entire lifespan (Brod *et al.* 2012; Das *et al.* 2012; de Zwaan *et al.* 2012; Ebejer *et al.* 2012). One area of public health concern is the relationship between ADHD and both substance use and substance use disorders (SUD). Some study results suggest that the presence of ADHD predicts the use of licit and illicit substances and, especially, of related SUD (Baker *et al.* 2012; Klein *et al.* 2012; De Alwis *et al.* 2014); for review see (Charach *et al.* 2011; Lee *et al.* 2011). This is problematic, as regular substance use and

* Address for correspondence: N. Estévez, Epidemiology, Biostatistics and Prevention Institute (EBPI), University of Zurich, Hirschengraben 84, 8001 Zurich, Switzerland.
(Email: natalia.estevezgomez@uzh.ch)

corresponding disorders can lead to further impairments in life domains, wherein those with ADHD already experience significant disadvantages.

The transition from adolescence to adulthood is particularly a critical stage of life for all young adults because it is characterised by considerable changes in every life domain (e.g., entering the workforce) (Gotham *et al.* 2003). Additionally, substance use and associated problems often increase during these years (Rehm *et al.* 2006; Toumbourou *et al.* 2007). Due to their symptoms, individuals with ADHD may experience more difficulties adapting to new situations and coping with the many challenges this life period introduces. Under these circumstances, they may be more vulnerable to using licit and illicit substances, and to developing SUD (Baker *et al.* 2012). For all these reasons, achieving better insights into the relationship between ADHD and substance use and related disorders in the young may be crucial to preventing negative consequences and reducing the burden of ADHD later in life.

A considerable body of research already exists investigating this relationship. However, results are inconsistent, with some studies failing to identify the aforementioned link between ADHD and substance use and related disorders, or only identifying an association for some substances (Lee *et al.* 2011; Galera *et al.* 2013; Madsen & Dalsgaard, 2014). Lack of sample representativeness and small sample sizes may have contributed to these inconsistent results. Indeed, previous studies were often limited by the use of convenience samples (e.g., from patient or student populations). Also because of the small samples, not all studies adjusted for potential confounders (Charach *et al.* 2011; Lee *et al.* 2011). Thus, it remains unclear if ADHD really is predictive of substance use and SUD, or if this link is mediated by other variables such as co-morbid psychiatric disorders or specific socio-demographic characteristics. Another limitation of previous studies is that the most investigated individuals during childhood and early adolescence, when the absence of positive associations between ADHD and SUD might merely be because subjects were too young (Kessler *et al.* 2005); for a review of limitations, see (Charach *et al.* 2011; Galera *et al.* 2013). Furthermore, previous studies mainly focused on the relationship between ADHD and SUD. Few examined the influence of ADHD on more general substance use patterns – like the age of first use, lifetime prevalence and the risky use of particular substances – that may be precursors to SUD. Identifying target use patterns may help to prevent the development of substance-related pathology in individuals with ADHD.

The aim of the present study was to clarify the association between adult ADHD and (1) substance use, and (2) SUD. This included investigating more general use patterns, thereby providing information about experimentation with and risky use of particular substances. To avoid some of the limitations of previous studies, a large, representative sample of young Swiss men was surveyed. Due to the contradicting previous findings concerning the role of other factors, this study examined whether ADHD was associated with the outcomes of interest independent of relevant co-morbid psychiatric disorders (i.e., antisocial personality disorder (ASPD) and major depression (MD) (Estévez *et al.* 2014; Regier *et al.* 1990)) and socio-demographics. We hypothesised that ADHD in young men would be significantly associated with substance use (experimentation and risky use) and SUDs, independent of other factors.

Methods

Study design

Data were extracted from the '*Cohort Study on Substance Use Risk Factors*' (*C-SURF*), designed to assess substance use patterns within a cohort of young Swiss men. The Ethics Committee for Clinical Research at Lausanne University Medical School (protocol number 15/07) approved the study protocol and informed written consent was obtained from all participants.

The sample was recruited at three of the six centres that recruit men for military service, covering 21 of 26 Swiss cantons (recruitment: August 2010–November 2011). Switzerland has a mandatory army recruitment process, such that all young men are called up at roughly 19 years of age to determine their eligibility for military or civil service, versus no service. As no pre-selection to army conscription exists, this procedure allowed us to access a representative sample of young Swiss men. The army centres were used only to enrol participants into the study; both the study itself and the men's decision to participate were entirely independent of the army. Data were drawn from baseline assessments collected between September 2010 and March 2012.

