

Poremećaj ovisnosti o psihoaktivnim tvarima u osoba s poremećajem pažnje/hiperaktivnosti

/ *Substance Use Disorder in Individuals with Attention Deficit Hyperactivity Disorder*

Daniela Cvitković¹, Gabriela Miklenić¹, Saša Jevtović²

¹ Edukacijsko rehabilitacijski fakultet, Sveučilište u Zagrebu, Zagreb, Hrvatska; ² Medicinski fakultet, Sveučilište u Zagrebu; Klinika za psihijatriju i psihološku medicinu, Klinički bolnički centar Zagreb, Zagreb, Hrvatska

¹ Faculty of Education and Rehabilitation Sciences, University of Zagreb, Zagreb, Croatia; ² University of Zagreb School of Medicine, Department of Psychiatry and Psychological Medicine, Clinical Hospital Centre Zagreb, Zagreb, Croatia

ORCID:

0000-0003-3490-4799 (Daniela Cvitković)

0000-0003-3837-4705 (Saša Jevtović)

Poremećaj pažnje/ hiperaktivnosti (engl. *attention deficit hyperactivity disorder*, ADHD) jedan je od najčešćih neurorazvojnih poremećaja. Riječ je o trajnom i kompleksnom stanju koje se reflektira u svim životnim područjima. Kod osoba s ADHD-om prisutni su česti komorbidni poremećaji uključujući poremećaj ovisnosti o psihoaktivnim tvarima. Cilj ovog narativnog pregleda je ukazati na problem ovisnosti o psihoaktivnim tvarima kod pacijenata s ADHD-om te sumirati dosadašnje rezultate istraživanja koji ukazuju na važnost prepoznavanja ADHD-a kod pacijenata s poremećajem ovisnosti o psihoaktivnim tvarima. Istraživanja ukazuju kako rano prepoznavanje ADHD-a i tretman mogu kod nekih osoba prevenirati, tj. smanjiti rizik za poremećaj ovisnosti o psihoaktivnim tvarima. Preklapanje u simptomima ADHD-a i ovisnosti o psihoaktivnim tvarima otežava postavljanje dijagnoze ADHD-a. Pacijenti s ADHD-om imaju raniji početak ovisnosti, kod njih je više recidiva i problemi su kompleksniji što zahtijeva drugačiji tretman i pristup u odnosu na pacijente s poremećajem ovisnosti koji nemaju ADHD.

/ Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorder. It is a persistent and complex condition that affects all areas of life. Patients with ADHD often have comorbid disorders, including substance use disorder (SUD). The aim of this narrative review is to highlight the problem of substance use disorder in patients with ADHD and to summarize the studies conducted so far which indicate the importance of recognizing ADHD in patients with SUD. Research suggests that early recognition of ADHD and its treatment can prevent, i.e. reduce the risk of substance use disorder in some individuals. The overlap between the symptoms of ADHD and SUD makes ADHD difficult to diagnose. In patients with ADHD, addiction sets in earlier, there are more relapses and the problems are more complex, requiring a different treatment and approach compared to patients with SUD who do not have ADHD.

ADRESA ZA DOPISIVANJE /

CORRESPONDENCE:

Izv. prof. dr. sc. Daniela Cvitković
Edukacijsko rehabilitacijski fakultet
Borongajska 83 f
10000 Zagreb, Hrvatska
E-pošta: daniela.cvitkovic@erf.unizg.hr

KLJUČNE RIJEČI / KEY WORDS:

ADHD / ADHD
Poremećaj ovisnosti o psihoaktivnim tvarima / *Substance Use Disorder*
Tretman ovisnika / *Treatment of Addicts*

TO LINK TO THIS ARTICLE: <https://doi.org/10.24869/spsih.2024.315>

Poremećaj pažnje/hiperaktivnosti (engl. *attention deficit hyperactivity disorder*, ADHD) jedan je od najčešćih neurorazvojnih poremećaja koji karakteriziraju simptomi poremećaja pažnje i/ili hiperaktivnosti i impulzivnosti (1). Prema svjetskim podacima prevalencija ADHD-a kod djece je između 2,6 i 4,5 %, (2) dok je kod odraslih oko 2,9 % (3).

Istraživanja pokazuju da kod osoba s ADHD-om postoji značajan deficit izvršnih funkcija, primarno inhibicije, radnog pamćenja i planiranja (4). U usporedbi s općom populacijom imaju više poteškoća u odnosima, rizik za uključivanjem u delinkventna ponašanja je veći (5), uspjeh u školi je često niži (6), a odrasli se suočavaju s poteškoćama u radnom okruženju i svakodnevnim obavezama (7). ADHD je trajno, kompleksno stanje koje rezultira trajnim, dugoročnim posljedicama u svim aspektima života (8).

ADHD dolazi često u komorbiditetu s raznim drugim poremećajima uključujući poremećaj ovisnosti o psihoaktivnim tvarima.

Cilj ovog narativnog preglednog rada je da prikazom istraživanja o poremećaju ovisnosti o psihoaktivnim tvarima kod osoba s ADHD-om odgovori na pitanje zašto je važno posebno obratiti pažnju na ovu skupinu pacijenata. Konkretnije, ovim radom sažeto će se prikazati teorije i nalazi istraživanja o mehanizmima u podlozi povezanosti ADHD-a i poremećaja ovisnosti o psihoaktivnim tvarima. Obrazložit će se kompleksnost problema kod osoba s ADHD-om i komorbidnim poremećajem ovisnosti o psihoaktivnim tvarima. Prikazat će se sažeto dosadašnje spoznaje o spolnim razlikama u ovisnosti o psihoaktivnim tvarima kod osoba s ADHD-om. Obrazložit će se i važnost dijagnosticiranja ADHD-a kod pacijenata s poremećajem ovisnosti o psihoaktivnim tvarima te općenito važnost ranog postavljanja dijagnoze ADHD-a.

Kako bi se odgovorilo na postavljene ciljeve pretražene su u razdoblju od 10. 10. do 18. 11. 2023.

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders characterized by symptoms of attention and/or hyperactivity and impulsivity disorders (1). According to the worldwide data, the prevalence of ADHD in children is between 2.6 and 4.5 % (2), while in adults it is around 2.9 % (3).

Studies show that there is a significant deficit in executive functions in ADHD patients, primarily relating to inhibition, working memory and planning (4). Compared to the general population, they experience more difficulties in relationships, have a higher risk of engaging in delinquent behavior (5), their academic success is often lower (6), and adults face difficulties in the work environment and in their daily responsibilities (7). ADHD is a persistent, complex condition that leads to lasting, long-term consequences for all aspects of life (8).

ADHD often occurs in comorbidity with various other disorders, including substance use disorder (SUD).

The aim of this narrative review is to answer the question of why it is important to pay particular attention to this patient group by presenting research on SUD in individuals with ADHD. Specifically, this paper briefly presents the theories and study findings relating to the underlying mechanisms of the connection between ADHD and SUD. The complexity of the problem in individuals with ADHD and comorbid SUD will be explained. We will present a summary of the current findings regarding the gender differences in terms of SUD in individuals with ADHD. The importance of diagnosing ADHD in patients with SUD and the importance of early diagnosis of ADHD in general will be explained.

In order to achieve the set objectives, the databases Google Scholar and Scopus were searched in the period from October 10 to November 18,

baze podataka *Google Scholar* i koristeći pristup koji je postavljen široko i koristi kombinacije ključnih riječi ADHD ili *attention deficit hyperactivity disorder* sa SUD ili *substance use disorder* ili *drug dependence* ili *alcohol disorder/dependence*; ili *nicotine dependence*. Kriterij odabira bili su cjeloviti znanstveni radovi na engleskom ili hrvatskom jeziku u području poremećaja ovisnosti o psihoaktivnim tvarima kod osoba s ADHD-om.

MEHANIZMI U PODLOZI POVEZANOSTI ADHD-a I OVISNOSTI O PSIHOAKTIVNIM TVARIMA

Postoje dokazi za neurobiološka preklapanja ADHD-a i poremećaja ovisnosti o psihoaktivnim tvarima. U PET i fMRI studijama pronađene su sličnosti između pacijenata s ADHD-om i onih sa poremećajem ovisnosti o psihoaktivnim tvarima (9). Studije na blizancima i cjelogenomske studije pridruživanja upućuju također na zajedničku nasljednu podlogu kod ADHD-a i poremećaju ovisnosti o psihoaktivnim tvarima (10,11).

Young i Sedgwick (12) u recentnom radu navode kako je vjerojatno da složeno međudjelovanje nekoliko medijacijskih čimbenika ima ulogu u konzumiranju psihoaktivnih tvari kod osoba s ADHD-om te navode o postojanju dokaza za više teorijskih modela poput teorije deficita / disfunkcije dopamina, teorije samoliječenja, teorije bihevioralne dezinhibicije, teorije komorbiditeta. Isto tako istraživanja ukazuju na okolinske rizike za razvoj ovisnosti o psihoaktivnim tvarima, a koji su prisutniji u populaciji osoba s ADHD-m (13,14).

Teorije deficita /disfunkcije dopamina i bihevioralne dezinhibicije

Prema teoriji deficita/disfunkcije dopamina simptomi ADHD-a mogu se dijelom objasniti izmijenjenom regulacijom dopamina, posebice

2023 using a broad approach which searched for combinations of the keywords ADHD or *attention deficit hyperactivity disorder* with SUD or *substance use disorder* or *drug dependence* or *alcohol disorder/dependence*; or *nicotine dependence*. The selection criteria included complete scientific papers written in English or Croatian in the field of SUD in individuals with ADHD.

