Naturalistic Exploratory Study of the Associations of Substance Use on ADHD Outcomes and Function

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Research Article

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Abstract

Background: Although Attention Deficit Hyperactivity Disorder (ADHD) is associated with an increased risk of substance use disorder (SUD), existing literature on how SUD interacts with ADHD outcomes is limited. This study investigates whether SUD among individuals with ADHD is associated with worse ADHD outcomes and prognosis, and the association between overall functioning and SUD. In addition, we seek to understand whether heavy cannabis use is a better predictor of poorer outcomes compared to SUD status alone.

Method: We conducted a retrospective analysis on 50 ADHD patient charts, which were allocated based on SUD status. Subgroup analysis was performed on the total sample population, with allocation based on heavy cannabis use.Mann-Whitney and Chi-Square tests were used for both the primary and subgroup analyses.

Results: SUD status highly correlated with more ADHD-related cognitive impairments and poorer functional outcomes at the time of diagnosis. ADHD patients with comorbid ADHD-SUD scored significantly lower ($p=<0.0001$) on objective cognitive testing (the continuous performance test). The correlation with poorer ADHD outcomes was more pronounced when groups were allocated based on heavy cannabis use status, where in addition to significantly lower objective cognitive testing scores ($p=0.0011$), heavy cannabis use was associated with more severe fine motor hyperactivity and self-reported hyperactivity/impulsivity scores ($p=0.0088$ and 0.0172, respectively).

Conclusion: Future research is needed to determine how substance abuse can be a barrier to improved ADHD outcomes, and the effect cannabis and other substances have on cognitive function and pharmacotherapy of ADHD.

Background

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized as a persistent pattern of inattention, hyperactivity, and/or impulsivity[1]. Decades of neuroimaging research have shown multiple ADHD-related neurocirculatory abnormalities throughout the brain, which brings our understanding of ADHD to be due to delayed or disrupted brain function. These brain regions have been shown to be responsible for higher order executive functions; including executive control over behavior, attention, social cognition, and networks supporting primary sensory and motor functions[3, 14]. Childhood ADHD is associated with several functional impairments including reduced school performance and academic attainment, and social rejection[1]. In adults, ADHD is associated with poorer occupational performance and attainment, attendance, interpersonal conflicts, as well as a higher probability of unemployment and substance abuse[1]. Substance use disorder (SUD) is characterized by a problematic pattern of substance abuse regardless of short and long term consequences, leading to clinically significant impairment or distress[1]. While ADHD and SUD are different disorders, they often coexist with each other. Children with ADHD are estimated to be 2.64 times more likely to develop SUD, and

individuals with ADHD are at an increased risk of substance misuse/dependence, including cannabis misuse[2, 15, 16].

Cannabis use in youth, regardless of ADHD diagnosis, has shown that it may lead to poorer performance on tasks that require attention functioning, decreased verbal working memory, and decreased executive functioning[12, 17, 18]. A study investigating the effects of cannabis on ADHD patients' response inhibition, showed that cannabis use was significantly associated with a slower continuous performance test (CPT) hit rate response[33]. Another study showed evidence that suggests that early onset of regular cannabis use may disrupt neuromaturation, especially in networks responsible for executive functions and rewards[32]. Additionally, cannabis misuse results in negative changes in brain regions associated with response inhibition[3, 22], and these declines in neuropsychological functioning are thought to be more likely to manifest among daily (or almost daily) cannabis users[11]. Cannabis use seems to be increasing among adults and adolescents[18]. Despite cannabis being associated with symptoms similar to ADHD, there are still studies that investigate the therapeutic use of cannabinoids in ADHD patients[5] and show that cannabis is perceived to be beneficial for some individuals with ADHD[19].

While there is conflicting literature around cannabis use on ADHD outcomes, there is only a small amount of literature that specifically investigates SUD (and cannabis use alone) on objective cognitive testing and all-around function in society. Additionally, current literature on SUD and ADHD have high variability in conclusions, and many limitations including inability to control for confounders.

The Integrated Auditory and Visual Continuous Performance test (IVA/CPT) is a standardized test that has been validated for diagnostic accuracy in comparison to clinician diagnosed ADHD, with EEG correspondence. The IVA/CPT computes a sustained auditory and visual attention quotient (SAAQ and SVAQ, respectively), response quotient, and fine motor hyperactivity quotient. The attention quotient consists of a summary of separate audio and visual measures of vigilance (a measure of inattention based on omission of errors), focus (total variability of mental processing speed for correct responses), and speed (average reaction time for correct responses). The response control quotient is comprised of separate auditory and visual scores for prudence (a measure of impulsivity and response inhibition based on commission errors), consistency (a measure of one's ability to stay on task by variability in response times), and stamina (a measure of sustained effort over time by comparing mean reaction times of the first 200 correct responses vs last 200 correct responses)[27].

Our explorative study seeks to understand: 1) how do the cognitive profiles of patients who have ADHD and SUD differ from patients with ADHD without SUD, and 2) Does substance use disorder among adults in a naturalistic outpatient community setting result in more functional impairment and worse ADHD outcomes.

Methodologies

Research Design

The study is a retrospective analysis and chart review of the first 50 newly diagnosed patients between the dates of January 1st, 2017 and June 1st, 2019 – the first 25 ADHD patients without SUD, and the first 25 ADHD patients with SUD.

