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Psychoses Induced by Synthetic Cathinone Use

Yuldasheva Khurziyo Fakhiddinovna[1,*], Khayredinova Ilnara Ilgizovna[2]

[1]Head of the Compulsory Treatment Department at the Tashkent Regional Branch of the Republican Specialized Scientific-Practical Medical Center for Mental Health, Narcology Service, Tashkent, Uzbekistan
[2]PhD., Senior Lecturer at the Department of Psychiatry and Narcology, Tashkent Medical Academy, Head of the Department of Narcology and Toxicology at the Republican Specialized Scientific-Practical Medical Center for Mental Health, Tashkent, Uzbekistan

Abstract **Relevance.** In recent years, there has been an increase in the use of synthetic cathinones, which are a group of novel psychoactive substances. One of the most significant consequences of their use is the development of psychotic disorders; however, the relationship between synthetic cathinones and psychosis remains insufficiently studied. **Objective.** To conduct a systematic literature review aimed at identifying and summarizing data on the impact of synthetic cathinone use on the development of psychoses, as well as to clarify the features of this association and the possible mechanisms involved. **Methods.** A literature search was conducted in the PubMed and Google Scholar databases (2013–2024), including studies containing information on psychotic symptoms in patients who used synthetic cathinones. The analysis included works describing clinical cases with confirmed use of synthetic cathinones and the development of psychotic disorders. Articles without specific data on the substances used or psychiatric symptoms were excluded. **Results.** The final sample included 15 studies analyzing 29 cases of psychosis induced by synthetic cathinone use. The most common symptoms were hallucinations (41%) and delusional disorders (28%). Nearly half of the patients (48%) exhibited psychomotor agitation and aggression. Psychosis was registered in men in 86% of the cases, with a median age of 29 years. Psychosis most frequently developed after the use of MDPV, α-PVP, and mephedrone. **Discussion.** The findings confirm that synthetic cathinones have a high potential to induce psychoses, causing acute hallucinatory-delusional disorders with a high incidence of aggression and suicidal behavior. Cathinone-induced psychoses resemble amphetamine and cocaine psychoses in their clinical presentation but are often accompanied by more pronounced emotional disturbances. Polysubstance abuse and pre-existing psychiatric disorders are identified as risk factors increasing the likelihood of psychotic episodes. **Conclusions.** The use of synthetic cathinones is associated with the risk of both acute and chronic psychosis. While compounds in this group share similar activity, they differ in symptom severity. The findings highlight the need for early diagnosis, preventive measures, and further research into the mechanisms underlying cathinone-induced psychosis.

Keywords Synthetic cathinones, Psychosis, Hallucinations, Delusions, Polysubstance abuse, Mental disorders, Psychostimulants

1. Introduction

In recent decades, the spread of novel psychoactive substances (NPS) has become one of the major challenges in modern psychiatry and addiction medicine [1]. Among NPS, synthetic cathinones hold a particularly significant place. Synthetic cathinones are a class of psychoactive substances that are derivatives of the natural compound cathinone, which is found in the plant *Catha edulis* (khat), native to East Africa and the Arabian Peninsula [2]. Chemically, cathinone is the β-ketone analogue of amphetamine, which is why it is often referred to as a "natural amphetamine." This structural similarity explains its strong stimulant properties and its impact on the central nervous system, comparable to amphetamines and other psychostimulants.

Synthetic cathinones first appeared on the market in the early 21st century and were initially sold under various commercial names to circumvent legal restrictions. They were marketed as "bath salts," "plant fertilizers," "carpet cleaners," "stain removers," and other similar products not intended for human consumption [3]. These substances were readily available online, in specialty shops, tobacco stores, gas stations, and adult stores, which contributed to their popularity among users [4,5]. Manufacturers often labeled the packaging with phrases like "not for human consumption," "research chemicals," or "for external use only" to avoid regulatory oversight [3,6].

By the early 2010s, due to an increasing number of toxic reactions, acute psychoses, and fatal outcomes associated with synthetic cathinone use, several countries, including the United States and various European nations, began banning their legal sale [7]. In 2011, several synthetic cathinones

* Corresponding author:
hurziuldaseva@gmail.com (Yuldasheva Khurziyo Fakhiddinovna)
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were added to the list of controlled substances in the U.S., followed by similar measures in other countries. Despite these restrictions, online sales remain active, and the illicit market continues to offer new synthetic cathinone derivatives, complicating efforts to control their distribution.