MECHANISMS UNDERLYING THE ASSOCIATION BETWEEN ADHD AND SUBSTANCE USE DISORDER

There is evidence of neurobiological overlap between ADHD and substance use disorder. Similarities were observed between ADHD patients and SUD patients in PET and fMRI studies (9). Studies conducted on twins and genome-wide association studies also point to a common hereditary basis for ADHD and substance use disorder (10, 11).

In a recent paper, Young and Sedgwick (12) observed that the complex interaction of multiple mediating factors likely plays a role in psychoactive substance use in individuals with ADHD, and postulated that there is evidence to support several theoretical models such as dopamine deficiency/dysfunction theory, self-medication theory, behavioral disinhibition theory and comorbidity theory. Studies also point to environmental risks for the development of psychoactive substance use, which are more prevalent in the population of people with ADHD (13, 14).

Dopamine deficiency/dysfunction and behavioral disinhibition theories

According to the dopamine deficiency/dysfunction theory, ADHD symptoms can be partly explained by altered dopamine regulation, particularly relating to dopamine transport-

prijenosnika dopamina (15). Dopamin ima važnu ulogu u kontroli pokreta, kognitivnim funkcijama, emocijama, motivaciji i mehanizmu nagrađivanja. Teorija deficita transfera dopamina predlaže da se neki od simptoma ADHD-a mogu objasniti time što dopaminergičke stanice, koje kod neurotipičnih osoba predviđaju nagradu prije nego što se ona pojavi, kod osoba s ADHD-om to ne uspijevaju (16).

Slično je sa poremećajem ovisnosti o psihoaktivnim tvarima. Tako je primjerice dostupnost dopaminskih receptora smanjena kod osoba s poremećajem ovisnosti o alkoholu, smanjeno je i otpuštanje dopamina u limbičkim područjima mozga, što ukazuje na smanjenu osjetljivost na nagradu kod osoba s poremećajem ovisnosti o alkoholu (17). Ova teorija djelomično može objasniti simptome poput hiperaktivnosti i impulzivnosti te ju možemo povezati s teorijom bihevioralne dezinhibicije prema kojoj su zbog slabe samokontrole i impulzivnosti osobe s ADHD-om sklonije isprobavati nove stvari i tražiti uzbuđenja (12). Dva moždana puta koji imaju ključnu ulogu u procesiranju nagrade su mezolimbčki i mezokortikalni moždani putevi te se oni povezuju i s ovisnošću i s ADHD-om (18). Mezolimbčki put je povezan s impulzivnošću i motivacijom, dok je mezokortikalni put povezan s prepoznavanjem pogrešaka, izvršnim funkcijama i održavanjem cilju usmjerenih ponašanja (18). Kod mnogih osoba početno konzumiranje droga povezano je s impulzivnošću i traženjem uzbuđenja (18), a impulzivnost odnosno poteškoća samoregulacije jedan je od glavnih simptoma ADHD-a (19). Impulzivnost je također povezana s povećanom konzumacijom alkohola i povećanim rizikom za razvoj ovisnosti o alkoholu i drogama (20,21).

Moglo bi se reći da ADHD karakterizira abnormalna senzitivnost na odgađanje nagrade, jer njihove dopaminergičke stanice ne predviđaju pojačanje, odnosno nagradu na adekvatan način (16). Smanjena osjetljivost na nagradu, kao posljedica smanjene razine dopamina kod oso-

ers (15). Dopamine plays an important role in movement control, cognitive functions, emotions, motivation, and reward mechanisms. The theory of dopamine transfer deficiency suggests that some of the symptoms of ADHD can be explained by the fact that dopaminergic cells, which in neurotypical individuals predict a reward before it appears, are not successful in individuals with ADHD (16).

A similar situation is with the substance use disorder. For example, the availability of dopamine receptors is reduced in individuals with alcohol use disorder, and the release of dopamine in the limbic regions of the brain is also reduced, indicating a reduced receptivity to reward in individuals with alcohol use disorder (17). This theory can partially explain symptoms such as hyperactivity and impulsivity, and we can link it with the theory of behavioral disinhibition according to which ADHD patients tend to try new things and seek excitement due to a lack of self-control and pronounced impulsivity (12). The two brain pathways that play a key role in reward processing are the mesolimbic and mesocortical brain pathways, which have been linked both to addiction and ADHD (18). The mesolimbic pathway is associated with impulsivity and motivation, while the mesocortical pathway is associated with error detection, executive functions and maintaining goal-directed behavior (18). In many people, initial substance use is connected with impulsivity and sensation-seeking (18), and impulsivity i.e. difficulty with self-regulation is one of the main symptoms of ADHD (19). Impulsivity is also associated with increased alcohol consumption and an increased risk of alcohol and drug dependence (20, 21).

It could be said that ADHD is characterized by abnormal sensitivity to reward delays, because their dopaminergic cells do not adequately predict reinforcement or reward (16). Reduced susceptibility to rewards due to lower dopamine levels stimulates behaviors related to im-

ba s ADHD-om potiče ponašanja koja uključuju impulzivno traženje nagrade i traženje novosti (18).

Teorija samoliječenja

Prema teoriji samoliječenja osobe s ADHD-om sklonije su zlorabi psihoaktivnih tvari zbog potrebe za smanjenjem simptoma deficita pažnje, impulzivnosti i hiperaktivnosti.

U više studija utvrđeno je kako se kod osoba s ADHD-om koji su uzimali nikotin preko flastera poboljšala pažnja (22-24). Isto tako pacijenti koji su uzimali flastere nikotina izvijestili su o poboljšanju pažnje i općenito poboljšanju svog stanja za razliku od kontrolne grupe koja je dobivala placebo (25). U jednom je istraživanju nikotin poboljšao bihevioralnu kontrolu kod visoko impulzivnih osoba (26). Slično je utvrđeno s konzumacijom kokaina. Osobe s ADHD-om i poremećajem ovisnosti o psihoaktivnim tvarima mogu doživjeti kratkoročne prednosti uzimanja kokaina kompenzirajući dopaminergički nedostatak (27). Druge supstance kao što su kanabis i alkohol same po sebi ne smanjuju simptome ADHD-a, ali neki pojedinci smatraju kako im pomažu da se osjećaju smirenije i lakše se nose sa stresom (28).

Teorije komorbiditeta

ADHD je često u komorbiditetu s drugim poremećajima poput poremećaja u ponašanju, opozicijsko protestnog poremećaja, anksioznosti i depresivnog poremećaja, a koji se povezuju s poremećajem ovisnosti o psihoaktivnim tvarima. Mnogi s poremećajima ovisnosti o psihoaktivnim tvarima imaju također poremećaj raspoloženja ili anksiozni poremećaj; prema jednoj studiji čak 63,2 % (29). Van Emmerik-van Oortmerssen *et al.* (30) su utvrdili u međunarodnoj studiji na velikom uzorku ispitanika kako je prevalencija antisocijalnog poremećaja, graničnog poremećaja ličnosti i poremećaja raspo-

pulsive reward seeking and novelty seeking in individuals with ADHD (18).

Self-medication theory

According to the self-medication theory, individuals with ADHD tend to abuse psychoactive substances in order to reduce the symptoms of attention deficit, impulsivity and hyperactivity.

Multiple studies have found that individuals with ADHD who used nicotine patches improved their attention (22-24). Likewise, patients taking nicotine patches also reported improvements in attention and an overall improvement in their condition as opposed to the placebo control group (25). In one study, nicotine improved behavioral control in highly impulsive individuals (26). Similar results were obtained with regard to cocaine use. Individuals with ADHD and substance use disorder may experience short-term benefits from cocaine use thus compensating for the dopaminergic deficiency (27).

Other substances such as cannabis and alcohol do not reduce ADHD symptoms in their own right, but some individuals believe that they help them feel calmer and cope better with stress (28).

Comorbidity theories

ADHD is often in comorbidity with other disorders such as behavioral disorders, oppositional defiant disorder, anxiety and depressive disorders, which are all associated with substance use disorder. Many individuals with substance use disorder also suffer from a mood or anxiety disorder, and according to one study their prevalence is as much as 63.2 % (29). In an international study conducted on a large sample of respondents, Van Emmerik-van Oortmerssen *et al.* (30) found that the prevalence of antisocial disorder, borderline personality disorder and mood disorder is higher in addicts who also have ADHD, compared to addicts without ADHD.

loženja veća kod ovisnika koji imaju i ADHD u odnosu na ovisnike bez ADHD-a.

Iako postoje studije u kojima se pokazalo da je ADHD prediktor ovisnosti o psihoaktivnim tvarima neovisno o poremećaju u ponašanju (31-34), u više longitudinalnih i transverzalnih studija utvrđeno je kako se osobe s dijagnozom ADHD-a koje nisu imali komorbidni poremećaj u ponašanju ili opozicijsko protestni poremećaj nisu razlikovale u zloporabi droga u odnosu na kontrolnu grupu (35-37).

Okolinski čimbenici rizika za ovisnost o psihoaktivnim tvarima

Okolinski čimbenici poput nepovoljnih životnih iskustava, vršnjačkog pritiska i dostupnost psihoaktivnih supstancija mogu pridonijeti razvoju ovisnosti o psihoaktivnim tvarima.

Budući da su djeca s ADHD-om izloženija nepovoljnim životnim iskustvima u odnosu na djecu bez ADHD-a (38,39) za pretpostaviti je da je poveznica između nepovoljnih okolinskih prilika kod djece i mladih s ADHD-om i poremećaja ovisnosti o psihoaktivnim tvarima još snažnija, što je potvrđeno u nekim istraživanjima koja slijede.

