



Novel psychoactive substances (NPS) as a risk factor for psychosis: A systematic review of the literature

Alessio Mosca^{a,*}, Gianluca Mancusi^a, Stefania Chiappini^{b,c}, Andrea Miuli^a, Clara Cavallotto^a, John Martin Corkery^b, Gilberto Di Petta^d, Arianna Pasino^a, Maria Chiara Santovito^a, Carlotta Marrangone^a, Maria Chiara Vicinelli^a, Mauro Pettorruso^a, Giovanni Martinotti^{a,b}, Fabrizio Schifano^b

^a Department of Neuroscience, Imaging and Clinical Sciences, "G. D'Annunzio" University, Chieti 66100, Italy

^b Psychopharmacology, Drug Misuse and Novel Psychoactive Substances Research Unit, School of Health, Medicine and Life Sciences, University of Hertfordshire, Hertfordshire AL10 9EU, UK

^c UniCamillus International University of Medical Sciences, Via di S. Alessandro 8, Rome, Italy

^d Department of Neuroscience Department of Mental Health, ASL Napoli 2, Napoli, Nord, Italy

ARTICLE INFO

Keywords:

Abuse
Drug abuse
Drug misuse
New psychoactive substances
NPS
Psychosis
Schizophrenia
Synthetic cannabinoids
Substance-induced-psychosis
Stimulants

ABSTRACT

Novel psychoactive substances (NPS) are increasingly used by young individuals for their psychoactive effects and have been frequently associated with the emergence of psychotic symptoms and schizophrenia spectrum disorders. However, it remains unclear whether NPS use directly increases the risk of psychosis onset or whether individuals with a predisposition to psychosis are more likely to engage in NPS use. This systematic review aims to explore the relationship between NPS consumption and the risk of developing psychotic symptoms. Out of 4477 identified studies, 95 met the inclusion criteria.

Findings: indicate that synthetic cannabinoids are the most frequently implicated substances, showing a strong association with acute psychosis and, in some cases, with persistent or relapsing psychotic disorders. The presence of Schneiderian First Rank Symptoms in some cases highlights a phenomenological overlap with schizophrenia, suggesting a possible risk of transition. Synthetic cathinones, phenethylamines, and other NPS classes were also linked to a broad range of psychotic manifestations, including disturbances in thought content and perceptual abnormalities. Although many episodes appeared transient, a notable proportion evolved into persistent psychotic states, supporting the hypothesis that NPS may either unmask latent vulnerabilities or directly contribute to the development of chronic psychotic disorders.

These results underline the critical importance of systematically assessing NPS use in individuals presenting with first-episode psychosis and call for increased clinical and public health awareness regarding the psychiatric risks associated with these substances.

1. Introduction

Over the past twenty years, alongside traditional psychoactive substances, the spread of New Psychoactive Substances (NPS) has been increasingly documented, becoming a major public health problem (Schifano et al., 2015). The United Nations Office on Drugs and Crime (UNODC) and the European Monitoring Centre for Drugs and Drug

Addiction (EMCDDA) define NPS as "substances of abuse, either in pure form or in preparations, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances but may pose a public health threat" (EMCDDA, 2019; UNODC United Nations Office on Drugs and Crime, 2020). These substances are often synthesized to mimic the psychoactive effects of controlled substances such as cannabis, cocaine, ecstasy, and lysergic acid

* Correspondence to: Department of Neuroscience, Imaging and Clinical Sciences, "G. D'Annunzio" University, via dei Vestini 31, Chieti 66100, Italy.

E-mail addresses: alessio.mosca@unich.it (A. Mosca), g.mancusi@hotmail.com (G. Mancusi), stefania.chiappini@unicamillus.org (S. Chiappini), andreamiuli@live.it (A. Miuli), clara.cavallotto@laconchiglia.srl (C. Cavallotto), j.corkery@herts.ac.uk (J.M. Corkery), gilbertodipetta@alice.it (G. Di Petta), pasino.arianna@gmail.com (A. Pasino), santovitomchiara@gmail.com (M.C. Santovito), carlotta.marrangone@gmail.com (C. Marrangone), mchiaravicinelli@gmail.com (M.C. Vicinelli), mauro.pettorruso@hotmail.it (M. Pettorruso), giovanni.martinotti@gmail.com (G. Martinotti), f.schifano@herts.ac.uk (F. Schifano).

<https://doi.org/10.1016/j.neubiorev.2025.106431>

Received 28 April 2025; Received in revised form 6 October 2025; Accepted 18 October 2025

Available online 19 October 2025

0149-7634/© 2025 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

diethylamide (LSD), bypassing existing drug regulations (they are marketed as “legal highs”), making their detection at routine screening tests and control more challenging (Chiappini et al., 2024a, 2024b). They include a heterogeneous group of recreational drugs such as synthetic cannabinoids (SCRAs), synthetic cathinones, phencyclidine-type substances, phenethylamines, piperazines, tryptamines, aminoindanes, opioids, benzodiazepines, and plant-based substances. Many are marketed as “legal” alternatives or substitutes for Traditional Drugs of Abuse (TDA), despite their association with acute toxicity, unpredictable effects, limited safety data, and significant psychiatric risks (Chiappini et al., 2021a, 2021b; EMCDDA, 2022). NPS have become a global concern, with reports from 141 countries; according to the United Nations Office on Drugs and Crime (UNODC), by November 2023, a total of 1330 NPS had been documented based on data provided by governments, laboratories, and partner organizations (UNODC United Nations Office on Drugs and Crime, 2024).

The spread of NPS occurs within the context of dramatic social transformations over the past three decades, shaping the postmodern era, in particular increasing individualization, shifts in social roles, evolving concepts of self-identity and intimacy, and altered perceptions of the future (Whitley, 2008). These features have an impact on risk factors for mental disorders, the dynamics of clinical interactions, patterns of help-seeking behavior, and treatment outcomes (Martinotti et al., 2021a). In this context, the phenomenon of “psychonauts” has emerged in recent decades (Schifano et al., 2021), representing a group of individuals who deliberately explore altered states of consciousness through the use of NPS. They often have extensive knowledge of pharmacology and pharmaceuticals and actively participate in sharing their drug-related experiences online, by online fora, social media platforms and specialized websites: this digital interaction creates a global community where psychonauts can have access to a vast knowledge about NPS and also offers an easy and anonymous access to online pharmacies and marketplaces (Davey et al., 2012). The proliferation of NPS is closely linked to acceleration in interconnectivity which characterizes the “digital revolution” (Bucci et al., 2019; Davey et al., 2012). However, psychonauts represent only one subgroup of users. Recent evidence indicates that NPS consumption is also highly prevalent in vulnerable populations such as prisoners and homeless individuals, where use is often associated with severe health risks and limited access to care (Chiappini et al., 2024a, 2024b). Recently, synthetic cannabinoids have also been detected in e-cigarettes seized from English schools, highlighting their diffusion among adolescents and the increasing diversity of routes of administration (Cozier et al., 2025).

Concerning NPS use, an especially alarming aspect is the severe psychopathological impact they can have, including risks of developing psychotic disorders, self-harm, suicide, dependence, withdrawal symptoms, and fatal intoxication or poisoning (Chiappini et al., 2021a, 2021b; Schifano et al., 2021). In particular, NPS intake may be associated with the onset of *de novo* psychosis in vulnerable individuals - substance/medication induced psychotic disorders (SIPD) - (Fiorentini et al., 2021; Schifano et al., 2021) or with the potential to trigger schizophrenia and other conditions within the psychotic spectrum - primary psychotic disorders (PPD) - (Papanti et al., 2013a). Additionally, there are ongoing concerns about persistent substance-induced psychoses, known as SREP (Substance-Related Exogenous Psychosis) (Martinotti et al., 2021b; Papanti et al., 2013b).

Aim of the study: The risks associated with NPS use for mental health are not yet fully understood and may indeed pose severe psychopathological consequences. The main outcome of this systematic review was to investigate any correlation between the use of NPS and the onset of psychotic symptoms, performing a literature review of the current related knowledge. A qualitative assessment of psychotic symptoms associated with the use of novel psychoactive substances (NPS) has also been conducted, with the aim of characterizing potential differences in psychopathological features based on the pharmacodynamic properties of the substances.

2. Materials and methods

2.1. Systematic review procedures

A systematic electronic search was performed on 13 August 2025 on the following search engines: PubMed, Scopus, and Web of Science (WoS). For PubMed and WoS the following search strategy was used: ("NPS" OR "new psychoactive substances" OR "novel psychoactive substances" OR "synthetic cannabinoids" OR "phenethylamines" OR "synthetic cathinones" OR "tryptamines" OR "piperazines" OR "new synthetic opioids" OR "designer benzodiazepines" OR "Spice" OR "JWH-018" OR "K2") AND ("psychosis" OR "hallucination" OR "delusion" OR "schizophrenia" OR "delusional" OR "schizoaffective") NOT review NOT animal. While for Scopus a slightly different search strategy was used: (TITLE-ABS-KEY ("NPS") OR TITLE-ABS-KEY ("new psychoactive substances") OR TITLE-ABS-KEY ("novel psychoactive substances") OR TITLE-ABS-KEY ("synthetic cannabinoids") OR TITLE-ABS-KEY ("phenethylamines") OR TITLE-ABS-KEY ("synthetic cathinones") OR TITLE-ABS-KEY ("tryptamines") OR TITLE-ABS-KEY ("piperazines") OR TITLE-ABS-KEY ("new synthetic opioids") OR TITLE-ABS-KEY ("designer benzodiazepines") OR TITLE-ABS-KEY ("Spice") OR TITLE-ABS-KEY ("JWH-018") OR TITLE-ABS-KEY ("K2") AND TITLE-ABS-KEY ("psychosis") OR TITLE-ABS-KEY ("hallucination") OR TITLE-ABS-KEY ("delusion") OR TITLE-ABS-KEY ("schizophrenia") OR TITLE-ABS-KEY ("delusional") OR TITLE-ABS-KEY ("schizoaffective") AND NOT TITLE-ABS-KEY (review) AND NOT TITLE-ABS-KEY (animal))).

The systematic review was structured in accordance with the PRISMA guidelines (Page et al., 2021). Identified studies were assessed at title/abstract and full text screening against eligibility criteria.

Only original articles written in English that report data on the correlation between NPS and psychosis (delusion, hallucination or schizophrenia). All studies not original and not written in English that report other substances misuse, or do not relate to psychosis were excluded.

2.2. Protocol and registration

Current research methods were approved by PROSPERO (identification code CRD42022383323).

2.3. Data synthesis strategy

The selection and eligibility phase of the articles were carried out independently by Man. G., P.A., S.M.C., V.M.C., and C.C., and then subjected to a final cross-check by Mi. A. and C.S. All discordant cases were evaluated by M.A., P.M., and M.G. Any unsolved doubts by the team of the topic covered in the article were clarified directly with the author(s), if contactable. The data were collected in a Word table containing the first author's name and year of publication of the study, study design, demographic variables (gender, age, psychiatric history), details on the drugs taken (dosage and route of administration), details on symptomatology (non-psychotic psychiatric symptoms, disturbances of thought, hallucinations), and details on the outcome (psychedelic experience, acute psychosis with remission, onset with persistence, psychotic relapse). The exclusion criteria for both selection phases were: 1) non-original research (e.g., re-view, metanalysis, commentary, editorial, letter to the editor without data available, and book chapter); 2) non-full-text articles (e.g., meeting abstract); 3) language other than English; 4) animal/in vitro studies; 5) articles not dealing with the misuse of the NPS selected (cannabinoids, phenethylamines, cathinones, tryptamines, piperazines, new synthetic opioids, designer benzodiazepines) and 6) articles not dealing with psychotic symptoms or schizophrenic spectrum disorder. From a total of 4324 articles (PubMed = 1853; Scopus = 2228; WoS = 242; other sources = 1), after deduplication (n = 1100), 3224 records were screened. Among the articles screened 2374 were considered not relevant to the subject reading title

and abstract, 222 were not written in English, and 277 were non-original articles. Of the 351 full-text articles assessed for eligibility, 184 did not match the inclusion criteria for the review and 56 were unavailable. Finally, 111 articles were included in the systematic review (Fig. 1).

2.4. Risk of bias assessment

Risk of bias was evaluated for all included studies. For non-case report articles, the ROBINS-I tool was applied across its seven domains (Sterne et al., 2016): confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result. For case reports, the CARE checklist was used to assess completeness and transparency of reporting (Gagnier et al., 2013). Two reviewers independently performed the assessments, with discrepancies resolved by discussion and consensus.

3. Results

3.1. General features

A total of 111 studies were included in the present systematic review, comprising case reports, case series, observational studies, retrospective analyses, and controlled trials. These studies addressed the use of NPS and reported on the sociodemographic, clinical, and comorbid profiles of the individuals involved. Findings related to the 95 articles are described in detail and organised by specific molecule and alphabetical order of authors (Table 1).

The main NPS categories identified were synthetic cannabinoids (SCRAs) (Abouchedid et al., 2016; Altintas et al., 2016; Altintop, 2020; Barceló et al., 2017; Bassir Nia et al., 2016; Bebaria et al., 2012; Benford and Caplan, 2011; Berry-Cabán et al., 2013; Besli et al., 2015; Bonaccorso et al., 2018; Celofiga et al., 2014; Di Petta, 2016; Durand et al., 2015; El Zahran et al., 2019; Every-Palmer, 2011; Glue et al., 2013; Haro et al., 2014; Hermanns-Clausen et al., 2018; Hoyte et al., 2012; Hurst et al., 2011; Johnson et al., 2011; Kekelidze et al., 2019; Kotan et al., 2017; Kuzucuoglu et al., 2018; Malik et al., 2021; Mathews et al., 2019; Monte et al., 2017; Müller et al., 2010; Oluwabusi et al., 2012; Ozer et al., 2016; Öznur et al., 2018; Peglow et al., 2012; Rahmani et al., 2014; Roberto et al., 2016; Robson et al., 2021; Satodiya and Palekar, 2020; Simmons et al., 2011; Skryabin and Vinnikova, 2018, 2019; Sönmez and Köşger, 2016; Sweet et al., 2017; Theunissen et al., 2019, 2022; Tofighi and Lee, 2012; Tung et al., 2012; Udow et al., 2018; Waugh et al., 2016; Welter et al., 2017), synthetic cathinones (Albert et al., 2022; Batisse et al., 2014; Blanco et al., 2021; Chan et al., 2013; Chou et al., 2021; Dolengevich-Segal et al., 2016; Fujita et al., 2018; Murray et al., 2012; Nina, 2018; Paul et al., 2021; Roberts et al., 2017; Romanek et al., 2017; P. Simonato et al., 2018; Truscott et al., 2013; Umebach et al., 2016), PCP-like substances (Dunlop et al., 2020; Zidkova et al., 2017), phenethylamines (Bretaudeau Deguigne et al., 2015; Forrester, 2014; Gee et al., 2016; Hill et al., 2013; Liakoni et al., 2017; Madsen et al., 2017; Miyajima et al., 2008; Papaseit et al., 2018, 2020; Rose et al., 2013; Schetz et al., 2022; Stoller et al., 2017), piperazines (Austin and Monasterio, 2004; Bossong et al., 2010; Thompson et al., 2010; Wilkins et al., 2007), amphetamine-type stimulants (Daveluy et al., 2016; Lafferty et al., 2016; Ricci et al., 2022; White et al., 2019), tryptamines (Alatrash et al., 2006; Rosenberg, 1964; Szara et al., 1966), 13 cases of poly-substance use (Beck et al., 2015; Caloro et al., 2016, 2018; Ciucă Anghel et al., 2022; Hondebrink et al., 2015; Kamijo et al., 2016; Khullar et al., 2014; Kihara and Day, 2014; Liakoni et al., 2015; Martinotti et al., 2021c; Matsumoto et al., 2016; Stevenson and Tudenham, 2014; Tancer and Johanson, 2001) and 7 cases of NPS not belonging to the above-mentioned categories (Anderson et al., 2015; El-Higaya et al., 2011; Janiri et al., 1991; Lagoutte-Renosi et al., 2021; Moccia et al., 2019; Täljemark and Johansson, 2012; Wilcox, 2012).

Regarding synthetic cannabinoids (SCRAs), the majority of studies

focused on unspecified SCRAs, followed by Spice, JWH-018, and K2, with a marked predominance of male subjects and a mean age ranging between 15 and 40 years. Although "Spice" was initially the brand name for a specific product containing synthetic cannabinoids, it later became a generic term used to describe a wide range of similar substances (National Institute on Drug Abuse (NIDA National Institute on Drug Abuse, 2024)). Most studies were case reports or observational in nature. Several authors reported psychiatric comorbidities such as schizophrenia, schizoaffective disorder, mood disorders, and substance use disorders. However, many cases did not document any medical or psychiatric comorbidities.

The group of synthetic cathinones mostly included observational studies and case series, also showing a predominance of male subjects with a mean age typically between 20 and 40 years. Some patients exhibited substance-induced psychotic episodes, mood disorders (e.g., depression, bipolar disorder), or personality disorders. In some cases, medical comorbidities were also documented.

The limited number of studies involving phencyclidine (PCP) analogues primarily consisted of adult male patients, often without psychiatric comorbidities but with frequent medical conditions.

