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Cognitive dysfunction in adolescents with substance use disorder

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Abstract

Background Substance abuse is a major health problem, associated with multiple clinical correlates. Cognitive dysfunctions were among the most relevant health problems associated with substance abuse among adolescents. The aim of the study is investigate the main cognitive domains affected in a sample of adolescents with substance use disorders. A case-control comparison was performed between 100 substance abusers versus 40 controls. The Mini-International Neuropsychiatric Interview v.5, Addiction Severity Index, Wisconsin Card Sorting Test, socioeconomic scale, and multiple historical variables investigated.

Results Substance abusers showed higher mean than control as regard all other WCST domains. The difference between two groups was statistically significant. Cannabis substance mostly affects early conceptualization and problem-solving abilities, while inhalants affect predominantly sustained attention, and alcohol mostly affect cognitive flexibility. Polysubstance use is more harmful to most of the executive function domain than mono substance use.

Conclusions The substance use disorders are a major health problem accompanied cognitive dysfunction among adolescents and associated with increased rates of executive dysfunction. Cognitive flexibility, sustained attention, problem-solving abilities, and early conceptualization are the most domains affected.

Keywords Cognitive dysfunction, Substance use disorder, Adolescents, Wisconsin Card

Background

Adolescence had a vulnerable developmental time where important changes take place in young cases's bodies, brains, and sociocultural environments, perhaps making them more susceptible to substance use and psychiatric comorbidity [1]. According to numerous studies, the majority of individuals who eventually start using drugs or alcohol did it when they were still teenagers [2].

During youth, early adulthood, cases had most prone to start abusing substances, including alcohol, illegal narcotics, and prescription medicines. By the time they had been seniors, about 70% of high school kids would had tried alcohol, 50% would had used illegal drugs, and more than 20% would had used prescription medications for purposes other than those prescribed [3].

Biologically, the teenage years are a critical window of vulnerability to drug abuse, because the brain is still developing and malleable (a property known as neuroplasticity), and some brain areas are less mature than others. The parts of the brain that process feelings of reward and pain, crucial drivers of drug use, are the first to mature during childhood. What remains incompletely developed during the teen years are the PFC and its connections to other brain regions. PFC is responsible for assessing situations, making sound decisions, and controlling our emotions and impulses; typically, this circuitry is not mature until a person is in his or her mid-20s [4].

Substance abuse has a major impact on individuals, families, and communities as its effects are cumulative,

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contributing to costly social, physical, and mental health problems. Substance use often initiates during adolescence, and over 80% of drug users began using during adolescence [5].

The substance use disorders are a major health problem among youth, and it is more prevalent in male sex in Egyptian population. Tramadol dependency is at the top of all substances abused in Egypt, followed by polysubstances. Smoking, cannabis, and opiate are the most prevalent types [6]. Smoking, cannabis, and opiates are more frequent, and polysubstance use is much common worldwide [7].

Substance exposure during adolescence may adversely affect cognitive functioning, as measured by neuropsychological tests and functional neuroimaging tasks. Adolescent alcohol and marijuana users have poorer performance on working memory, verbal learning and memory, visuospatial functioning, and psychometric motor speed tasks, and poorer performance has been observed with higher doses and an earlier age of onset [8, 9]. Moreover, marijuana users appear to suffer additional attentional deficits [10], and the cognitive deficits may be sustained in chronic users [11].

There had many different estimates that range from roughly 30–80% of cases with substance use disorders who had cognitive impairment. These deficiencies could be as mild as the brief effects of cannabis use or as severe as the moderate executive control deficits seen in long-term cocaine users, even after several months of abstinence. These estimates include the long-term visuospatial information processing abnormalities found in non-demented individuals with alcohol use disorders, even if they do not include alcoholics who had permanent deficits such Wernicke-Korsakoff syndrome [12].

Recent studies had found deficiencies in a variety of functions, including learning, memory, executive functioning, problem-solving, visuospatial, verbal ability, speed of information processing, connected to excessive alcohol, and other substance use problems [13, 14]. Additionally, polysubstance use disorder had linked to widespread deficits, critical deficiencies on neuropsychological tests of working memory, inhibition, flexibility, self-regulation, and decision-making had been described [15].