Participants

The present study used data from 5677 subjects. Detailed information about participation is presented in Fig. 1. As reported previously (Studer *et al.* 2013), participants and non-participants differ with respect to some substance use outcomes. However, these differences are small and statistically-significant largely

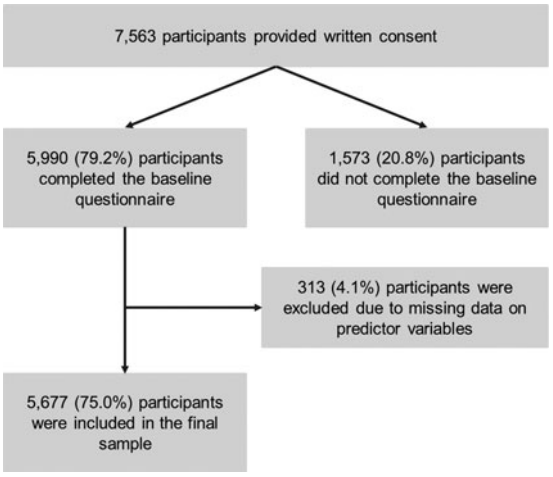

Fig. 1. Flow chart on participation.

due to the large sample, suggesting little effect of non-response on reported results. To avoid losing further data, subjects missing values on certain outcome variables were not excluded from analyses involving other variables. The exact number of participants used for each outcome variable is shown in Table 1.

Independent variables

Adult ADHD

ADHD over the past 12 months was assessed using the six-item Adult ADHD Self-Report Scale Screener (ASRS-v1.1), developed based on the DSM-IV diagnostic criteria by the World Health Organization (WHO) (Kessler *et al.* 2005, 2007). Responses were summated and dichotomised into 'no ADHD' (scores 0–13) and 'ADHD' (scores 14–24). Participants who failed to answer at least three items from the ASRS Screener were excluded ($n = 20$, 0.4%); meanwhile, missing responses for participants failing to answer only one or two items were replaced utilising nearest-neighbour hot-deck imputations, via a random recursive partitioning (RRP) dissimilarity matrix, implemented within the RRP package (Iacus & Porro, 2007) running in version 2.15 of the R statistical environment (R Team Core Development, 17).

Co-morbid disorders

MD was assessed using the Major Depressive Inventory (ICD-10) – WHO-MDI (Bech *et al.* 2001; Olsen *et al.* 2003). Responses were dichotomised to indicate the absence or presence of each symptom and coded as 'no MD' or 'MD'. MD was defined as the presence of at least five MDI items, with either item 1 or item 2 required among those five items (Bech *et al.* 2001). Participants were excluded when more than two items were unanswered.

ASPD was measured using the Mini International Neuropsychiatric Interview (MINI plus; Sheehan *et al.* 1998). Responses were dichotomised to indicate the absence or presence of each symptom and coded as 'no ASPD' or 'ASPD'. ASPD was defined as the presence of at least two symptoms before the age of 15 and three afterwards. Participants were excluded when more than two of the questions were unanswered.

Socio-demographic variables

Socio-demographic variables included age ('younger than 20 years' *v.* '20 years or older'), linguistic region ('German-' *v.* 'French-speaking'), residence ('rural' *v.* 'urban'), highest achieved education ('primary school' *v.* 'secondary vocational school' *v.* 'high school/university'), degree of financial autonomy ('financial autonomy' *v.* 'partial financial dependency' *v.* 'financial dependency'), maternal education ('primary school' *v.* 'secondary vocational school' *v.* 'high school/university') and family affluence ('above average' *v.* 'average' *v.* 'below average').

Outcome variables

The association between ADHD and substance use and SUD was assessed for alcohol, nicotine, cannabis and other illicit drugs. Outcomes of interest were: (1) variables related to subjects' experimentation with these substances (i.e., age at first use and lifetime use); (2) risky use of alcohol, nicotine and cannabis; and (3) the presence of SUD (again for alcohol, nicotine and cannabis). Only lifetime use was assessed for illicit drugs besides cannabis, because their use is rare.

Experimentation with substance use

For alcohol, nicotine and cannabis use, questions about the respective age at first use were assessed and answers categorised into 'very early-onset' (≤ age 12), 'early-onset' (13 through 15), 'late-onset' (≥ age 16) and 'no use'.