Every patient had been assessed and diagnosed by a psychiatrist after a full psychiatric evaluation, and in addition, completed a set of questionnaires to gain more information on the personal history and level of functioning. All patients were tested by the IVA/CPT.

The independent variables in the study are ADHD patients with substance use disorder (SUD group), and ADHD patients without substance use disorder (Non SUD group).

The dependent variables are as follows; demographics (age, gender), suicide risk level, medical comorbidities, alcohol and substance use history, psychiatric comorbid disorders, IVA/CPT score, number of non-valid IVA/CPT scores, parental breakups, family history of substance use disorder, childhood adversity events such as sexual and physical abuse, highest attained education level, interactions with the law, and employment status. The dependent variable data is collected from diagnosed patients through the many questionnaires' given to all patients at the clinic. These dependent variables function as markers for ADHD response and function. They serve as a way to gain more background information on each patient to better understand their profiles and to better identify potential confounding variables, helping with the analysis and interpretation of the results. Subgroup analyses will be done comparing heavy cannabis users (CU group) with non-heavy cannabis users (Non CU group) within the SUD and non-SUD population sample.

Participants

Participants are going to be split into two groups; 1) participants with ADHD who have DSM-5 defined SUD, and 2) participants with ADHD who do not have DSM-5 defined SUD.

Inclusion criteria: newly diagnosed patients with ADHD who are under the care of a psychiatrist specializing in ADHD, between the dates of January 1st, 2017 and June 1st, 2019.

Exclusion criteria: Patients who got diagnosed with ADHD;

- Without an Integrated Auditory and Visual Continuous Performance test
- Whose reported substance use is too ambiguous to determine substance use status (in accordance with the DSM-5 Substance use disorder and intoxication criteria), or have skipped section(s) in the substance use questionnaire.

Participant recruitment and allocation

In order to obtain our target of 50 patient charts in total, the supervising investigator reviewed patient charts sequentially (by decreasing date), starting on June 1st, 2019 until 25 charts in each group are identified. The maximum date range is from January 1st, 2017 to June 1st, 2019. All substances in the

DSM-5 SUD criteria were used to allocate patient charts based on substance use status except for nicotine and caffeine, as these are substances that can enhance ADHD-related cognition[1] and would serve as a confounding variable in our analysis. If patients do not meet the other DSM-5 criteria for SUD, but uses nicotine or caffeine, then they would be allocated to the Non SUD group. Alternately, if someone meets other DSM-5 SUD criteria for substances other than nicotine and caffeine, and use nicotine and/or caffeine, then they would be included in the SUD group. Whether someone uses nicotine or caffeine will not be an exclusion criteria, however information on nicotine use between groups were collected and analyzed in order to control for this variable.

When patient charts meet inclusion and exclusion criteria, and meet DSM-5 criteria for SUD, the chart will then be used for the ADHD with SUD group (SUD group). When patient charts meet inclusion and exclusion criteria, and do not meet DMS-5 criteria for SUD, the chart will then be used in the ADHD without SUD group (Non SUD group). The maximum number of charts to be reviewed in order to attain our goal of 25 charts per group, was set at 500 charts. This selection process was chosen as a way of randomization, to control for selection & allocation bias, where participant selection is dependent on when they got diagnosed, not on the choice of the researchers.

After the primary analysis, Subgroup analyses was done comparing heavy cannabis users (CU group) with those who either do not use cannabis, or light users of cannabis that's below the heavy cannabis use threshold (Non CU group). Heavy cannabis use in this study is defined as use 3 times a week or greater, or last use within 72 hours at the time of diagnosis among weekly users - as this population would be expected to still have relatively high cannabinoid levels in their system[30]. There was no use of cannabis within 72 hours in patients that used cannabis less than weekly.

Outcome measures

Measures of cognition and ADHD outcomes:

- Measure of ADHD outcomes were classified and calculated based on objective cognitive testing or subjective patient report.
- Objective cognitive testing measures were calculated based on participant's completion of the Integrated Visual and Auditory Continuous Performance task. The following objective measures are computed by the IVA/CPT; Sustained Auditory & Visual Attention Quotients (SAAQ and SVAQ, respectively), and Fine motor Hyperactivity. Fine Motor Hyperactivity measures off-task impulsive fine motor activity with the mouse, and is computed as a severity score (none, mild, moderate, severe and extreme)
- Severity score on ADHD symptoms were calculated based on self-reported symptoms consistent with the DSM-5 diagnostic criteria for Inattention and Hyperactivity/Impulsivity. Both hyperactivity/impulsivity and inattention measures were ranked out of 9 – if participants meet any

of the 9 symptoms in each checklist, then they were given a point for the respective symptom. For both Inattention and Hyperactivity/Impulsivity checklists, if adult participants had 5 points out of 9 or less, then their symptom severity is mild (given a score of 1). If 6 or 7 points out of 9 then symptom severity is moderate (given a score of 2), and if 8 or 9 points out 9, then symptom severity is severe (given a score of 3).

Education level:

- Highest attained education level was ranked as follows: 1= less then grade 10, 2 = grades 10-12, 3= completion of grade 12, 4= Community college, 5= Bachelor's degree, 6= completion of Master's degree, 7=Doctorate degree.

