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# Possible correlations between cocaine use, generalized anxiety and panic disorders in adolescents and young adults: a review of the literature

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## ABSTRACT

**BACKGROUND:** Substance use disorders have been associated with a vast range of harmful behaviors. The purpose of this review is to evaluate the possible correlations between anxiety disorders, especially generalized anxiety disorder (GAD), panic disorder (PD), panic attacks and cocaine use among adolescents and young adults.

**METHODS:** A literature search was conducted to evaluate pertinent studies up to July 06, 2020 in Google Scholar, PubMed, Embase and PsycInfo databases.

**RESULTS:** A total of 20 articles were considered eligible; most studies reported that young people who experienced PD, panic attacks or GAD were more likely to have been cocaine users, with the risk being higher when individuals were addicted.

**CONCLUSIONS:** The association between cocaine use, PD and GAD, poses significant challenges to health providers of adolescents and young adults, as comorbidity complicates the treatment, prognosis and course of the disorders.

**Key Words:** *Panic disorder; generalized anxiety disorder; cocaine use; substance use; adolescents*

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## Introduction

Substance use and substance use disorders (SUDs) are vital public health problems [1], as they are associated with a vast range of harmful behaviors, besides premature mortality [2]. Numerous studies indicate a positive correlation between problematic substance use and psychiatric disorders [3,4]. People diagnosed with a psychiatric disorder are twice and four times as likely to be diagnosed with an alcohol and drug use disorder, respectively, compared with patients without a psychiatric disorder [5]. The underlying causes have not been adequately studied, but one interpretation could entail substance use as self-medication [6,7]; however, the chronological relationship between substance use and psychiatric disorders is controversial. Legal or illicit substance use has been associated with anxiety disorders [8-12].

Anxiety disorders include a range of clinical syndromes, such as panic disorder (PD), generalized anxiety disorder (GAD), social anxiety disorder (SAD), obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD) and agoraphobia [4,13]. All of the above conditions, although characterized by anxiety, nervousness, tension and a variety of physical symptoms, each have specific psychopathological characteristics [14]. The overall prevalence of anxiety disorders, in the general population, is high. According to population surveys, up to 33.7% of people are affected by an anxiety disorder during their lifetime, but there is a natural decrease with advancing age [15, 16].

The hallmark of PD is the recurrence and unexpected seizures of severe anxiety, known as panic attacks. Panic attacks are characterized by physical and cognitive symptoms, such as sweating, shortness of breath, tachycardia, tremor, which emerge precipitously and reach their peak within 10 minutes [4]. The prevalence of PD, globally, ranges from 1.7 to 3.7% [17,18]. A diagnosed panic disorder may be present with or without agoraphobia [4]. Agoraphobia usually develops in response to panic attacks. The main feature of agoraphobia is the manifestation of anxiety when the person is in situations or places where help – in case of an unexpected panic attack – may not be available or escape may be difficult [19].

GAD, is a relatively common and debilitating anxiety disorder characterized by excessive stress and anxiety in various aspects of life. Although pathological anxiety is the main feature of this disorder, most

patients experience multiple physical symptoms, such as tension, irritability, fatigue, sleep disturbances, sweating, dizziness, palpitations and difficulty concentrating [20]. Anxiety disorders and substance use have been studied by many researchers, with many studies investigating the causal link between a particular type of anxiety disorders and the legal and / or illicit substance use. Proper recognition of anxiety disorder is very important for an effective intervention given the high rates of comorbidity [4]. According to the available literature, the correlation between anxiety disorders and substance use / abuse is often seen in people who experience negative emotions and, consequently, use these substances as a form of treating and relieving anxiety symptoms [21,22]. On the contrary, studies have also shown that substance use can affect the development of psychiatric disorders [23].

The use of cocaine, powder or crack, by high school students, has an annual prevalence (used at least once during the previous year) of about 7% globally [23,24]. Its use had been more frequent in the mid-1980s (above 14%), probably due to a decrease in heroin availability, and increased availability and affordable price of cocaine [25,26]. A lower incidence was recorded in the early 90's (almost 4%), and has an average of about 7% per year prevailing in the new century [23]. Cocaine use and cocaine use disorder (CUDs) have been associated with a number of adverse effects, such as increased vulnerability to serious medical conditions or infections, increased hospitalization, and even death [27-30].