Additionally, these questions were used to specify whether conscripts had ever (1) consumed alcohol, (2) smoked a cigarette or (3) used cannabis. Lifetime use of each of the afore-mentioned substances was coded as 'no use' or 'at least one-time use'. Additionally, participants were asked whether they had ever used any illicit drugs other than cannabis (for a list of all included illicit drugs, see Baggio *et al.* 2013). Illicit drug use also was coded as 'no use' or 'at least one-time use'.

Table 1. *Socio-demographic characteristics, co-morbid variables and substance use outcomes according to adult ADHD*

		All Participants		Participants without ADHD		Participants with ADHD			
	Total[a]	*n*	%	*n*	%	*n*	%	χ^2	*p*
Alcohol									
Age of onset	5677								
No use		189	3.3	180	3.3	9	3.9	17.01	<0.001
Late (≥16)		1450	25.5	1413	25.9	37	16.2		
Early (13–15)		3343	58.9	3204	58.8	139	61.0		
Very early (≤12)		695	12.2	652	12.0	43	18.9		
Ever consumed alcohol	5677	5488	96.7	5269	96.7	219	96.1	0.28	0.595
Risky alcohol use	5646	2633	46.6	2504	46.2	129	57.1	10.32	0.001
Alcohol abuse/dependence	5677	2084	36.7	1949	35.8	135	59.2	51.76	<0.001
Nicotine									
Age of onset	5665								
No use		2214	39.1	2153	39.6	61	26.8	30.88	<0.001
Late (≥16)		1406	24.8	1354	24.9	52	22.8		
Early (13–15)		1461	25.8	1390	25.6	71	31.1		
Very early (≤12)		584	10.3	540	9.9	44	19.3		
Ever smoked a cigarette	5665	3451	60.9	3284	60.4	167	73.2	15.16	<0.001
Risky nicotine use	5658	1189	21.0	1113	20.5	76	33.3	21.72	<0.001
Nicotine dependence	5342								
Very mild to moderate		5160	96.6	4958	96.8	202	91.4	18.87	<0.001
Severe		182	3.4	163	3.2	19	8.6		
Cannabis									
Age of onset	5677								
No use		2974	52.4	2896	53.1	78	34.2	51.62	<0.001
Late (≥16–20)		1642	28.9	1570	28.8	72	31.6		
Early (13–15)		936	16.5	872	16.0	64	28.1		
Very early (≤12)		125	2.2	111	2.0	14	6.1		
Ever used cannabis	5669	2703	47.7	2553	46.9	150	66.1	32.09	<0.001
Risky cannabis use	5664	539	9.5	491	9.0	48	21.1	37.14	<0.001
Cannabis dependence	5639	492	8.7	440	8.1	52	23.5	63.30	<0.001
Other illicit drugs									
Ever used other illicit drugs	5657	988	17.5	914	16.8	74	32.6	37.58	<0.001
Co-morbid disorders									
ASPD	5677	931	16.4	848	15.6	83	36.4	69.33	<0.001
MD	5677	147	2.6	116	2.1	31	13.6	114.10	<0.001
Socio-demographics									
Age	5677								
<20		3407	60.0	3291	60.4	116	50.9	8.26	0.004
≥20		2270	40.0	2158	39.6	112	49.1		
Linguistic region	5677								
German		2569	45.3	2499	45.9	70	30.7	20.30	<0.001
French		3108	54.7	2950	54.1	158	69.3		
Residence	5677								
Rural		1872	33.0	1807	33.2	65	28.5	2.14	0.143
Urban		3805	67.0	3642	66.8	163	71.5		
Education	5677								
Primary school		2843	50.1	2729	50.1	114	50.0	5.76	0.056
Secondary vocational school	1626	28.6	1573	28.9	53	23.2			
High school/university		1208	21.3	1147	21.0	61	26.8		
Financial autonomy	5677								
Financial autonomy		1336	23.5	1299	23.8	37	16.2	9.30	<0.010

Continued

Table 1. *Continued*

		All Participants		Participants without ADHD		Participants with ADHD			
	Total[a]	*n*	%	*n*	%	*n*	%	χ^2	*p*
Partial financial dependency	2424	42.7	2327	42.7	97	42.5			
Financial dependency		1917	33.8	1823	33.5	94	41.2		
Mother's education	5677								
Primary school		766	13.5	724	13.3	42	18.4	16.41	<0.001
Secondary vocational school	3536	62.3	3423	62.8	113	49.6			
High school/university		1375	24.2	1302	23.9	73	32.0		
Family affluence/income	5677								
Above average		2525	44.5	2430	44.6	95	41.7	1.62	0.444
Average		2334	41.1	2240	41.1	94	41.2		
Below		818	14.4	779	14.3	39	17.1		

ADHD, attention-deficit/hyperactivity disorder; ASPD, antisocial personality disorder; MD, major depression.
[a]Total number of participants (*n*) recorded for this variable, *n* varies slightly between variables due to missing data.