Suicide Risk:

- Was graded as either mild, moderate or severe, and was given the numerical values 1, 2 and 3 respectively. Participants were ranked based on the rules of The Nova Scotia Tool for Suicide Risk assessment. Patients were ranked as severe if they had an active plan or intent of suicide with ongoing suicidal ideation. Participants were moderate if they had suicidal ideation, multiple risk factors but not current intent nor plan. Participants were low risk if they had no history of cutting or suicide attempts.

Substance and alcohol use:

- The substance use questionnaire asks about the daily amount, frequency, and date of last use for the following substances; alcohol, cannabis, hallucinogens, stimulants, cocaine, pain medication not prescribed, and barbiturates. Nicotine use was inquired by checking a yes or no box depending on whether one currently uses it, with a space for the participant to elaborate if they feel necessary. Caffeine use wasn't collected.

Statistical analysis

T tests and Chi squared tests were used to see if there is any statistical significance between substance use disorder status and measures of ADHD outcome and function. Odds ratios were calculated for each comparison. We also used these tests to see if cannabis abuse of varying frequencies and quantities have any significant differences between identified dependent variables.

Results

Demographics

Table 1 provides demographic information and statistical tests (Mann-Whitney and Chi-Square test) for both primary analysis groups (SUD vs Non SUD) and secondary analysis groups (CU group vs Non CU

group). This table also provides the subject count in each group. The groups were not statistically different in terms of age, gender and confounding medication use.

Table 1. Demographics

Outcome Measures	SUD n=25	Non SUD n=25	CU n=22	Non CU n=28	P values	
					SUD vs Non SUD	CU vs Non CU
Median Age (25th /75th percentile)	29 (23.5/ 36.5)	30 (28/37)	29.5 (22.7 /36.2)	29.5 (24.5 /39.5)	0.8211	0.5188
Gender	M:16 F:9	M:11 F:14	M: 14 F: 8	M:13 F: 15	0.156	0.226
Confounding Meds						
Nicotine	Yes: 9	Yes: 4	Yes: 8	Yes: 5	0.107	0.139
Benzodiazepines PRN	Yes: 2	Yes: 4	Yes: 1	Yes: 5	0.663	0.318

Substance use

Table 2 provides information around substance use frequency, which shows how many participants used a given substance according to frequency.

Cannabis was the most commonly used drug for the SUD group, whereas alcohol was the most common substance used in the Non SUD group – although alcohol use was still higher for the SUD group compared to the Non SUD group. Cocaine and Hallucinogen

use was the least used substance in both groups in terms of frequency. We chose a more conservative threshold as to whether one's cannabis use met SUD status as the substance was recently legalized in the country. Cannabis use would be considered a substance use disorder if the frequency of use was more than two times per week and meets other

SUD criteria, while being used with other substances, and contributed to functional impairment.

Table 2. Substance Use

Substance	Frequency	SUD	Non SUD
Cannabis	Daily	15	0
	2-6 times per week	4	0
	Weekly-Monthly	3	5
	2-6 times per year	2	5
	Yearly or never used	1	15
Alcohol	Daily	3	0
	2-6 times per week	1	1
	Weekly	4	2
	1-3 times per month	11	5
	2-6 times per year	2	8
	Yearly or never used	2	9
	Frequency not reported	2	n/a
Cocaine	Use within 1 year	13	0
	History of use (>1year)	7	2
	Never used	5	23
Hallucinogens	Use within 1 year	5	0
	History of use (>1year)	7	2
	Never used	13	23

IVA/CPT Primary Analysis

In order to test our hypothesis that Substance use among the ADHD population results in worse ADHD outcomes, statistical analysis (Mann-Whitney Non Parametric T test) was done between SUD groups and Non SUD groups. Table 3 provides the statistical results around objective and subjective cognitive testing between SUD and Non SUD groups, subject counts, and median values. The results indicate that the SUD group had poorer performance and differed significantly for all IVA/CPT measures. The groups did not differ statistically for the

reported number of ADHD symptoms. All measures had a sample size of 25 for each group, except for IVA/CPT SAAQ and SVAQ where quotients were excluded if the computers detected idiopathic or random responding errors, and calculated a non-valid IVA/CPT score. There was one non-valid IVA/CPT score in each group.

Table 3. Cognitive Testing

Outcome Measures		P value	Medians (n)	
			SUD	Non SUD
Objective Measures via IVA/CPT	IVA/CPT SAAQ	0.0064**	44.5 (24)	80 (25)
	IVA/CPT SVAQ	0.0001***	18 (25)	81.5 (24)
	IVA/CPT Average	<0.0001***	38 (25)	83 (25)
	Fine Motor Hyperactivity	0.0946	2 (25)	1 (25)
Subjective DSM-5 ADHD questionnaire scores	Inattention Symptoms	0.0565	2 (25)	1 (25)
	Hyperactivity & Impulsivity Symptoms	0.2841	1 (25)	1 (25)

*P ≤ 0.05,** P ≤ 0.01), ***P ≤ 0.001.