Anxiety and mood disorders are closely linked to CUDs. In particular, cocaine use can cause panic attacks, phobic reactions, compulsions and obsessions, which may persist after cessation of use [31-33]. The comorbidity between cocaine use and social phobia [34] and post-traumatic stress disorder [35,36] tends to occur among people with severe cocaine use / abuse and family or personal history of disorders [37]. Cocaine users seeking treatment also report significant levels of anxiety and panic, as a side effect of cocaine use [31,38].

Thus, the purpose of the present review is to identify and highlight through the available literature the possible correlations between anxiety

disorders, especially GAD, PD and panic attacks, and cocaine use among adolescents and young adults.

## Methods

### *Data Sources*

A literature review was conducted in the following electronic databases: Google Scholar, PubMed, Embase and PsycInfo, with end-of-search date July 06, 2020. The following search algorithm was used: (cocaine OR coke OR bernice OR crack OR blow OR “crack cocaine”) AND (teens OR teenagers OR adolescence OR adolescent OR adolescents OR “young adults” OR “younger adults” OR youthful OR youngster OR young) AND (“generalized anxiety disorder” OR GAD OR “panic disorder” OR “panic attack”). Snowball method was moreover utilized to scan reference records of retrieved full-content articles in order to search manually for additional relevant literature.

### *Eligibility Criteria, Data Extraction, Analysis*

The inclusion criteria for this review are the following:

1. Articles written in English.
2. Studies should be conducted only on humans
3. Articles published at any time
4. Original research articles and studies were selected (cross-sectional, case series / control, clinical and cohort studies). Case reports, dissertations, conference posters and newspaper articles were excluded
5. Anxiety disorders or symptoms (GAD, PA, PD) data could be measured by self – reported surveys, diagnostic criteria (DSM – III, DSM – III – R, DSM – IV, ICD – 10), standardized scales or diagnosed by healthcare professionals
6. Cocaine use or cocaine use disorder data should be presented, analyzed and discussed in eligible studies and an association with either GAD or PA and PD should be reported. Studies which included cocaine users who developed any other anxiety disorder, except GAD, PA and PD, were excluded.
7. Population spanning adolescents (14 – 17 years) or young adults (< 30 years)

No limitations, such as ethnicity, country or journal, were considered.

Using these criteria, two independent reviewers (P.I and K.E) screened the titles and the abstracts of the retrieved articles. After this initial screening, the relevant

full texts were read, and the ones that met the inclusion criteria were collected.

From the analysis, the following data were extracted for each study: PMID or DOI, name of first author and year of publication, region / country where the study was conducted, language, study period and design, sample size and selection of sample, percentage of males, mean age and age range, study population, statistical analysis, type and assortment of cocaine use, time of cocaine use, assessment for diagnosis of GAD and panic disorder and correlation between cocaine – GAD, cocaine – panic disorder.

## Results

### *Study selection*

After the search in databases, 3620 articles were retrieved in total, including duplicates. After removal of duplicates (n = 3010), 610 items were selected for extensive review. From them, 457 items were excluded as irrelevant to the topic and three articles as reviews. The remaining 150 full – text articles were subjected to further consideration; of them, two articles were excluded because of language. Finally, 20 articles were included in the review [2-4,13,23,25,27,31,33,40-51]; half of them (n = 10) were cross-sectional [2-3,13,23,25,33,40,45,46,50], seven were case-control [27,31,43,47-51], two were cohort studies [41,44], and one was case- crossover [42]. The included relevant studies are presented in Table 1.

### *Descriptive Analysis of the Included Studies*

Based on geographical distribution, the studies investigated the following populations: 15 studies were conducted in the USA [2, 23, 27, 31, 33, 40-44, 47-51], four studies presented data from Brazil [4,13,45,48] and one study included participants from Spain [25]. Eight studies enrolled young adults between 18 and 30 years old [13, 25, 33,41,43-45,47], four studies enrolled participants >18 years old [2,31,50, 51], three studies included only adolescents between 14 and 18 years old [4,23,46] and one study included adolescents and young adults > 14 years old [42]. However, three studies used a wide age range criterion including adolescents, young adults and adult participants [27,40,48], whereas another study referred to adults in general, without further study referred to adults in general, without further specification [49].