Obiteljske prilike utječu na razvoj ovisnosti o psihoaktivnim tvarima; negativne interakcije roditelj-dijete, visoke razine negativnog utjecaja i emocionalni stres povećavaju rizik od poremećaja ovisnosti o drogama kod adolescenata (40). Roditelji djece s ADHD-om češće imaju lošiju komunikaciju sa svojom djecom i pružaju manje podrške, što može utjecati na početak konzumacije nikotina (41). Utvrđeno je također kako adolescenti s ADHD-om češće imaju roditelje pušače (42). S druge strane, pozitivni aspekti roditeljstva poput znanja o tome što dijete radi, s kim se druži, u koje je aktivnosti uključen i sl. smanjuju rizik za ovisnost o drogama i ta veza je još jača u obiteljima djece s ADHD-om, nego kod tipičnih obitelji (41).

Although the results of some studies have shown that ADHD is a predictor of substance use disorder independent of a behavioral disorder (31-34), it was observed in several longitudinal and cross-sectional studies that there was no difference between individuals diagnosed with ADHD who did not have a comorbid behavioral disorder or oppositional defiant disorder and the control group when it came to substance abuse (35-37).

Environmental risk factors for psychoactive substance use

Environmental factors such as unfavorable life experiences, peer pressure and availability of psychoactive substances can contribute to the development of psychoactive substance use.

Since children with ADHD are more exposed to adverse life experiences when compared to children without ADHD (38, 39), it is to be assumed that the link between adverse environmental conditions of children and young people with ADHD and substance use disorder is even stronger, as confirmed in some of the following studies.

Family circumstances affect the development of psychoactive substance use; negative parent-child interactions, high levels of negative influence and emotional stress increase the risk of drug addiction disorder in adolescents (40). Parents of children with ADHD are more likely to have poor communication with their children and to provide less support, which may affect the start of nicotine consumption (41). It was also observed that adolescents with ADHD more frequently have parents who smoke (42). On the other hand, the positive aspects of parenting, such as knowing what the child is doing, who they associate with, what activities they are involved in etc., reduce the risk of drug addiction and this relationship is even stronger in families of children with ADHD than in typical ones (41).

Zlostavljanje je rizični faktor za zlorabu opojnih sredstava te jedno istraživanje pokazuje kako je još veći rizični faktor kod osoba s ADHD-om (13). Temeljem podataka velike studije koja uključuje internacionalni uzorak više europskih zemalja utvrđeno je kako je veća stopa ADHD-a kod pacijenata s poremećajem ovisnosti o psihoaktivnim tvarima koja su bila izložena traumama u djetinjstvu (verbalno, fizičko, seksualno i emocionalno zlostavljanje ili zanemarivanje te obiteljsko nasilje) u usporedbi s onima bez traume (43). Za razliku od tog istraživanja Garcia *et al.* nisu potvrdili medijacijski utjecaj ADHD-a između zlostavljanja i ovisnosti o psihoaktivnim tvarima. U jednom se istraživanju neuspjeh u školi pokazao kao medijator veze između ADHD-a i pušenja cigareta kod adolescenata (45).

Postoje istraživanja koja povezuju stigmatizaciju koju doživljavaju osobe s ADHD-om s posezanjem za psihoaktivnim tvarima. Stigmatizacija okoline kod osoba s ADHD-om može naime dovesti do smanjenog samopoštovanja i lošije prilagodbe, što u konačnici može dovesti do problema u ponašanju i problema mentalnog zdravlja, između ostalog i do zlorabe opojnih sredstava (46).

Osobe s ADHD zbog teškoća koja proizlaze iz tog poremećaja imaju manje pozitivnih interakcija s vršnjacima i veća je vjerojatnost za udruživanjem s devijantnim vršnjačkim grupama (14). Pripadnost devijantnim vršnjačkim grupama ima medijacijski učinak između ADHD-a i uporabe psihoaktivnih supstanci (14) što znači kako je vjerojatnije da će se djeca s ADHD-om nego djeca bez ADHD-a družiti s devijantnim vršnjacima i, kao rezultat toga, vjerojatnije će koristiti psihoaktivne tvari. Štoviše, odnos između devijantne pripadnosti vršnjacima i upotrebe supstanci bio je snažniji za adolescente s ADHD-om, što ukazuje da jednom kada su uronjeni u devijantnu grupu vršnjaka, adolescenti s ADHD-om su ranjiviji na negativne društvene utjecaje te skupine. Slične rezultate

Abuse is a risk factor for substance abuse and one study shows that it is an even higher risk factor in individuals with ADHD (13). Based on data from a large study involving an international sample from several European countries, it was determined that ADHD rates were higher in patients with substance use disorder who had been exposed to trauma (verbal, physical, sexual and emotional abuse or neglect, and family violence) in childhood, when compared to patients without trauma (43). In contrast to this study, Garcia *et al.* were unable to confirm the mediating influence of ADHD between abuse and psychoactive substance use. One study determined that poor school performance mediates the relationship between ADHD and cigarette smoking in adolescents (45).

In some studies, a link was found between the stigmatization experienced by individuals with ADHD and the use of psychoactive substances. In individuals with ADHD, stigmatization from the environment can lead to reduced self-esteem and poorer adjustment, which can ultimately lead to behavioral and mental health problems, including, among other things, substance abuse (46).

Due to issues arising from the disorder, individuals with ADHD have fewer positive interactions with peers and are more likely to associate with deviant peer groups (14). Associating with deviant peer groups has a mediating effect between ADHD and the use of psychoactive substances (14), which means that children with ADHD are more likely to associate with deviant peers than children without ADHD and, as a result, are more likely to use psychoactive substances. Moreover, the connection between deviant peer groups and substance use was stronger in adolescents with ADHD, suggesting that once immersed in a deviant peer group, adolescents with ADHD are more vulnerable to the negative social impacts of that group. Similar results were obtained by Garcia *et al.* while studying the connection between deviant peer groups and marijuana consumption (44).

dobili su Garcia *et al.* proučavajući vezu između devijantne vršnjačke grupe i konzumiranja marihuane (44).

VEĆI RIZIK ZA OVISNOST O PSIHOAKTIVNIM TVARIMA OSOBA S ADHD-om

Eme (18) navodi kako, sudeći po prevalenciji adolescenata i mladih s ADHD-om koji su u tretmanima za ovisnost u odnosu na opću populaciju te longitudinalnim praćenjima osoba s ADHD-om, možemo zaključiti o većem riziku za ovisnost o psihoaktivnim tvarima kod osoba s ADHD-om. Istraživanja pokazuju da je među onima koji su u tretmanu za ovisnost o drogama veliki postotak osoba s ADHD-om i kreće se između 20 % za mlade i oko 30 % za odrasle s ADHD-om (47,48); slično je i za ovisnost o alkoholu i nikotinu (49,50). Između 17 % i 45 % odraslih osoba s ADHD-om ima povijest ovisnosti o alkoholu ili zloporabe alkohola te između 9 % i 30 % ima povijest ovisnosti ili zloporabe droga (51). Osobe s ADHD-om češće su ovisnici o nikotinu neovisno o tome imaju li konduktivni poremećaj (52). Biederman i sur. proveli su istraživanje u kojem su ispitivali konzumaciju alkohola kod osoba kojima je kao djeci postavljena dijagnoza ADHD-a u usporedbi s kontrolnom skupinom (32). Pokazalo se da ispitanici s ADHD-om imaju jednaku šansu razvoja ovisnosti o alkoholu kao i neurotipični ispitanici, no postojala je statistički veća šansa da ispitanici s ADHD-om razviju ovisnost o alkoholu u kombinaciji s ovisnošću o drogama.

Longitudinalnim praćenjem pokazalo se kako je ADHD rizični čimbenik za poremećaj ovisnosti o psihoaktivnim tvarima (53-55). Osobe s ADHD-om imaju dva do tri puta veći izgled za razvoj poremećaja zloporabe psihoaktivnih supstancija (4,56). Tako je, primjerice u jednoj studiji, ovisnost o kokainu kod odraslih s ADHD-om iznosila 21 %, a kod osoba bez ADHD-a 10 % (57). Djeca kojima je dija-

HIGHER RISK OF PSYCHOACTIVE SUBSTANCE USE IN INDIVIDUALS WITH ADHD

Eme (18) states that, based on the prevalence of adolescents and young population with ADHD undergoing addiction treatment as compared to the general population, and the longitudinal observation of ADHD patients, we can conclude that there is a higher risk of psychoactive substance use in ADHD patients. Studies show that there is a high percentage of individuals with ADHD among those being treated for drug addiction, ranging from 20% in adolescents to around 30% for adults with ADHD (47, 48). Similar results were obtained for alcohol and nicotine dependence as well (49, 50). Between 17% and 45% of adults with ADHD have a history of alcohol dependence or abuse, and between 9% and 30% have a history of drug dependence or abuse (51). Individuals with ADHD are more likely to develop nicotine dependence, regardless of whether they have a conductive disorder (52). Biederman et al. (32) conducted a study in which they analyzed alcohol consumption in individuals diagnosed with ADHD in childhood, compared to a control group. It was found that respondents with ADHD had the same odds of developing alcohol dependence as the neurotypical respondents, but there was a statistically higher chance that respondents with ADHD would develop alcohol dependence in combination with drug dependence.

The results of longitudinal monitoring showed that ADHD is a risk factor for substance use disorder (53-55). Individuals with ADHD are two to three times more likely to develop substance use disorder (4, 56). In one study, for example, the prevalence of cocaine addiction in adults with ADHD amounted to 21 %, while it was 10 % in individuals without ADHD (57). Children diagnosed with ADHD are almost three times more likely to try marijuana (56). Biederman et al. (32) found that adults with ADHD are twice as likely to develop drug ad-

gnosticiran ADHD imaju gotovo tri puta veću vjerojatnost da će probati marihuanu (56). Biederman *et al.* su utvrdili da odrasli s ADHD-om imaju dvostruko veće izgleda za razvoj ovisnosti o drogama u usporedbi s općom populacijom, čak i kada su povezani psihijatrijski poremećaji kontrolirani (32). Isto tako, u studijama u kojima je kontroliran utjecaj drugih komorbidnih poremećaja poput anksioznosti, depresivnosti nađena je izravna veza ADHD-a i ovisnosti o psihoaktivnim tvarima (53,55).