Comorbid Disorders Comparisons

Table 4a provides the statistical results for various psychiatric related measures between SUD and Non SUD groups. Mann-Whitney Non Parametric T test was used to compare median scores between groups. This table shows that the SUD group had significantly more traits consistent to borderline and antisocial personality disorder. These were calculated based on participants responses to symptom questionnaire consistent with the DSM-5 criteria for borderline personality disorder (BPD) and antisocial personality disorder, which were converted into a ratio (symptoms checked off divided by total symptoms). These differences were not found for Cluster C personality disorder traits. Table 4a also shows that the SUD group population had a significantly higher suicide risk. One participant in the

Non SUD group was excluded in the analysis of personality traits, as they were in late adolescence and therefore did not receive the DSM-5 personality trait questionnaire.

Table 4b provides the statistical results for dichotomous variables relating to psychiatric health, and therefore Chi-square tests were used to calculate significance. This table shows that more patients in the SUD group met DSM-5 diagnostic criteria for borderline personality disorder and generalized anxiety disorder. There were no statistically significant differences between groups for the following self-reported measures: history of self-harm, in-patient psychiatric hospitalizations, family history of SUD, and previous psychotherapy. As past psychiatric hospitalizations had an expected cell count less then 5 on the Chi-Square, Yates Continuity Corrected Chi-Square was also done to determine a corrected P value of 0.4616. One participant in the Non SUD group was excluded in the analysis of borderline personality disorder diagnosis, as they were in late adolescence and therefore did not receive the DSM-5 personality disorder questionnaire.

Table 4a. Psychiatric Data

Outcome Measures	P value	Medians (n)	
		SUD	Non SUD
Borderline Personality Traits According to DSM-5 Criteria	0.0147*	0.385 (25)	0.154 (24)
Antisocial Personality Traits According to DSM-5 Criteria	0.0122*	0.25 (25)	0 (24)
Cluster C Personality Traits According to DSM-5 Criteria	0.1883	0.4 (25)	0.2 (24)
Suicide Severity Risk	0.0337*	1 (25)	1 (25)
Major Depressive Disorder Severity According to DSM-5	0.001***	3 (25)	2 (25)

*P ≤ 0.05,** P ≤ 0.01), ***P ≤ 0.001.

Table 4b. Psychiatric Data

Outcome Measures	P Value	%Yes (n)	
		SUD	Non SUD
Borderline Personality Disorder According to DSM-5 Criteria	0.0147*	44 (25)	12.5 (24)
Generalized Anxiety Disorder According to DSM-5 Criteria	0.0087**	80 (25)	44 (25)
History of Self Harm	0.1452	48 (25)	28 (25)
Past Psychiatric Hospitalizations	0.2695	24 (25)	12 (25)
Family History of SUD	0.8741	44 (25)	32 (25)
Previous Psychotherapy	0.5637	64 (25)	56 (25)

*P ≤ 0.05,** P ≤ 0.01), ***P ≤ 0.001.

Level of Functioning and adversity factors

In order to test our hypothesis that comorbid ADHD and SUD results in poorer functional impairment within society, data pertaining to violence, interactions with law, academic and occupational achievement and trauma history was analyzed (Table 5). Chi-square tests were used for all variables to calculate statistical significance, except for ‘highest attained education level’ where the Mann-Whitney test was used, as we were comparing medians.

Significance was found for measures relating to violence, charges, physical abuse, and poor relationship with parents. In terms of academic and occupational achievement, significance was found for not completing high school, and the highest attained education level. The SUD group had a median education level at grade 12, whereas those in the non SUD group had a median college degree education level. History of failing grade, academic difficulty, and dropping out of college/university were approaching significance at an alpha level of 0.05, and met significance with an alpha level of 0.1.

As the event rate for some variables were low, the Yates continuity chi-square was used if any cell in the chi-square had an expected count less than 5. These variables, along with their corrected P values, are as follows; Drinking/Drugging Leads to Violence (P=0.0145), Previous Charges (P=0.0538), Previous Arrests (=0.2472), Previous Jail time (P>0.99), Dropped out of College or University (P=0.2097), and Current Employment (P>0.99).

Table 5. Societal Functioning and Adversities

Outcome Category	Outcome Measures	P Value	Percentage Yes (n)	
			SUD	Non SUD
Violence Related	Got in Trouble due to Temper/Violence	0.0081**	40 (25)	8 (25)
	Drinking/Drugging Leads to Violence	0.0043**	28 (25)	0 (25)
Interactions With Law	Previous Charges	0.0206*	28 (25)	4 (25)
	Previous Arrests	0.1228	24 (25)	8 (25)
	Previous Jail time	0.5515	8 (25)	4 (25)
Reported abuse	Physical Abuse	0.0469*	36 (25)	12 (25)
	Sexual Abuse	0.1853	32 (25)	16 (25)
Academic and Occupational Achievement	Failed Grades: 1 to 12	0.0588	40 (25)	16 (25)
	Dropped out of College or University	0.0910	20 (25)	4.17 (24)
	Didn't Complete High school	0.0288*	32 (25)	7.69 (25)
	Academic Difficulty	0.0874	56 (25)	32 (25)
	Highest attained Education	0.0104*	Median: 3	Median: 4
	Current Employment	0.7328	80 (25)	76 (25)
Regarding Parental Relationships	Poor/No Relationship with parents	0.0007***	45.8 (24)	4 (25)
	Parental Split During Childhood/Adolescence	0.5637	44 (25)	36 (25)

*P ≤ 0.05,** P ≤ 0.01), ***P ≤ 0.001.