**Table 1: Eligible studies – examining association between cocaine use and panic disorder or / and generalized anxiety disorder – Demographic characteristics**

First author (year)	Region, Country	Language	Study Period	Study Design	Sample Size	Percentage of males	Mean age	Age Range
Sareen et al., 2006	USA, Ontario	English	Early 1990s	Cross-sectional	NCS (n=5877), OHS (n=8116)	Not reported	Not reported	NCS 15 – 54 OHS 15 – 64
Alvarado et al., 2010	USA	English, France, Spanish	2000 – 2002	Cohort study	1692	46.7% (2000 – 2002)	21 years	18 – 22 years
Valentiner et al., 2004	USA	English	2004	Cross-sectional	399	Not reported	18.4 years	18 – 24 years (young adults)
O'Brien et al., 2005	USA	English, France, Spanish	1994 – 1997	Case – crossover	1071	Not reported	Not reported	Youth was 12 – 17 years and 18 years and older
Deacon et al., 2000	USA	English	2000	Case – control	279	52%	19.7 years	Young adults
Newcomb et al., 1987	USA – Los Angeles	English	1980 – 1984	Cohort study	739	30%	21.5 years	19 – 24 years
Kligus & Pumariega, 2009	USA – South Carolina	English	2009	Cross-sectional	31	23 boys from 31	16 years	14 – 17 years
Narvaez et al., 2014	Pelotas, southern Rio Grande do Sul, Brazil	English	Not reported	Cross-sectional	1560	82.1%	Not reported	18 – 24 years
Ohanessian, 2014	USA	English	Spring of 2007	Cross-sectional	905	54%	16.1 years	15 – 17 years
Buckner et al., 2011	USA, Washington, DC	English	Not reported	Case – control	304	58.6%	43 years	19 – 66 years
Mackesy – Amuti et al., 201	USA, Chicago	English	Not reported	Case – control	570	62%	23 years	18 – 25 years
Zubaran et al., 2013	Brazil	English	Not reported	Case – control	100	88%	20.1 years	11 – 40 years
Ziordonis et al., 1994	USA	English	June 1986 – July 1988	Case – control	263	74% White, 61% African America	27 White, 29 African American	Adults
Conway et al., 2006	USA	English	2001 – 2002	Cross-sectional	43093	Not reported	Not reported	18 years and older
De matos et al., 2018	Brazil	English	2007 and 2009	Cross-sectional	1560	43.6%	21 years	18 – 24 years
Pires et al., 2014	Brazil	English, Spanish	July 2009 – December 2009	Cross-sectional	1081	28.7%	Not reported	14 – 19 years old (adolescent)
Herrero et al., 2008	Barcelona, Spain	English	End of 2003 – 2006	Cross-sectional	139	62.6%	23.8 years	18 – 30 years
Bianco et al., 2018	USA	English	2001 – 2002	Cross-sectional	43093	Not reported	Not reported	18 years or older
Anthony et al., 1989	USA	English	1980 – 1984	Case-control	5896	Not reported	29.7 years	18 – 44 years
Weiss et al. 1986 [	USA	English	Not reported	Case-Control	30	63.3%	29.7±5.8 years	21-42 years

\* NESARC: National Epidemiological Survey of Alcohol and Related Conditions, UCPel: Universidade Católica de Pelotas

Regarding gender distribution in the included studies, eight studies did not report the gender distribution [2,31,33,40,42,49-51], and the other 12 studies recruited both male and female participants [4, 13, 23, 25, 27, 41, 43, 44-48]. Among the latter, five investigated mainly male participants [23,25,45,47,48], whereas two studies investigated mainly female participants (more than 60% males or females in the population, respectively) [4,44], and five studies demonstrated an approximately balanced male – female ratio [13,27,41,43,46].

### Assessment of cocaine use

The majority of the studies used questionnaires (interviews), whereas others used screening tests or medical records to establish the cocaine use. Specifically, 15 studies used interviews [2,27,31,33,40-43,45, 48-50], one used history data which were obtained from self-

report questionnaire [51], four studies used rating scales [44,46] or screening tests [4,13] to check current and lifetime substance use and two studies did not report their methods [23,25].