Risky substance use

Risky alcohol use was assessed using questions about the usual quantity and frequency of alcohol consumption and the frequency of risky single-occasion drinking (RSOD), defined as consuming at least six standard drinks on a single occasion, over the preceding 12 months. This variable was dichotomised into 'no risky use' (including those who never or only occasionally drink alcohol) versus 'risky use' (including conscripts reporting either RSOD at least monthly or risky-volume drinking). Risky-volume drinking was defined as at least 21 standard drinks per week. For detailed information about the assessment and coding of these variables; see (Gmel *et al.* 2010).

Risky nicotine use was dichotomised into 'no risky use' (including those who never or only occasionally smoke cigarettes) versus 'risky use' (smoking at least one cigarette daily). Risky cannabis use was dichotomised into 'no risky use' (using cannabis at most once per week or not at all) versus 'risky use' (using cannabis more than once weekly).

SUD

Alcohol abuse and dependence were assessed via questionnaires (Knight *et al.* 2002) based upon DSM-IV diagnostic criteria. The questions were adapted from the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) (Bucholz *et al.* 1994; Hesselbrock *et al.* 1999). Abuse was defined as a positive response to any of the four abuse criteria and the absence of dependence. Dependence was defined as a positive response to any three or more of seven dependence criteria (Knight *et al.* 2002). For our purposes, a variable was created with the followed categories: 'no abuse or dependence' (also including those who consume no alcohol) and 'abuse or dependence'.

Nicotine dependence was assessed using the six-item Fagerström Test for Nicotine Dependence (FTND revised version; Heatherton *et al.* 1991; Bleich *et al.* 2002). Summation scores were categorised into 'no or very mild dependence' (scores 0–2), 'mild dependence' (scores 3–4), 'moderate dependence' (score 5), 'severe dependence' (scores 6–7) and 'very severe dependence' (scores 8–10). To reduce the number of outcomes, the first three and last two categories were grouped together, generating a binary variable: 'no use to moderate dependence' *v.* 'severe dependence'.

Cannabis dependence was measured with the ten-item Cannabis Use Disorder Identification Test (CUDIT revised version; Adamson & Sellman, 2003). Three of the items were modified according to Annaheim *et al.* (2010). Answers were summated and dichotomised into 'no dependence' (scores 0–7) and 'dependence' (scores 8–40).

Statistical analysis

All statistical analyses reported below, were performed using the statistical package SPSS 20.0. Socio-demographic, co-morbidity and substance use characteristics were compared between participants with and without ADHD using Pearson chi-square analysis. To examine the association between ADHD and substance use and SUD, binomial and

multinomial logistic regression analyses were performed using ADHD as a predictor. From this, unadjusted and adjusted odd ratios (OR) were calculated. In the adjusted models, (1) socio-demographic variables alone, and (2) socio-demographic characteristics and co-morbid disorders were included. To further identify associations between co-morbid disorders and substance use outcomes, unadjusted regression analyses also were performed for ASPD and MD.

Results

For socio-demographic characteristics, co-morbidity variables and substance use outcomes for participants with and without adult ADHD; see Table 1. Detailed regression analysis results for all investigated substances are presented in Tables 2 for lifetime use, risky substance use and SUD, and in Table 3 for age of first use. Unadjusted and adjusted ORs and 95% confidence intervals (95% CI) for ADHD, ASPD and MD are shown.

Alcohol

No significant difference between participants with and without ADHD was identified in terms of ever having used alcohol (Table 2). However, more conscripts with ADHD reported an early or very early age of alcohol use onset than those without ADHD (Table 3). Furthermore, young men with ADHD were more likely to report risky alcohol use and alcohol use disorders (Table 2). Adjusting for socio-demographic variables did not substantially change the results for any of the alcohol-related outcomes (data not shown). When also adjusting for ASPD and MD, the positive association between ADHD and risky alcohol use only decreased slightly. In contrast, the ORs for the relationships of ADHD with age of first alcohol use and with alcohol use disorders, although still significant, were reduced. Sensitivity regression analyses using the co-morbid disorders (ASPD and MD) separately revealed that this reduction was mainly due to the adjustment for ASPD and not MD. The effect of ASPD remained stable for both outcomes even after adjusting for socio-demographics, MD and ADHD. In contrast to ADHD and ASPD, MD exhibited an inverse association with lifetime alcohol use.