Subgroup analyses

Although subgroup analyses can be difficult to interpret, we elected to compare heavy cannabis users (CU group) with non-heavy cannabis users (Non CU group). Table 6 provides information on the influence of heavy cannabis use on ADHD outcomes and function. Participants in both SUD and Non SUD groups were allocated to the CU subgroup if they used cannabis 3 or more times per week, or used within 72 hours of being diagnosed with ADHD among weekly users. If not, the participant would be allocated to the Non CU subgroup.

The CU group differed significantly from the Non CU group by having more impairment in objective and subjective cognitive functioning. Fine motor activity and Hyperactivity/impulsivity symptoms were significantly higher in the CU group – both of which were not seen when comparing groups by SUD status. No significant differences were found when comparing inattention symptoms. Like the

comparison of SUD groups, the CU subgroups had significantly poorer performance on IVA/CPT, higher suicide risk, poorer education attainment, more borderline and antisocial personality traits, and higher major depression disorder severity.

Table 6. Cannabis Subgroup Analysis

Outcome Measures	P value	Medians (n)	
		CU	Non CU
IVA/CPT SAAQ	0.0121*	43 (21)	77 (28)
IVA/CPT SVAQ	0.0045**	12 (22)	80 (27)
IVA/CPT Average	0.0011***	38.75 (22)	80.5 (28)
Fine Motor Hyperactivity	0.0088**	2 (22)	1 (28)
DSM-5 ADHD Inattention Symptoms	0.0714	2 (22)	1 (28)
DSM-5 ADHD Hyperactivity & Impulsivity Symptoms	0.0172*	1 (22)	1 (28)
Suicide Risk	0.0042**	2 (22)	1 (28)
Education Level Attainment	0.0316*	3 (22)	4 (28)
Borderline Personality Disorder According to DSM-5 Criteria	0.0027**	% yes: 50	% yes: 11.1
Antisocial Personality Traits According to DSM-5 Criteria	0.0256*	0.25 (22)	0 (27)
Cluster C Personality Traits According to DSM-5 Criteria	0.5983	0.4 (22)	0.4 (27)
DSM-5 defined Major Depressive Disorder Severity	0.001***	3 (22)	2 (28)

*P ≤ 0.05,** P ≤ 0.01), ***P ≤ 0.001.

Discussion

We aimed to investigate how substance abuse among the ADHD population may interact with different outcomes measures, and how the profiles of ADHD patients differ according to SUD status. Our results show that according to IVA/CPT results between groups (Figure 1, Table 3), SUD status is highly correlated with more impaired ADHD-related cognitive outcomes at the time of diagnosis, to both auditory and visual information (P values are 0.0064 and 0.0001, respectively).

No significant difference was found between groups for reported number of ADHD symptoms (Figure 2, Table 3). The SUD group had a median inattention severity of moderate while the Non SUD group had a median Inattention severity of mild, with a p value of 0.0565. As for Hyperactivity/Impulsivity symptoms, both groups had a median severity of mild, although the SUD group had 4 participants with severe symptoms, and the Non SUD group had 1 (Figure 2).

Although no significant differences were found for fine motor hyperactivity (Figure 3, Table 3), significance was trending towards the SUD group having more impulsive fine motor activity (P value

0.0946). The median severity scores were mild and none for the SUD and Non SUD group respectively, and more participants in the SUD group had extreme and severe symptom severity.

Subgroup analyses investigating heavy cannabis abuse shows even more impairment in objective and subjective ADHD outcomes. (Table 6). Significance was found for IVA/CPT SAAQ and SVAQ scores (P values 0.0121 and 0.0045, respectively), Fine motor hyperactivity (P value 0.0088), and Subjective hyperactivity/impulsivity symptoms (P value 0.0172). Like SUD status, Subjective Inattention symptoms were not significant, but were trending towards significance with a P value of 0.0714.

These results suggest that SUD status at diagnosis predicts poorer ADHD outcomes and prognosis. These results bring up the question of how ADHD and SUD interact with one another, and the other factors (genetic, epigenetic, neurodevelopmental, and environmental) that interplay to produce a more severe ADHD phenotype. Are individuals with severe ADHD symptoms (i.e. more deficits in response inhibition, less able to engage in future goal-oriented behaviour, and impulsivity) more likely to abuse substances[8], and/or do the substances themselves directly impair cognition or neurodevelopment through pharmacologic means. Some researchers suggest that youth with ADHD are more likely to initiate substance use earlier, escalate to more frequent substance use, and engage in binge drinking by adult[13, 28]. Another explanation is that the ADHD patients with comorbid disorders such as anxiety or mood disorders, are more likely to abuse substances to the point of meeting SUD criteria[9]. Additionally, mood and anxiety disorders are also highly comorbid with SUD, with co-occurrence lifetime rate of 40.3% for major depression[23], and 29.9% for anxiety disorders[4, 27, 29]. Some of the symptoms of anxiety and mood disorders can overlap with ADHD[20, 21, 26, 27].