Methods

This case-control study had carried out on 100 cases (as case group) who attended the Suez Canal University Hospital, Addiction Centers and Clinics in the Suez Canal region. They had been evaluated, after meeting inclusion criteria between October 2019 and December 2021, with 40 healthy control subjects (as control group) chosen from the healthy blood donors who had matched to the case group in terms of sociodemographic data.

The study included cases between the ages of 13 to 19 who had of either gender and had substance use disorders diagnosed in accordance with the International Classification of Diseases (ICD-10) criteria. Cases with neurodevelopmental disorders, epilepsy, severe head trauma, neurologic deficits, sensory deficits such as hearing or vision loss, low IQ, had intoxicated, or had undergone withdrawal had not been included.

Each participant in the study underwent the following:

- A full thorough psychiatric sheet including sociodemographic information
- Full physical and neurological testing to rule out organic or neurological comorbidities
- A structured interview conducted by a psychiatrist using the Arabic version of the Mini-International Neuropsychiatric Interview v.5 (M.I.N.I. child) [16, 17].
- Testing for urine toxicity both during and after detoxification
- Psychometric evaluation

Teen-addiction severity index

It had a structured, objective face-to-face interview that allowed the assessor to comment, including confidence ratings to show whether the information might be misinterpreted as well as severity ratings (indicating how severe the assessor believes had the need for treatment or counseling). Chemical usage, school performance, employment, support, family ties, peer, social interactions, legal status (involvement with criminal justice programme), mental health status, and a list of contacts for more information are among the issues that had been assessed [18].

It was translated into Arabic by official office. The Arabic draft was translated into English again.

The back-translated version was compared with the original English version to verify that the questions were properly translated. All of the back-translated items were worded similarly to the original ones. Under the direction of the research supervisors, a pilot study with a sample of adolescents had been conducted.

El-Gilany et al. socioeconomic's scale

The occupation domain, education domain, home sanitation domain, family possessions domain, family domain, economic domain, and healthcare domain made comprised the socioeconomic rating in this study sample [19].

The Wisconsin Card Sorting Test

The test could be given to individuals between the ages of 6.5 and 89; it makes use of several abilities, such as attention, working memory, and visual processing. It had been used to assess a person's proficiency in abstract reasoning as well as their capacity to switch up their problem-solving methods when necessary.

The WCST consists of 128 response cards, four stimulus cards with variously shaped shapes (crosses, circles, triangles, or stars), colours (red, blue, green, or yellow), and numbers on them (one, two, three, or four). Before the subject, on the table, are the four stimulus cards [20].

Following WCST scoring, the following domains had been offered:

- The total number of trials conducted
- Number of categories completed
- Tries to successfully finish first category
- Perseverative response
- Error numbers
- Non-perseverative errors and failure to maintain set

Statistical analysis

The statistical analysis of data was done by using Excel programme for figures, SPSS (SPSS, Inc., Chicago, IL, USA) program, and Statistical Package for Social Science version 16. To test the normality of data distribution, K-S (Kolmogorov-Smirnov) test had been done. Only critical data revealed to be nonparametric. N.B: All tested data revealed to be parametric. One-way analysis of variance (ANOVA) was used to explore group differences in age, years of education, and other variables when appropriate in subsequent analysis. Group differences regarding gender were examined using $\times 2$ analysis.

Group differences on the subscale scores were examined using a multivariate analysis of covariance (MANCOVA), including years of education and economic subscales as covariates. Group differences on the WCST were analysed using univariate ANOVAs. In all these comparisons, we conducted post hoc one-way ANOVAs or Mann-Whitney tests to examine possible differences between subgroups of adolescents with substance use disorder classified according to their primary drug of choice. We conducted three multiple regression analyses to examine the predictive effects of severity of addiction (as measured by the teen addiction severity index subscales) on WCST scales scores. p-value had been critical if ≤ 0.05.