Nicotine

Young men with ADHD were more likely to report having smoked a cigarette at some time in their life (Table 2) and having started smoking at a very early age than men without this disorder (Table 3). Additionally, more men with ADHD reported risky nicotine use and nicotine dependence (Table 2). Adjusting for socio-demographic variables did not change these results (data not shown), while also correcting for co-morbid disorders reduced the ORs for all outcomes. ORs were reduced but remained significant for age of onset, ever having smoked, and risky nicotine use. For nicotine dependence, only a trend was detected ($p < 0.10$). The observed reduction was due to the inclusion of ASPD in the model, which was significantly associated with all nicotine-related outcomes, even after correcting for all other variables. Conversely, MD was not associated with any nicotine-related outcome except nicotine dependence.

Cannabis and other illicit drugs

More young men with ADHD reported having used cannabis and other illicit drugs at some time than those without ADHD (Table 2). They also more often reported an early or very early age of first cannabis use and were less often non-users than men without ADHD (Table 3). Conscripts with ADHD also more often admitted to risky cannabis use and cannabis dependence (Table 2). Similar to alcohol- and nicotine-related outcomes, the positive association between ADHD and outcomes related to illicit substance use did not change after correcting for socio-demographic variables (data not shown), but did after adjusting for co-morbid disorders. For co-morbid conditions, the effect of ADHD was reduced but still significant for most outcomes. Only the positive association between ADHD and early-onset cannabis use failed to achieve statistical significance after this correction. As for alcohol- and nicotine-related outcomes, ASPD displayed a constant association with most drug-related variables, except for cannabis dependence and very early onset of cannabis use, for which ORs were reduced after adjustments were made. MD was only related to cannabis dependence and the use of other illicit drugs.

A *post-hoc* power analysis conducted with G*power (Faul *et al.* 2009) revealed that, for a type 1 error of 5% and a sample of 5677 participants, the power to detect an OR of 1.5, which corresponds to a small effect size (Rosenthal, 1996), is 83.3% if the response probability of the dependent variable is 4%. For this prevalence, medium effects (OR = 2.5; Rosenthal, 1996) can be detected with a power of 100%. This is true under the assumption that the dependent variable and independent variable of interest are correlated with control variables to $R^2 = 0.20$. For a dependent variable with a prevalence of 3%, only medium effect sizes (OR = 2.5) would yield sufficient power of 80%. In fact, the power for this case would again be 100%. The

Table 2. *Logistic regression analyses with licit and illicit substances as outcomes*