Regarding phenethylamines, the included studies mostly involved young male users. Psychiatric comorbidities such as depression, substance use disorders, and in some instances, psychotic disorders were observed.

Evidence regarding Piperazines was derived from a small number of observational studies and case reports with minimal information on psychiatric or medical comorbidities.

For amphetamine-type stimulants, available data suggested a predominance of young adult males, while medical comorbidities were occasionally noted, psychiatric comorbidities were infrequently reported.

Studies involving tryptamines were scarce and, in most cases, did not report significant psychiatric or medical comorbidities.

Numerous studies documented concurrent use of multiple NPS (polyabuse), with a substantial presence of psychiatric disorders including schizophrenia, mood disorders, personality disorders, and substance use disorders. Again, this group was predominantly composed of young adult males.

Regarding other substances, a few studies explored substances that did not fall into the aforementioned categories. These cases typically involved young adult males, with occasional reports of psychiatric conditions such as paranoid schizophrenia, while medical comorbidities were rarely described.

For detailed information on study design, substance type, and the sociodemographic and clinical characteristics of the subjects included, please refer to Table 1.

3.2. Symptomatology

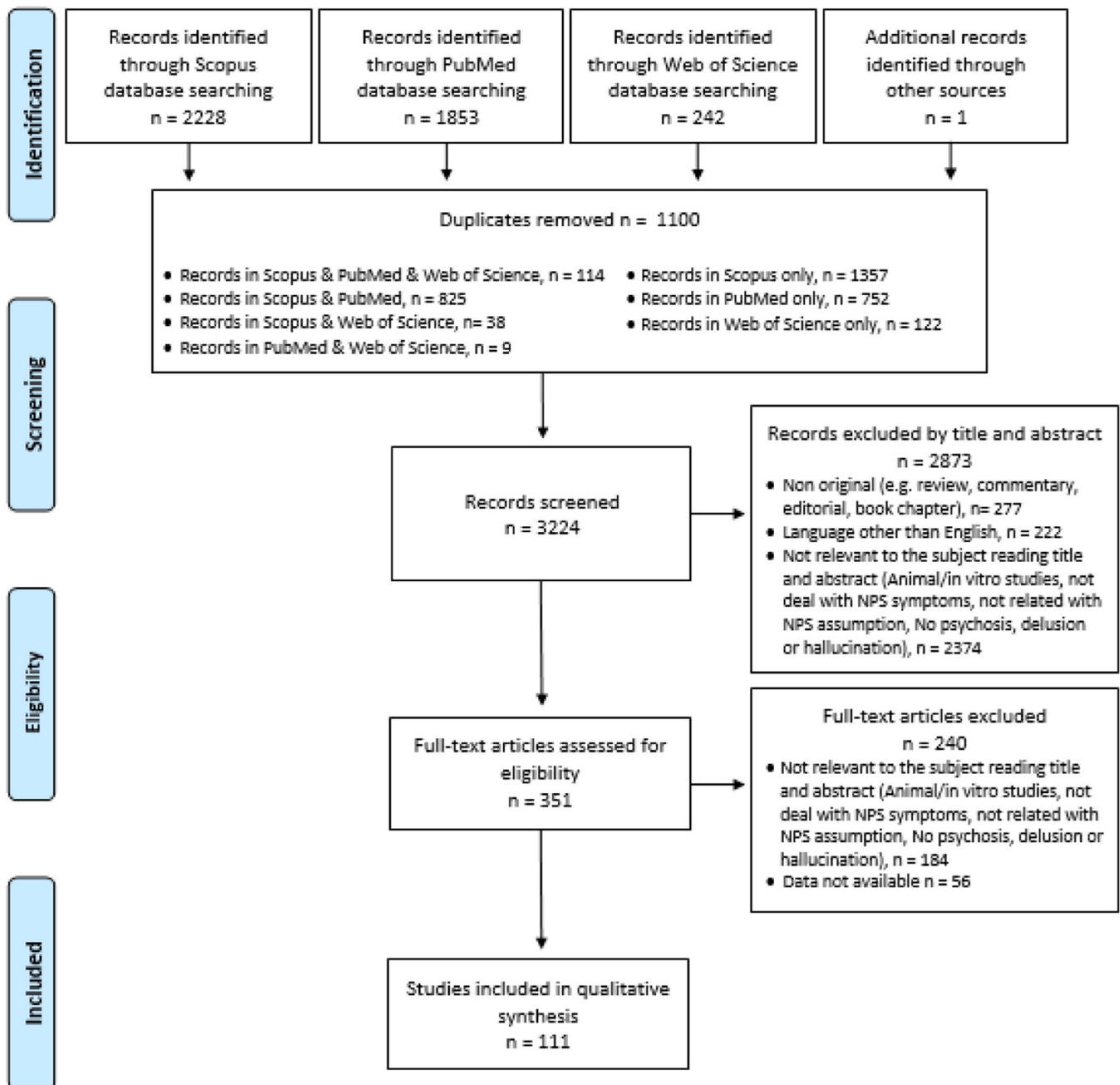
Regarding the psychopathological manifestations associated with the use of NPS, the results are presented in Table 2, table specifying the substance used, route of administration, psychiatric comorbidities, and specific symptomatology - including non-psychotic psychiatric symptoms, negative symptoms, thought disturbances, and hallucinations.

A wide range of acute psychiatric symptoms was reported following the use of SCRAs, with smoking being the most common route of administration. Users often presented with agitation, anxiety, suicidal ideation, and disorganized behavior. Disturbances in thought processes - such as paranoia, thought blocking, and delusional thinking - were frequently documented, along with both auditory and visual hallucinations. Some reports also described complex delusional states (e.g., Capgras syndrome, mystical or supernatural delusions), negative symptoms (e.g., flat affect, alogia, avolition), and dissociative phenomena.

Synthetic cathinones were associated with high levels of agitation, confusion, anxiety, and in some cases, severe behavioral dysregulation



PRISMA Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *BMC Med* 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Fig. 1. Prisma flow diagram of the methodology of the systematic literature review.

Table 1

Sociodemographic and clinical characteristics of individuals with psychosis associated with NPS.

Name, Year	Substance	Study design	Population (N, M, F)	Mean age± Standard deviation	Psychiatric comorbidity	Medical comorbidity (Yes;No)
SYNTHETIC CANNABINOIDS						
Abouchedid et al., (2016)	JWH–18	Case report	F= 1	19	Depression	No
Alhassan et al. (2024)	Spice	Case report	N = 1, F= 1	51	No	No
Altintas et al., (2016)	Unspecified SCRA	Single-center cross-sectional analysis	M= 50	MA= 25,9 ± 5,5	NA	NA
Altintop et al., 2020	Unspecified SCRA	Retrospective study	N = 352 M= 330 F= 22	MA= 26,9 ± 8,3	NA	NA
Barceló et al., (2017)	5F-ADB, MMB–2201	Case series	N = 5 M= 4 F= 1	Case 1= 17 Case 2= 17 Case 3= 17 Case 4= 14 Case 5= 21	No	No
Bassir Nia et al. (2016)	Unspecified SCRA	Retrospective review	N = 594 M= 444 F= 150	MA= 40,6 ± 12,9	Schizophrenia, Schizoaffective disorder, Bipolar disorder, MDD, others	NA
Bebarta et al., (2012)	Spice	Case series	Case 1=M Case 2= 2 Case 3=M	Case 1= 19 Case 2= 19 Case 3= 23	No	No
Berry-Cabàn et al., 2013	Spice	Case report	M= 1	20	Schizoaffective disorder	No
Besli et al., (2015)	Unspecified SCRA	Case series	N = 16 M= 15 F= 1	MA= 15,4 ± 1,7	NA	NA
Bonaccorso et al., (2018)	Unspecified SCRA	Case series	Case 1=M Case 2=F Case 3=M Case 4=M	Case 1= 28 Case 2= 32 Case 3= 20 Case 4= 39	Paranoid schizophrenia, Schizoaffective disorder, Bipolar disorder	NA
Celofiga et al., (2014)	Unspecified SCRA	Case series	M= 4	Case 1= 35 Case 2= 21 Case 3= 27 Case 4= 29	Paranoid schizophrenia, Undifferentiated schizophrenia	NA
Dawn Benford et al., 2011	Spice	Case report	M= 1	20	No	No
Di Petta (2016)	Unspecified SCRA	Case report	M= 1	28	Previous psychosis in substance abuse	No
Durand et al., (2015)	Unspecified SCRA	Case report	M= 1	23	No	No
Every-Palmer et al., 2011	JWH–018	Cohort study	M= 15	MA= 34 ± 7,9	Schizophrenia, Schizoaffective disorder, Borderline personality	NA
El Zahran et al., (2019)	Cumyl–4- cyano-BINACA	Case report	M= 1	29	No	NA
Glue et al., (2013)	K2	Retrospective observational study	N = 17 M= 10 F= 7	MA= 26,1 ± 10	Affective disorder, Psychotic episodes	NA
Haro et al., (2014)	JWH–081, JWH–250, JWH–203, JWH–019	Letter to editor-case report	F= 1	19	NA	NA
Hermanns-Clausen et al. (2013)	AB-CHMINACA,MDMB- CHMICA	Prospective observational study	N = 44 M= 39 F= 5	MA= 20,5	NA	NA
Helge Müller et al., 2009	Spice	Case report	M= 1	25	History of cannabis induced recurrent psychotic episodes	NA
Hoyte et al., (2012)	Unspecified SCRA	Observational study	N = 1898 M= 1005 F= 893	MA= 22,5 ± 8,86	NA	NA
Hurst et al., (2011)	Spice	Case Series	M= 10	MA= 23	No	No
Johnson et al., (2011)	Spice	Case report	M= 1	23	NA	NA
Simmons et al., (2011)	JWH–018, JWH–073	Case series	M= 3	Case 1= 25 Case 2= 21 Case 3= 19	No	NA
Kekelidze et al., (2019)	JWH, AB-PINACA, TMCP	Interventional study	N = 43 M= 38 F= 5	MA= 25	NA	NA
Kotan et al., (2017)	Unspecified SCRA	Cross-sectional study	M= 74 N SC users= 33 N SC and C users= 41	MA SC users= 24,7 ± 6,8 MA SC and C users= 25,7 ± 7,6	No	No

(continued on next page)

Table 1 (continued)

Name, Year	Substance	Study design	Population (N, M, F)	Mean age± Standard deviation	Psychiatric comorbidity	Medical comorbidity (Yes;No)
Kuzucuoglu et al., (2018)	Bonzai	Case series	M= 8	MA= 21,6 ± 4,7	NA	NA
Malik et al., (2021)	K2	Case series	Case 1=M Case 2=F	Case 1= 31 Case 2= 36	Schizophrenia, SUD	Yes
Mathews et al., (2019)	Unspecified SCRA	Observational study	N = 90 M= 23,3 % F= 66,7 %	MA= 19,9 ± 2,3	NA	NA
Monte et al., (2017)	Unspecified SCRA	Cohort study	N = 353 M= 297 F= 56	MA= 25	NA	NA
Oluwabusi et al., (2012)	K2	Case series	M= 2	Case 1= 16 Case 2= 17	No	NA
Ozer et al., (2016)	Unspecified SCRA	Case report	M= 1	17	No	No
Öznur et al., (2018)	Unspecified SCRA	Prospective observational study	M= 166	MA= 21,04 ± 1,04	NA	NA
Peglow et al., (2012)	Spice	Case report	M= 1	59	Post traumatic stress disorder, SUD	No
Rahmani et al. (2014)	Unspecified SCRA	Case series	M= 2	Case 1= 17 Case 2= 17	No	NA
Roberto et al., (2016)	Unspecified SCRA	Case report	M= 1	18	No	No
Robson et al., (2021)	Unspecified SCRA	Observational study	N = 113 M= 81 F= 32	MA= 28,4 ± 10,1	Schizophrenia	NA
Satodiya et al., 2020	K2	Case Report	M= 1	32	Schizophrenia	NA
Skryabin et al., 2019	Unspecified SCRA	Observational study	M= 60	MA= 23,6 ± 3,5	SC dependence, cannabis use disorder, SC abuse	NA
Skryabin et al., (2018)	Spice	Longitudinal, observational cohort study	M= 46	MA= 23,2 ± 3,5	NA	NA
Sönmez et al. 2016	Unspecified SCRA	Case report	M= 1	31	No	No
Sweet et al., (2017)	Unspecified SCRA	Case report	M= 1	47	NA	NA
Theunissen et al. (2019)	JWH-018	Placebo-controlled double blind	N = 24 M= 10 F= 14	MA= 22,8 ± 3,05	Occasional users of cannabis	No
Theunissen et al., (2019)	JWH-018	Placebo-controlled crossover study	M= 17	MA= 23,4 ± 3,1	Occasional users of cannabis	No
Tofighi et al., 2012	K2, JWH-018	Case report	M= 1	48	No	No
Tung et al., (2012)	Spice	Case report	M= 1	36	No	No
Udow et al., (2018)	Unspecified SCRA	Case report	F= 1	70	Occasional visual hallucinations for many years with preserved insight	Yes
Waugh et al., (2016)	Unspecified SCRA	Retrospective study	N = 510 M= 80.8 % F= 19.2 %	MA= 21	NA	NA
Welter et al., (2017)	Unspecified SCRA	Prospective pilot survey	N = 21 M= 15 F= 6	MA= 25,6 ± 5,8	Paranoid schizophrenia, Depression without psychosis, Schizoaffective disorder, other	NA
WILLIAMS and HIMMELSBACH (1846)	Pyrahexyl compound	Interventional study	N = 12 (prisoner patients, M)	24–33	One case with schizophrenia; others with psychopathic/antisocial or paranoid traits	No
Yazici et al. (2017)	Synthetic cannabinoids (“Bonzai”)	Case report	N = 2, M= 2	Case 1= 26 Case 2= 30	History of polysubstance use; hypomanic symptoms in one case	No
SYNTHETIC CATHINONES/ BATH SALTS						
Albert et al., (2022)	α-PVP (“Flakka”), α-PHP, α-PHP	Case Report	F= 1	21	Substance induced paranoid psychotic episode	NA
Batisse et al., (2014)	NRG3, mephedrone, MDPV	Case series	N = 21 M= 20 F= 1	MA= 38,1 ± 8,32	SUD	Yes
Blanco et al., (2021)	N-ethylpentylone	Observational study	N = 9 M= 6 F= 3	MA= 27	NA	NA
Chan et al., (2013)	6–2-aminopropylbenzofuran (6-APB)	Case report	M= 1	21	No	No

(continued on next page)

Table 1 (continued)

Name, Year	Substance	Study design	Population (N, M, F)	Mean age± Standard deviation	Psychiatric comorbidity	Medical comorbidity (Yes;No)
Chou et al., (2021)	Toxic coffee packets	Retrospective analysis	N = 60 M= 47 F= 13	MA= 28,85 ± 9,24	History of psychiatric disorder	NA
Dolengevich-Segal et al., (2016)	Mephedrone	Case report	M= 1	25	ADHD, SUD	Yes
Douglas et al., 2012	Methylenedioxypyrovalerone (MDPV)	Retrospective study	N = 30 M= 21 F= 9	MA= 28,6 ± 7,8	NA	NA
Fujita et al., (2018)	α-PHP	Case report	M= 1	39	NA	NA
Paul et al., (2021)	α-PVT	Retrospective study	N = 44 M= 39 F= 6	MA= 36	NA	NA
Roberts et al., (2017)	Mexedrone, 3-methoxy-2-methylamino-1-4-methylphenyl propanone	Observational case series	M= 11	MA= 30	No	No
Romanek et al., (2017)	Unspecified cathinones	Cohort study	N = 81 M= 52 F= 29	MA= 34	NA	NA
Schloerkeremper et al. (2018)	Unspecified cathinones	Case report	F= 1	20	NA	NA
Simonato et al., (2018)	Alpha-PVP	Case report	M= 1	28	Substance induced psychosis, schizoid personality disorder	NA
Truscott et al., (2013)	NA	Case report	M= 1	32	SUD	Yes
Umebachi et al., (2016)	α- pyrrolidinovalerophenone	Retrospective case series	N = 8 M= 6 F= 2	MA= 27	Depression, Bipolar disorder	NA
PCP-LIKE DRUGS						
Dunlop et al., (2020)	3-hydroxyphencyclidine (3-HO-PCP)	Case report	M= 1	56	NA	Yes
Zidkova et al., (2017)	3-Methoxy-Phencyclidine	Case series	M= 2	Case 1= 37 Case 2= 40	No	Yes
PHENETHYLAMINES						
Brethaudau Deguigne et al., (2015)	2C-P	Case series	M= 2	MA= 20,4 ± 1,95	No	No
Gee et al. (2016)	25 C, 25B, 25I-NBOMes	Case series	N = 10 M= 8 F= 2	MA= 27 ± 6,1	NA	NA
Hill et al., (2013)	25I-NBOMe	Case series	M= 7	MA= 21,5 ± 3,41	Depression, SUD	Yes
Liakoni et al., (2017)	2,5-Dimethoxy-4-ethylphenethylamine (2C-E)	Retrospective study	M= 1	19	NA	NA
Madsen et al., (2017)	NBOMes	Retrospective study	N = 43 M= 32 F= 11	MA= 21	NA	NA
Forrester (2014)	25I-NBOMe, 25C-NBOMe and ND NBOMe	Observational study	N = 25 M= 22 F= 3	MA= 17 ± 2,9	NA	NA
Miyajima et al., (2008)	2C-T-4	Case report	M= 1	MA= 40	SUD	NA
Papaseit et al., (2018)	2C-B	Non controlled prospective observational study	N = 16 M= 8 F= 8	MA= 33,3 ± 3,7	NA	NA
Papaseit et al., (2020)	2,5-Dimethoxy-4-ethylphenethylamine (2C-E)	Non-controlled prospective observational study	N = 10 M= 6 F= 4	MA= 27 ± 4	No	No
Rose et al. (2013)	25I-NBOMe	Case report	M= 1	18	NA	NA
Schetz et al., (2022)	25I-NBOMe	Retrospective analysis	Control group= 43 Study group= 15	MA control group= 24 MA study group= 23	NA	NA
Stoller et al. (2017)	2C-P	Case report	M= 1	19	No	NA
PIPERAZINE						
Austin and Monasterio et al., 2004	Rapture	Case report	M= 1	20	No	NA
Bossong et al. (2010)	mCPP	Observational study	N = 79	NA	NA	NA
Thompson et al. (2010)	BZP, TFMPP	Randomised, double-blind,	N = 35 M= 22 F= 13	MA= 24	No	No