Naročito su simptomi nepažnje povezani s ovisnostima o nikotinu (33,58), alkoholu i drogama (33).

U Hrvatskoj nedostaje istraživanja o konzumiranju psihoaktivnih tvari kod osoba s ADHD-om. U nedavnom istraživanju provedenom za potrebe diplomskog rada utvrđeno je na prigodnom uzorku kako ne postoji razlika u konzumaciji nikotina i alkohola između odraslih osoba s ADHD-om i onih bez ADHD-a, no osobe s ADHD-om u značajno većoj mjeri konzumiraju ilegalne droge (59). S obzirom na veći udio ispitanika ženskog spola ove rezultate možemo smatrati preliminarnima i uzeti ih s oprezom.

SPOLNE RAZLIKE U OVISNOSTI O PSIHOAKTIVNIM TVARIMA KOD OSOBA S ADHD-om

Dosadašnja istraživanja o eventualnim spolnim razlikama s obzirom na vjerojatnost za razvoj ovisnosti o psihoaktivnim tvarima i težinu poremećaja kod osoba s ADHD-om daju oprečne rezultate.

U nešto ranijim istraživanjima nisu utvrđene spolne razlike u kroničnom uzimanju droga (60) ili je stopa ADHD-a bila veća kod muških adolescenata, ovisnika od droga (61).

Prema novijim istraživanjima djevojke i odrasle žene s ADHD-om u većem su riziku za

diction when compared to the general population, even when the associated psychiatric disorders are controlled (32). Moreover, studies in which the influence of other comorbid disorders such as anxiety and depression was controlled, found a direct link between ADHD and substance use disorder (53, 55).

Attention deficit symptoms are particularly associated with dependence on nicotine (33, 58), alcohol and drugs (33).

There are no studies in Croatia on the use of psychoactive substances among individuals with ADHD. A recent study conducted on a convenience sample as part of a diploma thesis, found that there is no difference in nicotine and alcohol consumption between adults with ADHD and those without ADHD, however, those with ADHD consume illegal substances to a significantly higher extent (59). Given the higher proportion of female respondents, these results should be regarded as preliminary and treated with caution.

GENDER-SPECIFIC DIFFERENCES IN PSYCHOACTIVE SUBSTANCE USE IN INDIVIDUALS WITH ADHD

Previous studies on possible gender differences when it came to the likelihood of developing substance use disorder and the severity of the disorder in individuals with ADHD have yielded contradictory results.

Some earlier studies found no gender differences in chronic drug abuse (60), or the ADHD rates were higher in male adolescents, drug addicts (61).

According to recent studies, girls and adult women with ADHD are at a higher risk of developing drug, or alcohol (64), dependence disorder compared to male individuals with ADHD (62-64). The results of a recent study also show that impulsivity and hyperactivity have greater

razvoj poremećaja ovisnosti o drogama u odnosu muške osobe s ADHD-om (62-64) te o alkoholu (64). Rezultati jedne studije ukazuju kako impulzivnost i hiperaktivnost imaju veću prediktivnu snagu za poremećaj ovisnosti o alkoholu i drogama i zlorabu alkohola i droga kod djevojaka (65). Isto tako žene s ADHD-om koje puše duhan imaju veće simptome kod odvikavanja za vrijeme rane apstinencijske faze (66).

KOMPLEKSNOŠT PROBLEMA KOD OSOBA S KOMORBIDNIM ADHD-OM I POREMEĆAJEM OVISNOSTI O PSIHOAKTIVNIM TVARIMA

Dosadašnja istraživanja ukazuju na kompleksnije teškoće kod ovisnika s ADHD-om u odnosu na ovisnike bez komorbidnog ADHD-a. Tako je nepovoljan utjecaj droga, alkohola na kognitivne funkcije potvrđen u više istraživanja. Konzumacija alkohola kod adolescenata smanjuje volumen sive tvari i razvoj bijele tvari (67), povećava deficit pažnje (68) i dovodi do poteškoća u verbalnom pamćenju, vizuospatialnim funkcijama, brzini procesuiranja informacija i kognitivne kontrole (69). Budući da su ove kognitivne funkcije kod osoba s ADHD-om već oštećene (70), učestala konzumacija alkohola još nepovoljnije djeluje na razvoj adolescenata koji imaju ADHD (71). Konzumacija alkohola također povećava impulzivnost, a osobe s ADHD-om osjetljivije su na akutni dezinhbirajući učinak alkohola (72). Slično je s kokainom pa su utvrđena veća oštećenja kognitivnih funkcija u skupini ovisnika o kokainu koji imaju ADHD u odnosu na skupinu ovisnika koji nemaju ADHD (73). U usporedbi s osobama bez ADHD-a, oni s ADHD-om ranije počinju konzumirati kokain te ga konzumiraju češće i više (74). Isto tako, osobe s ADHD-om imaju veća oštećenja povezana s konzumacijom marihuane i drugih zabranjenih droga, neovisno o

predictive power for alcohol and drug dependence disorders, and alcohol and drug abuse in girls (65). In addition, women with ADHD who smoke tobacco have more severe cessation symptoms in the early withdrawal phase (66).

COMPLEXITY OF THE ISSUE IN INDIVIDUALS WITH COMORBID ADHD AND SUBSTANCE USE DISORDER

Previous studies have shown that addicts with ADHD experience more complex difficulties compared to addicts without comorbid ADHD. The adverse effect of drugs and alcohol on cognitive function have been confirmed in a number of studies. Alcohol consumption in adolescents reduces grey matter volume and white matter development (67), increases attention deficit (68) and leads to problems with verbal memory, visuospatial functions, speed of information processing and cognitive control (69). As these cognitive functions are already impaired in individuals with ADHD (70), frequent alcohol consumption has an even more unfavorable effect on the development of adolescents with ADHD (71). Alcohol consumption also increases impulsivity, and individuals with ADHD are more sensitive to the acute disinhibitory effects of alcohol (72). It is similar with cocaine, as cocaine addicts with ADHD have been found to have higher cognitive impairment than non-ADHD addicts (73). Compared to individuals without ADHD, those with ADHD start using cocaine earlier, and use it more frequently and in larger amounts (74). Similarly, individuals with ADHD have greater impairments associated with the consumption of marijuana and other illicit drugs, regardless of whether they have a comorbid behavior disorder (52).

In addition to the more adverse effect on cognitive functions in addicts with ADHD, studies

tome imaju li komorbidni poremećaj ponašanja (52).

Osim nepovoljnijeg učinka na kognitivne funkcije kod ovisnika s ADHD-om istraživanja ukazuju na veću izraženost drugih problema poput ranijeg početka, više recidiva, većih teškoća pri odvikavanju, kompleksnijeg tijeka poremećaja.

Veći broj istraživanja jasno pokazuje kako adolescenti s komorbidnim poremećajem ovisnosti o drogama/alkoholu i ADHD-om imaju raniji početak i teži tijek poremećaja ovisnosti o drogama te je u njih više recidiva (57,74-79).

Slično je s konzumacijom duhana. Veća je vjerojatnost da će osobe s ADHD-om početi pušiti duhan u ranoj dobi i da će brže doći do faze redovne konzumacije duhana u odnosu na tipičnu populaciju (80). Odrasli pušači s ADHD-om imaju veću ovisnost o nikotinu (80). Podatci o broju konzumiranih cigareta/dan u odnosu na opću populaciju su neujednačeni. Prema rezultatima istraživanja Sanchez Garcia i suradnika osobe s ADHD-om puše više cigareta/dan (81), dok prema rezultatima Rhodes i suradnika nema razlike u broju cigareta/dan (80). Intenzivniji su simptomi odvikavanja od pušenja (49, 82) te osobe s ADHD-om mogu imati više poteškoća s prestankom pušenja u usporedbi s onima bez tog poremećaja (83,84).

VAŽNOST DIJAGNOSTICIRANJA ADHD-a U OSOBA S POREMEĆAJEM OVISNOSTI O PSIHOAKTIVNIM TVARIMA S OBZIROM NA SPECIFIČNOSTI TRETMANA

ADHD je važno prepoznati i dijagnosticirati kod ovisnika o psihoaktivnim tvarima, jer je tim osobama s komorbidnom dijagnozom ADHD-a potreban drugačiji pristup i tretman. Schellekens *et al.* (85) temeljem rezultata istraživanja predlažu da bi probir za ADHD trebao biti standardna procedura u liječenju osoba s

also suggest a greater severity of other problems, such as earlier onset, more relapses, greater difficulty in withdrawal, and a more complex course of the disorder.

The results of numerous studies clearly show that adolescents with comorbid drug/alcohol use disorder and ADHD have an earlier onset and a more severe course of addiction, and tend to relapse more frequently (57, 74-79).

The situation is similar with tobacco consumption. Individuals with ADHD are more likely to start smoking tobacco at a young age, and reach the regular tobacco use stage sooner than the typical population (80). Adult smokers with ADHD are more addicted to nicotine (80). Data on the number of cigarettes consumed per day compared to the general population is inconsistent. According to a study conducted by Sanchez Garcia *et al.*, individuals with ADHD smoke more cigarettes per day (81), while according to Rhodes *et al.*, there is no difference in the number of cigarettes per day (80). Symptoms of smoking cessation (49, 82) are more intense and individuals with ADHD may have more difficulty quitting smoking than those without the disorder (83, 84).