Studies investigating the effect cannabis has on brain structure and function shows that cannabis use is associated with altered brain structure and function[3, 7, 18, 22, 25, 32]. Our results support that notion, as we found that more cognitive impairment and poorer ADHD outcomes were seen when groups were allocated based on heavy cannabis use as appose to substance use status (which includes other substances such as alcohol).

Table 4 presents results relating to psychiatric data, by comparing medians between groups with continuous data (Table 4a) and contingency data with dichotomous variables (Table 4b). Results indicate that the SUD group had a higher prevalence of generalized anxiety disorder (P value 0.0087) and borderline personality disorder (P value 0.0147), a higher severity of major depression (P value 0.001), higher suicide risk (P value 0.0337), and more borderline and antisocial personality traits (P values 0.0147 and 0.0122, respectively).

Our study shows that the prevalence of comorbid BPD and ADHD in our total sample is 28.6%. The SUD group had significantly more comorbid ADHD and BPD then the Non SUD group (44% versus 12.5% comorbidity), with a P value of 0.0147. The prevalence of comorbid BPD and ADHD in other studies varies, with numbers such as 16%[24] and 38%[10].

The presence of comorbid ADHD and BPD is associated with more severe symptoms of BPD, worse outcomes, and poor response to treatment[24, 27, 31].

The results presented in Table 5 helps us understand how the profiles of ADHD patients differ based on SUD status in terms of psychosocial functioning. We found that the SUD group had significantly more deficits in measures of violence and educational attainment, more interactions with the law (charges), and more history of physical abuse and poor relationships with their parents. This emphasizes that the reasoning for high substance abuse and psychiatric comorbidity in the ADHD population are multifactorial. These variables may include the overlap of genetic and epigenetic vulnerabilities[6], and environmental influences such as trauma and poor social relationships. Exposure to such environmental influences may work synergistically with the neurodevelopmental influences to produce a more severe ADHD phenotype[16]. Psychiatric comorbidities and environmental adversities are high in the ADHD population, which emphasizes the importance of a personalized and tailored treatment approach that fits a patient's biopsychosocial narrative. An individual with ADHD whom has many other comorbidities would benefit from multimodal approach that may include biological (pharmacologic treatment for ADHD and comorbid psychiatric disorders) and psychosocial (psychoeducation, psychotherapy, family therapy, motivational interviewing, peer support groups) treatments, and any specialized treatments as needed (crisis management, withdrawal management, relapse prevention). To maintain such approaches, more emphasis and health care resource allocation needs to be put on supporting such approaches to improve accessibility.

Our study has several limitations; this study is a retrospective analysis with no blinding of participants or investigators. Identified patients are allocated into independent variable groups depending on their reported substance use on questionnaires. Therefore, whether a participant fits into the "ADHD with SUD" group or "ADHD without SUD" group is dependent on the integrity of their self-reported substance use patterns on questionnaires. Due to the study's retrospective nature, not all confounding variables were controlled for, which may include the chronicity of substance use (i.e. whether they used cannabis regularly during adolescence), age of ADHD diagnosis, and other comorbidities and social circumstances not asked about in the questionnaires.

Conclusion

Our study served as a pilot study and is exploratory in nature to gain more background information on SUD in the ADHD population, and how patients may differ in many psychosocial variables based on SUD status. Our results suggest that more research is needed to determine the effect that certain substances may have on neuromaturation and cognition, and how substances can be a barrier to improved ADHD outcomes. Considering how the use of cannabis recently became legalized in Canada, this study accentuates the need to further understand how cannabis use disorder interacts with cognitive functioning.

Abbreviations

ADHD: Attention-Deficit/Hyperactivity Disorder

BPD: Borderline Personality Disorder

CU: Heavy Cannabis use

IVA/CPT: Integrated Auditory and Visual Continuous Performance test

SAAQ: Sustained Auditory Attention Quotient

SVAQ: Sustained Visual Attention Quotient

SUD: Substance use Disorder

Declarations

Ethics approval and consent to participate:

This study had received full ethics approval and consent to participate by the Nova Scotia Health Authority Research Ethics Board, under the NSHA REB ROMEO File number 1024540

All methods within our study comply, and were carried out, in accordance with Institutional (NSHA-related policies and guidelines), national, and international guidelines.

Consent process: After discussions with the Nova Scotia Health Authority Research Ethics Board, a waiver of consent form was filled out and approved by NSHA REB. Informed consent wasn't required in our study as all patient charts were deidentified by their Psychiatrist prior to chart review.

Consent for publication: Not applicable

Availability of data and materials: Data pertaining to this study has been deidentified, and is stored on a password-protected laptop. The datasets generated and analysed during the current study are not publicly available as the public release of deidentified data was not approved by the NSHA Research Ethics Board – as that may jeopardize the privacy and confidentiality of study participants. However any particular materials are datasets that are not included in the publication, can be made available by contacting the corresponding author on reasonable request.

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Authors' contributions

BM and JS contributed to the development of the study design, and were involved in the allocation of participants into groups depending on SUD status. BM drafted the manuscript, and was involved in the background research, data collection, and statistical analysis under the supervision of JS. JS was involved in deidentifying patient information prior to data analysis and reviewed the statistical approach to ensure accuracy. BM and JS provided critical revisions throughout the development of the final manuscript. All Authors read and approved the final version of the manuscript for submission, and are personally accountable for ensuring integrity and accuracy of their contributions.