Results

The study, which involved 100 adolescent substance users who attended the psychiatric clinic as previously described and 40 matched healthy adolescents who underwent comprehensive evaluations and psychometric assessments using the aforementioned methods, produced the following findings:

- The difference between two groups had no statistical significance regarding father and mothers' education, daily income, socioeconomic scale, residency, and religion as shown in Table 1.
- There is lower mean than control as regard number of category completed (reflect the overall efficiency in the test performance), while they showed higher mean than control as regard all other WCST domains. The difference between two groups had statistically significance ($p = 0.05$) as shown in Table 2.
- The mono and polysubstance case groups had lower mean than control group as regard number of category completed and higher mean than control group as regard other WCST domains, and the difference between mono and polysubstance users'cases and control groups had statistically significance ($p = 0.05$). Polysubstance use case group shows higher mean than mono substance use group as regard number of perseverative errors; the difference between two groups had statistically significance ($p = 0.003$). Polysubstance use case groups show higher mean than mono substance use group as regard failure to maintain set, but the difference between two groups had no statistically significance as shown in Table 3.
- The combined cannabis use group had lower mean than non-cannabis use group and control group as regard all domains except failure to maintain set, and the difference had statistically significance ($p = 0.05$) which means that cannabis use might affect the executive function domains except sustained attention as shown in Table 4.
- The mono alcohol use group showed a higher mean than control, non-alcohol use group as regard number of perseverative errors, and the difference had statistically significance ($p = 0.029$) which means that alcohol use might affect flexibility domain critical. Mono alcohol use control groups showed a lower mean than combined alcohol use group and in non-alcohol user group as regard total number of errors; the difference had been statistically critical $p = 0.038$. Mono, combined, and non-alcohol use groups show lower mean than control groups as regard number of category completed and higher mean than control as regard numbers of trial to first category,

Table 1 Sociodemographic variables

		Cases $N = 100$		Controls $N = 40$		*p*-Value
		Mean ± SD		Mean ± SD		
Age		17 ± 1		17 ± 2		0.143
Education years		9 ± 3		10 ± 2		0.631
Father education		9 ± 3		10 ± 2		0.105
Mother education		12 ± 3		13 ± 2		0.071
Income daily		72 ± 51		39 ± 10		0.213
		N	%	*N*	%	
Gender	**Males**	84	84%	33	82.50%	0.401
	Females	16	16%	7	17.50%	
Marital	**Single**	98	98%	39	97.50%	0.292
	Married	2	2%	1	2.50%	
Religion	**Moslem**	97	97%	39	97.50%	0.387
	Christian	3	3%	1	2.50%	
Residency	**Rural**	37	37%	14	35.00%	0.604
	Urban	63	63%	26	65.00%	
Occupation	**Student**	80	80%	33	82.50%	0.199
	Working	20	20%	7	17.50%	
Socioeconomic scale	**Very low**	19	19%	8	20%	0.209
	Low	35	35%	14	35%	
	Middle	39	39%	16	40%	
	High	7	7%	2	5 %	

Shows that difference between two groups had not statistically critical regarding father and mothers' education, daily income, socioeconomic scale, residency, and religion

Table 2 Comparison between cases and control group regarding the WCST domains

	Cases	Control group	*p*-Value
	Mean ± SD	Mean ± SD	
Number of categories completed	2 ± 1	5 ± 1	0.047*
Trials to first category	32 ± 4	20 ± 3	0.036*
Failure to maintain set	2 ± 1	1 ± 1	0.042*
Total number of errors	60 ± 15	34 ± 4	0.049*
Number of perseverative errors	32 ± 8	18 ± 3	0.001**
Number of perseverative responses	44 ± 5	26 ± 4	0.027*
Number of non-perseverative errors	28 ± 7	16 ± 5	0.039*

*p-value < 0.05 significance. **p-value < 0.01 significance. Shows that lower mean than control as regard number of category completed (reflect the overall efficiency in the test performance), while they showed higher mean than control as regard all other WCST domains. The difference between two groups had statistically critical ($p = 0.05$)

and the difference had statistically significance $p = 0.05$ as shown in Table 5.