IMPORTANCE OF DIAGNOSING ADHD IN INDIVIDUALS WITH SUBSTANCE USE DISORDER WITH REGARD TO THE TREATMENT SPECIFICITIES

It is important to recognize and diagnose ADHD in those addicted to psychoactive substances, as these individuals with a comorbid diagnosis of ADHD require a different approach and treatment. Based on their study results, Schellekens *et al.* (85) suggest that screening for ADHD should be a standard procedure in the treatment of individuals with addiction, i.e. substance use disorder.

ovisnošću, odnosno poremećajem zlorabe supstancija.

Zbog sličnosti u simptomima, ADHD se, ako nije dijagnosticiran u djetinjstvu, često previdi u ovisnika (86), budući da dugotrajna zloraba psihoaktivnih tvari poput marihuane, kokaina, metamfetamina, alkohola i sl. dovodi do oštećenja kognitivnih funkcija, pažnje, pamćenja, izvršnih funkcija (87). Unatoč navedenim sličnostima u simptomima istraživanja pokazuju kako je moguće pouzdano dijagnosticirati ADHD čak i kod onih koji nisu u potpunosti apstinenti (47), a Van de Glind *et al.* (54) su uspjeli dokazati na međunarodnom uzorku kako je upitnik za samoprocjenu simptoma ADHD-a kod odraslih *The Adult ADHD Self-Report Scale* (ASRS) dovoljno dobra mjera za probir ADHD-a u populaciji pacijenata s ovisnosti o psihoaktivnim tvarima. Procjena ADHD-a uključuje kompletnu anamnezu uključujući razvojnu povijest bolesti, kao i mentalno stanje pojedinca te funkcioniranje u svim situacijama; podatke koji se prikupljaju od pacijenta ali i od bliskih srodnika (54). Osobito je važno prikupiti podatke o simptomima koji su bili prisutni prije poremećaja ovisnosti o psihoaktivnim tvarima i koji su prisutni u razdoblju apstinencije kako bi se utvrdilo radi li se o primarnim simptomima ili su potaknuti konzumacijom psihoaktivnih tvari (88).

Dijagnozu ADHD-a važno je postaviti što ranije u dječjoj dobi, budući da liječenje stimulansima tijekom djetinjstva može smanjiti rizik od razvoja poremećaja ovisnosti o psihoaktivnim tvarima, osobito ako se s terapijom započne rano (53,58,90). Isto tako psihosocijalne intervencije usmjerene na djecu s ADHD-om, ali i na roditelje, učitelje i vršnjake mogu prevenirati razvoj poremećaja ovisnosti o psihoaktivnim tvarima (81,91).

Osim toga, važno je što ranije dijagnosticirati ADHD kod pacijenata s poremećajem ovisnosti o psihoaktivnim tvarima jer, kao što sadašnja istraživanja pokazuju, tretman ovi-

Due to the similarity of symptoms, ADHD in addicts is often overlooked if it had not been diagnosed in childhood (86), since long-term abuse of psychoactive substances such as marijuana, cocaine, methamphetamine, alcohol etc. leads to impaired cognitive, as well as attention, memory and executive functioning (87). Despite these similarities in symptoms, studies have shown that ADHD can also be reliably diagnosed even in individuals who are not completely abstinent (47), and the authors Van de Glind *et al.* (54) were able to demonstrate on an international sample that the Adult ADHD Self-Report Scale (ASRS), a self-assessment questionnaire of ADHD symptoms in adults, is a sufficient measure for ADHD screening in the population of patients with psychoactive substance use. The assessment of ADHD involves a complete medical history, including developmental and medical history, as well as the individual's mental state and functioning in all situations; and the data collected from the patients, but also from their close relatives (54). It is particularly important to collect data on the symptoms that were present before the substance use disorder and those that are present during the period of abstinence, in order to determine whether they are primary symptoms or whether they were triggered by the use of psychoactive substances (88).

It is important to diagnose ADHD as early as possible in childhood, since stimulant therapy in childhood can reduce the risk of developing substance use disorder, especially if therapy is started early (53, 58, 90). Similarly, psychosocial interventions aimed at children with ADHD, but also at parents, teachers and peers, can prevent the development of substance use disorder (81, 91).

In addition, it is important to diagnose ADHD as early as possible in patients with substance use disorder because, as previous research suggests, the treatment of addiction should probably be different for people with a diagnosis of

snosti kod osoba s komorbidnom dijagnozom ADHD-a vjerojatno treba biti drugačiji. U preglednom radu Zaso *et al.* (92) zaključuju kako je znanje o liječenju komorbidnog ADHD-a i ovisnosti o psihoaktivnim tvarima u adolescenciji ograničeno. Čini se da tretman koji bi uključivao medikamentnu terapiju nije naročito učinkovit u liječenju poremećaja ovisnosti o psihoaktivnim tvarima u osoba s ADHD-om. Istraživanja pokazuju da osobe koje imaju izraženije simptome ADHD-a i koje su u tretmanu zbog poremećaja zlorabe tvari imaju manju dobit od terapije (60) te postoji manja vjerojatnost da će napredovati tijekom terapije i ostati u terapiji (86). Buduća bi se istraživanja trebala usmjeriti na donošenje odgovora o najboljoj medikamentnoj terapiji za osobe s ADHD-om koje imaju komorbidni poremećaj zlorabe tvari (85).

Zulauf i sur. (18) zaključuju kako je u tretman adolescenata i mladih odraslih osoba s ADHD-om i poremećajem ovisnosti o psihoaktivnim tvarima potrebno uključiti obitelj. Nakon što je uzimanje psihoaktivnih tvari pod kontrolom, u liječenju mogu biti učinkovite strukturirane psihoterapije poput kognitivno bihevioralnog tretmana (18). No, potrebna su buduća placebo kontrolirana klinička ispitivanja na velikim uzorcima kako bi se ispitala učinkovitost psihoterapijskih intervencija, budući da u dosadašnjim istraživanjima ne možemo isključiti alternativna objašnjenja poput utjecaja placeba ili tzv. efekta Hawthorne (92).

RASPRAVA

Dosadašnja istraživanja jasno su utvrdila vezu između ADHD-a i ovisnosti o psihoaktivnim tvarima, što ukazuje na potrebu probira na ADHD kod ovisnika o psihoaktivnim tvarima. Temeljem pregleda istraživanja o mehanizmi-ma povezanosti ADHD-a i poremećaja ovisnosti možemo zaključiti kako nema jednoznačnog odgovora o razlozima povezanosti te je vjero-

comorbid ADHD. In their review article, Zaso *et al.* (92) concluded that knowledge about the treatment of comorbid ADHD and adolescent psychoactive substance use is limited. Medication-only treatment does not appear to be particularly effective in the treatment of substance use disorder in individuals with ADHD. Studies show that people with more severe ADHD symptoms who are being treated for substance use disorder are less likely to benefit from therapy (60), and they are less likely to make progress during therapy and remain in therapy (86). Future studies should focus on finding the best medication therapy for ADHD patients with comorbid substance use disorder (85).

Zulauf *et al.* (18) observed that family involvement is necessary in the treatment of adolescents and young adults with ADHD and substance use disorder. Once psychoactive substance use is under control, structured psychotherapies such as cognitive behavioral therapy can be effective in treatment (18). However, future placebo-controlled clinical trials on large samples are necessary in order to investigate the effectiveness of psychotherapeutic interventions, because studies conducted so far could not rule out alternative explanations such as the placebo effect or the so-called Hawthorne effect (92).

DISCUSSION

Previous studies have clearly established an association between ADHD and substance use disorder, indicating the need for screening for ADHD in individuals using psychoactive substances. Based on a review of studies addressing the mechanisms of association between ADHD and substance use disorder, we can conclude that there is no clear answer as to the reasons for the association, and that a combination of neurobiological and environmental factors is likely to be the cause. There

jatno odgovorna kombinacija neurobioloških i okolinskih čimbenika. Postoje dokazi o zajedničkoj genetskoj podlozi, o neurobiološkim preklapanjima. Isto tako postoje istraživanja koja upućuju na okolinske čimbenike povezanosti. Važno je nastaviti ispitivanje rizičnih i protektivnih čimbenika okoline kako bismo unaprijedili prevenciju razvoja ovisnosti o psihoaktivnim tvarima kod osoba s ADHD-om.

Neka istraživanja idu u prilog teoriji komorbiditeta, no s druge strane rezultati drugih istraživanja opovrgavaju ovu teoriju. Preporučuje se nastaviti s kontroliranim longitudinalnim studijama s međunarodnim uzorcima kako bi se donijeli jasniji zaključci.

S obzirom na oprečne rezultate potrebno je daljnje istraživanje spolnih razlika kod osoba s komorbidnim ADHD-om i poremećajem ovisnosti o psihoaktivnim tvarima. Moguće je da se s godinama stopa zlorabe psihoaktivnih tvari u žena s ADHD-om povećala. ADHD u žena se sve više otkriva, za razliku od prije kada je smatran većinom muškim poremećajem, što je također moglo utjecati na razlike između ranijih i recentnijih istraživanja. Ono što posebno nedostaje u dosadašnjim istraživanjima jest usmjeravanje na moguće različite tretmane i metode prevencije s obzirom na različitosti u razvoju i funkcioniranju muškaraca i žena. Moguće je da su različiti rizični, ali i protektivni faktori važni za razvoj poremećaja ovisnosti kod žena s ADHD-om u odnosu na muškarce s ADHD-om.

Za sada nema definitivnog odgovora na pitanje o najboljem tretmanu za pacijente s poremećajem ovisnosti s komorbidnim ADHD-om jer ima malo istraživanja na ovom području. Ono što se do sada zna jest da klasičan tretman za poremećaj ovisnosti nije dovoljan, kao ni medikamentna terapija namijenjena ADHD-u. Istraživanja podržavaju multimodalni tretman koji bi uključivao adekvatan odabir medikamenata zajedno s odgovarajućom psihosocijalnom intervencijom.

is evidence of a common genetic background, neurobiological overlaps. There are also studies that point to environmental factors in terms of association. It is important to further investigate the environmental risk and protective factors in order to improve the prevention of psychoactive substance use development in individuals with ADHD.