	Licit substances			
	Ever consumed alcohol		Ever smoked a cigarette	
	Crude OR [CI]	Adjusted OR [CI][a]	Crude OR [CI]	Adjusted OR [CI][a]
ADHD				
No	1.00	1.00	1.00	1.00
Yes	0.83 [0.42–1.65]	0.97 [0.48–1.99]	1.79 [1.33–2.42]***	1.51 [1.11–2.06]**
ASPD				
No	1.00	1.00	1.00	1.00
Yes	2.02 [1.22–3.34]**	2.19 [1.31–3.68]**	2.88 [2.43–3.41]***	2.80 [2.36–3.33]***
MD				
No	1.00	1.00	1.00	1.00
Yes	0.34 [0.19–0.61]***	0.38 [0.20–0.70]**	1.10 [0.78–1.54]	0.89 [0.63–1.28]
	Risky alcohol use		Risky nicotine use	
	Crude OR [CI]	Adjusted OR [CI][a]	Crude OR [CI]	Adjusted OR [CI][a]
ADHD				
No	1.00	1.00	1.00	1.00
Yes	1.55 [1.18–2.03]**	1.44 [1.09–1.90]*	1.94 [1.46–2.57]***	1.62 [1.19–2.21]**
ASPD				
No	1.00	1.00	1.00	1.00
Yes	2.29 [1.98–2.64]***	2.27 [1.96–2.64]***	2.64 [2.27–3.08]***	2.57 [2.19–3.01]***
MD				
No	1.00	1.00	1.00	1.00
Yes	1.00 [0.72–1.39]	0.91 [0.65–1.29]	1.59 [1.11–2.28]*	1.24 [0.84–1.84]
	Alcohol abuse/dependence		Nicotine dependence	
	Crude OR [CI]	Adjusted OR [CI][a]	Crude OR [CI]	Adjusted OR [CI][a]
ADHD				
No	1.00	1.00	1.00	1.00
Yes	2.61 [1.99–3.41]***	2.10 [1.58–2.80]***	2.86 [1.74–4.70]***	1.68 [0.96–2.93]†
ASPD				
No	1.00	1.00	1.00	1.00
Yes	3.56 [3.08–4.12]***	3.51 [3.02–4.07]***	3.35 [2.46–4.56]***	3.04 [2.20–4.19]***
MD				
No	1.00	1.00	1.00	1.00
Yes	1.46 [1.05–2.03]*	1.14 [0.80–1.62]	5.14 [3.12–8.46]***	3.83 [2.21–6.63]***
	Illicit substances			
	Ever used cannabis		Ever used other illicit drugs	
	Crude OR [CI]	Adjusted OR [CI][a]	Crude OR [CI]	Adjusted OR [CI][a]
ADHD				
No	1.00	1.00	1.00	1.00
Yes	2.20 [1.67–2.92]***	1.74 [1.30–2.34]***	2.39 [1.79–3.18]***	1.61 [1.18–2.21]**
ASPD				
No	1.00	1.00	1.00	1.00
Yes	3.34 [2.86–3.89]***	3.22 [2.76–3.77]***	3.70 [3.16, 4.33]***	3.58 [3.05–4.21]***
MD				
No	1.00	1.00	1.00	1.00
Yes	1.30 [0.94–1.81]	1.01 [0.71–1.44]	2.14 [1.50–3.06]***	1.63 [1.01–2.40]*

Continued

Table 2. *Continued*

	Risky cannabis use		Cannabis dependence	
	Crude OR [CI]	Adjusted OR [CI][a]	Crude OR [CI]	Adjusted OR [CI][a]
ADHD				
No	1.00	1.00	1.00	1.00
Yes	2.70 [1.94–3.76]***	1.84 [1.28–2.65]**	3.48 [2.51–4.82]***	2.24 [1.56–3.24]***
ASPD				
No	1.00	1.00	1.00	1.00
Yes	4.26 [3.52–5.14]***	4.00 [3.29–4.86]***	5.33 [4.39–6.47]***	4.94 [4.04–6.04]***
MD				
No	1.00	1.00	1.00	1.00
Yes	2.01 [1.30–3.12]**	1.35 [0.84–2.19]	3.00 [2.00–4.51]***	2.00 [1.25–3.11]**

ADHD, attention-deficit/hyperactivity disorder; ASPD, antisocial personality disorder; MD, major depression.
$^{+}p < 0.10$, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$; OR, Odds ratio; CI, 95% confidence interval.
[a]Adjusted for socio-demographic variables and co-morbid disorders.

prevalence rates of nearly all the dependent variables used in this study were considerably greater than 4%. Thus, the sample size was more than sufficient to detect small effect sizes with a higher power than the standard level of 80%.

Discussion

The present study investigated the association between adult ADHD and both the use of licit and illicit substances and the presence of SUD. Since young adulthood represents a critical stage of life wherein substance use and associated problems often increase, associations were investigated in a large, representative sample of young men drawn from the general Swiss population.

Young men with ADHD were more likely to have used nicotine, cannabis and other illicit drugs at some time in their life, but no more likely to have consumed alcohol. These findings are consistent with a previously-reported meta-analysis on substance use and ADHD (Lee *et al.* 2011) that included 27 prospective follow-up studies that followed children into adolescence and/or adulthood, but mainly used small, selective samples. Our results also agree with findings reported recently for a representative sample of the U.S. population (NESARC project) (De Alwis *et al.* 2014), which included a broader age range than the present study (18 years and older, mean age: 37.5–49.2 depending on the subgroups studied), but also accounted for co-morbid disorders and relevant socio-demographic characteristics. Additionally, the presence of ADHD was associated with the age of first use of nicotine, cannabis and alcohol. Compared with young men without ADHD, those with this disorder were more likely to try alcohol while still 15 years old or younger and to use nicotine and cannabis before age 13. Altogether, these results suggest that the presence of ADHD may contribute to a propensity to experiment with licit and illicit substances, and that this is especially true at early ages.