(continued on next page)

Table 1 (continued)

Name, Year	Substance	Study design	Population (N, M, F)	Mean age± Standard deviation	Psychiatric comorbidity	Medical comorbidity (Yes;No)
Wilkins et al., (2007)	Benzylpiperazine (BZP) and trifluorophenylmethypiperazine (TFMPP)	Placebo controlled trial Observational study	NA	NA	NA	NA
STIMULANTS						
AMPHETAMINE-TYPE						
Daveluy et al., (2016) Lafferty et al., (2016)	Methiopropamine (MPA) Ethylphenidate	Case report Cross sectional study	M= 1 N = 413 M= 317 F= 96	30 N = 1 % MA< 20; N = 20 % 20 <MA< 29; N = 53 % 30 <MA< 39; N = 23 % 40 <MA< 49; N = 3 % 50 <MA< 59; N = 1 % MA> 60	No NA	Yes NA
Ricci et al. (2022) White et al., (2019)	Methamphetamine Methiopropamine (MPA)	Case report Short communication	M= 1 N = 11 M= 9 F= 2	25 MA= 24	NA NA	NA NA
TRYPTAMINE						
Alatrash et al. (2006)	5-methoxy-N,N-diisopropyl-tryptamine	Case report	M= 1	23	NA	NA
Rosenberg,(1964)	N,N-Dimethyltryptamine	Randomized control trial	M= 6	MA= 30	No	No
Szara et al., (1966)	N,N-diethyltryptamine	Randomized control trial	M= 20	NA	Schizophrenia	NA
POLYABUSE						
Beck et al., (2015)	MDPV, alpha-pyrrolidinovalephorone (a-PVP), methylene	Retrospective study	N = 201 M= 143 F= 58	MA= 36	NA	NA
Caloro et al., (2016)	Amphetamines, heroin, synthetic cannabinoids, benzylglycinamide	Case report	F= 1	24	NA	Yes
Caloro et al., (2018)	Phencyclidine, methoxphenidine, methoxyphencyclidine, ethylorketamine, norketamine, deschlorketamine	Case report	M= 1	32	SUD	NA
Ciucia et al., 2022	Synthetic cannabinoids, synthetic cathinones	Retrospective study	N = 604 M= 527 F= 77	MA= 29,9 ± 6,7	Personality disorder, Depressive episode, Psychotic disorder, Schizophrenia	NA
Hondebrink et al., (2015)	2C-B, 4-FA, MXE, 6-APB	Observational study	N = 30	MA= 22 ± 3,8	NA	NA
Kamijo et al. (2014)	Synthetic cannabinoids, synthetic cathinones, methoxetamine	Multicenter retrospective survey	N = 518 M= 425 F= 93	MA= 28,4 ± 8,4	NA	NA
Kihara et al., 2014	NRG-3 Cathinone- related, mephedrone, MDPV	Case report	M= 1	35	No	No
Khullar et al., (2014) Liakoni et al., (2015)	Synthetic cannabinoides Cocaine, cannabis, opioid, MDMA, heroin, ketamine, LSD	Case report Observational study	M= 1 N = 216 M= 148 F= 68	20 N = 42 16 <MA< 20, N = 79 21 <MA< 30, N = 55 31 <MA< 40, N = 40 MA> 40	SUD NA	No No
Martinotti et al. (2021)	Depressors, stimulants, cannabinoids, empathogens, dissociatives, opioids	Observational study	N = 110 M= 76 F= 34	MA= 32,57 ± 9,15	Bipolar disorder, Psychotic episode, Cluster B personality disorder, SUD, Alcohol abuse, Paranoid schizophrenia, Schizoaffective disorder, Manic episode, Depression, Anxiety disorder	NA

(continued on next page)

Table 1 (continued)

Name, Year	Substance	Study design	Population (N, M, F)	Mean age± Standard deviation	Psychiatric comorbidity	Medical comorbidity (Yes;No)
Matsumoto et al., (2016)	Unspecified NPS	Observational cross-sectional study	Group 1: N = 123 M= 112 F= 11 Group 2: N = 355 M= 317 F= 38	Group 1: MA= 28,2 ± 7,9 Group 2: MA= 23,3 ± 8,4	NA	NA
Stevenson et al., 2014	Methoxyphenylcyclidine (3-MeO-PCP), methylenedioxypyrovalerone (MDPV)	Case report	M= 1	20	NA	Yes
Tancer & Johanson et al., 2001	MDMA, mCPP	Randomized control trial	N = 22 M= 8 F= 14	MA= 23,6	No	No
OTHER						
Anderson et al., (2015)	El blanco	Case report	M= 1	30	Paranoid schizophrenia	NA
El-Higaya et al., (2011)	Compound 4-fluorotropacocaine (pFBT), Desoxypipradrol (2DPMP)	Case series	Case 1=M Case 2=M	Case 1= 20 Case 2= 40	Case 1: previous SUD Case 2: No	No
Janiri et al., (1991)	Zipexprol	Observative study	N = 30 M= 19 F= 11	MA= 22,6 ± 1,8	Somatoform disorder, Conduct disorder, Affective disorders, Antisocial personality disorder, Dependent personality disorders	NA
Lagoutte-Renosi et al., 2021	5-MeODALT, Alpha-pyrrolidinovalerophenone, a synthetic cathinone (flakka)	Case report	Case 1 =M Case 2=M	Case 1 = 34 Case 2 = 32	Depression, anxiety	NA
Taljemark et al., 2012	4-OH- MET (metocin)	Case report	M= 1	17	No	No
Wilcox et al., 2012	α-Methyltryptamine	Observational	N = 15 M= 8 F= 7	MA= 39	No	No
Moccia et al., (2019)	Methoxetamine	Case report	M= 1	23	NA	NA

N = Number of subjects; M=Male; F=Female; MA=Mean Age; NA= not applicable; SC=Synthetic Cannabinoids; SCRA=Synthetic Cannabinoid Receptor Agonists; SUD= Substances Use Disorder; C=cannabis.

including hypersexuality and aggression. Delusional thoughts were frequently observed, often accompanied by vivid auditory and visual hallucinations. In a few cases, tactile, olfactory, and cenesthetic hallucinations were also described. Comorbid psychiatric conditions included substance use disorders, attention deficit and hyperactivity disorder (ADHD), and affective disorders.

PCP-like compounds were typically associated with confusion, reduced consciousness, and visual hallucinations. In one case, delusional ideation and aggressive behavior were also reported.

Phenethylamines showed a high prevalence of agitation, confusion, derealization, and emotional instability. Several cases exhibited delusional thinking and paranoia, along with intense hallucinations, often multimodal (visual, auditory, and occasionally tactile or olfactory). Psychotic episodes were frequently reported, especially in association with NBOMe and 2C-series compounds.

Piperazines were associated with anxiety, agitation, insomnia, paranoia, and persecutory delusions. Hallucinations - both auditory and visual - were commonly reported, sometimes in combination with olfactory phenomena.

Amphetamine-type stimulants intoxication clinically presented with agitation, paranoia, thought insertion, and persecutory delusions. Hallucinations were common and often complex, involving frightening visual distortions and command auditory hallucinations. Cases of depression, suicidal ideation, and social withdrawal were also reported.

Tryptamine users experienced agitation, perceptual distortions, paranoia, and dissociative symptoms. One early trial reported schizophrenia-like symptoms such as thought disorder and paranoid ideation.

In cases involving the combined use of multiple NPS or other psychoactive drugs, patients frequently displayed severe agitation, emotional lability, suicidal ideation, bizarre or religious delusions, and a range of hallucinations (including visual, auditory, tactile, and olfactory). Several reports noted complex delusional systems, often with

preserved insight or alternating lucidity. Comorbid psychiatric conditions were common and included schizophrenia, mood disorders, personality disorders, and substance use disorders.

Other compounds. Less frequently reported substances showed heterogeneous psychiatric symptoms, ranging from anxiety, logorrhea, and persecution delusions to dissociative states and hallucinations of various sensory modalities.

For detailed information on the substance used, route of administration, psychiatric comorbidities, and specific symptomatology - including non-psychotic psychiatric symptoms, negative symptoms, thought disturbances, and hallucinations - please refer to Table 2.

3.3. Symptomatology and outcomes

A further analysis was conducted, reporting for each substance the total number of subjects included across studies, as well as the number of articles providing information on specific psychotic symptomatology, such as “Thought and ideation disturbances”, “Hallucinations”, “Negative Symptoms”, and “Psychedelic experience”. Similarly, the number of articles reporting specific outcome data - namely “Acute psychosis with remission”, “Onset with persistence”, and “Psychotic relapse” - was also recorded. These findings are presented in Table 3.

SCRA accounted for the largest portion of the sample (N = 4813). Among these, thought and ideation disturbances were reported in 37 cases, hallucinations in 40, and negative symptoms in 10. Psychedelic experiences were documented in 16 subjects. Acute psychosis with full remission occurred in 38 cases, while persistent psychotic symptoms were reported in 9 cases, and psychotic relapses in 10.

Synthetic cathinones (N = 269) were also associated with significant psychopathological burden. Thought disturbances were present in 11 subjects, and hallucinations in 9, while psychedelic-like experiences were observed in 3 individuals. Acute psychosis with remission occurred in 13 cases, whereas no persistent symptoms or relapses were reported.

Table 2
Psychiatric symptomatology associated with Novel Psychoactive Substances (NPS).

SUBSTANCE								
Name, Year	Substance	Psychiatric comorbidity	Administration	Poly-abuse (substance)	Non-psychotic psychiatric symptoms	Negative Symptoms	Thought and ideation disturbances	Hallucinations
<i>SYNTHETIC CANNABINOIDS</i>								
Abouché et al., (2016)	JWH-18	Depression	Smoked	LSD	NA	NA	NA	Unspecified visual hallucinations
Alhassan et al. (2024)	Spice	No	Smoked	Cannabis (occasional)	Severe agitation, aggression, disorganized behavior, bizarre conduct (hiding keys in vagina)	Poor hygiene, social withdrawal during acute phase	Persecutory delusions, conspiracy ideas, illogical and circumstantial thinking	Visual hallucinations, auditory hallucinations
Altintas et al., (2016)	Unspecified SCRA	NA	NA	Cannabis, alcohol, stimulant, opioid	Suicidal ideation, suicide attempt	NA	NA	NA
Altintop et al., 2020	Unspecified SCRA	NA	NA	NA	NA	NA	Unspecified psychosis	NA
Barceló et al., (2017)	5F-ADB, MMB-2201	No	Smoked	Cannabis	Agitation, confusion; anxiety, suicide attempted	No	Delusions of influence and grandeur, altered language, bradypsychia	No
Bassir Nia et al. (2016)	Unspecified SCRA	Schizophrenia, Schizoaffective disorder, Bipolar disorder, MDD, others	Smoked	Cannabis	Agitation; suicidal ideation, mood symptoms	No	Thought disorganization, internally preoccupation	No
Bebarta et al., (2012)	Spice	No	Smoked	Acetaminophen, dextromethorphan, doxylamine	Aggression, agitation, sedation; panic	No	Paranoia	Visual and somatic hallucinations
Berry-Cabàn et al., 2013	Spice	Schizoaffective disorder	Smoked	Mephedrone, cannabis, alcohol	No	Aspecific negative symptoms	Thought-blocking, disorganized behaviors, disorganized thinking, paranoid delusion, referential delusion, loss of ego boundaries	Verbal hallucinations
Besli et al., (2015)	Unspecified SCRA	NA	Smoked	Alcohol, amphetamines	Agitation, unconsciousness	NA	NA	Perceptual changes (disturbance of vision, sense of smell and body perception)
Bonaccorso et al., (2018)	Unspecified SCRA	Paranoid schizophrenia, Schizoaffective disorder, Bipolar disorder	Smoked	Crack, cocaine, heroin, alcohol, MDMA, cannabis, legal highs	Agitation, verbal and physical aggression, sexual disinhibition, bizarre behavior	NA	Disorganization. Delusional mood, persecutory and grandiose delusions	Second- and third-person auditory hallucinations
Celofiga et al., (2014)	Unspecified SCRA	Paranoid schizophrenia, Undifferentiated schizophrenia	Smoked	NA	Agitation Mood changes, anxiety, elevated affect	Unspecified negative symptoms (antecedents to the use of SCRA)	Chronic paranoid and grandiose delusions, bizarre behaviour, formal thought symptoms	Haptic hallucinations

(continued on next page)

Table 2 (continued)

SUBSTANCE								
Dawn Benford et al., 2011	Spice	No	Smoked	NA	Severe anxiety	NA	Paranoia	Unspecified auditory and visual hallucinations
Di Petta, 2016	Unspecified SCRA	Previous psychosis in substance abuse	Smoked	Salvia divinorum, cocaine, efedrine, ketamine, alcohol	Agitation, Suicide attempts, irrational behavior	NA	Magical delusions, mystical ideas, delusions of greatness and persecution, full of bizarre details (UFO, superheroes, and power), Capgras syndrome, Ekbom syndrome, twilight state of consciousness promotes illusions	Visual or auditory hallucinations
Durand et al., (2015)	Unspecified SCRA	No	NA	Cannabis	Agitation	NA	Persecutory/mystical delusions	NA
Every-Palmer et al., 2011	JWH-018	Schizophrenia, Schizoaffective disorder, Borderline personality	Smoked	No	Agitation, disorganization	NA	Paranoid, disorganization, fear and alert status, impulse to do evil things, sense of the end of the world	NA
El Zahran et al., (2019)	Cumyl-4- cyano-BINACA	No	Smoked	No	Agitation	NA	Visual hallucinations	NA
Glue et al., (2013)	K2	Affective disorder, Psychotic episodes	NA	NA	Homicidal ideation. Affective changes (anxious, depressive), intense suicidal thinking/behavior	NA	Paranoia, thought disorder, disorganized behavior	NA
Haro et al., (2014)	JWH-081, JWH-250, JWH-203, JWH-019	NA	NA	NA	Laughter forfeit, derealization, depersonalization, movement disorder similar to catatonia	Soliloquy with personal hygiene deteriorated	Self-references when eating or walking	Visual hallucinations
Hermanns-Clausen et al. (2018)	AB-CHMINACA,MDMB- CHMICA	NA	Oral, smoked, sniffed	Amphetamines	Restlessness/agitation, amnesia. Anxiety	NA	Acute psychosis, self-mutilating behavior	NA
Helge Müller et al., 2009	Spice	History of cannabis induced recurrent psychotic episodes	Smoked	No	Increased anxiety	NA	Delusions of influence (controlled through a chip implanted in his abdomen)	Imperative voices
Hoyte et al., (2012)	Unspecified SCRA	NA	Smoked	No	Agitation, irritability, drowsiness, lethargy, confusion, dizziness	NA	Paranoia, unspecified delusions	Unspecified hallucinations
Hurst et al., (2011)	Spice	No	Smoked	Cannabis, alcohol	Insomnia, psychomotor agitation. Suicidal ideation, anxiety	Flat affect, alogia	Paranoid delusions, thought blocking, disorganized speeches, disorganized behavior, psychomotor retardation	Auditory hallucinations, Visual hallucinations

(continued on next page)

Table 2 (continued)