Some studies support the theory of comorbidity, but on the other hand, the results of other studies refute this theory. It is recommended to continue with controlled longitudinal studies on international samples, in order to draw clearer conclusions.

Given the conflicting results, further research on the gender differences in individuals with comorbid ADHD and substance use disorder is necessary. It is possible that the rate of psychoactive substance abuse in women with ADHD has increased over the years. ADHD in women is being identified more frequently, unlike in the past when it was considered primarily a male disorder, which may also have influenced the differences between the earlier and more recent studies. What is particularly lacking in previous studies is a focus on possible different treatments and prevention methods, considering the differences in development and functioning between males and females. It is possible that different risk and protective factors are important for the development of addictive disorders in women with ADHD compared to men with ADHD.

There is so far no definitive answer to the question of the best treatment for patients with substance use disorder and comorbid ADHD, because there are few studies in this area. What is known so far is that traditional treatment for substance use disorder is not sufficient, nor is the medication treatment intended for ADHD. Studies support a multimodal treatment that would include an adequate selection of medications along with an appropriate psychosocial intervention.

Ovim narativnim pregledom nastojalo se u prikazu istraživanja odgovoriti na pitanje zašto je važno posebno obratiti pažnju na skupinu pacijenata s poremećajem ovisnosti o psihoaktivnim tvarima s komorbidnim ADHD-om. Istraživanja jasno pokazuju povezanost između tih dvaju poremećaja. Iako uzroci čestog komorbiditeta nisu do kraja razjašnjeni, rezultati istraživanja idu u prilog zaključku kako je riječ o kombinaciji neurobioloških čimbenika i čimbenika okoline. Kod ove skupine pacijenata lošije su prognoze s obzirom na poremećaj ovisnosti zbog čestih recidiva i izraženijih simptoma poremećaja, a rano prepoznavanje ADHD-a i terapija stimulansima mogu smanjiti rizik za poremećaj ovisnosti o psihoaktivnim tvarima. Rezultati istraživanja ukazuju na potrebu za drugačijim tretmanom ovisnika s komorbidnim ADHD-om koji bi osim medikamentne terapije uključivao i druge pristupe. Iduća istraživanja trebala bi se usmjeriti na dobivanje odgovora na pitanje o najboljem tretmanu za poremećaj ovisnosti o psihoaktivnim tvarima u pacijenata s ADHD-om te se dodatno usmjeriti na spolne razlike s obzirom na specifičnosti procjene i tretmana.

This aim of this narrative review was to answer the question of why it is important to pay particular attention to the group of patients with substance use disorder and comorbid ADHD. Studies clearly show an association between these two disorders. Although the causes of frequent comorbidity are not yet fully understood, research results suggest that it is a combination of neurobiological and environmental factors. The prognosis for this patient group is poorer in terms of substance use disorder, due to frequent relapses and more pronounced symptoms of the disorder. Early recognition of ADHD and stimulant therapy can reduce the risk of substance use disorder. Study findings point to the need for a different treatment of addicts with comorbid ADHD, which includes other approaches in addition to medication. Future studies should focus on obtaining an answer to the question of the best treatment for substance use disorder in patients with ADHD, and should additionally focus on gender differences, taking into account the specificity of assessment and treatment.

LITERATURA/REFERENCES

1. American Psychiatric Association DS, American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. Washington, DC: American psychiatric association, 2013.
2. Polanczyk GV, Salum GA, Sugaya LS, Caye A, Rohde LA. Annual research review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *J Child Psychol Psychiatry* 2015;56(3):345-65. doi:10.1111/jcpp.12381.
3. Faraone SV, Biederman J. What is the prevalence of adult ADHD? Results of a population screen of 966 adults. *J Atten Disord* 2005;9(2):384-91. doi: 10.1177/1087054705281478.
4. Willcutt EG, Doyle AE, Nigg JT, Faraone SV, Pennington BF. Validity of the executive function theory of attention-deficit/hyperactivity disorder: a meta-analytic review. *Biol Psychiatry* 2005;57(11):1336-46. doi:10.1016/j.biopsych.2005.02.006.
5. Sciberras E, Roos LE, Efron D. Review of prospective longitudinal studies of children with ADHD: mental health, educational, and social outcomes. *Curr Atten Disord Rep* 2009;1(4):171-7.
6. Arnold LE, Hodgkins P, Kahle J, Madhoo M, Kewley G. Long-term outcomes of ADHD: academic achievement and performance. *J Atten Disord* 2020;24(1):73-85. doi: 10.1177/1087054714566076.
7. Biederman J, Faraone SV, Spencer TJ, Mick E, Monuteaux MC, Aleardi M. Functional impairments in adults with self-reports of diagnosed ADHD: A controlled study of 1001 adults in the community. *J Clin Psychiatry* 2006;67(4):524-40. doi: 10.4088/jcp.v67n0403.
8. Di Lorenzo R, Balducci J, Poppi C, Arcolin E, Cutino A, Ferri P *et al.* Children and adolescents with ADHD followed up to adulthood: A systematic review of long-term outcomes. *Acta Neuropsychiatrica* 2021;33(6):283-98. doi: 10.1017/neu.2021.23.
9. Frodl T. Comorbidity of ADHD and substance use disorder (SUD): a neuroimaging perspective. *J Atten Disord* 2010;14(2):109-20. doi: 10.1177/1087054710365054.

10. Derks EM, Vink JM, Willemsen G, van den Brink W, Boomsma DI. Genetic and environmental influences on the relationship between adult ADHD symptoms and self-reported problem drinking in 6024 Dutch twins. *Psychol Med* 2014;44(12):2673-83. doi: 10.1017/S0033291714000361.
11. Vink J, Schellekens A. Relating addiction and psychiatric disorders. *Science* 2018;361(6409):1323-4.
12. Young S, Sedgwick O. Attention deficit hyperactivity disorder and substance misuse: An evaluation of causal hypotheses and treatment considerations. *Expert Rev Neurother* 2015;15(9):1005-14. doi: 10.1586/14737175.2015.1059756.
13. De Sanctis VA, Newcorn, JH, Halperin, JM. A prospective look at substance use and criminal behavior in urban ADHD youth: what is the role of maltreatment history on outcome? *Atten Defic Hyperact Disord.* 2014;6(2):79-86. doi: 10.1007/s12402-013-0124-8.
14. Marshal MP, Molina BS, Pelham Jr WE. Childhood ADHD and adolescent substance use: an examination of deviant peer group affiliation as a risk factor. *Psychol Addict Behav* 2003;17(4):293. doi: 10.1037/0893-164X.17.4.293.
15. Spencer TJ, Biederman J, Madras BK, Faraone SV, Dougherty DD, Bonab A *et al.* In vivo neuroreceptor imaging in attention-deficit/hyperactivity disorder: a focus on the dopamine transporter. *Biol Psychiatry* 2005;57(11):1293-300. doi: 10.1016/j.biopsych.2005.03.036.
16. Tripp G, Wickens JR. Neurobiology of ADHD. *Neuropharmacology* 2009;57(7-8):579-89. doi: 10.1016/j.neuropharm.2009.07.026.
17. Volkow ND, Wang GJ, Telang F, Fowler JS, Logan J, Jayne M *et al.* Profound decreases in dopamine release in striatum in detoxified alcoholics: possible orbitofrontal involvement. *J Neurosci* 2007;27(46):12700-6. doi: 10.1523/JNEUROSCI.3371-07.2007.
18. Eme R. ADHD and risky substance use in male adolescents. *Child Adoles Psychopharmacol* 2017;22(3):1-8.
19. Barkley RA. The important role of executive functioning and self-regulation in ADHD. *Child Neuropsychol* 2011;113(21):41-56.
20. Adan A, Forero DA, Navarro JF. Personality traits related to binge drinking: a systematic review. *Front in Psychiatry* 2017; 8:134. doi: 10.3389/fpsyt.2017.00134.
21. Kozak K, Lucatch AM, Lowe DJE, Balodis IM, MacKillop J, George TP. The neurobiology of impulsivity and substance use disorders: implications for treatment. *Ann N Y Acad Sci* 2019;1451(1):71-91. doi: 10.1111/nyas.13977.
22. Levin ED, Conners CK, Sparrow E, Hinton SC, Erhardt D, Meck WH *et al.* Nicotine effects on adults with attention-deficit/hyperactivity disorder. *Psychopharmacology (Berl)* 1996;123(1):55-63. doi: 10.1007/BF02246281.
23. Potter AS, Newhouse PA. Acute nicotine improves cognitive deficits in young adults with attention-deficit/hyperactivity disorder. *Pharmacol Biochem Behav* 2008;88(4):407-417. doi: 10.1016/j.pbb.2007.09.014.
24. Conners CK, Levin ED, Sparrow E, Hinton SC, Erhardt D, Meck WH *et al.* Nicotine and attention in adult attention deficit hyperactivity disorder (ADHD). *Psychopharmacol Bull* 1996;32(1):67-74.
25. Gehricke JG, Whalen CK, Jamner LD, Wigal TL, Steinhoff K. The reinforcing effects of nicotine and stimulant medication in the everyday lives of adult smokers with ADHD: A preliminary examination. *Nicotine Tob Res* 2006;8(1):37-47. doi: 10.1080/14622200500431619.
26. Potter AS, Buccì DJ, Newhouse PA. Manipulation of nicotinic acetylcholine receptors differentially affects behavioral inhibition in human subjects with and without disordered baseline impulsivity. *Psychopharmacology* 2012;220(2):331-40. doi: 10.1007/s00213-011-2476-0.
27. Carli G, Cavicchioli M, Martini AL, Bruscoli M, Manfredi A, Presotto L *et al.* Neurobiological Dysfunctional Substrates for the Self-Medication Hypothesis in Adult Individuals with Attention-Deficit Hyperactivity Disorder and Cocaine Use Disorder: A Fluorine-18-Fluorodeoxyglucose Positron Emission Tomography Study. *Brain Connect* 2023;13(7):370-382. doi: 10.1089/brain.2022.0076.
28. Young S, Woodhouse E. Assessment and treatment of substance use in adults with ADHD: a psychological approach. *J Neural Trans (Vienna)* 2021;128(7):1099-108. doi: 10.1007/s00702-020-02277-w.
29. Bizzarri JV, Rucci P, Sbrana A, Gonnelli C, Massei GJ, Ravani *et al.* Reasons for substance use and vulnerability factors in patients with substance use disorder and anxiety or mood disorders. *Addict Behav* 2007;32(2):384-91. doi: 10.1016/j.addbeh.2006.04.005.
30. van Emmerik-van Oortmerssen K, van de Glind G, Koeter MW, Allsop S, Auriacombe M, Barta C *et al.* Psychiatric comorbidity in treatment-seeking substance use disorder patients with and without attention deficit hyperactivity disorder: results of the IASP study. *Addiction* 2014;109(2):262-72.
31. Groenman, AP, Schwersen LJS, Weeda W, Luman M, Noordermeer SDS, Heslenfeld DJ *et al.* Stimulant treatment profiles predicting co-occurring substance use disorders in individuals with attention-deficit/hyperactivity disorder. *Eur Child Adolesc Psychiatry* 2019;28(9):1213-22. doi: 10.1007/s00787-019-01283-y.
32. Biederman J, Wilens T, Mick E, Milberger S, Spencer TJ, Faraone SV. Psychoactive substance use disorders in adults with attention deficit hyperactivity disorder (ADHD): effects of ADHD and psychiatric comorbidity. *Am J Psychiatry* 1995; 152(11): 1652-1658. doi: 10.1176/ajp.152.11.1652.
33. Molina BS, Pelham Jr WE. Childhood predictors of adolescent substance use in a longitudinal study of children with ADHD. *J Abnorm Psychol* 2003;112(3):497. doi: 10.1037/0021-843x.112.3.497.
34. Gau SS, Chong MY, Yang P, Yen CF, Liang KY, Cheng ATA. Psychiatric and psychosocial predictors of substance use disorders among adolescents: longitudinal study. *Br J Psychiatry* 2007;190(1):42-8. doi: 10.1192/bjp.bp.106.022871.
35. August GJ, Winters KC, Realmuto GM, Fahnhorst T, Botzet A, Lee S. Prospective study of adolescent drug use among community samples of ADHD and non-ADHD participants. *J AM Acad Child Adolesc Psychiatry* 2006;45(7):824-32. doi: 10.1097/01.chi.0000219831.16226.f8.

36. Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult follow-up of hyperactive children: antisocial activities and drug use. *J Child Psychol Psychiatry* 2004;45(2):195-211. doi: 10.1111/j.1469-7610.2004.00214.x.
37. Torok M, Darke S, Kaye S. Attention deficit hyperactivity disorder and severity of substance use: The role of comorbid psychopathology. *Psychol Addict Behav* 2012;26(4):974-9. doi: 10.1037/a0027846.
38. Brown NM, Brown SN, Briggs RD, Germán, M, Belamarich, PF, Oyeku, SO. Associations between adverse childhood experiences and ADHD diagnosis and severity. *Acad Pediatr* 2017;17(4):349-55. doi: 10.1016/j.acap.2016.08.013.
39. Lugo-Candelas C, Corbeil T, Wall M, Posner J, Bird H, Canino G *et al.* ADHD and risk for subsequent adverse childhood experiences: Understanding the cycle of adversity. *J Child Psychol Psychiatry* 2021;62(8):971-8. doi: 10.1111/jcpp.13352.
40. Wills TA, McNamara G, Vaccaro D, Hirky AE. Escalated substance use: a longitudinal grouping analysis from early to middle adolescence. *J Abnorm Psychol* 1996; 105(2):166-180. doi: 10.1037//0021-843x.105.2.166.
41. Walther CA, Cheong J, Molina BS, Pelham Jr WE, Wymbs BT *et al.* Substance use and delinquency among adolescents with childhood ADHD: the protective role of parenting. *Psychol Addict Behav* 2012;26(3):585-98. doi: 10.1037/a0026818.
42. Kalyva E. Prevalence and influences on self-reported smoking among adolescents with mild learning disabilities, attention deficit hyperactivity disorder, and their typically developing peers. *J Intellect Disabil* 2007;11(3):267-79. doi: 10.1177/1744629507080790.
43. Konstenius M, Leifman A, van Emmerik-van Oortmerssen K, van de Glind G, Franck J, Moggi F *et al.* Childhood trauma exposure in substance use disorder patients with and without ADHD. *Addict Behav* 2017;65:118-24. Epub 2016 Nov 07. <http://dx.doi.org/10.1016/j.addbeh.2016.10.016>.
44. Garcia BH, Vazquez A, Moses JO, Cromer KD, Marrow AS, Villodas M. Risk for substance use among adolescents at-risk for childhood victimization: The moderating role of ADHD. *Child Abuse Negl* 2021;114:104977. doi:10.1016/j.chiabu.2021.104977.
45. Flory K, Malone PS, Lamis DA. Childhood ADHD symptoms and risk for cigarette smoking during adolescence: School adjustment as a potential mediator. *Psychol Addict Behav* 2011;25(2):320. doi:10.1037/a0022633.
46. Mueller AK, Fuermaier AB, Koerts J, Tucha L. Stigma in attention deficit hyperactivity disorder. *ADHD attention deficit and hyperactivity disorders* 2012;4:101-14. doi: 10.1007/s12402-012-0085-3.
47. van Emmerik-van Oortmerssen K, van de Glind G, van den Brink W, Smit F, Crunelle CL *et al.* Prevalence of attention-deficit hyperactivity disorder in substance use disorder patients: a meta-analysis and meta-regression analysis. *Drug Alcohol Depend* 2012;122(1-2):11-9. doi: 10.1016/j.drugalcdep.2011.
48. Notzon D, Pavlicova M, Glass A, Mariani J, Mahony A, Brooks DJ *et al.* ADHD is highly prevalent in patients seeking treatment for cannabis use disorders. *J Atten Dis* 2020;24(11):1487-92. doi: 10.1177/1087054716640109.
49. Ohlmeier MD, Peters K, Kordon A, Seifert J, Wildt BT, Wiese B *et al.* Nicotine and alcohol dependence in patients with comorbid attention-deficit/hyperactivity disorder (ADHD). *Alcohol Alcohol* 2007;42(6):539-43. doi: 10.1093/alcac/agg069.
50. Pomerleau OF, Downey KK, Stelson FW, Pomerleau CS. Cigarette smoking in adult patients diagnosed with attention deficit hyperactivity disorder. *J Subst Abuse* 1995;7(3):373-8. doi: 10.1016/0899-3289(95)90030-6.
51. Wilens TE. Attention-deficit/hyperactivity disorder and the substance use disorders: the nature of the relationship, subtypes at risk, and treatment issues. *Psychiatr Clin North Am* 2004;27(2):283-301. doi: 10.1016/S0193-953X(03)00113-8.
52. Rooney M, Chronis-Tuscano A, Yoon, Y. Substance Use in College Students With ADHD. *J Attend Disord* 2012;16(3): 221-234. doi: 10.1177/1087054710392536.
53. Wilens TE, Martelon M, Joshi G, Bateman C, Fried R, Petty C *et al.* Does ADHD predict substance-use disorders? A 10-year follow-up study of young adults with ADHD. *J Am Acad Child Adolesc Psychiatry* 2011 Jun;50(6):543-553. doi: 10.1016/j.jaac.2011.01.021.
54. Van De Glind G, Van Emmerik-van Oortmerssen K, Carpentier PJ, Levin FR, Koeter MW, Barta C *et al.* The International ADHD in Substance Use Disorders Prevalence (IASP) study: background, methods and study population. *Int J Methods Psychiatr Red* 2013 Sep;22(3):232-44. doi: 10.1002/mpr.1397.
55. Ilbegi S, Groenman AP, Schellekens A, Hartman CA, Hoekstra PJ, Franke B *et al.* Substance use and nicotine dependence in persistent, remittent, and late-onset ADHD: a 10-year longitudinal study from childhood to young adulthood. *J Neurodevel Disord* 2018 Dec;10(1):42. doi: 10.1186/s11689-018-9260-y.
56. Lee SS, Humphreys KL, Flory K, Liu R, Glass K. Prospective association of childhood attention-deficit/hyperactivity disorder (ADHD) and substance use and abuse/dependence: a meta-analytic review. *Clin Psychol Rev* 2011 Apr;31(3):328-41. doi: 10.1016/j.cpr.2011.01.006.
57. Lambert NM, Hartsough CS. Prospective study of tobacco smoking and substance dependencies among samples of ADHD and non-ADHD participants. *J Learn Disabil*. 1998 Nov-Dec;31(6):533-44. doi: 10.1177/002221949803100603.
58. Burke JD, Loeber R, Lahey BB. Which aspects of ADHD are associated with tobacco use in early adolescence? *J Child Psychol Psychiatry* 2001;42(4):493-502.
59. Miklenić G. Povezanost ADHD-a i konzumacije psihoaktivnih supstanci kod odraslih osoba (diplomski rad). Sveučilište u Zagrebu. Edukacijsko-rehabilitacijski fakultet, 2023.
60. Wilens TE, Biederman J, Mick E. Does ADHD affect the course of substance abuse? Findings from a sample of adults with and without ADHD. *Am J Addict* 1998;7(2):156-63.
61. Latimer WW, Stone AL, Voight A, Winters KC, August GJ. Gender differences in psychiatric comorbidity among adolescents with substance use disorders. *Exp and Clin Psychopharmacol* 2002;10(3):310-5. doi: 10.1037//1064-1297.10.3.310.
62. Ottosen C, Petersen L, Larsen JT, Dalsgaard S. Gender differences in associations between attention-deficit/hyperactivity disorder and substance use disorder. *J Am Acad Child Psychiatry* 2016;55(3):227-34. doi: 10.1016/j.jaac.2015.12.010.