Most researchers created a drug use questionnaire using the drug category sheet in the Structured Clinical Interview and asked the respondents to answer “yes” or “no” to the question regarding ever use of any form of cocaine, including crack, snorting, powder, leaves, free base, or coca paste, even once [27,33,40,41,43,49,50]. One study used psychiatric interview to evaluate the main addictive substance and the one causing the most salient dependence [48], whereas one study used the National Household Surveys on Drug Abuse (NHSDA) questions to define cocaine use, include crack or smoking, in the past month or in the past 12 months [42]. In addition, one

study administered all participants to Mini International Neuropsychiatric Interview (MINI), a clinical interview based on DSM – IV and ICD – 10 criteria for the diagnosis of Axis I disorders (Narvaez et al., 2014), one study used an audio computer – assisted self – interview (ACASI) to assess drug use among other parameters [48] and one study used Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM – IV (AUDADIS – IV) for advance measurement of substance use and mental disorders [2].

Moreover, two studies used rating scale to evaluate the frequency of cocaine use during the past 6 months with the following categories: (1) “Never”, (2) “Once or Twice”, (3) “A few times”, (4) “Once a month”, (5) “Once a week”, (6) “Once a day” and (7) “More than once a day” [44,47]. One study used screening test, and especially the self – applied Alcohol Smoking and Substance Involvement Screening Test (ASSIST 2.0/OMS), to evaluate the frequency of use and the possible dependence in a list of several legal or illicit psychoactive / psychotropic substances, included crack cocaine [4,13].

### ***Establish Panic Disorder / Generalized Anxiety Disorder Diagnosis***

The majority of the studies used DSM – III / DSM – III R (n = 5) [23,40,44,49,51] and DSM – IV / DSM – IV – TR / ICD – 10 (n = 7) [2,27,45, 47,48,50] criteria to establish GAD diagnosis. Moreover, one study used 41 item Screen for Child Anxiety Related Disorders (SCARED) [46], to assess a child’s recent anxiety symptoms and one study Mini International Neuropsychiatric Interview (MINI) [13] to evaluate the number of stressful events during the last year, whereas 7 studies did not report the diagnostic method [4,25,31,33,41-43]. Similarly, the majority of studies used DSM – III / DSM – III – R (n = 5) [23,40,41,44,49] and DSM – IV / DSM – IV – TR / ICD – 10 (n = 10) [2,25,27,33,42,43,45, 47,48,50] criteria to establish PD diagnosis. Furthermore, one study applied diagnostic interview schedule [31], one study used SCARED [47] and one used MINI [4]. Two studies did not report the diagnostic method [13, 51].

### ***Panic Disorder***

Herrero et al., (2008) [25] with their study highlighted the moderately high incidence of psychiatric comorbidity (42.4%, CI 34 – 51%) in a sa-

-mple of young cocaine users that were recruited on the street. The most common Axis I disorders were mood disorders (26.6%) and anxiety disorders (13%), with panic disorder correlated 4.3% [25].

The majority of studies observed correlations between cocaine use and PD. Conway et al., (2006) [50] found virtually positive and statistically significant (p < 0.05) associations between specific cocaine and anxiety disorders, especially PD with agoraphobia. A few years later, Pires et al., (2014) [4], also found a strong relation between panic disorder and substance use (included cocaine or / and crack). Especially, subjects who used – at least once – one of the substances, showed at least two times higher likelihood to have current panic disorder [4].

According to one study [44] several significant relationships were observed between cocaine use and indicators of psychopathology, including panic and phobia symptoms, but a negative association was found between cocaine use and panic / phobia symptoms and panic disorder diagnosis. Especially the authors indicated that females with a panic / phobia disorder were significantly less likely to have used substances that may impair their thought processes and motor behavior, or diminish their sense of control, such as cocaine.

### ***Panic attacks***

Antony et al., (1989) [31] showed statistically significant associations between the risk of panic attack and use of cocaine (RR = 3.2). Subjects who had used cocaine during follow – up were 14 times more likely to experience a panic attack, as compared with subjects who did not use cocaine during the follow – up interval (CI 2.4 – 85.6) [31]. Similarly, O’ Brien et al., (2005) [42], based on case – crossover estimates, demonstrated that cocaine use was associated with a 3 – to – 4 – fold increased occurrence of panic attack (RR = 3.3, p = 0.049, CI 1.0 – 13.7) [42]. Same results were found from the study by Alvarado et al., (2010) [41], that revealed a modest, but statistically robust association linking use of cocaine at least once with the occurrence of a panic attack – like experience (OR = 1.9, p = .003) [41].