SUBSTANCE									
Johnson et al., (2011)	Spice	NA	Smoked	No	Mild to moderate. cognitive impairment. Changes in mood.	NA	Altered speech, paranoid delusions of persecution, sense of the end of the world, loss of ego boundaries, sense of revelation, disorganized and tangential thought	Changes in perception	
Simmons et al., (2011)	JWH-018, JWH-073	No	Smoked	No	Agitation, amnesia, bizarre behaviour	NA	Paranoia, unspecified delusions	No	
Kekelidze et al., (2019)	JWH, AB-PINACA, TMCP	NA	NA	NA	Anxiety, fear. Disorientation (in place, time and self), dreamlike clouding of consciousness, catatonic disorders (in form of sub stupor), catalepsy, profound impairments to consciousness	NA	Perceptual delusions, delusional experiences, severe disintegration of all components of thought, degraded self-awareness	Multiple vivid and dynamic pareidolias, scene-like visual hallucinations, tactile and auditory hallucinations, daydream-like fantastic hallucination	
Kotan et al., (2017)	Unspecified SCRA	No	NA	N SC and C users= 41	Irritability, nervousness. Loss of motivation; anxiety	Loss of motivation	NA	NA	
Kuzucuoglu et al., 2018	Bonzai	NA	NA	NA	Anxiety, panic. Confusion, sleepiness, agitation, amnesia	NA	NA	Auditory hallucination	
Malik et al., (2021)	K2	Schizophrenia, SUD	NA	NA	Aggressivity	NA	Bizarre behavior, delusional self-inflicted injury to the eye	NA	
Mathews et al., (2019)	Unspecified SCRA	NA	NA	NA	Relaxed/stoned, lightheadedness, confusion, time distortion. Anxiety, depression, euphoria, panic attack	NA	Paranoia, confused/ cloudy thinking, racing thoughts	Auditory hallucinations, visual hallucinations	
Monte et al., (2017)	Unspecified SCRA	NA	NA	NA	Agitation	NA	Unspecified delusion	Unspecified hallucinations	
Oluwabusi et al., (2012)	K2	No	Smoked	NA	Insomnia. Low mood hyperactivity, anxiety symptoms	Lack of interest in usual daily social activities	Paranoid delusions, grandiose delusions, somatic preoccupation, disorganized behavior	Musical auditory hallucinations, colorful visual hallucinations	
Ozer et al., (2016)	Unspecified SCRA	No	Smoked	No	Anxiety, agitation, irritability, confusion, insomnia, anorexia. Dysphoric mood,	No	Capgras syndrome, persecutory delusions	Unspecific hallucinations	

(continued on next page)

Table 2 (continued)

SUBSTANCE								
Öznur et al., (2018)	Unspecified SCRA	NA	Smoked, oral	Cannabis, alcohol	suicidality with self-injury Suicidal ideas, euphoria	NA	Scepticism	NA
Peglow et al., (2012)	Spice	Post traumatic stress disorder, SUD	Smoked	No	Traumatic flashbacks	No	Disorganized, bizarre behavior	Visual hallucinations
Rahmani et al. (2014)	Unspecified SCRA	No	Smoked	Cannabis, LSD, psilocybin, mushrooms, spice, bath salts, oxycodone	Insomnia sleep, irritability, mild agitation	No	Delirium of influence and possession, mystical delusions, sense of the end of the world, Capgras syndrome, bizarre and disorganized behaviors	Auditory hallucinations, visual hallucinations
Roberto et al., (2016)	Unspecified SCRA	No	Smoked	No	Confusion, amnesia, agitation, insomnia, catatonia. Elevated mood	Intermittent mutism, avolition	Thought disorganization, paranoid delusions, persecution ideation	Unspecific auditory hallucinations
Robson et al., (2021)	Unspecified SCRA	Schizophrenia	Smoked, oral	Alcohol	Agitation, irritability, sleep disorder, memory disturbance. Anxiety, mood disturbance, cognitive impairment, suicidality	No	Psychosis, paranoid reaction	Unspecific auditory hallucinations
Satodiya et al., 2020	K2	Schizophrenia	Smoked	NA	No	Monotone speech, minimal gestures, social withdrawal, lack of spontaneity, blunted affect, avolition	No	No
Skryabin et al., 2019	Unspecified SCRA	SC dependence, cannabis use disorder, SC abuse	NA	NA	Catatonia. Anxiety, motor retardation with elements of catatonia, motor agitation	NA	Kandinsky- Clerambault syndrome, delusions of influence, automatisms, telepathy, thought broadcasting, thought insertion, delusional ideas of interpretation, persecutory delusions, delusional ideas of a philosophical and esoteric nature, cenestopathic automatisms	Tactile hallucinations, pseudo hallucinations, acute verbal hallucinations with threatening monologues or dialogues from somewhere behind a wall or behind their backs
Skryabin et al., (2018)	Spice	NA	NA	NA	Psychomotor agitation. Anxious-depressive	Negative symptoms of schizophrenia	Kandinsky-Clerambault syndrome, persecutory delusions, paranoia	Threatening monologues or

(continued on next page)

Table 2 (continued)

SUBSTANCE								
Sönmez et al. 2016	Unspecified SCRA	No	Smoked	No	symptoms, mild hypomania Distressed mood. Agitation, insomnia, self and etero harming ideation, irritation, bursts of anger insomnia	No	Delusions of persecution and reference, shape and content of thought altered	dialogs, unspecific visual hallucinations No
Sweet et al., (2017)	Unspecified SCRA	NA	Smoked	NA	Psychomotor agitation	No	Paranoia	NA
Theunissen et al. (2022)	JWH-018	Occasional users of cannabis	Smoked	No	Dissociative effects, amnesia, derealization, depersonalization, induced feelings of confusion	No	No	Altered internal and external perception
Theunissen et al., (2019)	JWH-018	Occasional users of cannabis	Smoked	No	Confusion, drowsiness, low and transient dissociation, amnesia, confusion	No	No	Higher external and internal perception
Tofghi et al., 2012	K2, JWH-018	No	Oral	No	Sedation, depersonalization	no	No	No
Tung et al., (2012)	Spice	No	Smoked	Poly-substances abuse	Agitation, insomnia. Dysphoric mood	NA	Persecutory delusion, disorganized thoughts, disorganized behaviour, irrelevant speech, bizzarre behaviours	Auditory hallucination
Udow et al., (2018)	Unspecified SCRA	Occasional visual hallucinations for many years with preserved insight	Oral	No	Anxiety.	NA	Persecutory delusions	Bizarre visual hallucinations
Waugh et al., (2016)	Unspecified SCRA	NA	NA	Alcohol, opioids, benzodiazepines	Agitation	NA	NA	NA
Welter et al., (2017)	Unspecified SCRA	Paranoid schizophrenia, Depression without psychosis, Schizoaffective disorder, other	NA	NA	NA	Motor retardation, blunted affect, poor rapport, emotional withdrawal	Persecution delusions, disorganization behaviour, grandiosity	Unspecific hallucinations
WILLIAMS and HIMMELSBACH, (1846)	Synthetic cannabinoids ("Bonzai")	None reported	Smoked	No	Agitation, irritability, insomnia, craving, severe anxiety	NA	Persecutory and jealous delusions; disorganized behavior	Elementary auditory hallucinations; visual hallucinations (grasping in the air)
Yazici et al. (2017)	Pyrahexyl compound	Schizophrenia (1 case); psychopathic/antisocial traits	Oral	No	Euphoria, garrulousness, reduced concentration, irritability, indifference, poor hygiene	Apathy, loss of interest, neglect of personal hygiene	Circumstantial thought, paranoia in one case, manic reaction during withdrawal	Transient auditory and visual hallucinations in one case (paranoid psychotic episode)

(continued on next page)

Table 2 (continued)

SUBSTANCE								
SYNTHETIC CATHINONES/ BATH SALTS								
Albert et al., (2022)	α -PVP ("Flakka"), α -PHP, α -PHIP	Substance induced paranoid psychotic episode	Ketamine, cocaine, amphetamine, methamphetamine, gamma hydroxybutyrate (GHB), heroin	No	Poorly oriented in time and place, attention deficits	NA	Persecutory and somatic delusion, logorrhea	No
Batisse et al., (2014)	NRG3, mephedrone, MDPV	SUD	Intravenous injection, snorted, smoked, oral	NRG3, mephedrone, MDPV, cocaine, F-hydroxybutyric acid, alcohol	Agitation, acute sexual behavior disorder with hypersexuality, violent behavior with endangerment, maiming. Anxiety, suicidal ideas, suicidal attempt	NA	Unspecific psychotic symptoms	Auditory hallucinations, visual hallucinations
Blanco et al., (2021)	N-ethylpentylone	NA	NA	MDMA, benzodia- zepines, amphetamine and/or methamphetamine, cocaine, 5F-NPB 22, butylone, cannabis, heroin	Agitation, confusion	NA	NA	Unspecified visual hallucinations
Chan et al., (2013)	6-2-aminopropylbenzofuran (6-APB)	No	NA	6-APB, JWH-122, THC	Agitation, amnesia, self-harm, suicidal ideation	NA	Paranoia, delusional thoughts, belief that one of his friends might be dead, delusions of guilt	NA
Chou et al., (2021)	Toxic coffee packets	History of psychiatric disorder	Oral	NA	Agitation, combative behavior, delirium. Low mood	NA	NA	Unspecific visual hallucinations
Dolengevich-Segal et al., (2016)	Mephedrone	ADHD, SUD	NA	No	Psychomotor restlessness, tiredness. Anxiety	NA	Delusions of influence, delusions of persecution	Visual hallucinations, cenesthopathy (insects crawling under the skin)
Douglas et al., 2012	Methylenedioxypyrovalerone (MDPV)	NA	NA	Amphetamine, cannabis, vanilla sky, cocaine, venlafaxine, herbal product, butane	Agitation, insomnia	NA	Paranoid ideation	Auditory hallucinations, tactile hallucinations
Fujita et al., (2018)	α -PHP	NA	NA	Flunitrazepam	Fear, restlessness. Anxiety	NA	NA	Unspecific Hallucinations
Paul et al., (2021)	α -PVT	NA	Intravenous	NA	Agitation, mild stimulation, aggressive and violent behavior, confusion	NA	Paranoid ideation	Unspecified hallucinations
Roberts et al., (2017)	Mexedrone, 3-methoxy-2-methylamino-1-4-methylphenyl propanone	No	Smoked, oral	Present, not specified	Agitation	NA	Mystical/ supernatural/ demonic delusions, paranoia	Visual hallucination, auditory hallucinations ("ghosts and dead people")
Romanek et al., (2017)	Unspecified cathinones	NA	NA	Alcohol, opiates/opioids, cocaine, benzodiazepines, cannabis, pregabalin	Agitation	NA	Prolonged psychosis	NA
Schloerkeremper (2018)	Unspecified cathinones	NA	NA	Methamphetamine	Aggressiveness, agitation	NA	Paranoid delusions	NA

(continued on next page)

Table 2 (continued)

SUBSTANCE								
Simonato et al., (2018)	Alpha-PVP	Substance induced psychosis, schizoid personality disorder	Smoked	Cannabis, skunk, alcohol, NPS	Stimulation with mental euphoria, insomnia, sexual arousal. High levels of physical energy, panic attacks, anxiety	NA	Ekbom's syndrome, severe persecutory delusion	Unspecific auditory hallucinations Unspecific visual hallucinations
Truscott et al., (2013)	NA	SUD	Snorting	No	Aggressive behavior	NA	NA	NA
Umebachi et al., (2016)	α -pyrrolidinovalerophenone	Depression, Bipolar disorder	Rectal insertion, inhalation	NA	Agitation	NA	Paranoid delusions	NA
PCP-LIKE DRUGS								
Dunlop et al., (2020)	3-hydroxyphencyclidine (3-HO-PCP)	NA	Sniffing, rectal insertion	Cough syrup	Confusion, reduced consciousness	NA	NA	Visual hallucinations
Zidkova et al., (2017)	3-Methoxy-Phencyclidine	No	Oral	Alcohol	NA	NA	NA	NA
PHENETHYLAMINES								
Breitaudeau Deguigne et al., (2015)	2C-P	No	Oral, sniffing	Alcohol, cannabis	Severe agitation, confusion, disorientation	NA	Loghorrea, delirium	NA
Gee et al. (2016)	25 C, 25B, 25I-NBOMes	NA	Sniffing, oral, intravenous	Alcohol nicotine, cannabis, amphetamine, methamphetamine, caffeine	Violent agitation, sympathomimetic syndrome	NA	NA	NA
Hill et al., (2013)	25I-NBOMe	Depression, SUD	Intravenous, oral, snorting	Alcohol	Agitation, aggression, chaotic feeling, self-harming behavior, derealization. Euphoria	NA	Unspecified psychosis	Unspecified auditory hallucinations, unspecified visual hallucinations ("shapes moving around or animal running around together")
Liakoni et al., (2017)	2,5-Dimethoxy-4-ethylphenethylamine (2C-E)	NA	NA	Alcohol	Agitation, confusion	NA	Severe hallucinations	NA
Madsen et al., (2017)	NBOMes	NA	NA	Alcohol, cannabis, amphetamine, cocaine, benzodiazepines, methylenedioxymethamphetamine	Agitation	NA	Unspecified psychosis	Unspecified hallucinations
Forrester (2014)	25I-NBOMe, 25C-NBOMe and ND NBOMe	NA	Oral, smoked	Alcohol, cannabis, mushrooms, synthetic cathinone	Empathic feelings, change in consciousness, unusual body sensations, agitation, aggression, violent behavior, insomnia. Euphoria	NA	Paranoia	Unspecified hallucinations
Miyajima et al., (2008)	2C-T-4	SUD	Oral	NA	Anxiety, sexual disinhibition	NA	Delusional state, incoherent speech, sense of the end of the world	NA
Papaseit et al., (2018)	2C-B	NA	Oral	No	Psychosomatic anxiety	NA	NA	Auditory hallucinations with voices, visual hallucinations (animals, things,

(continued on next page)

Table 2 (continued)

SUBSTANCE								
Papaseit et al., (2020)	2,5-Dimethoxy-4-ethylphenethylamine (2C-E)	No	NA	No	Confusion, drowsiness, pleasure feelings. Euphoria	NA	NA	insects, people, lights, spots) Auditory hallucinations (sounds, voices), visual hallucinations (things, people, lights, spots)
Rose et al. (2013)	25I-NBOMe	NA	NA	Cannabis	Severe agitation; aggressiveness, bizarre behavior	NA	NA	Unspecified hallucinations
Schetz et al., (2022)	25I-NBOMe	NA	NA	NA	Derealization episodes, depersonalization episodes, suicidal thoughts, agitation. Depression, panic reactions	NA	Bizarre delusions	Auditory hallucinations, visual pseudohallucinations (visual snow, afterimages, flashes of colors, geometric shapes and halos around objects)
Stoller et al. (2017)	2C-P	No	Oral	Alcohol, tetrahydrocannabinol, opiates	Agitation	NA	NA	Unspecified hallucinations
<i>PIPERAZINE</i>								
Austin and Monasterio et al., 2004	Rapture	No	Oral	Cannabis, nitrous oxide	Anxiety	NA	Persecution delusions, poisonous delirium	Auditory hallucinations, visual hallucinations, olfactory hallucinations
Bossong et al. (2010)	mCPP	NA	Oral	NA	Dizziness, agitation; Anxiety	NA	Unspecified delusion, paranoia	Unspecified hallucinations
Thompson et al. (2010)	BZP, TFMPP	No	Oral	Alcohol, benzodiazepines	Agitation, insomnia; Anxiety	NA	Unspecified delusion	Unspecified hallucinations
Wilkins et al., (2007)	Benzylpiperazine (BZP) and trifluorophenylmethylpiperazine (TFMPP)	NA	NA	NA	Insomnia, poor appetite, hot/cold flushes, heavy sweating, confusion, irritability, feelings of aggression, suicidal thoughts. Mood swings	NA	Paranoia	Auditory hallucinations, visual hallucinations
<i>STIMULANTS</i>								
<i>AMPHETAMINE-TYPE</i>								
Daveluy et al., (2016)	Methiopropamine (MPA)	No	Oral	Cannabis	Confusion, incoherent speech	NA	Paranoid delusion	Unspecified hallucinations
Lafferty et al., (2016)	Ethylphenidate	NA	Injection	NA	Anxiety	NA	Thought insertion, paranoia	Unspecified visual hallucinations, unspecified tactile hallucinations, unspecified auditory hallucinations
Ricci et al. (2022)	Methamphetamine	NA	Smoked	Methamphetamine, cocaine, cannabis	Erratic sleep, poor appetite with weight loss.	Social withdrawal,	Paranoid ideation, ideas of reference, delusions of persecution	Visual hallucinations and illusions (frightening animals, (continued on next page)

Table 2 (continued)