- The combined opioid use group shows a higher mean than control group, non-opioid use group as regard number of perseverative response, total number of errors, and the difference had statistically significance ($p = 0.039$) and ($p = 0.05$), respectively, which means that opioid use impairs flexibility critical. Combined opioid and non-opioid use groups show a lower mean than control group as regard number of category completed, and the difference had statistically significance $p = 0.043$. Combined opioid and non-opioid use groups show a higher mean than control group as regard number of perseverative errors, failure to maintain set, and trials to first category, but it had no statistically significance as shown in Table 6.
- The combined benzodiazepine use group shows a lower mean than non-benzodiazepine use group as regard number of perseverative errors, and the difference had statistically significance $p = 0.01$. Combined benzodiazepine use groups show a lower mean than control group as regard number category completed, higher mean than control group as regard number of non-perseverative errors, trials to first category, and the difference had statistically significance $p = 0.05$ as shown in Table 7.
- The combined inhalant use group shows lower mean than control group, non-inhalant use group as regard number of category completed, and the difference had statistically significance $p = 0.034$.

Table 3 Comparison between mono and polysubstance use groups with control group regarding WCST domains

	Mono		Poly		Control group		*p*-Value
	N = 100				*N* = 40		
	N	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	
Number of categories completed	15	3 ± 1	85	2 ± 1	40	5 ± 1	0.043*
Trials to first category	15	31 ± 2	85	35 ± 4	40	20 ± 3	0.039*
Failure to maintain set	15	10	85	2 ± 1	40	1 ± 1	
Total number of errors	15	43 ± 2	85	63 ± 14	40	34 ± 4	0.047*
Number of perseverative errors	15	22* ± 2	85	34 ± 8	40	18 ± 3	0.003**
Number of perseverative responses	15	42 ± 3	85	44 ± 5	40	26 ± 4	0.05*
Number of non-perseverative errors	15	21 ± 3	85	29 ± 7	40	16 ± 5	0.042*

*p-value < 0.05 significance. **p-value < 0.01 significance. Shows that mono and polysubstance case groups had lower mean than control group as regard number of category completed and higher mean than control group as regard other WCST domains; the difference between mono and polysubstance users' cases and control groups had statistically critical ($p = 0.05$). Polysubstance use case group shows higher mean than mono substance use group as regard number of perseverative errors; the difference between two groups had statistically critical ($p = 0.003$). Polysubstance use case groups show higher mean than mono substance use group as regard failure to maintain set, but the difference between two groups had not statistically critical

Table 4 Comparison between combined cannabis and non-cannabis use cases with control group regarding WCST domains

	Combined cannabis use group		Non-cannabis use group		Control group		*p*-Value
	N = 100				*N* = 40		
	N	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	
Number of categories completed	73	2 ± 1	27	3 ± 1	40	5 ± 1	0.05*
Trials to first category	73	32 ± 3	27	33 ± 4	40	20 ± 3	0.047*
Failure to maintain set	73	2 ± 1	27	1 ± 1	40	1 ± 1	
Total number of errors	73	61 ± 14	27	58 ± 18	40	34 ± 4	0.036*
Number of perseverative errors	73	33 ± 8	27	31 ± 10	40	18 ± 3	0.043*
Number of perseverative responses	73	44 ± 5	27	45 ± 5	40	26 ± 4	0.05*
Number of non-perseverative errors	73	28 ± 7	27	27 ± 8	40	16 ± 5	0.038*

*p-value < 0.05 significance. Shows that combined cannabis use group had lower mean than non-cannabis use group, control group as regard all domains except failure to maintain set, and the difference had statistically critical ($p = 0.05$) which means that cannabis use might affect the executive function domains except sustained attention

Table 5 Comparison between alcohol, combined alcohol, and non-alcohol use groups with control group regarding WCST domains

	Combined alcohol use group		Non-alcohol use group		Mono alcohol use group		Control group		*p*-Value
	N = 100						*N* = 40		
	N	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	
Number of categories completed	35	3 ± 1	56	3 ± 1	9	4 ± 1	40	5 ± 1	0.05*
Trials to first category	35	32 ± 3	56	33 ± 4	9	31 ± 1	40	20 ± 3	0.047*
Failure to maintain set	35	2 ± 1	56	2 ± 1	9	10	40	1 ± 1	0.1
Total number of errors	35	58 ± 14	56	64 ± 15	9	44 ± 2	40	34 ± 4	0.038*
Number of perseverative errors	35	28 ± 7	56	24 ± 9	9	32 ± 2	40	18 ± 3	0.029*
Number of perseverative responses	35	43 ± 4	56	45 ± 5	9	42 ± 2	40	26 ± 4	0.7
Number of non-perseverative errors	35	25 ± 8	56	31 ± 6	9	21 ± 4	40	16 ± 5	0.6