Because of their initial legal status, these substances were also known as "legal highs" and were often perceived by users as a safer alternative to other popular stimulants such as cocaine and amphetamine [8]. Additionally, each product package may contain a different amount or even type of drug than what is listed on the label, meaning that users often do not know exactly what or how much they are consuming [6].

The stimulant effects of synthetic cathinones are explained by their action on the brain's neurotransmitter systems, particularly their impact on dopamine, norepinephrine, and serotonin levels. Like amphetamines, synthetic cathinones enhance the release of monoamines and inhibit their reuptake, leading to increased arousal, euphoria, and heightened motor activity [9]. However, their effects are accompanied by serious side effects, including psychotic disorders, anxiety, aggression, paranoia, and cognitive impairments.

One of the most concerning aspects of synthetic cathinone use is their potential to induce psychotic disorders. Research shows that acute psychosis may develop during intoxication with these substances, characterized by hallucinations, delusions, paranoid ideation, agitation, and aggressive behavior. In some cases, psychotic symptoms persist over time, potentially leading to lasting mental disturbances resembling endogenous psychoses.

Despite a significant number of clinical observations, the relationship between synthetic cathinone use and the development of psychotic disorders remains insufficiently understood. Several key questions remain: What is the prevalence of psychosis among synthetic cathinone users? What symptoms dominate the clinical presentation of cathinone -induced psychosis? Are there differences in psychotic manifestations depending on the specific compound used? What role do pre-existing mental disorders and polysubstance abuse play in the development of these conditions?

Objective of the Study.

This study presents a systematic literature review aimed at identifying and summarizing existing data on the relationship between synthetic cathinone use and the development of psychosis, as well as clarifying the characteristics of this association and possible underlying mechanisms.

2. Materials and Methods

The authors conducted a comprehensive literature search to identify all relevant scientific articles describing cases of synthetic cathinone abuse that included sufficiently detailed information on acute and chronic psychiatric symptoms and/or disorders.

The search was carried out in the PubMed and Google Scholar databases, covering all publications from January 1, 2013, to July 1, 2024.

Search queries included the class of synthetic cathinones, individual substances from the synthetic cathinone group, and the associated mental health symptoms. Specifically, the following keywords were used (individually or in combination): *"synthetic cathinones," "mephedrone," "alpha-PVP."*

In addition, terms describing psychopathological outcomes of use were employed, such as *"psychotic disorders," "mental disorders," "substance use disorders," "substance abuse," "hallucinations," "delusions."* Descriptors for major psychiatric diagnoses were also included: *"schizophrenia," "bipolar disorder," "major depressive disorder," "anxiety disorders," "post-traumatic stress disorder."*

Potentially relevant studies were also selected manually by reviewing the reference lists of the screened and selected publications.

Inclusion criteria covered only studies that described a correlation between synthetic cathinone use and psychopathological outcomes. Included studies had to provide sufficient details about the case history, and synthetic cathinone presence had to be confirmed either through toxicological analysis or reported by the patient or their relatives. Studies published in English and Russian were considered.

Exclusion criteria included works that provided generalized data without specifying the psychoactive substance used, review articles, book chapters, books, symposium materials, letters to the editor, and studies unrelated to the topic.

Article selection was carried out in several stages. Initially, titles and abstracts were screened to remove duplicates and studies that did not meet the inclusion criteria. Articles that failed to meet criteria based on their abstract were excluded. The remaining publications underwent a full-text review to determine their eligibility. Additionally, cross-references from the selected studies were analyzed. Duplicate entries and irrelevant studies were removed. Following the final analysis, 15 studies that met the inclusion criteria were selected and included in the final list.

3. Results

In the 15 studies included in the final selection [10–24], a total of 29 cases of synthetic cathinone use were reported.

Frequency and Nature of Psychotic Symptoms

Analysis of the collected cases revealed that hallucinations and delusional disorders are the most frequently occurring symptoms following the use of synthetic cathinones. Hallucinations—primarily visual and, less frequently, auditory—were observed in approximately 12 out of 29 cases (~41%). Delusional symptoms, mainly of a paranoid nature (persecutory ideas, ideas of reference, etc.), were present in around 8 patients (~28%). In some reports, explicit mention of delusions was absent; however, paranoid behavior and pronounced suspiciousness were noted, which essentially reflect a delusional mindset.