SUBSTANCE					Suicidal thoughts, depression	difficulty concentrating		bodily distortions, demonic faces while staring at inanimate objects), auditory hallucinations (commanding voices) Unspecified hallucinations
White et al., (2019)	Methiopropamine (MPA)	NA	NA	NA	Agitation, confusion, reduced level of consciousness	NA	NA	
<i>TRYPTAMINE</i>								
Alatrash et al. (2006)	5-methoxy-N,N-diisopropyl- tryptamine	NA	Oral	NA	Agitation	NA	NA	Unspecified hallucinations
Rosenberg,(1964)	N,N-Dimethyltryptamine	No	Injection	No	Anxiety, euphoria	NA	Perceptual distortions	NA
Szara et al., (1966)	N,N-diethyltryptamine	Schizophrenia	NA	NA	Empathogen-like effect, body misperceptions, distortions of time	NA	Paranoid ideation; loosening of associative thinking	Unspecified hallucinations
<i>POLYABUSE</i>								
Beck et al., (2015)	MDPV, alpha- pyrrolidinovalerophenone (a- PVP), methylene	NA	NA	MDPV, alpha- pyrrolidinovalerophenone (a- PVP), methylene	Agitation, reduced level of consciousness	NA	Delusions	Unspecified hallucinations
Caloro et al., (2016)	Amphetamines, heroin, synthetic cannabinoids, benzylglycinamide	NA	NA	Amphetamines, heroin, synthetic cannabinoids, benzylglycinamide	Agitation, aggression, insomnia, irritability, rage bouts, psychomotor retardation. Emotional instability	NA	Persecutory, bizarre sexual delusion, speaking alone; accelerated speech	NA
Caloro et al., (2018)	Phencyclidine, methoxyphenidine, methoxyphencyclidine, ethylmorketamine, norketamine, deschlorketamine	SUD	NA	Phencyclidine, methoxyphenidine, methoxyphencyclidine, ethylmorketamine, norketamine, deschlorketamine	Extreme anguish, verbal and physical aggression	NA	Religious delusion, paranoia	NA
Ciuca et al. (2022)	Synthetic cannabinoidds, synthetic cathinones	Personality disorder, Depressive episode, Psychotic disorder, Schizophrenia	NA	Heroin/opiate, cannabis, alcohol, benzodiazepines, cocaine	Euphoria, drowsiness, loss of appetite, decreased sexual appetite, decreased activity, personality changes, confusion, motor incoordination, agitation, hyperactivity, aggression, irritability	NA	Slowed thinking, disorganized thought, delusion of grandeur and persecution	Visual hallucinations, illusions, perceptual distortions
Hondebrink et al., (2015)	2C-B, 4-FA, MXE, 6-APB	NA	NA	MDMA, cocaine, alcohol	Dizziness, confusion, agitation, insomnia, ataxia, sympathomimetic effect. Anxiety,	NA	Paranoia, perceptual anomalities, psychosis	Unspecified hallucinations

(continued on next page)

Table 2 (continued)

SUBSTANCE								
Kamijo et al. (2014)	Synthetic cannabinoids, synthetic cathinones, methoxetamine	NA	Inhaled, oral, sniffed, inserted anally	Cannabis, alcohol benzodiazepines	euphoria, dysphoria Agitation, irritability, anxiety, fear, confusion, abnormal behavior, aggressive behavior, inability to speak, short-term memory deficits, drowsiness, panic attacks, seizures, stupor. Suicidal ideation	NA	Dissociative symptoms (derealization, depersonalization, and catatonic-like state), agitation, combative or violent behavior, delusion, paranoia	Unspecified hallucinations
Kihara et al., 2014	NRG-3 Cathinone- related, mephedrone, MDPV	No	Inhalation, oral	NRG-3 Cathinone- related, mephedrone, MDPV	Agitation, passivity of volition, energetic despite sleep, prosopagnosia, episodes of consciousness but not responsiveness, agitation, reduced sleep, confusion. Anxiety	NA	Depersonalization, derealization, prosopagnosia, persecutory delusions, abnormal writhing movements	Visual hallucinations (people shooting at him), auditory hallucinations (sexual moans), tactile hallucinations (metal objects thrown at him), olfactory hallucinations
Khullar et al., (2014)	Synthetic cannabinoides	SUD	Oral, smoked	Cannabis	Aggressive behavior, agitation, insomnia, listlessness, shivers, loss of inhibitions. Anxiety, dysphoria, euphoria, self-mutilation, suicidal thoughts	No	Paranoia	Unspecified hallucinations
Liakoni et al., (2015)	Cocaine, cannabis, opioid, MDMA, heroin, ketamine, LSD	NA	Oral, smoked	Pentylone, tramadol F53	NA	NA	Delusional parasitosis	Unspecified hallucinations
Martinotti et al. (2021)	Depressors, stimulants, cannabinoids, empathogens, dissociatives, opioids	Bipolar disorder, Psychotic episode, Cluster B personality disorder, SUD, Alcohol abuse, Paranoid schizophrenia, Schizoaffective disorder, Manic episode, Depression, Anxiety disorder	NA	Stimulants, cannabinoids, depressors, empathogens, dissociatives, opioids, psychedelics	Psychomotor agitation, aggression, self-harm, suicidality stand out. Suicidality	NA	Reference and paranoid delusions (paraphrenic delusions, with a feeling of unreality, while the ability to analyze the feeling is preserved)	NA

(continued on next page)

Table 2 (continued)

SUBSTANCE								
Matsumoto et al., (2016)	Unspecified NPS	NA	NA	NPS	Amnesic syndrome	NA	NA	NA
Stevenson et al., 2014	Methoxyphencyclidine (3-MeO-PCP), methylenedioxypyrovalerone (MDPV)	NA	Inhalation, snorting	Butane gas	NA	NA	Delusions (talking to spirits of dead people, travelling to different worlds and having a girlfriend with whom he had children, his house would be used as a base for superheroes so he would need to get rid of his father who lived in the house)	Panoramic visual hallucinations, auditory hallucinations (friends talking to him from pictures, voice saying "kill him", persistent voice repeating his thoughts)
Tancer and Johanson (2001)	MDMA, mCPP	No	Oral	MDMA, mCPP	NA	NA	NA	Unspecified hallucinations
OTHER								
Anderson et al., (2015)	El blanco	Paranoid schizophrenia	Powder drink	NA	NA	NA	NA	NA
El-Higaya et al., (2011)	Compound 4-fluorotropacocaine (pFBT), Desoxypipradrol (2DPMP)	Case 1: previous SUD	Snorted	NA	NA	NA	NA	NA
Janiri et al., (1991)	Zipeprol	Case 2: No Somatoform disorder, Conduct disorder, Affective disorders, Antisocial personality disorder, Dependent personality disorders	Oral	NA	NA	NA	NA	NA
Lagoutte-Renosi et al. (2021)	5-MeODALT, Alpha-pyrrolidinovalerophenone, a synthetic cathinone (flakka)	Depression, anxiety	Inhaled	No	Agitation, disorientation, stereotyped movements and muscle spasticity. Logorrhea	NA	Ideas of persecution	Unspecified hallucinations
Taljemmark et al., 2012	4-OH- MET (metocin)	No	Inhaled	Cannabis	Severe agitation. Acute suicidality	Mute, apathetic	NA	NA
Wilcox et al., 2012	α -Methyltryptamine	No	NA	No	Euphoria, anxiety, depressed mood	NA	NA	Unspecified visual hallucinations
Moccia et al., (2019)	Methoxetamine	NA	Intravenous	Alcohol, cannabis, ketamine, LSD	Affective withdrawal, motivational anhedonia	Emotional blunting, curbing of interests, diminished social drive, impoverished speech; motivational anhedonia	Detachment from reality, absorption in imaginative thoughts	Unspecified visual hallucinations, unspecified auditory hallucinations

N = Number of subjects; M=Male; F=Female; MA=Mean Age; NA= not applicable; SC=Synthetic Cannabinoids; SCRA=Synthetic Cannabinoid Receptor Agonists; SUD= Substances Use Disorder; C=cannabis.

PCP-like compounds were evaluated in a very small sample ($N = 3$), with one case each of hallucinations, psychedelic experience, and acute psychosis with remission, but no persistent outcomes.

Phenethylamines ($N = 158$) were linked to 11 cases of disordered thinking and 8 reports of hallucinations. No negative symptoms were observed, though 10 subjects reported psychedelic experiences. Acute psychosis with remission was also documented in 10 individuals, with only one case resulting in a psychotic relapse.

Piperazines ($N = 115$) were associated with lower frequencies of symptoms overall, including 4 cases each of thought disturbances and hallucinations, and 3 reports of psychedelic-like experiences. Only 2 cases developed acute psychosis with remission; no persistent symptoms or relapses were observed.

Amphetamine-type stimulants ($N = 426$) presented with 3 cases of thought disturbances and 4 cases of hallucinations, along with one report of negative symptoms and 4 psychedelic experiences. Acute psychosis was reported in 4 cases, with no persistence or relapse.

Tryptamines ($N = 27$) showed a lower incidence of symptoms, with 2 cases each of thought disturbances and hallucinations, and 3 reports of psychedelic experiences. No cases of acute or persistent psychosis were noted.

Poly-substance use ($N = 2154$) revealed 11 cases of thought disorders, 9 of hallucinations, and 9 individuals reporting psychedelic experiences. Acute psychosis with remission occurred in 10 subjects, with 3 cases persisting over time and 5 individuals experiencing a relapse.

For further details, see Table 3.

3.4. First rank symptoms

Although they have been recently de-emphasized in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 (American Psychiatric Association, 2013), Kurt Schneider's First Rank Symptoms (FRS) have been widely used in psychiatric diagnostic classification systems to diagnose schizophrenia since the late 1970s, and they remain among the most suggestive symptoms of the disorder (Moskowitz and Heim, 2018). These include voices conversing or arguing, voices commenting on one's behavior, somatic passivity experiences, thought insertion, thought withdrawal, thought interference/'made' thoughts, 'made' feelings, 'made' impulses or actions, audible thoughts, thought broadcasting, and delusional perception (Schneider, 1959).

To further explore which NPS are more likely to induce symptom profiles suggestive of schizophrenia, a focused analysis was conducted on the presence of FRS as defined by Kurt Schneider. Table 4 reports the number of studies in which FRS were documented, relative to the total number of subjects analyzed per substance class.

Among synthetic cannabinoids ($N = 4813$), auditory or verbal hallucinations were the most frequently reported FRS ($n = 9$), followed by experiences of thought withdrawal, insertion, interruption, or broadcasting ($n = 2$), passivity phenomena or delusions of control/influence ($n = 3$), and delusional perception ($n = 1$).

For synthetic cathinones ($N = 269$), 4 cases of auditory/verbal hallucinations and one case of passivity phenomenon were reported, with no documented instances of thought-related disturbances or delusional perception.

Among phenethylamines ($N = 158$), 4 cases of auditory/verbal hallucinations were identified, whereas no other FRS were reported.

In the piperazine group ($N = 115$), 2 cases of auditory hallucinations were observed, without other FRS features.

The amphetamine-type stimulant category ($N = 426$) included 2 cases of auditory hallucinations and 1 case of thought broadcasting/insertion-related symptoms.

No FRS were identified in the PCP-like compounds ($N = 3$) or tryptamines ($N = 27$) groups.

3.5. Risk of bias

The ROBINS assessment indicated an overall low-to-moderate risk of bias. The domains most affected were *confounding* and *missing data*, likely attributable to the wide range of publication years across the included studies. Evaluation of the selection-related domains (*reported result* and *participants*) as well as *measurement of outcomes* suggested a moderate overall risk of bias. By contrast, the domains *deviations from intended interventions* and *classification of interventions* consistently demonstrated a low risk of bias in the included studies (see Fig. 2).

Application of the CARE checklist, used to assess the transparency of the included case report, revealed a general presence of the investigated items, with no article showing a predominance of "absent" assessments (see Appendix 1).

4. Discussion

4.1. NPS and Substance/medication induced psychotic disorders (SIPD)

This systematic review provides a comprehensive synthesis of the existing literature on the association between NPS and psychosis. To the best of our knowledge, this work represents the first review to investigate the association between the overall misuse of NPS and psychosis. The evidence confirms that several classes of NPS can induce a wide array of psychopathological symptoms, ranging from mild perceptual alterations and affective disturbances to acute psychotic episodes indistinguishable from primary psychotic disorders, including schizophrenia.

According to the DSM-5, Substance/Medication-Induced Psychotic Disorder (SIPD) is characterized by the presence of delusions and/or hallucinations directly attributable to the physiological effects of a substance or medication, as determined by clinical history, physical examination, or laboratory findings (American Psychiatric Association, 2013; Fraser et al., 2012).

The scientific literature consistently distinguishes Primary Psychotic Disorders (PPD) - such as schizophrenia, brief psychotic episodes, schizotypal disorder, and delusional disorder - from SIPD (Fraser et al., 2012; Fusar-Poli et al., 2016). Conceptually, SIPD is defined as psychotic symptoms temporally related to psychoactive substance or medication exposure, while PPD refers to primary psychotic disorders with multifactorial etiology, including genetic vulnerability, neurobiological predisposition, and psychosocial stressors (van Dam et al., 2014; Wilson et al., 2018).

Moreover, positive symptoms and cognitive impairments (e.g., in memory, visual attention, and language) tend to resolve more rapidly in SIPD compared to PPD (Dawe et al., 2011; Helle et al., 2014).

Patients with SIPD are also less likely to have a family history of psychosis, but show higher levels of insight, as well as more severe hostility and anxiety than those with PPD. They are also more frequently associated with forensic histories, antisocial personality disorder diagnoses, and past traumatic experiences (Fraser et al., 2012). Additionally, patients with SIPD exhibit a higher prevalence of visual hallucinations, greater rates of suicidal ideation within the previous year, more frequent episodes of violent behavior, and an increased likelihood of a family history of substance misuse (Caton et al., 2005). This variation in symptomatology may reflect differences in perceived control, emotional distress, and the coping strategies employed by affected individuals (Bach and Hayes, 2002; Bak et al., 2003). However, in clinical practice the boundaries are often blurred: a substantial overlap exists between SIPD and PPD, and many patients initially diagnosed with SIPD later transition to a schizophrenia spectrum disorder (Murrie et al., 2020). Thus, SIPD and PPD may be better understood as conditions along a continuum, with shared vulnerability factors, rather than as entirely separate entities.

A significant gender disparity was observed across the studies, with the majority of subjects in the SIPD group being male - a finding

Table 3
Distribution of psychotic symptoms and outcomes across NPS classes.

Substance	Population tot*	SYMPTOMATOLOGY**				OUTCOME**		
		Thought and ideation disturbances	Hallucinations	Negative Symptoms	Psychedelic experience	Acute psychosis with remission	Onset with persistence	Psychotic relapse
SYNTHETIC CANNABINOIDS	N = 4829	41	42	13	16	44	9	10
SYNTHETIC CATHINONES/BATH SALTS	N = 269	11	9	0	3	13	0	0
PCP-LIKE DRUGS	N = 3	0	1	0	1	1	0	0
PHENETHYLAMINES	N = 158	11	8	0	10	10	1	0
PIPERAZINE	N = 115	4	4	0	3	2	0	0
STIMULANTS	N = 426	3	4	1	4	4	0	0
AMPHETAMINE-TYPE								
TRYPTAMINE	N = 27	2	2	0	3	0	0	0
POLYABUSE	N = 2154	11	9	0	9	10	3	5

N = Number of subjects
* Number of subjects
**Number of articles

Table 4
First Rank Symptoms (FRS) in psychosis associated with Novel Psychoactive Substances (NPS).

	First Rank Symptoms				
	Population tot	Auditory/ verbal hallucination	thought withdrawal/ insertion/ interruption/ broadcasting	Passivity phenomenon/delusion of control/influence	Delusional Perception
SYNTHETIC CANNABINOIDS	N = 4829	12	2	3	1
SYNTHETIC CATHINONES/BATH SALTS	N = 269	4	0	1	0
PCP-LIKE DRUGS	N = 3	0	0	0	0
PHENETHYLAMINE	N = 158	4	0	0	0
PIPERAZINE	N = 115	2	0	0	0
STIMULANTS	N = 426	2	1	0	0
AMPHETAMINE-TYPE					
TRYPTAMINE	N = 27	0	0	0	0

N = Number of subjects
* Number of subjects
**Number of articles

consistent with existing literature (Bach and Hayes, 2002). However, the age range of individuals affected by NPS use was broader, ranging from adolescents as young as 16 (Oluwabusi et al., 2012) to older adults up to 70 years old (Udow et al., 2018). This wide age range emphasizes the importance of considering NPS use as a potential risk factor for psychosis across different life stages.

Among all substance classes, SCRAAs stand out as the most strongly implicated in the onset of psychotic symptoms. Indeed, several studies have highlighted their ability to induce psychotic states (Papanti et al., 2013b; Skryabin and Vinnikova, 2019). This is consistent with prior research indicating that SCRAAs possess high potency at CB1 receptors and lack cannabidiol’s modulating properties, thereby creating a

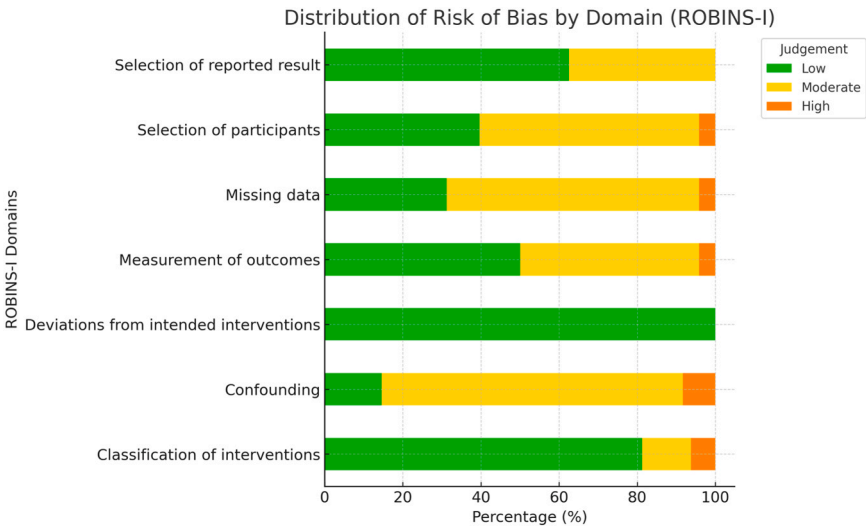


Fig. 2. Summary of risk of bias assessment using the ROBINS-I tool across the included non-case report studies.

neurochemical imbalance conducive to psychosis (Malaca et al., 2021; Theunissen et al., 2022). The breadth and severity of symptoms - ranging from agitation and persecutory delusions to auditory hallucinations - underscore the psychotogenic potential of this class.