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Figures

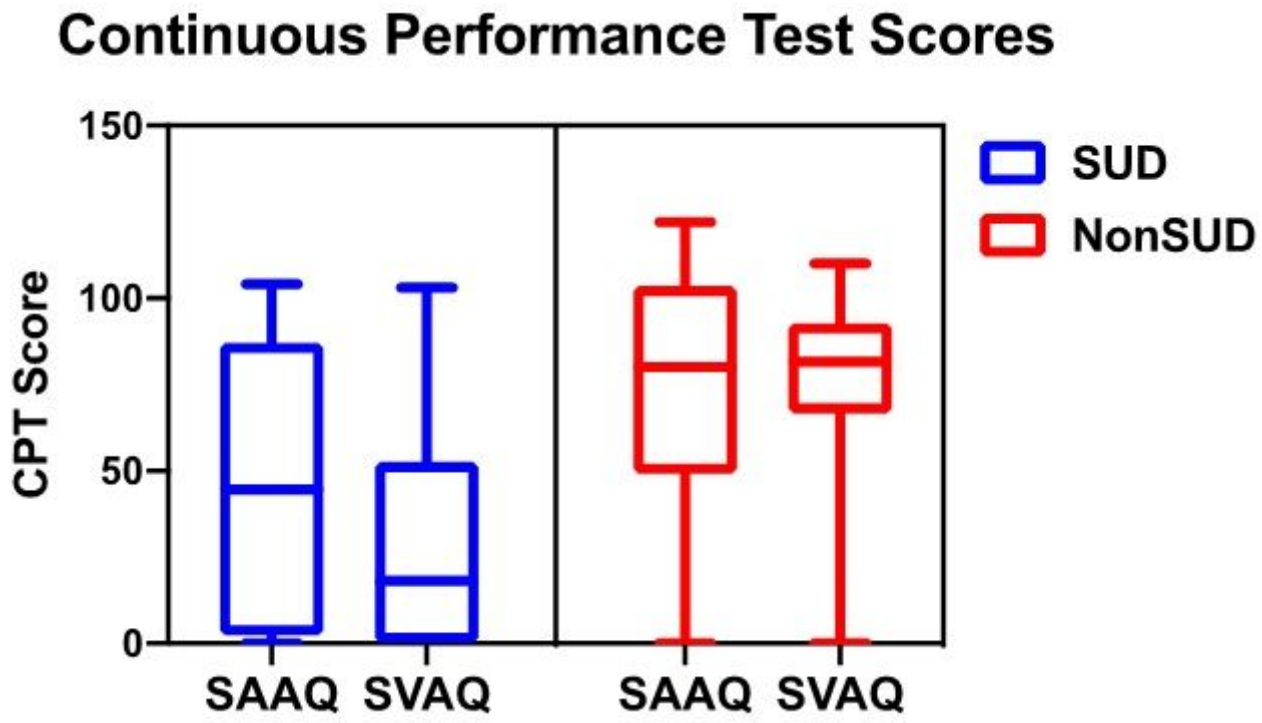

Figure 1

Objective Sustained Auditory and Visual Quotients (SAAQ and SVAQ, respectively) calculated from IVA/CPT, and shows a Box and Whisper plot with min/max range, interquartile ranges, and medians