*p-value < 0.05 significance. Shows that mono alcohol use group showed a higher mean than control, non-alcohol use group as regard number of perseverative errors, and the difference had statistically critical ($p = 0.029$) which means that alcohol use might affect flexibility domain critical. Mono alcohol use and control groups showed a lower mean than combined alcohol use group and non-alcohol user group as regard total number of errors, and the difference had statistically critical $p = 0.038$. Mono, combined, and non-alcohol use groups show lower mean than control groups as regard number of category completed and higher mean than control as regard numbers of trial to first category, and the difference had statistically critical $p = 0.05$

Table 6 Comparison between mono opioid, combined opioid, and non-opioid use groups with control group regarding WCST domains

	Combined opioids use group		Non-opioids use group		Mono opioids use group		Control group		*p*-Value
	N = 100						*N* = 40		
	N	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	
Number of categories completed	**38**	**3 ± 1**	**60**	**3 ± 1**	**2**	**4 ± 2**	**40**	**5 ± 1**	**0.043***
Trials to first category	**38**	**33 ± 4**	**60**	**32 ± 4**	**2**	**31**	**40**	**20 ± 3**	**0.1**
Failure to maintain set	**38**	**2 ± 1**	**60**	**2 ± 1**	**2**	**1**	**40**	**1 ± 1**	**0.1**
Total number of errors	**38**	**62 ± 13**	**60**	**59 ± 15**	**2**	**42 ± 1**	**40**	**34 ± 4**	**0.05***
Number of perseverative errors	**38**	**33 ± 8**	**60**	**32 ± 9**	**2**	**22**	**40**	**18 ± 3**	**0.1**
Number of perseverative responses	**38**	**48 ± 5**	**60**	**42 ± 10**	**2**	**43**	**40**	**26 ± 4**	**0.039***
Number of non-perseverative errors	**38**	**29 ± 6**	**60**	**27 ± 8**	**2**	**20 ± 1**	**40**	**16 ± 5**	**0.07**

**p*-value < 0.05 significance. Shows that combined opioid use group shows a higher mean than control group, non-opioid use group as regard number of perseverative response, and total number of errors; the difference had statistically critical ($p = 0.039$) and ($p = 0.05$), respectively, which mean that opioid use impairs flexibility critical. Combined opioid and non-opioid use groups show a lower mean than control group as regard number of category completed, and the difference had statistically critical $p = 0.043$. Combined opioid and non-opioid use groups show a higher mean than control group as regard number of perseverative errors, failure to maintain set, and trials to first category, but it had not statistically critical

Table 7 Comparison between combined benzodiazepine and non-benzodiazepine use groups with control group regarding WCST domains

	Combined benzodiazepine use group		Non-benzodiazepine use group		Control group		*p*-Value
	N = 100				*N* = 40		
	N	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	
Number of categories completed	**37**	**2 ± 1**	**63**	**2 ± 1**	**40**	**5 ± 1**	**0.031***
Trials to first category	**37**	**33 ± 4**	**63**	**32 ± 3**	**40**	**20 ± 3**	**0.027***
Failure to maintain set	**37**	**2 ± 1**	**63**	**1 ± 1**	**40**	**1 ± 1**	
Total number of errors	**37**	**68 ± 14**	**63**	**56 ± 12**	**40**	**34 ± 4**	
Number of perseverative errors	**37**	**31 ± 8**	**63**	**37 ± 8**	**40**	**18 ± 3**	**0.01****
Number of perseverative responses	**37**	**46 ± 5**	**63**	**43 ± 4**	**40**	**26 ± 4**	**0.09**
Number of non-perseverative errors	**37**	**31 ± 7**	**63**	**26 ± 7**	**40**	**16 ± 5**	**0.046***

**p*-value < 0.05 significance. ***p*-value < 0.01 significance. Shows that combined benzodiazepine use group shows a lower mean than non-benzodiazepine use group as regard number of perseverative errors; the difference had statistically critical $p = 0.01$. Combined benzodiazepine use groups show a lower mean than control group as regard number category completed, higher mean than control group as regard number of non-perseverative errors, and trials to first category; the difference had statistically critical $p = 0.05$

Combined inhalant use group shows higher mean than control, non-inhalants use groups as regard trial to first category, failure to maintain set, total number of errors, number of perseverative errors, number of perseverative responses, and the difference had statistically significance $p = 0.05$, which means that inhalant's use impairs early conceptualization and sustained attention and flexibility domains. Combined inhalant use group shows higher mean than control and non-inhalants use groups as regard number of non-perseverative errors, but the difference had no statistically significance as shown in Table 8.