Synthetic cathinones, often labeled “bath salts,” showed similar but somewhat less extensive associations. These compounds have stimulant-like properties and have been associated with hyperactivity, mood dysregulation, and psychotic symptoms, particularly paranoia and hallucinations, in line with existing literature (Daswani et al., 2024). While acute presentations can be severe and clinically indistinguishable from stimulant-induced psychosis (e.g., amphetamines or cocaine) (Lin et al., 2023), data on long-term outcomes are limited. The available evidence suggests that synthetic cathinones may induce acute psychosis, but they are less frequently associated with persistence or recurrence compared to SCRA.

Other NPS classes, such as phenethylamines, piperazines, amphetamine-type stimulants, and tryptamines, were also implicated in inducing psychotic or schizophrenia-like symptoms. Phenethylamines, in particular, demonstrate a notable capacity to induce multimodal hallucinations and complex delusional states, often accompanied by intense derealization or mystical experiences. Notably, phenethylamines are most frequently associated with psychedelic effects and with clinical outcomes characterized as “acute psychosis with remission”. While these experiences can resemble brief psychotic episodes, they may also represent drug-induced altered states of consciousness that require careful differential diagnosis. The psychotic potential of these substances may be underestimated, especially in recreational or experimental contexts.

Another critical observation relates to poly-substance use, which was frequently reported in the included studies. The co-use of multiple psychoactive substances - often including alcohol, cannabis, stimulants, and hallucinogens - makes it difficult to isolate the specific effects of individual NPS. However, polyabuse patterns themselves may represent a distinct risk profile for the development of psychosis, possibly due to synergistic or cumulative neurotoxic effects (Martinotti et al., 2021d; Schifano et al., 2021).

Our findings are consistent with existing literature, confirming the capacity of NPS to induce SIPD, characterized by a higher occurrence of visual hallucinations, a greater prevalence of suicidal ideation within the past year, more frequent episodes of violent behavior, and an increased likelihood of a family history of substance misuse (Caton et al., 2005; Dawe et al., 2011).

4.2. NPS and transition to schizophrenia

Evidence in the literature has shown that a significant proportion of individuals with SIPD later develop a diagnosis of schizophrenia. Reported transition probabilities vary across studies, ranging from 25 % (Murrie et al., 2020) to 44 % (Arendt et al., 2005) and up to 66 % (Addington et al., 2006). Studies consistently indicate that cannabis is the substance most strongly associated with transition to schizophrenia (Myran et al., 2023; Rognli et al., 2023), followed by amphetamines (Chiang et al., 2019; Kittirattanapaiboon et al., 2010). Although the ability of NPS to unmask latent schizophrenia has been documented (Papanti et al., 2013a; van Amsterdam et al., 2015), no study to date has evaluated which specific NPS carries the highest risk of triggering schizophrenia in predisposed individuals. Our results indicate that SCRA and polydrug use are most frequently associated with the onset of persistent psychosis. However, the clinical outcomes of psychotic episodes were not consistently reported across the studies included in this review; in fact, outcome data were missing for approximately half of the cases. Moreover, most studies did not clarify whether the persistence of symptoms reflected a chronic drug-induced, psychotic condition or a true transition to schizophrenia.

To conduct a preliminary evaluation, we assessed the presence of negative symptoms (e.g., blunted affect, avolition, alogia), which are

typically linked to chronic or primary psychotic disorders (Correll and Schooler, 2020). SCRA were associated with negative symptoms in 10 reported cases (Berry-Cabán et al., 2013; Celofiga et al., 2014; Haro et al., 2014; Hurst et al., 2011; Kotan et al., 2017; Oluwabusi et al., 2012; Roberto et al., 2016; Skryabin and Vinnikova, 2018, 2019; Welter et al., 2017), followed by amphetamine-type stimulants in one case (Ricci et al., 2022).

Given their historical status as pathognomonic features of schizophrenia in classical psychiatric literature, we also examined the presence of Kurt Schneider's FRS, including thought insertion, auditory hallucinations, and delusions of control (Schneider, 1959). FRS have been widely used in diagnostic classification systems for schizophrenia since the late 1970s (Moskowitz and Heim, 2018). Although their diagnostic reliability is currently under debate (Peralta and Cuesta, 2023), recent evidence suggests that FRS correctly identify individuals with schizophrenia in 75–95 % of cases (Soares-Weiser et al., 2015). Consequently, their potential reintroduction as core diagnostic criteria in DSM-6 remains a subject of active expert discussion (Moritz et al., 2024).

In our review, FRS were most commonly observed in cases involving SCRA. Specifically, auditory/verbal hallucinations were reported in 9 articles; thought withdrawal, insertion, interruption, or broadcasting in 2; passivity phenomena or delusions of control/influence in 3; and delusional perception in 1 article. The co-occurrence of negative symptoms and FRS supports the hypothesis that SCRA may be more strongly associated with a transition to schizophrenia/PPD than other NPS. Nonetheless, further research is warranted to validate this association.

4.3. NPS and persistent psychosis

Although only a minority of cases progressed to persistent psychosis, SCRA appeared most frequently associated with such outcomes, suggesting a possible risk of triggering enduring psychiatric conditions or unmasking latent vulnerability. This may reflect the typically sporadic nature of NPS use - since many individuals experiment only once and do not develop dependence - as well as potential reporting bias in the available studies. Consequently, conclusions regarding long-term risk should be drawn with caution, and further longitudinal research is needed to clarify the true extent of chronic outcomes. Phenethylamines were also implicated in one such case (Schetz et al., 2022), as was polysubstance use. Other substance classes primarily led to substance-induced psychosis without a clear trend toward chronicity. However, we lack sufficient data to determine whether the chronic psychoses associated with SCRA and phenethylamines represent true psychopathological onsets or are better characterized as exogenous substance-related exogenous psychoses (SREP). SREP is described as a form of persistent psychosis induced by substances that can be clinically and phenomenologically distinguished from schizophrenia Schizophrenia/PPD in terms of clinical presentation, epidemiology, etiological models, and response to treatment (Martinotti et al., 2021d; Mosca et al., 2023). In this context, the term “Spicephrenia” has been coined to describe chronic psychoses, distinguishable from schizophrenia, induced by the use of “Spice”, or SCRA (Papanti et al., 2013a). Methamphetamine has also been associated with this particular type of chronic psychosis (Chiang et al., 2019; Voce et al., 2019), although our data did not show an association with amphetamine-type stimulants.

4.4. Final considerations

From a nosological standpoint, this review raises significant questions about the boundaries between primary psychotic disorders and substance-induced psychoses.

The analysis of outcomes revealed a concerning trend: while many patients achieved full remission from acute NPS-induced psychotic episodes, a considerable minority developed persistent symptoms or

experienced recurrent psychotic episodes. This is likely attributable to the potent neurochemical effects of NPS (Bennett et al., 2017; Giorgetti et al., 2021; Martin S., 2019), as well as the rapid sociocultural changes characteristic of postmodernity (Martinotti et al., 2021b). These findings underscore the potential long-term psychiatric consequences of NPS use, especially among individuals with a personal or familial vulnerability to psychosis.

The conventional definition of SIPD does not adequately capture the phenomenon of persistent psychosis, which displays clinical differences from PPD. SREPs pose additional diagnostic challenges, particularly in differentiating substance-induced psychopathology from primary psychiatric disorders (Martinotti et al., 2021d). The progression from substance-induced-psychosis to chronic psychotic disorder remains poorly understood, and further research is necessary to elucidate these phenomena.

5. Limitations

This review has several limitations. Many of the included studies were case reports or small case series, limiting the generalizability of the findings. Nonetheless, these case reports were included because they often represent the first clinical signals of newly emerging NPS and provide detailed phenomenological descriptions of psychotic presentations that are rarely captured in larger studies. Their contribution should therefore be considered as hypothesis-generating, while higher-quality observational and controlled studies provide the more robust evidence base. In addition, the heterogeneity of methodologies, populations, and outcome measures complicates direct comparisons across studies. The heterogeneity of methodologies, populations, and outcome measures also complicates direct comparisons across studies. Another limitation concerns the apparent low frequency of hallucinations and delusions reported in our tables when compared with large-scale emergency department studies (e.g., Hoyte et al., 2012, who reported psychotic symptoms in 9.4 % of cases). This discrepancy most likely reflects reporting bias: many case reports and observational studies included in our review did not provide systematic information on psychotic symptoms, and several emergency cohorts aggregated these presentations under broader diagnostic labels without specifying phenomenology. Moreover, since information on subjects' substance use patterns was reported only under the 'Psychiatric comorbidity' column in Table 1, it was therefore not possible to determine whether the cases involved single episodes of use, harmful use, or dependence on NPS. This substantially limits the extent to which reliable conclusions can be drawn about the actual risk these substances may carry for the development of psychosis. Therefore, the numbers presented in Table 3 should be interpreted as the frequency with which symptoms were reported in published studies, rather than as accurate estimates of prevalence. Our tables are intended primarily to map the phenomenological diversity of presentations rather than to quantify their epidemiological distribution. Furthermore, the presence of psychiatric or medical comorbidities and poly-substance use often limits the ability to attribute symptoms to a single compound.

6. Conclusions

The findings of this systematic review underscore the significant psychotogenic potential of novel psychoactive substances (NPS), particularly SCRA, which emerged as the most consistent and potent inducers of acute psychosis and schizophrenia-like symptomatology. These compounds were associated with a broad range of psychotic features, including hallucinations, delusions, thought disorganization, and negative symptoms, with First Rank Symptoms (FRS), traditionally regarded as hallmark indicators of schizophrenia, reported in a limited number of cases...

The data also suggest that other NPS classes - such as synthetic cathinones, phenethylamines, piperazines, and amphetamine-type

stimulants - can contribute to the development of psychotic symptoms, though often with differing phenomenological profiles and generally less frequent associations with FRS or long-term outcomes. Nevertheless, in vulnerable individuals, including those with preexisting psychiatric conditions or a genetic predisposition to psychosis, the use of these substances may act as a precipitating factor for the onset or exacerbation of psychotic illness (Schifano et al., 2021).

Clinically, these findings suggest the potential importance of systematically inquiring about NPS use in individuals presenting with new-onset psychosis, especially in atypical or acute cases; however, the current evidence does not allow firm recommendations regarding screening, incidence, or impact on management and outcomes.

These findings carry relevant public health implications. The widespread availability of NPS - especially among adolescents and young adults - combined with the lack of awareness of their psychiatric risks among both consumers and mental health professionals, represents a growing concern for mental health services worldwide. An integrated approach, combining toxicological screening and thorough clinical inquiry into NPS use, should be considered essential in all cases of first-episode psychosis, especially when presentation is atypical, rapidly progressive, or resistant to treatment. Moreover, preventive treatment strategies should be implemented to reduce the risk of progression to chronic psychotic states and the development of schizophrenia (Chiappini et al., 2024a, 2024b; Martinotti et al., 2022).

Future research should aim to clarify the neurobiological mechanisms underpinning the psychosis-inducing effects of different NPS, identify individual vulnerability factors (e.g., genetic, neurodevelopmental, or trauma-related), and explore the longitudinal trajectories of NPS-induced psychosis. Finally, the review has important public health implications. The increasing availability of NPS, often perceived as legal or "safe" alternatives to classical illicit drugs, poses a serious threat, particularly among adolescents and young adults. Educational campaigns, preventive strategies, and regulatory interventions are urgently needed to curb the spread of these substances and to inform users about their potential psychiatric risks. Improved regulatory control, harm reduction strategies, and targeted educational campaigns are urgently needed to reduce the burden of NPS-related psychiatric morbidity.

Author Contributions

M.A. M.G. conceived the idea of this paper; data were extracted by Man. G., P.A., S.M.C., V.M.C., and C.C., whilst Mi.A., M.A. C.S. and P.M. supervised all stages of the process and were consulted to resolve any possible disagreement. M.A., M.G. and C.S. drafted the first version and revised it after contributions from M.G., S.F., C.J.M., P.M. and D.P.G. All authors approved the final version. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

S.F. (Schifano Fabrizio) was a member of the UK Advisory Council on the Misuse of Drugs (ACMD; 2011–2019) and is currently a member of the EMA Advisory Board (Psychiatry). M.G. has been a consultant and/or a speaker and/or has received research grants from Angelini, Doc Generici, Janssen-Cilag, Lundbeck, Otsuka, Pfizer, Servier, Recordati. C. J.M. is a member of the ACMD's Novel Psychoactive Substances and Technical Committees. C.S., V.G., M.A., Mi. A., S.G., G.G., d'A.G. D.C.F., C.R., C.C., P.M., G.A.: nothing to be declared.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Funding

This research received no external funding.

Appendix 1. CARE Checklist - Case Reports

Author (year)	Title	Keywords	Abstract	Introduction	Patient information	Clinical findings	Timeline	Diagnostic assessment	Therapeutic intervention	Follow-up and outcomes	Discussion	Patient perspective	Informed consent
Abouché et al. (2016)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Present
Albert et al. (2022)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Alhassan et al. (2024)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Anderson (2015)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Austin and Monasterio (2004)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Barceló et al. (2017)	Present	Present	Absent	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Batisse et al. (2014)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Bebarta et al. (2012)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Benford and Caplan (2011)	Present	Present	Absent	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Berry-Cabán et al. (2013)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Besli et al. (2015)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Bonaccorso et al. (2018)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Bretaudéau-Deguigne et al. (2015)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Caloro (2016)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Caloro (2018)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Celofiga et al. (2014)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Chan et al. (2013)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Present
Daveluy (2016)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Di Petta (2016)	Present	Absent	Absent	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Dolengevich-Segal (2016)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Dunlop et al., (2020)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Durand et al. (2015)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
El-Higaya et al. (2011)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Present
El Zahran et al. (2019)	Present	Present	Absent	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Fujita et al. (2018)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Gee et al. (2016)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Alatrash et al. (2006)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Haro et al. (2014)	Present	Absent	Absent	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Hill et al. (2013)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Present
Hurst et al. (2011)	Present	Present	Absent	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Johnson et al. (2011)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Khullar et al. (2014)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Kihara and Day (2014)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Kuzucuoglu et al. (2018)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Lagoutte-Renosi et al. (2021)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Malik et al. (2021)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Miyajima et al. (2008)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Moccia (2019)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Müller et al. (2009)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Oluwabusi et al. (2012)	Present	Absent	Absent	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Ozer et al. (2016)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Present
Peglow et al. (2012)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Rahmani et al. (2014)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Ricci (2022)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Roberto et al. (2016)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Present
Rose et al. (2013)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Satodiya and Palekar (2020)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Absent	Present	Absent	Present
Schloemerkemper (2018)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Simmons et al. (2011)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Simonato (2018)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Sönmez and Köşger (2016)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Stevenson (2014)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Stoller et al. (2017)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent

(continued on next page)

(continued)

Author (year)	Title	Keywords	Abstract	Introduction	Patient information	Clinical findings	Timeline	Diagnostic assessment	Therapeutic intervention	Follow-up and outcomes	Discussion	Patient perspective	Informed consent
Sweet et al. (2017)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Taljemark & Johansson (2012)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent
Tofighi and Lee (2012)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Truscott (2013)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Tung et al. (2012)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Udow et al. (2018)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent
Yazici et al. (2017)	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Present	Absent	Absent
Zidkova (2017)	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent

Data availability statement

Not applicable.

References

Abouchedid, R., Ho, J.H., Hudson, S., Dines, A., Archer, J.R.H., Wood, D.M., Dargan, P.I., 2016. Acute toxicity associated with use of 5F-Derivations of synthetic cannabinoid receptor agonists with analytical confirmation. *J. Med. Toxicol.* 12 (4), 396–401. <https://doi.org/10.1007/s13181-016-0571-7>.

Addington, J., Chaves, A., Addington, D., 2006. Diagnostic stability over one year in first-episode psychosis. *Schizophr. Res.* 86 (1–3). <https://doi.org/10.1016/j.schres.2006.04.018>.

Alatrash, G., Majhail, N.S., Pile, J.C., 2006. Rhabdomyolysis after ingestion of ‘foxy,’ a hallucinogenic tryptamine derivative. *Mayo Clin. Proc.* 81 (4). <https://doi.org/10.4065/81.4.550>.

Albert, N., Catthoor, K., Morrens, M., 2022. Akathisia after chronic usage of synthetic cathinones: a case study. *Front. Psychiatry* 13. <https://doi.org/10.3389/fpsyt.2022.1046486>.