On the contrary, Deacon et al., (2000) [43], indicated that non – clinical panickers were not more likely than non – panickers to report having used cocaine. These results suggested that the use of cocaine is probably

not inducing many panic attacks in non-clinical populations [43]. Correspondingly, Valentiner et al., (2004) [33] did not find a strong relationship between panic attacks and cocaine use, with the results showing that panickers were significantly more likely to report sedative / opioid / stimulant and other drug use, whereas, were not significantly more likely to report alcohol / tobacco / cannabis / hallucinogen and cocaine use, compared with non-panickers. Even more than that, the results did not find any correlation between number and severity of panic attacks among panickers who did and did not report substance use, especially cocaine use [33].

### **Generalized Anxiety Disorder**

Weiss et al., (1986) [51] found that the rate of affective disorder in the sample of hospitalized chronic cocaine abusers was found to be significantly higher (3.3%) than that in a group of opiate and depressant abusers admitted to the same facility [51]. It is worthy to note that the prevalence of each anxiety disorder was consistently much higher among respondents with dependence than for those with abuse (eg cocaine use disorder and GAD = 10.4%, cocaine abuse and GAD = 8.1%, cocaine dependence and GAD = 14.7%). Among gender, the associations between specific anxiety disorders and drug use disorders were nearly all positive and statistically significant, and few gender differences were observed (eg the associations between panic disorder with agoraphobia and cocaine dependence were greater for men than for women) [51]. Sareen et al., (2006) [40], who conducted two surveys found that among those with lifetime use of cocaine, among other drugs, approximately one-third of participants had at least one lifetime anxiety disorder diagnosis (OR 2.0) (NCS OR 2.39 for GAD and OHS OR 1.39 for PD) [40].

The results from the study of Kilgus and Pumariega (2009) demonstrated that cocaine-preferring adolescents have higher comorbidity and more anxiety disorders (GAD 9.7%) than the general population of adolescents. Additionally, more boys met threshold criteria for anxiety disorders (43% vs. 25%); overanxious and generalized anxiety disorders were reported together. Same results demonstrated to study of Narvaez et al., (2014) [45], who also found a strong association between lifetime crack cocaine use, substance use disorders and psychiatric disorders, included generalized anxiety disorder (20.5%) among

other [45].

Zubaran et al., (2013) [48] investigated anxiety symptoms among inhalant cocaine user and crack cocaine users and found that both crack and inhalant users encounter critical side effects of anxiety, with inhalant users presented significantly more anxiety symptoms than crack users. Particularly, 90% crack users and 53.1% of inhalant users demonstrated the absence or low levels of anxiety whereas 10% and 46.9% demonstrated the presence of anxiety, respectively. Among crack and inhalant users who experienced anxiety, 4% and 28.6% presented light to moderate levels of anxiety, while 6% and 18.4% presented moderate to severe levels of anxiety, respectively [49]. In contrast, de Matos et al., (2018) [13] indicated a scare relationship between crack cocaine use and GAD (the prevalence of GAD was significantly higher among those who abused / were dependent on stimulant substances like crack cocaine [2%]) [13].

Ziedonis et al., (1994) [49], who studied the psychiatric comorbidity and differences in current and lifetime rates for specific disorders among African-American and White cocaine users, discovered that the current and lifetime rates both for psychiatric disorders and cocaine use disorders did not differ significantly for the two racial groups. Whereas, compared with African Americans, Whites had altogether higher rates of lifetime attention deficit disorder, major depression, alcohol dependence and conduct disorder, while African-American addicts, especially women, were more likely to meet criteria for a current diagnosis of anxiety disorders and phobia [49]. On the other hand, both men and women cocaine users reported frequently feelings of nervousness, tenseness and restlessness (anxious mood and diagnosis of GAD), among other symptoms such as low interest or / and energy, depressed mood, psychotic proneness, impaired cognitive functions, sleep disturbance, lack of purpose in life, etc.[44].