Early substance use initiation has repeatedly been linked to the development of SUD (Ernst *et al.* 2006; Odgers *et al.* 2008; Gmel *et al.* 2010). The early initiation patterns observed in our study, together with these previous reports, suggest that early initiation may be an important precursor of pathological substance use patterns in men with ADHD. Therefore, preventive interventions should be implemented during childhood and early adolescence in males with ADHD to reduce their likelihood of developing later pathological substance use patterns.

ADHD was also associated with risky consumption of alcohol, nicotine and cannabis. These results are in accordance with previous findings and may be related to the difficulty those with ADHD have regulating their consumption. For instance, in one study on college students (Baker *et al.* 2012), ADHD sufferers were more likely to report difficulties stopping their drinking once started, leading to more risky drinking. Men with ADHD who have tried nicotine also appear to be more likely to become regular smokers than those who have not, as demonstrated in a cross-sectional study of adolescents (Madsen & Dalsgaard, 2014). In addition to difficulties controlling substance use, several studies indicated that not only nicotine, but also cannabis and other illicit drugs are often used by individuals with ADHD as self-medication to reduce their symptoms (Wilens, 2007; Wilens *et al.* 2007; Frei *et al.* 2010; Silva *et al.* 2014), which may further increase both their likelihood of using these substances regularly and their subsequent risk of SUD.

Table 3. *Multinomial regression analyses with age of first use of alcohol, nicotine and cannabis as outcome*

Alcohol use	Very early-onset (≤12 years)[a]		Early-onset (13–15 years)[a]		No use[a]	
	Crude OR [CI]	Adjusted OR [CI][b]	Crude OR [CI]	Adjusted OR [CI][b]	Crude OR [CI]	Adjusted OR [CI][b]
ADHD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	2.52 [1.61–3.95]***	1.77 [1.10–2.84]*	1.66 [1.15–2.39]**	1.54 [1.05–2.24]*	1.91 [0.91–4.02]†	1.45 [0.67–3.14]
ASPD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	5.26 [4.10–6.74]***	5.16 [4.01–6.65]***	2.41 [1.96–2.98]***	2.41 [1.95–2.98]***	1.14 [0.67–1.94]	1.04 [0.60–1.78]
MD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	1.35 [0.81–2.25]	0.96 [0.56–1.65]	0.77 [0.52–1.15]	0.69 [0.46–1.04]†	2.67 [1.40–5.10]**	2.15 [1.10–4.19]*
Nicotine use	**Very early-onset (≤12 years)[a]**		**Early-onset (13–15 years)[a]**		**No use[a]**	
	Crude OR [CI]	Adjusted OR [CI][b]	Crude OR [CI]	Adjusted OR [CI][b]	Crude OR [CI]	Adjusted OR [CI][b]
ADHD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	2.12 [1.40–3.21]***	1.67 [1.08–2.59]*	1.33 [0.92–1.92]	1.19 [0.81–1.73]	0.74 [0.51–1.08]	0.79 [0.54–1.15]
ASPD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	3.68 [2.92–4.64]***	3.50 [2.76–4.43]***	2.20 [1.81–2.68]***	2.17 [1.78–2.65]***	0.65 [0.52–0.80]***	0.65 [0.52–0.81]***
MD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	1.52 [0.86–2.69]	1.04 [0.57–1.89]	1.21 [0.76–1.94]	0.99 [0.61–1.60]	1.07 [0.69–1.67]	1.12 [0.72–1.76]
Cannabis use	**Very early-onset (≤12 years)[a]**		**Early-onset (13–15 years)[a]**		**No use[a]**	
	Crude OR [CI]	Adjusted OR [CI][b]	Crude OR [CI]	Adjusted OR [CI][b]	Crude OR [CI]	Adjusted OR [CI][b]
ADHD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	2.75 [1.50–5.03]***	1.95 [1.02–3.74]*	1.60 [1.13–2.26]**	1.30 [0.90–1.87]	0.59 [0.42–0.81]***	0.67 [0.48–0.93]*
ASPD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	5.12 [3.52–7.44]***	4.66 [3.18–6.83]***	2.74 [2.28–3.31]***	2.64 [2.18–3.19]***	0.50 [0.41–0.59]***	0.50 [0.42–0.60]***
MD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	2.07 [0.86–4.99]	1.16 [0.46–2.96]	1.55 [0.97–2.47]†	1.16 [0.71–1.89]	0.96 [0.65–1.43]	1.08 [0.72–1.62]

ADHD, attention-deficit/hyperactivity disorder; ASPD, antisocial personality disorder; MD, major depression; OR, odds ratio; CI, 95% confidence interval.