Discussion

The study, conducted in 2021 at the Faculty of Medicine Suez Canal University Hospital, the psychiatric hospitals, Clinics of the Suez Canal regional area, examined the relationship between substance use and executive function in a sample of adolescents who had been mostly from the same cultural background and who did not had developmental or psychological delays. Toxicology screening, semi-structured interviews (mini-kid), the Teen Addiction Severity Index scale, the WCST, and a social classification scale had all been performed on the 140 cases we evaluated, who had split into two groups of 100 cases and 40 controls.

Table 8 Comparison between combined inhalants and non-inhalants use groups with control group regarding WCST domains

	Combined inhalants use group		Non-inhalant use group		Control group		*p*-Value
	N = 100				*N* = 40		
	N	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	
Number of categories completed	**21**	**1 ± 1**	**79**	**3 ± 1**	**40**	**5 ± 1**	**0.034***
Trials to first category	**21**	**37 ± 4**	**79**	**31 ± 3**	**40**	**20 ± 3**	**0.01****
Failure to maintain set	**21**	**3 ± 1**	**79**	**1 ± 1**	**40**	**1 ± 1**	**0.03***
Total number of errors	**21**	**76 ± 8**	**79**	**56 ± 13**	**40**	**34 ± 4**	**0.05***
Number of perseverative errors	**21**	**41 ± 3**	**79**	**30 ± 8**	**40**	**18 ± 3**	**0.01****
Number of perseverative responses	**21**	**49 ± 4**	**79**	**43 ± 4**	**40**	**26 ± 4**	**0.04***
Number of non-perseverative errors	**21**	**35 ± 5**	**79**	**26 ± 7**	**40**	**16 ± 5**	**0.07**

**p*-value < 0.05 significance. ***p*-value < 0.01 significance. Shows that combined inhalant use group shows lower mean than control group, non-inhalant use group as regard number of category completed, and the difference had statistically critical $p = 0.034$. Combined inhalant use group shows higher mean than control, non-inhalants use groups as regard trial to first category, failure to maintain set, total number of errors, number of perseverative errors, and number of perseverative responses; the difference had statistically critical $p = 0.05$, which mean that inhalants use impairs early conceptualization, sustained attention, and flexibility domains. Combined inhalant use group shows higher mean than control, non-inhalants use groups as regard number of non-perseverative errors, but the difference had not statistically critical

In this investigation, there had no discernible difference in the sociodemographic characteristics of the cases and the control group.

In all WCST domains, our investigation discovered a substantial difference between the case and control groups. On the basis of our findings, the majority of research conducted to evaluate this issue, including those conducted in Spain [21–23], the USA [24], 2011, and Brazil [25], reached to the same conclusion: there had been a global decline in executive function related to substance use. Adolescent substance use might had a negative impact on performance as determined by neuropsychological testing and functional neuroimaging activities [8].

This conclusion might be explained by the fact that altered function, including changes in the well-known "executive" domains of attention, inhibition/regulation, working memory, and decision-making, had a defining characteristic of substance use disorders. It had been acknowledged that a fundamental impairment in addiction, a potentially critical target for intervention, had poor (sometimes referred to as "top down") regulation of downstream motivational processes, whether appetitive (reward, incentive salience) or aversive (stress, negative affect) [26].

In this study, polydrug use impaired executive functions in the majority of domains more than mono substance use, which had been consistent with research from Meyerhoff [27], Gustavson [28], Schmidt et al. [29], Formiga et al. (2001), and studies from San Francisco, Brazil [30], while this could be explained biologically and socially, it had been challenging to compare or assess substance use patterns across cases with various backgrounds.