In addition to classic psychotic manifestations, nearly half of the cases were accompanied by marked agitation and aggression. In 14 patients (~48%), psychomotor agitation or aggressive behavior (often both simultaneously) were present. A considerable number of patients also demonstrated disorganized behavior: in approximately 24% of cases, bizarre actions or incoherent speech were reported during the peak of psychosis.

Some episodes involved behavior dangerous to the patient themselves—for example, in one case, self-injury (auto-aggression) was noted during psychosis [22]. Several patients exhibited suicidal tendencies while intoxicated: suicidal thoughts or attempts were documented in 3 cases (~10%) [10,11,23].

Moreover, some individuals experienced cognitive impairments and altered states of consciousness. Isolated reports described confusion, disorientation, memory loss, and, in one case, loss of consciousness [10]. Anxiety was reported as a comorbid symptom in three patients. Thus, the spectrum of psychopathological manifestations associated with synthetic cathinone use is broad—ranging from classic hallucinations and delusions to intense agitation, aggression, and behavioral disorganization, sometimes accompanied by affective and cognitive symptoms.

Age and Gender Distribution

Cases of psychosis associated with synthetic cathinone use were distributed unevenly by gender: the vast majority of patients were male. In the presented sample, 25 out of 29 cases (~86%) involved male individuals. Only 4 cases (14%) involved female patients [11,13,18,21], indicating a clear predominance of men among those developing such psychoses.

The age of the patients ranged from 17 to 46 years, covering late adolescence to middle adulthood. The median age was approximately 29 years, with the majority of cases occurring in young adults aged 20 to 30. Only a few cases involved adolescents (the youngest patient was 17 years old) or individuals over 40. Overall, the results suggest that the most vulnerable group for developing psychosis in the context of cathinone use are young adult males of working age.

Association of Psychosis with Different Synthetic Cathinones

Psychotic episodes were recorded following the use of various substances from the synthetic cathinone group, with certain compounds appearing particularly frequently. The most commonly reported were MDPV (3,4-methylenedioxypyrovalerone) and 4-MMC (mephedrone), both featuring in a significant proportion of the cases.

MDPV was explicitly identified in several psychotic episodes and is associated with intense hallucinations and delusional ideas, often accompanied by pronounced agitation. Mephedrone (4-MMC) was also repeatedly linked to the development of psychosis, including both acute delusional episodes immediately following use and chronic psychotic disorders in cases of prolonged abuse. Some cases involving mephedrone described the development of paranoid delusions and hallucinations, often in the context of polysubstance abuse.

Generic "bath salts"—synthetic cathinone-based mixtures—were mentioned in four cases [11,13,22]. These products often contain MDPV or related stimulants, consistent with the clinical presentations: patients experienced severe psychoses with vivid hallucinations, delusions, and episodes of aggression. In one such case, the individual exhibited extreme aggression and self-harm, highlighting the high risk associated with these substances.

Among the newer synthetic cathinone derivatives mentioned in the data were α-PVP and related compounds. α-PVP (alpha-PVP) appeared in several episodes: in one case, a 17-year-old girl experienced acute psychosis with auditory hallucinations and agitation [21], while in another, a 40-year-old man developed a prolonged psychotic state [24]. Chronic abuse of α-PVP has been linked to long-lasting psychosis; one case described the development of a "schizophrenia-like" psychosis following regular use.

Other similar cathinones, such as α-PHP and α-PHiP, may also induce psychosis. In the dataset, α-PHP (alpha-PHP) was associated with a combination of hallucinations, delusions, and severe anxiety in a 39-year-old patient, while α-PHiP led to agitation and bizarre behavior.

Special attention should be given to cases involving ephylone and eutylone—relatively new synthetic cathinones. In a series of ephylone (Ephylone) intoxications among young adults (aged 18–32), psychosis mainly manifested as psychomotor agitation, aggression, and incoherent speech, with hallucinations reported less frequently. Eutylone (Eutylone), in one case involving a 32-year-old man with a complicated medical history, caused pronounced abnormal behavior, culminating in loss of consciousness [10].

MDPHP and butylone, less frequently encountered cathinones, were also associated with psychotic symptoms (e.g., aggressive behavior with MDPHP). Overall, various members of the cathinone class similarly exhibit the potential to provoke acute psychotic disorders.