†$p < 0.10$, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

[a]Reference category: late onset (16 years or later).

[b]Adjusted for socio-demographic variables and co-morbid disorders.

Indeed, consistent with previously-published findings (Charach *et al.* 2011; Lee *et al.* 2011; De Alwis *et al.* 2014), we also observed a positive association between ADHD and the presence of SUD, with the probability of an alcohol or cannabis use disorder approximately two times greater among men with ADHD than those without. However, contrary to most studies investigating the contribution of ADHD to nicotine dependence, our results demonstrate only a borderline significance after adjusting for co-morbidity and socio-demography. This may be due to the small number of subjects we had in the 'severe dependency' category and to our use of a binary variable for analysis. Indeed, additional multinomial regression analysis using four categories ('no or very mild dependence', 'mild dependence', 'moderate

dependence' and 'severe dependence') revealed a significant association between ADHD and severe nicotine dependence, but not with mild or moderate dependency (data not shown). Therefore, in young men, ADHD may contribute to nicotine dependence at least in more extreme cases. Considering that the impairments that adults with ADHD experience can have a cumulative effect over their lifespan (Brod *et al.* 2012) and may even be exacerbated by co-morbidity with SUD, the high frequency of SUD already observed in our young subjects is alarming. Further efforts should be undertaken to prevent the development of such disorders in young males with ADHD.

When controlling for co-morbid disorders, our analyses revealed that the association between ADHD and licit and illicit substance use and the development of SUD was reduced when adjusting for ASPD. As such, the positive association between ADHD and substance use patterns reported in previous studies that did not control for co-morbidity, may be partially mediated by ASPD. Consistent with our results, some of those few studies that did control for co-morbidity identified the increased use of licit and illicit substances and the presence of SUD in subjects who also reported conduct problems and antisocial behaviour during childhood and adolescence (Lee *et al.* 2011). A recent meta-analysis (Serra-Pinheiro *et al.* 2013) addressing the relationship between ADHD and the use of illicit drugs and SUD found that, although the risk of these use patterns was higher among those with versus without ADHD, differences were not statistically significant after correcting for conduct problems and antisocial behaviours. However, as suggested by the authors, it is possible that the power of this meta-analysis was insufficient to detect any other than strong associations. In fact, after adjusting for ASPD, we identified weak or moderate associations between ADHD and substance use and SUD, whereas for ASPD such associations were greater (i.e., moderate or large according to Rosenthal, 1996). Thus, insufficient power might explain the lack of significance observed in previous studies. Investigations using large enough samples to also detect small or medium effects could be crucial to elucidating whether ADHD is associated with particular substance use patterns and the roles of conduct problems and antisocial behaviours in such associations. Additionally, our findings suggest that males with ADHD may benefit from interventions that also address the association between ASPD and substance use and misuse.

Study limitations

The following limitations of our study must be considered. First, women were excluded from our sample, though evidence exists that women differ from men in the association between ADHD and substance use and SUD (Galera *et al.* 2010). Second, our assessment of ADHD, co-morbid disorders and all SUD was performed using self-reports and did not include any confirmatory diagnostic assessment. However, we only used well-validated and previously-used scales (Heatherton *et al.* 1991; Bucholz *et al.* 1994; Sheehan *et al.* 1998; Hesselbrock *et al.* 1999; Bech *et al.* 2001; Olsen *et al.* 2003; Kessler *et al.* 2007; Annaheim *et al.* 2010). Third, the medical history for ADHD and mental disorders was not assessed. Therefore, we do not know the clinical status of our study participants or whether they had received or continued to receive any treatment. Fourth, with respect to reporting age of first use and lifetime use, recall bias cannot be excluded. Finally, the cross-sectional data collection prevents us from drawing causal inferences.

In summary, our findings suggest that young men with ADHD are susceptible to experimenting with different licit and illicit substances, especially at earlier ages, and more likely to exhibit risky use patterns and ultimately develop some SUD. These patterns are also highly associated with ASPD. Therefore, early preventive interventions that address the ASPD co-morbidity issue might be crucial to preventing the development of SUDs, which themselves often increase illness burden in men affected by ADHD.

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Declaration of Interest

None.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration (study protocol approved by the Ethics Committee for Clinical Research at Lausanne University Medical School, protocol number 15/07).

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