Due to the short sample size, lack of cases who only used cannabis at the time of the trial, there had been no cases who only used cannabis. Cannabis use critically affects all executive function domains, as demonstrated by studies conducted in the Netherlands by Jager et al. [31], Boston by Dahlgren et al. [32], and in Israel by Cohen K., Weinstein [33]; more specifically, it critical affects adolescents' working memory and flexibility, as demonstrated by Morinet al [34].. Block et al. [35] also found this in his study using a sample of Europeans and Americans, respectively. This conclusion had backed by convergent evidence from structural neuroimaging studies, which show that regular cannabis use had linked to neuronal changes in a number of areas of the brain that had been important for working memory, including a shrinkage of the hippocampus and amygdala. These changes also had a relationship with the quantity of cannabis use dependence [36].

The flexibility and initial conceptualization of the adolescent cases had been critically impacted by alcohol use in our study, which had been consistent with Sanhueza et al. [37]'s findings in a related study conducted in Madrid. Powell et al. [38]'s mega study, however, found that alcohol had an impact on every domain of the executive functions; this might be explained by the smaller sample size. Numerous studies revealed that heavy drinkers had lower cerebellar activity in response to a reward processing test (wheel of fortune), frontal, parietal brain activation in response to inhibition, and working memory tasks [39, 40].

In line with research conducted in Egypt by Bassiony et al. [41] and Tehran by Rezapour et al. [42], opioid usage severely impacted executive functioning in our

study, particularly flexibility [42]. Although other studies conducted in China by Li et al. [43], Germany by Brand et al. [44], Florida by Valdes, Lunsford [45], Finland by Rapeli et al. [46], and Finland by Brand et al. [44] did not arrive at the same precise results, this had likely because they used different psychometric tools for evaluating the executive functions. This had been explained by research that shows how opiates cause atrophy, apoptosis by upregulating GDNF, downregulating apoptotic markers including Caspase 3 and 8, and inducing pro-inflammatory indicators.

Additionally, it causes prefrontal cortex neuronal loss, microgliosis, and astrogliosis. Other negative effects of opiate use include behavioural disruption and impairment. Overall, opiate use led to the activation of the neuroinflammatory response, which in turn caused neurodegeneration in the prefrontal cortex [47].

In line with research conducted in Italy by Federico et al., benzos usage in this study adversely impacted executive functioning, particularly flexibility and problem-solving skills [48]. Despite the fact that studies conducted in Bangladesh by Chowdhury et al. [49] and Mexico by Contreras-González et al. [49], it indicated that benzodiazepines influence all domains of executive function.

This study found that inhalant use considerably affected executive functions, which had been consistent with research from studies conducted in Australia, the USA, Turkey, and Mexico. These investigations found that inhalant use critical affected all domains of executive function. Recent research on the executive functioning of inhalant users had found impairments in information processing speed, self-monitoring, visual, motor speed, working memory, psychomotor function, and spatial problem-solving [50, 51].

Conclusions

Adolescents' substance use problems had a serious health issue that had also accompanied by impairment. Cannabis had the greatest impact on early conceptualization and problem-solving skills, whereas alcohol and inhalants mostly impair flexibility and sustained attention, respectively. Contrary to mono substance use, polysubstance use had been more detrimental to the majority of the executive function area.

Abbreviations

ICD-10	International Classification of Diseases
WCST	The Wisconsin Card Sorting Test
M.I.N.I. kid	The Mini-International Neuropsychiatric Interview v.5

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Authors' contributions

Study conception and design, AA, OY, AT, and HH. Data collection, HH, AA, and HE. Data analysis and interpretation, HH, AA, OY, and HE. Drafting of the article, AA, AT, and HH. Critical revision of the article, AA, AT, OY, and HH. The authors read and approved the final manuscript.

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Availability of data and materials

Available data and material.

Declarations

Ethics approval and consent to participate

An informed permission taken from the Medical Ethical Committee, Number: 3684 (30/8/2018). Consent from the case or the case legal guardian as cases had still minors taken at the beginning of the study based on information given about the nature of the study.

Consent for publication

Oral consent from the study subjects had been obtained for publication.

Competing interests

The authors declare that they have no competing interests.

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