Similarly, according to one study of Ohannessian et al., (2014) [46] the relationship between anxiety and substance use differs by sex and ethnicity / race. Especially, for African-American and Caucasian boys, higher levels of social and separation anxiety were related to less substance use. In contrast, higher levels of generalized anxiety disorder and panic disorder were related with more substance use for African-American boys. However, none of the anxiety disorders were related to substance use for African-American girls or

or Hispanic girls or boys [46].

### **Discussion**

Many of the investigated studies in this review found that adolescents and young adults who reported using of cocaine, have experienced PD or / and GAD, with risk being higher when individuals are addicted compared to use of cocaine [4, 13, 23, 25, 33, 40, 44, 45, 48, 50, 51]. In contrast to the studies that have documented positive relationship between cocaine use and PD / GAD, particularly, some studies have not identified an increased likelihood of anxiety disorders among cocaine users and non – users [33,44].

Large – scale epidemiological studies in US and European adult populations with SUDs [52,53], as well as community and clinical studies on substance – abusing / using youth people [54,55], reported a higher incidence of substance – related psychiatric disorders. This situation is so – called “Dual Diagnosis” [56]. The term “Dual Diagnosis” is used by many physicians to categorize patients diagnosed with both SUDs and psychiatric disorders. Patients with dual diagnosis constitute very heterogeneous groups, with many possible combinations of two or more diagnosed SUDs and psychiatric disorders. Therefore, they are associated with poor prognosis in treatment options. It should be noted that previous studies have recognized the need for new therapeutic approaches to address both problematic situations [38, 49]. One explanation for this dual diagnosis often point out that many people may use psychoactive substances to reduce negative emotions such as anxiety, panic attacks and depression [11]. Another explanation for high rates of dual diagnosis is that certain substances can cause panic attacks or other negative emotions [11,57].

Cocaine use and cocaine use disorder (CUDs) remain serious public health concerns. Cocaine use has also been associated with a number of adverse effects, such as increased vulnerability to serious medical conditions or infections, increased hospitalization, and even death [27-30]. However, although cocaine is a widely abused drug, it is not adequately studied in adolescent populations [23]. Given that both SUD and anxiety disorders often begin after adolescence, it is not surprising that there is some evidence that substance use behaviors and symptoms of anxiety disorders coexist during late adolescence [58].

Many of the investigated studies in this review found that adolescents and young adults who reported having experienced psychiatric disorders were more likely to report using sedatives, opioids, stimulants and other drugs, included cocaine. In particular, anxiety disorders, including PD and GAD, were the most prevalent mental disorders among cocaine users, with the risk being higher when individuals are addicted compared to use of cocaine. This strong association is consistent with the finding that the severity of these psychiatric conditions is positively correlated with the progression from abuse to addiction, as well as, with heavier use patterns [4,13,23,25,33,40,44,45,48,50,51].

Even so, the main evidence of the present review indicates that cocaine use in these age groups is associated with increased risk of developing panic attacks, as compared with non – cocaine use [31,41,42], a finding which is supported by clinical observations and laboratory data on the pharmacological activity of the drug [59]. Based on present and previous studies and case reports, cocaine use was associated with 3.3 – fold elevated incidence of panic attacks [31].

Furthermore, results from multiple – group analyzes showed that the relationships between anxiety and substance use differ by gender, ethnicity and race. In particular, higher levels of predicted GAD and PD symptoms and substance use were more common among African – American boys, followed by Caucasian youth. [46, 51].

In contrast to the studies that have documented positive relationship between cocaine use and psychiatric disorder in adolescents/young adults, particularly anxiety disorders (included GAD and PD), some studies have not identified an increased likelihood of anxiety disorders among cocaine users and non – users [33,44,58].

Although the present results revealed a number of correlations between cocaine use and psychiatric comorbidities, particularly anxiety disorders (PD and GAD), they were unable to identify the causal link between them. A reasonable hypothesis for this relationship is that they share similar predisposing factors or are subject to a common underlying pathology. A third explanation for the present findings includes the idea of using drugs as a form of self – medication to relieve the symptoms of a pre – existing disorder [33, 45], although long-term, drug use can worsen these symptoms [45].

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