63. Castellano-García F, Benito A, Jovani A, Fuertes-Sáiz A, Mari-Sanmillán MI, Haro G. Sex differences in substance use, prevalence, pharmacological therapy, and mental health in adolescents with attention-deficit/hyperactivity disorder (ADHD). *Brain Sci* 2022;12(5):590. doi: 10.3390/brainsci12050590.
64. Elkins IJ, Saunders GRB, Malone SM, Wilson S, McGue M, Iacono WG. Differential implications of persistent, remitted, and late-onset ADHD symptoms for substance abuse in women and men: a twin study from ages 11 to 24. *Drug Alcohol Depend* 2020;212:107947. doi: 10.1016/j.drugalcdep.2020.107947.
65. Sihvola E, Rose RJ, Dick DM, Korhonen T, Pulkkinen L, Raevuori A *et al.* Prospective relationships of ADHD symptoms with developing substance use in a population-derived sample. *Psychol Med* 2011;41(12):2615-23. doi: 10.1017/S0033291711000791.
66. McClernon FJ, Van Voorhees EE, English J, Hallyburton M, Holdaway A, Kollins SH. Smoking withdrawal symptoms are more severe among smokers with ADHD and independent of ADHD symptom change: results from a 12-day contingency-managed abstinence trial. *Nicotine Tob Res* 2011;13(9):784-92. doi: 10.1093/ntr/ntr073.
67. Squeglia LM, Tapert SF, Sullivan EV, Jacobus J, Meloy M, Rohlfing T *et al.* Brain development in heavy-drinking adolescents. *Am. J. Psychiatry* 2015;172 (6):531-42. doi: 10.1176/appi.ajp.2015.14101249.
68. Louth EL, Bignell W, Taylor CL, Bailey CD. Developmental ethanol exposure leads to long-term deficits in attention and its underlying prefrontal circuitry. *eNeuro* 2016;3(5). doi: 10.1523/ENEURO.0267-16.2016.
69. Squeglia LM, Gray KM. Alcohol and drug use and the developing brain. *Curr. Psychiatry Rep* 2016;18(5):46. doi: 10.1007/s11920-016-0689-y.
70. Coghill D, Toplak M, Rhodes S, Adamo N. Cognitive functioning in ADHD. *Oxford textbook of attention deficit hyperactivity disorder*. 2018, chapter 10, 94-102.
71. Luderer M, Quiroga JA, Faraone SV, Zhang-James Y, Reif A. Alcohol use disorders and ADHD. *Neurosci Biobehav Rev* 2021;128:648-60. doi: 10.1016/j.neubiorev.2021.07.010.
72. Weafer J, Fillmore MT, Milich R. Increased sensitivity to the disinhibiting effects of alcohol in adults with ADHD. *Exp. Clin. Psychopharmacol* 2009;17(2):113-21. doi: 10.1037/a0015418.
73. Wunderli MD, Vonmoos M, Niedecker SM, Hulka LM, Preller KH, Baumgartner MR *et al.* Cognitive and emotional impairments in adults with attention-deficit/hyperactivity disorder and cocaine use. *Drug Alcohol Depend* 2016;163:92-9. doi: 10.1016/j.drugalcdep.2016.03.026.
74. Carroll KM, Rounsaville BJ. History and significance of childhood attention deficit disorder in treatment-seeking cocaine abusers. *Compr Psychiatry* 1993;34(2):75-82. doi: 10.1016/0010-440x(93)90050-e.
75. Thompson LL, Riggs PD, Mikulich SK, Crowley TJ. Contribution of ADHD symptoms to substance problems and delinquency in conduct-disordered adolescents. *J Abnorm Child Psychol* 1996;24(3):325-347. doi: 10.1007/BF01441634.
76. Milberger S, Biederman J, Faraone SV, Chen L, Jones J. ADHD is associated with early initiation of cigarette smoking in children and adolescents. *J Am Acad Child Adolesc Psychiatry* 1997; 36(1):37-44. doi: 10.1097/00004583-199701000-00015.
77. McCabe SE, Dickinson K, West BT, Wilens TE. Age of onset, duration, and type of medication therapy for attention-deficit/hyperactivity disorder and substance use during adolescence: a multi-cohort national study. *J Am Acad Child Adolesc Psychiatry* 2016;55(6):479-86. doi: 10.1016/j.jaac.2016.03.011.
78. Young JT, Carruthers S, Kaye S, Allsop S, Gilseman J, Degenhardt L *et al.* Comorbid attention deficit hyperactivity disorder and substance use disorder complexity and chronicity in treatment-seeking adults. *Drug Alcohol Rev* 2015;34(6):683-93. doi: 10.1111/dar.12249.
79. Luderer M, Sick C, Kaplan-Wickel N, Reinhard I, Richter A, Kiefer F *et al.* Prevalence estimates of ADHD in a sample of inpatients with alcohol dependence. *J Atten Disord* 2020;24(14):2072-2083. doi: 10.1177/1087054717750272.
80. Wunderli MD, Vonmoos M, Niedecker SM, Hulka LM, Preller KH, Baumgartner MR *et al.* Cognitive and emotional impairments in adults with attention-deficit/hyperactivity disorder and cocaine use. *Drug Alcohol Depend* 2016;163:92-9. doi: 10.1016/j.drugalcdep.2016.03.026.
81. Rhodes JD, Pelham WE, Gnagy EM, Shiffman S, Derefinko KJ, Molina BS. Cigarette smoking and ADHD: An examination of prognostically relevant smoking behaviors among adolescents and young adults. *Psychol Addict Behav* 2016;30(5):588-600. doi: 10.1037/adb0000188.
82. Sanchez-Garcia NC, Gonzalez RA, Ramos-Quiroga JA, van den Brink W, Luderer M, Blankers M *et al.* Attention Deficit Hyperactivity Disorder Increases Nicotine Addiction Severity in Adults Seeking Treatment for Substance Use Disorders: The Role of Personality Disorders. *Eur Addict Res* 2020;26(4-5):191-200. doi: 10.1159/000508545.
83. McClernon FJ, Kollins SH, Lutz AM, Fitzgerald DP, Murray DW, Redman C, Rose JE. Effects of smoking abstinence on adult smokers with and without attention deficit hyperactivity disorder: results of a preliminary study. *Psychopharmacology (Berl)* 2008;197(1):95-105. doi: 10.1007/s00213-007-1009-3.
84. Covey LS, Manubay J, Jiang H, Norkick M, Palumbo D. Smoking cessation and inattention or hyperactivity/impulsivity: a post hoc analysis. *Nicotine Tob Res* 2008;10(12):1717-25. doi: 10.1080/14622200802443536.
85. Humfleet GL, Prochaska JJ, Mengis M, Cullen J, Munoz R, Reus V *et al.* Preliminary evidence of the association between the history of childhood attention-deficit/hyperactivity disorder and smoking treatment failure. *Nicotine Tob Res* 2005;7(3):453-60. doi: 10.1080/14622200500125310.
86. Schellekens AF, van den Brink W, Kiefer F, Goudriaan AE. Often overlooked and ignored, but do not underestimate its relevance: ADHD in addiction—addiction in ADHD. *Eur Addict Res* 2020;26(4-5):169-72. doi: 10.1159/000509267.
87. Kalbag AS, Levin FR. Adult ADHD and substance abuse: diagnostic and treatment issues. *Subst Use Misuse* 2005;40(13-14):1955-8. doi: 10.1080/10826080500294858.

88. Cadet JL, Bisagno V. Neuropsychological consequences of chronic drug use: relevance to treatment approaches. *Front Psychiatry* 2016; 6:189. doi: 10.3389/fpsy.2015.00189.
89. Martinez-Raga J, Szerman N, Knecht C, de Alvaro R. Attention deficit hyperactivity disorder and dual disorders. Educational needs for an underdiagnosed condition. *Int J Adolesc Med Health* 2013; 25(3), 231-43. DOI 10.1515/ijamh-2013-0057
90. Steinhausen HC, Bisgaard C. Substance use disorders in association with attention-deficit/hyperactivity disorder, co-morbid mental disorders, and medication in a nationwide sample. *Eur Neuropsychopharmacol* 2014;24(2):232-241. doi: 10.1016/j.euroneuro.2013.11.003.
91. Schoenfelder EN, Kollins SH. Prevention of health risk behaviors in ADHD youth: Is ADHD treatment enough? *ADHD Report* 2014;22(4):1-8.
92. Zaso MJ, Park A, Antshel KM. Treatments for adolescents with comorbid ADHD and substance use disorder: A systematic review. *J Attend Disord* 2020;24(9):1215-26. doi: 10.1177/1087054715569280.
93. Zulauf CA, Sprich SE, Safren SA, Wilens TE. The Complicated Relationship Between Attention Deficit/Hyperactivity Disorder and Substance Use Disorders. *Curr Psychiatry Rep* 2014;16(3)436. doi: 10.1007/s11920-013-0436-6.