Alhassan, A., Prahad, S.R., Burk, B.G., Fargason, R.E., Birur, B., 2024. New-Onset Prolonged Psychosis Following Synthetic Cannabinoid Use in an Older Patient: A Case Report. *Psychopharmacol. Bull.* 54 (1), 33–39. PMID: 38449474; PMCID: PMC10913866.

Altintas, M., Inanc, L., Oruc, G., Arpaciglu, S., Gulec, H., 2016. Clinical characteristics of synthetic cannabinoid-induced psychosis in relation to schizophrenia: a single-center cross-sectional analysis of concurrently hospitalized patients. *Neuropsychiatr. Dis. Treat.* 12. <https://doi.org/10.2147/NDT.S107622>.

Altintop, I., 2020. A 4-Year retrospective analysis of patients presenting at the emergency department with synthetic cannabinoid intoxication in Turkey. *J. Clin. Psychopharmacol.* 40 (5), 464–467. <https://doi.org/10.1097/JCP.0000000000001275>.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM) 5th ed.*

Anderson, C., Morrell, C., Marchevsky, D., 2015. A novel psychoactive substance poses a new challenge in the management of paranoid schizophrenia. *bcr2015209573 BMJ Case Rep.* <https://doi.org/10.1136/bcr-2015-209573>.

Arendt, M., Rosenberg, R., Foldager, L., Perto, G., Munk-Jørgensen, P., 2005. Cannabis-induced psychosis and subsequent schizophrenia-spectrum disorders: Follow-up study of 535 incident cases. *Br. J. Psychiatry* 187 (DEC.). <https://doi.org/10.1192/bjp.187.6.510>.

Austin, H., Monasterio, E., 2004. Acute psychosis following ingestion of ‘rapture. *Australas. Psychiatry* 12 (4). <https://doi.org/10.1111/j.1440-1665.2004.02137.x>.

Bach, P., Hayes, S.C., 2002. The use of acceptance and commitment therapy to prevent the rehospitalization of psychotic patients: a randomized controlled trial. *J. Consult. Clin. Psychol.* 70 (5), 1129–1139. <https://doi.org/10.1037/0022-006X.70.5.1129>.

Bak, M., Myin-Germeys, I., Hanssen, M., Bijl, R., Vollebergh, W., Delespaul, P., van Os, J., 2003. When does experience of psychosis result in a need for care? A prospective general population study. *Schizophr. Bull.* 29 (2), 349–358. <https://doi.org/10.1093/oxfordjournals.schbul.a007010>.

Barceló, B., Pichini, S., López-Corominas, V., Gomila, I., Yates, C., Busardó, F.P., Pellegrini, M., 2017. Acute intoxication caused by synthetic cannabinoids 5F-ADB and MMB-2201: a case series. *Forensic Sci. Int.* 273. <https://doi.org/10.1016/j.forsciint.2017.01.020>.

Bassir Nia, A., Medrano, B., Perkel, C., Galyner, I., Hurd, Y.L., 2016. Psychiatric comorbidity associated with synthetic cannabinoid use compared to cannabis. *J. Psychopharmacol.* 30 (12), 1321–1330. <https://doi.org/10.1177/0269881116658990>.

Batisse, A., Fortias, M., Bourgonne, E., Grégoire, M., Sec, I., Djeddar, S., 2014. Case series of 21 synthetic cathinones abuse. *J. Clin. Psychopharmacol.* 34 (3), 411–413. <https://doi.org/10.1097/JCP.0000000000000116>.

Bebarta, V.S., Ramirez, S., Varney, S.M., 2012. Spice: a new ‘legal’ herbal mixture abused by young active duty military personnel. *Subst. Abus.* 33 (2). <https://doi.org/10.1080/08897077.2011.637610>.

Beck, O., Franzen, L., Bäckberg, M., Signell, P., Helander, A., 2015. Intoxications involving MDPV in Sweden during 2010–2014: results from the STRIDA project. *Clin. Toxicol.* 53 (9), 865–873. <https://doi.org/10.3109/15563650.2015.1089576>.

Benford, D.M., Caplan, J.P., 2011. Psychiatric sequelae of spice, K2, and synthetic cannabinoid receptor agonists. *Psychosomatics* 52 (3). <https://doi.org/10.1016/j.psych.2011.01.004>.

Bennett, K.H., Hare, H.M., Waller, R.M., Alderson, H.L., Lawrie, S., 2017. Characteristics of NPS use in patients admitted to acute psychiatric services in southeast scotland: a retrospective cross-sectional analysis following public health interventions. *BMJ Open* 7 (12), e015716. <https://doi.org/10.1136/bmjopen-2016-015716>.

Berry-Cabán, C.S., Ee, J., Ingram, V., Berry, C.E., Kim, E.H., 2013. Synthetic cannabinoid overdose in a 20-year-old Male US soldier. *Subst. Abus.* 34 (1). <https://doi.org/10.1080/08897077.2012.677754>.

Besli, G.E., Ikiz, M.A., Yildirim, S., Saltik, S., 2015. Synthetic cannabinoid abuse in adolescents: a case series. *J. Emerg. Med.* 49 (5), 644–650. <https://doi.org/10.1016/j.jemermed.2015.06.053>.

Blanco, G., Vidler, D., Roper, C., Wood, D.M., Dargan, P.I., Keating, L., Macfarlane, R., Emmett, S., Johnson, G., Eddleston, M., Hill, S.L., Thomas, S.H.L., 2021. Acute toxicity from the synthetic cathinone n-ethylpentylone (ephylone) in the United Kingdom. *Clin. Toxicol.* 59 (12), 1270–1273. <https://doi.org/10.1080/15563650.2021.1909730>.

Bonaccorso, S., Metastasio, A., Ricciardi, A., Stewart, N., Jamal, L., Rujully, N.-U.-D., Theleritis, C., Ferracuti, S., Ducci, G., Schifano, F., 2018. Synthetic cannabinoid use in a case series of patients with psychosis presenting to acute psychiatric settings: clinical presentation and management issues. *Brain Sci.* 8 (7), 133. <https://doi.org/10.3390/brainsci8070133>.

Bosong, M., Brunt, T., Van Dijk, J., Rigter, S., Hoek, J., Goldschmidt, H., Niesink, R., 2010. mCPP: an undesired addition to the ecstasy market. *J. Psychopharmacol.* 24 (9), 1395–1401. <https://doi.org/10.1177/0269881109102541>.

Bretaudau Duguigne, M., Férec, S., Lelièvre, B., Bruneau, C., Diquet, B., Harry, P., Turcant, A., 2015. Report of five cases of 2,5-dimethoxy-4-(n)-propylphenethylamine (2C-P) intoxication following recreational use. *Toxicol. Anal. Et. Clin.* 27 (2). <https://doi.org/10.1016/j.toxac.2015.03.001>.

Bucci, S., Schwannauer, M., Berry, N., 2019. The digital revolution and its impact on mental health care. *Psychol. Psychother. Theory Res. Pract.* 92 (2), 277–297. <https://doi.org/10.1111/papt.12222>.

Caloro, M., Calabrò, G., De Pisa, E., Rosini, E., Kotzalidis, G.D., Lonati, D., Locatelli, C.A., Papa, P., Schifano, F., Girardi, P., 2018. Combined NMDA inhibitor use in a patient with Multisubstance-induced psychotic disorder. *J. Addict. Med.* 12 (3). <https://doi.org/10.1097/ADM.0000000000000390>.

Caloro, M., Calabrò, G., Kotzalidis, G.D., Cuomo, I., Corkery, J.M., Vento, A.E., Lionetto, L., De Filippis, S., Ranieri, V., Lonati, D., Locatelli, C.A., de Pisa, E., Di Tommaso, A., Girardi, P., Schifano, F., 2016. Use of benzylglycinamide by a HIV-seropositive polysubstance user: the changing pattern of novel psychoactive substance use among youths. *Addict. Behav.* 60, 53–57. <https://doi.org/10.1016/j.addbeh.2016.03.032>.

Caton, C.L., Drake, R.E., Hasin, D.S., Dominguez, B., Shrout, P.E., Samet, S., & Schanzer, B. (2005). Differences between early-phase primary psychotic disorders with concurrent substance use and substance-induced psychoses.[Erratum appears in Arch Gen Psychiatry. 2005 May;62(5):493 Note: Schanzer, W Bella [corrected to Schanzer, Bella]]. *Archives of General Psychiatry*, 62(2).

Celofiga, A., Koprivsek, J., Klavz, J., 2014. Use of synthetic cannabinoids in patients with psychotic disorders: case series. *J. Dual Diagn.* 10 (3). <https://doi.org/10.1080/15504263.2014.929364>.

Chan, W.L., Wood, D.M., Hudson, S., Dargan, P.I., 2013. Acute psychosis associated with recreational use of benzofuran 6-(2-Aminopropyl)Benzofuran (6-APB) and cannabis. *J. Med. Toxicol.* 9 (3). <https://doi.org/10.1007/s13181-013-0306-y>.

Chiang, M., Lombardi, D., Du, J., Makrum, U., Sitthichai, R., Harrington, A., Shukair, N., Zhao, M., Fan, X., 2019. Methamphetamine-associated psychosis: clinical presentation, biological basis, and treatment options. *Hum. Psychopharmacol. Clin. Exp.* 34 (5). <https://doi.org/10.1002/hup.2710>.

Chiappini, S., Cavallotto, C., Mosca, A., Di Carlo, F., Piro, T., Giovannetti, G., Pasino, A., Vicinelli, M., Lorenzini, C., Di Paolo, M., Pepe, M., Di Nicola, M., Ricci, V., Pettorosso, M., Martinotti, G., 2024a. Investigating the effectiveness of brexpiprazole in subjects with schizophrenia spectrum illness and Co-Occurring substance use