However, it can be noted that the more potent stimulants—such as MDPV and α-PVP—were more frequently linked to full-blown hallucinatory-delusional syndromes, whereas some newer cathinones (e.g., ephylone, hexen) primarily manifested as excessive agitation and aggression. No unique symptoms strictly attributable to a single substance were identified in the collected data—all synthetic cathinones, especially in high doses, are capable of inducing stimulant-type psychosis.

4. Discussion

The results of the conducted analysis confirm a high likelihood of developing psychotic disorders following the use of synthetic cathinones. Psychosis induced by these substances is primarily characterized by hallucinations, delusional disorders, agitation, aggression, and disorganized behavior—findings that align with previously published studies on the effects of stimulants on the central nervous system.

Comparison with Other Psychoactive Substances

Cathinone-induced psychoses share many features with those triggered by classic stimulants such as amphetamines and cocaine. In both cases, intense hallucinations, delusions, paranoid ideation, and aggressive behavior are common. However, unlike amphetamine-induced psychosis, cathinone -related psychoses may be accompanied by more pronounced emotional disturbances and a greater tendency toward suicidal behavior. There are also similarities with cannabinoid -induced psychoses, particularly those associated with synthetic THC analogs. Both classes of substances can provoke paranoia and anxiety disorders. However, cathinone psychoses are more often marked by hyperactivity, agitation, and aggression, whereas cannabinoid-related psychoses more frequently involve psychomotor retardation and affective lability.

Gender and Age Characteristics

The observed predominance of males (86%) among patients with cathinone-induced psychosis corresponds to data on gender differences in stimulant use more broadly. Studies show that men are more likely to use psychostimulants, exhibit higher rates of polysubstance abuse, and demonstrate a greater tendency toward aggressive behavior. The age range (17–46 years, median of 29) indicates that the highest risk of cathinone-related psychosis falls on young adults. This aligns with the age profile of new psychoactive substance (NPS) users, as confirmed by epidemiological research. Young adults are more likely to experiment with drugs and exhibit impulsive behavior.

Specific Features of Different Synthetic Cathinones

Our analysis confirmed that different synthetic cathinones share similar properties, although the intensity of symptoms may vary. MDPV and α-PVP were more frequently associated with vivid hallucinations and delusions, whereas ephylone and butylone more commonly led to agitation and aggressive behavior. Notably, about two-thirds of the patients exhibited polysubstance use, highlighting the complexity of diagnosing and interpreting cathinone-related psychoses. The concurrent use of THC, alcohol, cocaine, and other stimulants may have intensified psychopathological manifestations, which should be taken into account in clinical practice.

Psychopathological Consequences and Risk of Chronic Disorders

The collected data confirm that cathinone-induced psychoses may be both acute and chronic. In some cases, symptoms persisted for several months, and with prolonged use, the development of persistent psychotic disorders resembling schizophrenia was observed. These findings are consistent with research suggesting that long-term stimulant abuse can lead to lasting changes in the dopaminergic system, increasing the risk of chronic psychotic disorders. Moreover, the documented suicide attempts among patients with cathinone-induced psychosis warrant special attention. This suggests that the psychological impact of cathinones extends beyond classical psychosis, affecting affective and cognitive domains as well. These findings underscore the need for the development of specific diagnostic and treatment protocols.

Limitations of the Study

Despite the important findings obtained through the analysis, this study has several limitations:

- **Heterogeneity of data**: The reviewed cases included patients with diverse clinical and personal histories, which may have influenced the psychiatric manifestations.
- **Limited sample size**: The study is based on a relatively small number of published case reports, which limits the ability to draw definitive population-level conclusions.
- **Influence of concomitant substance use**: It is difficult to determine to what extent the psychoses were caused specifically by synthetic cathinones as opposed to their combination with other psychoactive substances.

5. Conclusions

The findings of this study confirm that the use of synthetic cathinones is associated with a high risk of developing both acute and chronic psychoses, accompanied by hallucinations, delusional disorders, agitation, aggression, and suicidal tendencies. The most vulnerable group appears to be young men between the ages of 20 and 30. While different cathinones demonstrate similar psychostimulant activity, the intensity and specific presentation of symptoms may vary depending on the compound's chemical structure. These results highlight the need for early diagnosis, preventive efforts, and further research aimed at exploring the long-term consequences of synthetic cathinone use.

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