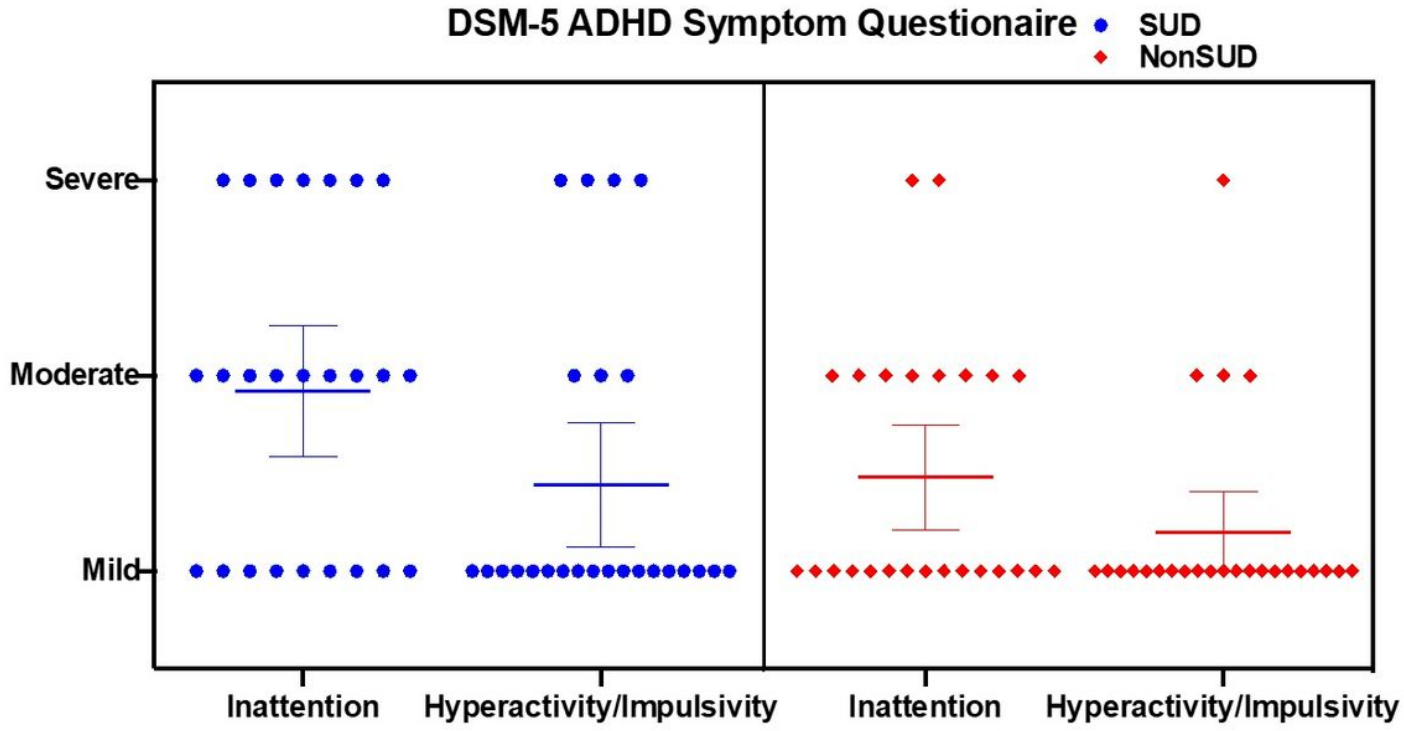

Figure 2

Subjective ADHD inattention and Hyperactivity/Impulsivity symptom scores, based on participants responses to the DSM-5 ADHD Symptom Questionaires. Consists of a Scatter Plot graph, with 95%confidence interval around mean scores

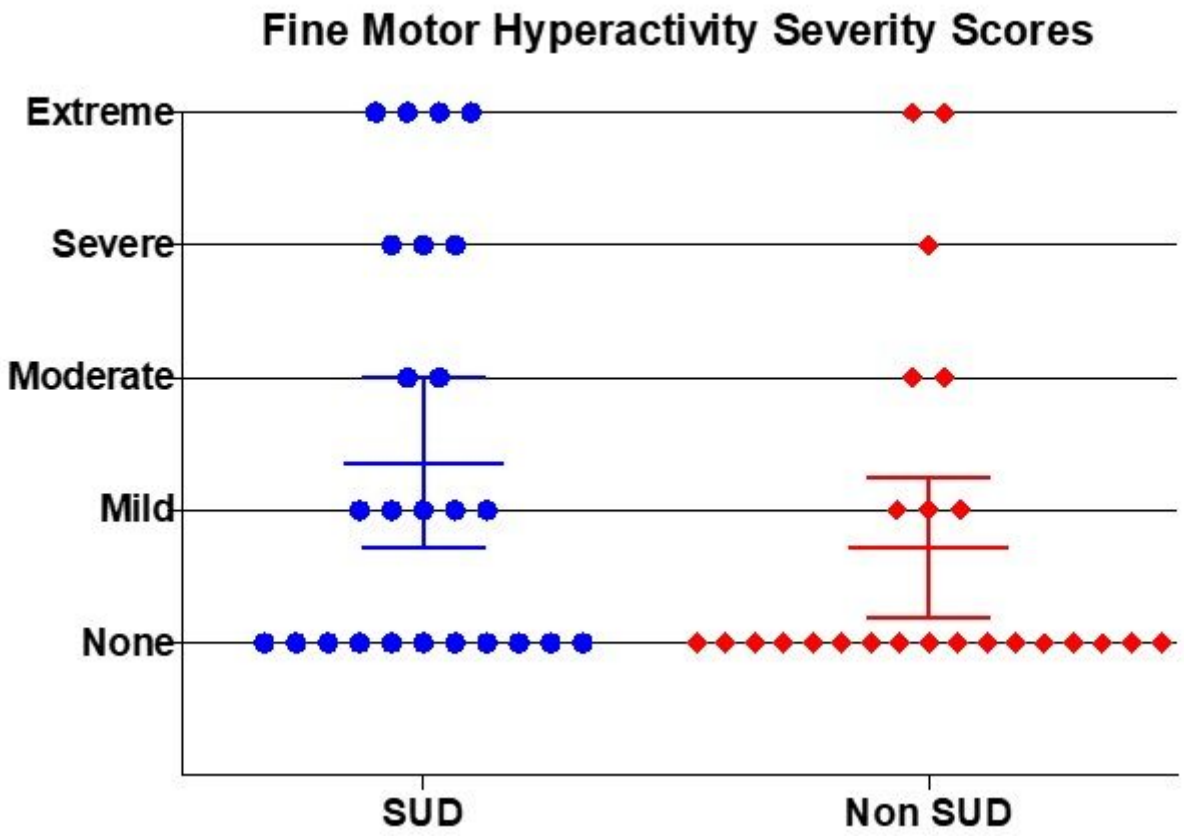

Figure 3

Objective Fine Motor Hyperactivity calculated from IVA/CPT, and shows a scatter plot graph with 95% Confidence Interval around mean scores.