- disorder: a prospective, multicentric, Real-World study. *Pharmaceuticals* 17 (4), 535. <https://doi.org/10.3390/ph17040535>.
- Chiappini, S., Miuli, A., Mosca, A., Pettorruso, M., Guirguis, A., John, M.C., Martiotti, G., Di Giannantonio, M., Schifano, F., 2021a. The benzydamine experience: a systematic review of benzydamine abuse. *Curr. Neuropharmacol.* 19 (10), 1728–1737. <https://doi.org/10.2174/1570159X19666210113151136>.
- Chiappini, S., Mosca, A., Miuli, A., Santovito, M.C., Orsolini, L., Corkery, J.M., Guirguis, A., Pettorruso, M., Martiotti, G., Di Giannantonio, M., Schifano, F., 2021b. New psychoactive substances and suicidality: a systematic review of the current literature. *Med. (Kaunas. Lith.)* 57 (6). <https://doi.org/10.3390/MEDICINA57060580>.
- Chiappini, S., Vaccaro, G., Mosca, A., Miuli, A., Stigliano, G., Stefanelli, G., Giovannetti, G., Carullo, R., d'Andrea, G., Di Carlo, F., Cavallotto, C., Pettorruso, M., Di Petta, G., Corkery, J.M., Guirguis, A., Stair, J.L., Martiotti, G., Fazel, S., Schifano, F., 2024b. New trends of drug abuse in custodial settings: a systematic review on the misuse of over-the-counter drugs, prescription-only-medications, and new psychoactive substances. *Neurosci. Biobehav. Rev.* 162, 105691. <https://doi.org/10.1016/j.neubiorev.2024.105691>.
- Chou, H.-H., Hsieh, C.-H., Chaou, C.-H., Chen, C.-K., Yen, T.-H., Liao, S.-C., Seak, C.-J., Chen, H.-Y., 2021. Synthetic cathinone poisoning from ingestion of drug-laced “instant coffee packets” in Taiwan. *Hum. Exp. Toxicol.* 40 (9), 1403–1412. <https://doi.org/10.1177/0960327121996043>.
- Ciucă Anghel, D.-M., Anghel, E.-E., Stan, M., Tudor, G., Dumitriu, A.S., Paunica, S., Baconi, D.L., 2022. Psychological and psychiatric characterization of various groups of drugs users. *J. Mind Med. Sci.* 9 (2), 255–265. <https://doi.org/10.22543/2392-7674.1356>.
- Correll, C.U., Schooler, N.R., 2020. Negative symptoms in schizophrenia: a review and clinical guide for recognition, assessment, and treatment. *Neuropsychiatr. Dis. Treat.* 16. <https://doi.org/10.2147/NDT.S225643>.
- Cozier G.E., Gardner M., Craft S., Skumlien M., Spicer J., Andrews R., Power A., Haines T., Bowman R., Manley A.E., Sunderland P., Sutcliffe O.B., Husbands S.M., Hines L., Taylor G., Freeman T.P., Scott J., Pudney C.R. Synthetic cannabinoids in e-cigarettes seized from English schools. *Addiction*. 2025 Jun 26. doi: 10.1111/add.70110. Epub ahead of print. PMID: 40574414.
- Daswani, R.R., Choles, C.M., Kim, D.D., Barr, A.M., 2024. A systematic review and meta-analysis of synthetic cathinone use and psychosis. *Psychopharmacology* 241 (5). <https://doi.org/10.1007/s00213-024-06569-x>.
- Daveluy, A., Castaing, N., Cherifi, H., Richeva, C., Humbert, L., Faure, I., Labadie, M., Allorge, D., Haramburu, F., Molimard, M., Titier, K., 2016. Acute methiopropamine intoxication after “Synthacaine” consumption. *J. Anal. Toxicol.* <https://doi.org/10.1093/jat/bkw073>.
- Davey, Z., Schifano, F., Corazza, O., Deluca, P., 2012. e-Psychonauts: conducting research in online drug forum communities. *J. Ment. Health* 21 (4), 386–394. <https://doi.org/10.3109/09638237.2012.682265>.
- Dawe, S., Geppert, L., Occhipinti, S., Kingswell, W., 2011. A comparison of the symptoms and short-term clinical course in inpatients with substance-induced psychosis and primary psychosis. *J. Subst. Abuse. Treat.* 40 (1), 95–101. <https://doi.org/10.1016/j.jsat.2010.08.002>.
- Di Petta, G., 2016. “Synthetic psychosis” by novel psychoactive substances: A psychopathological understanding of a clinical case. In *An Experiential Approach to Psychopathology: What is it Like to Suffer From Mental Disorders?* https://doi.org/10.1007/978-3-319-29945-7_9.
- Dolengevich-Segal, H., Rodríguez-Salgado, B., Gómez-Arnau, J., Sánchez-Mateos, D., 2016. Severe psychosis, drug dependence, and hepatitis c related to *slamming* mephedrone. *Case Rep. Psychiatry* 2016, 1–5. <https://doi.org/10.1155/2016/8379562>.
- Dunlop, L.C., Wood, D., Archer, J., Hudson, S., Dargan, P., 2020. Severe toxicity to the new psychoactive substances 3-Hydroxyphenylcyclidine and N-Ethylhexedrone: an analytically confirmed case report. *J. Med. Toxicol.* 16 (1). <https://doi.org/10.1007/s13181-019-00734-x>.
- Durand, D., Delgado, L.L., De La Parra-Pellot, D.M., Nichols-Vinueza, D., 2015. Psychosis and severe rhabdomyolysis associated with synthetic cannabinoid use: a case report. *Clin. Schizophr. Relat. Psychoses* 8 (4). <https://doi.org/10.3371/CSRP.DUDE.031513>.
- El Zahran, T., Gerona, R., Morgan, B.W., Pomerleau, A.C., 2019. A novel synthetic cannabinoid (Cumyl-4-cyano-BINACA) resulting in hyperthermia, rhabdomyolysis, and renal failure in a 29-year-old patient: it's not meningitis. *Clin. Toxicol.* 57 (6), 421–422. <https://doi.org/10.1080/15563650.2018.1534241>.
- El-Higayni, E., Ahmed, M., Hallahan, B., 2011. Whack induced psychosis: a case series. *Ir. J. Psychol. Med.* 28 (1). <https://doi.org/10.1017/s0790966700011915>.
- EMCDDA (European Monitoring Centre for Drugs and Drug Addiction). (2019). EU Early Warning System operating guidelines.
- EMCDDA. (2022). EMCDDA operating guidelines for the European Union Early Warning System on new psychoactive substances.
- Every-Palmer, S., 2011. Synthetic cannabinoid JWH-018 and psychosis: an explorative study. *Drug Alcohol Depend.* 117 (2–3), 152–157. <https://doi.org/10.1016/j.drugalcdep.2011.01.012>.
- Fiorentini, A., Cantù, F., Crisanti, C., Cereda, G., Oldani, L., Brambilla, P., 2021. Substance-Induced psychoses: an updated literature review. *Front. Psychiatry* 12. <https://doi.org/10.3389/fpsyt.2021.694863>.
- Forrester, M.B., 2014. NBOME designer drug exposures reported to texas poison centers. *J. Addict. Dis.* 33 (3). <https://doi.org/10.1080/10550887.2014.950027>.
- Fraser, S., Hides, L., Phillips, L., Proctor, D., Lubman, D.I., 2012. Differentiating first episode substance induced and primary psychotic disorders with concurrent substance use in young people. *Schizophr. Res.* 136 (1–3). <https://doi.org/10.1016/j.schres.2012.01.022>.
- Fujita, Y., Mita, T., Usui, K., Kamijo, Y., Kikuchi, S., Onodera, M., Fujino, Y., Inoue, Y., 2018. Toxicokinetics of the synthetic cathinone α -Pyrrolidinohexanophenone. *J. Anal. Toxicol.* 42 (1), e1–e5. <https://doi.org/10.1093/jat/bkx080>.
- Fusar-Poli, P., Cappucciati, M., Rutigliano, G., Heslin, M., Stahl, D., Brittenden, Z., Caverzasi, E., McGuire, P., Carpenter, W.T., 2016. Diagnostic stability of ICD/DSM first episode psychosis diagnoses: Meta-analysis. *Schizophr. Bull.* 42 (6). <https://doi.org/10.1093/schbul/sbw020>.
- Gagnier, J.J., Kienle, G., Altman, D.G., Moher, D., Sox, H., Riley, D., 2013. CARE group. The CARE guidelines: consensus-based clinical case reporting guideline development (Nov-Dec). *Headache* 53 (10), 1541–1547. <https://doi.org/10.1111/head.12246>. PMID: 24266334.
- Gee, P., Schep, L.J., Jensen, B.P., Moore, G., Barrington, S., 2016. Case series: toxicity from 25B-NBOMe – a cluster of N-bomb cases. *Clin. Toxicol.* 54 (2), 141–146. <https://doi.org/10.3109/15563650.2015.1115056>.
- Giorgetti, A., Pascali, J.P., Fais, P., Pelletti, G., Gabbin, A., Franchetti, G., Cecchetto, G., Viel, G., 2021. Molecular mechanisms of action of novel psychoactive substances (NPS): a new threat for young drug users with Forensic-Toxicological implications. *Life (Basel Switz.)* 11 (5). <https://doi.org/10.3390/life11050440>.
- Glue, P., Al-Shaqsi, S., Hancock, D., Gale, C., Strong, B., Schep, L., 2013. Hospitalisation associated with use of the synthetic cannabinoid K2. *N. Z. Med. J.* 126 (1377).
- Haro, G., Ripoll, C., Ibáñez, M., Orengo, T., Liaño, V. M., Meneu, E., Hernández, F., Traver, F., 2014. Could spice drugs induce psychosis with abnormal movements similar to catatonia? *Psychiatry (N. Y.)* 77 (2). <https://doi.org/10.1521/psyc.2014.77.2.206>.
- Helle, S., Gjestad, R., Johnsen, E., Kroken, R.A., Jørgensen, H.A., Løberg, E.-M., 2014. Cognitive changes in patients with acute phase psychosis—Effects of illicit drug use. *Psychiatry Res.* 220 (3), 818–824. <https://doi.org/10.1016/j.psychres.2014.08.062>.
- Hermanns-Clausen, M., Kneisel, S., Szabo, B., Auwärter, V., 2013. Acute toxicity due to the confirmed consumption of synthetic cannabinoids: clinical and laboratory findings. *Addiction* 108 (3), 534–544. <https://doi.org/10.1111/j.1360-0443.2012.04078.x>. Epub 2012 Nov 1. PMID: 22971158.
- Hermanns-Clausen, M., Müller, D., Kithinji, J., Angerer, V., Franz, F., Eyer, F., Neurath, H., Liebetrau, G., Auwärter, V., 2018. Acute side effects after consumption of the new synthetic cannabinoids AB-CHMINACA and MDMB-CHMICA. *Clin. Toxicol.* 56 (6), 404–411. <https://doi.org/10.1080/15563650.2017.1393082>.
- Hill, S.L., Doris, T., Gurung, S., Katebe, S., Lomas, A., Dunn, M., Blain, P., Thomas, S.H.L., 2013. Severe clinical toxicity associated with analytically confirmed recreational use of 25I-NBOMe: case series. *Clin. Toxicol.* 51 (6), 487–492. <https://doi.org/10.3109/15563650.2013.802795>.
- Hondebrink, L., Nugteren-van Lonkhuyzen, J.J., Van Der Gouw, D., Brunt, T.M., 2015. Monitoring new psychoactive substances (NPS) in the Netherlands: data from the drug market and the poisons information centre. *Drug Alcohol Depend.* 147. <https://doi.org/10.1016/j.drugalcdep.2014.11.033>.
- Hoyte, C.O., Jacob, J., Monte, A.A., Al-Jumaan, M., Bronstein, A.C., Heard, K.J., 2012. A characterization of synthetic cannabinoid exposures reported to The National poison data system in 2010. *Ann. Emerg. Med.* 60 (4). <https://doi.org/10.1016/j.annemergmed.2012.03.007>.
- Hurst, D., Loeffler, G., McLay, R., 2011. Psychosis associated with synthetic cannabinoid agonists: a case series, 1119–1119 *Am. J. Psychiatry* 168 (10). <https://doi.org/10.1176/appi.ajp.2011.11010176>.
- Janiri, L., Mannelli, P., Persico, A.M., Diodato, S., Tempesta, E., 1991. Zipeprol is a newly abused antitussive with an opioid spectrum and hallucinogenic effects. *Drug Alcohol Depend.* 27 (2). [https://doi.org/10.1016/0376-8716\(91\)90030-3](https://doi.org/10.1016/0376-8716(91)90030-3).
- Johnson, L.A., Johnson, R.L., Alfonso, C., 2011. Spice: a legal marijuana equivalent. *Mil. Med.* 176 (6). <https://doi.org/10.7205/MILMED-D-10-00356>.
- Kamijo, Y., Takai, M., Fujita, Y., Hirose, Y., Iwasaki, Y., Ishihara, S., Yokoyama, T., Yagi, K., Sakamoto, T., 2014. A multicenter retrospective survey of poisoning after consumption of products containing synthetic chemicals in Japan. *Intern. Med.* 53 (21), 2439–2445. <https://doi.org/10.2169/internalmedicine.53.2344>. Epub 2014 Nov 1. PMID: 25366001.
- Kamijo, Y., Takai, M., Fujita, Y., Sakamoto, T., 2016. A multicenter retrospective survey of poisoning after consumption of products containing novel psychoactive substances from 2013 to 2014 in Japan. *Am. J. Drug Alcohol Abuse.* 42 (5), 513–519. <https://doi.org/10.1080/00952990.2016.1176177>.
- Kekelidze, Z.I., Klimenko, T.V., Kozlov, A.A., Shakhova, S.M., 2019. A differential approach to the treatment of acute psychosis due to consumption of synthetic cannabinoids. *Neurosci. Behav. Physiol.* 49 (2), 266–270. <https://doi.org/10.1007/s11055-019-00724-0>.
- Khullar, V., Jain, A., Sattari, M., 2014. Emergence of new classes of recreational drugs - synthetic cannabinoids and cathinones. *J. Gen. Intern. Med.* 29 (8). <https://doi.org/10.1007/s11606-014-2802-4>.
- Kihara, R., Day, E., 2014. Transient psychotic episodes following recreational use of NRG-3. *Prog. Neurol. Psychiatry* 18 (3). <https://doi.org/10.1002/pnp.331>.
- Kittirattanakulapoon, P., Mahatirunkul, S., Booncharoen, H., Thummawong, P., Dumrongchai, U., Chutha, W., 2010. Long-term outcomes in methamphetamine psychosis patients after first hospitalisation. *Drug Alcohol Rev.* 29 (4). <https://doi.org/10.1111/j.1465-3362.2010.00196.x>.
- Kotan, V.O., Baz Yüçens, B., Kotan, Z., Özkaya, G., Okay, İ.T., Tikir, B., Göka, E., 2017. Differences in sociodemographic characteristics, clinical features and serum liver function tests of Male cannabis and synthetic cannabinoid users. *Anadolu Psikiyatr. Derg.* 18(6). <https://doi.org/10.5455/apd.260524>.
- Kuzucuoğlu, T., Uçkun, S., Temizel, F., Arslan, G., Çevik, B., 2018. Intensive care unit outcomes of the cases with cannabinoid intoxication. *J. Med. Surg. Intensive Care Med.* 9 (3). <https://doi.org/10.5152/dcbdyd.2018.1596>.

- Lafferty, C., Smith, L., Coull, A., Shanley, J., 2016. The experience of an increase in the injection of ethylphenidate in lothian April 2014-March 2015. *Scott. Med. J.* 61 (2). <https://doi.org/10.1177/0036933016649871>.
- Lagoutte-Renosi, J., Richeval, C., Phanithavong, M., Wiart, J., Castex, E., Vanhoy, X., Hakim, F., Deheul, S., Tournébeiz, J., Allorge, D., Gaulier, J., 2021. Hair analysis can support the follow-up addiction care after acute new psychoactive substances intoxication: illustration by two cases. *Drug Test. Anal.* 13 (1), 227–234. <https://doi.org/10.1002/dta.2936>.
- Liakoni, E., Dolder, P.C., Rentsch, K., Liechti, M.E., 2015. Acute health problems due to recreational drug use in patients presenting to an urban emergency department in Switzerland. *Swiss Med. Wkly.* 145. <https://doi.org/10.4414/smw.2015.14166>.
- Liakoni, E., Müller, S., Stoller, A., Ricklin, M., Liechti, M.E., Exadaktylos, A.K., 2017. Presentations to an urban emergency department in Bern, Switzerland associated with acute recreational drug toxicity. *Scand. J. Trauma Resusc. Emerg. Med.* 25 (1), 26. <https://doi.org/10.1186/s13049-017-0369-x>.
- Lin, C.H., Chen, J.J., Chan, C.H., 2023. Comparison of psychiatric and clinical profiles between people who use synthetic cathinones and methamphetamine: a matched Case-Control study. *J. Clin. Psychopharmacol.* 43 (2). <https://doi.org/10.1097/JCP.0000000000001649>.
- Madsen, G.R., Petersen, T.S., Dalhoff, K.P., 2017. NBOMe hallucinogenic drug exposures reported to the danish poison information centre. *Dan. Med. J.* 64 (6).
- Malaca, S., Busardó, F.P., Nittari, G., Sirignano, A., Ricci, G., 2021. Fourth generation of synthetic cannabinoid receptor agonists: a review on the latest insights. *Curr. Pharm. Des.* 28 (32). <https://doi.org/10.2174/138161282766621115170521>.
- Malik, K., Kommana, S., Paul, J., Krakauer, M., 2021. Synthetic cannabinoid induced ocular self-injury. *Orbit* 40 (4), 326–328. <https://doi.org/10.1080/01676830.2020.1781199>.
- Martin S.R.E., 2019. Novel psychoactive substances: a toxicological challenge (July). *Bull. R. Coll. Pathol.* 187, 168–170.
- Martinotti, G., Chiappini, S., Mosca, A., Miuli, A., Santovito, M.C., Pettorruso, M., Skryabin, V., Sensi, S.L., Giannantonio, M., Di, 2022. Atypical antipsychotic drugs in dual disorders: current evidence for clinical practice. *Curr. Pharm. Des.* 28 (27), 2241–2259. <https://doi.org/10.2174/1381612828666220623092853>.
- Martinotti, G., De Risió, L., Vannini, C., Schifano, F., Pettorruso, M., Di Giannantonio, M., 2021a. Substance-related exogenous psychosis: a postmodern syndrome. *CNS Spectr.* 26 (1), 84–91. <https://doi.org/10.1017/S1092852920001479>.
- Martinotti, G., De Risió, L., Vannini, C., Schifano, F., Pettorruso, M., Di Giannantonio, M., 2021b. Substance-related exogenous psychosis: a postmodern syndrome. *CNS Spectr.* 26 (1), 84–91. <https://doi.org/10.1017/S1092852920001479>.
- Martinotti, G., De Risió, L., Vannini, C., Schifano, F., Pettorruso, M., Di Giannantonio, M., 2021c. Substance-related exogenous psychosis: a postmodern syndrome. *CNS Spectr.* 26 (1), 84–91. <https://doi.org/10.1017/S1092852920001479>.
- Martinotti, G., De Risió, L., Vannini, C., Schifano, F., Pettorruso, M., Di Giannantonio, M., 2021d. Substance-related exogenous psychosis: a postmodern syndrome. *CNS Spectr.* 26 (1), 84–91. <https://doi.org/10.1017/S1092852920001479>.
- Martinotti, G., Merino Del Villar, C., García Córdoba, A., Andrés Tubau, L., Castro Sánchez, I., Di Carlo, F., Chiappini, S., Pettorruso, M., Schifano, F., Giannantonio, M., 2021. Club Drugs and Psychiatric Sequelae: An Issue of Vulnerability and Previous Psychiatric History. *Int J Environ Res Public Health* 18 (13), 6944. <https://doi.org/10.3390/ijerph18136944>. PMID: 34209645; PMCID: PMC8297170.
- Mathews, E.M., Jeffries, E., Hsieh, C., Jones, G., Buckner, J.D., 2019. Synthetic cannabinoid use among college students. *Addict. Behav.* 93, 219–224. <https://doi.org/10.1016/j.addbeh.2019.02.009>.
- Matsumoto, T., Tachimori, H., Takano, A., Tanibuchi, Y., Funada, D., Wada, K., 2016. Recent changes in the clinical features of patients with new psychoactive-substances-related disorders in Japan: comparison of the nationwide mental hospital surveys on Drug-related psychiatric disorders undertaken in 2012 and 2014. *Psychiatry Clin. Neurosci.* 70 (12). <https://doi.org/10.1111/pcn.12434>.
- Miyajima, M., Matsumoto, T., Ito, S., 2008. 2C-T4 intoxication: acute psychosis caused by a designer drug, 243–243 *Psychiatry Clin. Neurosci.* 62 (2). <https://doi.org/10.1111/j.1440-1819.2008.01764.x>.
- Moccia, L., Tofani, A., Mazza, M., Covino, M., Martinotti, G., Schifano, F., Janiri, L., Di Nicola, M., 2019. Dorsolateral prefrontal cortex impairment in Methoxetamine-Induced psychosis: an ¹⁸F-FDG PET/CT case study. *J. Psychoact. Drugs* 51 (3), 254–259. <https://doi.org/10.1080/02791072.2019.1578444>.
- Monte, A.A., Calello, D.P., Gerona, R.R., Hamad, E., Campleman, S.L., Brent, J., Wax, P., Carlson, R.G., 2017. Characteristics and treatment of patients with clinical illness due to synthetic cannabinoid inhalation reported by medical toxicologists: a ToxIC database study. *J. Med. Toxicol.* 13 (2), 146–152. <https://doi.org/10.1007/s13181-017-0605-9>.
- Moritz, S., Borgmann, L., Heinz, A., Fuchs, T., Gallinat, J., 2024. Towards the DSM-6: results of a survey of experts on the reintroduction of First-Rank symptoms as core criteria of schizophrenia and on redefining hallucinations. *Schizophr. Bull.* 50 (5), 1050–1054. <https://doi.org/10.1093/schbul/sbae061>.
- Mosca, A., Chiappini, S., Miuli, A., Mancusi, G., Santovito, M.C., Di Carlo, F., Pettorruso, M., Corkery, J.M., Canessa, C., Martinotti, G., Di Giannantonio, M., 2023. Ibogaine/Noribogaine in the treatment of substance use disorders: a systematic review of the current literature. *Curr. Neuropharmacol.* 21 (11), 2178–2194. <https://doi.org/10.2174/1570159X211666221017085612>.
- Moskowitz, A., Heim, G., 2018. The role of dissociation in the historical concept of schizophrenia. In *Psychosis, Trauma and Dissociation*. Wiley, pp. 55–67. <https://doi.org/10.1002/9781118585948.ch4>.
- Müller, H., Sperling, W., Köhrmann, M., Huttner, H.B., Kornhuber, J., Maler, J.M., 2010. The synthetic cannabinoid spice as a trigger for an acute exacerbation of cannabis induced recurrent psychotic episodes. *Schizophr. Res.* 118 (s 1–3). <https://doi.org/10.1016/j.schres.2009.12.001>.
- Murray, D.B., Potts, S., Haxton, C., Jackson, G., Sandilands, E.A., Ramsey, J., Puchanawicz, M., Holt, D.W., Johnston, A., Nicholas Bateman, D., Dear, J.W., 2012. Ivory wave' toxicity in recreational drug users; integration of clinical and poisons information services to manage legal high poisoning. *Clin. Toxicol.* 50 (2). <https://doi.org/10.3109/15563650.2011.647992>.
- Murrie, B., Lappin, J., Large, M., Sara, G., 2020. Transition of Substance-Induced, brief, and atypical psychoses to schizophrenia: a systematic review and Meta-analysis. *Schizophr. Bull.* 46 (3), 505–516. <https://doi.org/10.1093/schbul/sbz102>.
- Myran, D.T., Harrison, L.D., Pugliese, M., Solmi, M., Anderson, K.K., Fiedorowicz, J.G., Perlman, C.M., Webber, C., Finkelstein, Y., Tanuseputro, P., 2023. Transition to schizophrenia spectrum disorder following emergency department visits due to substance use with and without psychosis. *JAMA Psychiatry* 80 (11), 1169. <https://doi.org/10.1001/jamapsychiatry.2023.3582>.
- NIDA (National Institute on Drug Abuse), 2024. Synthetic cannabinoids (K2/Spice). National Institutes of Health.
- Oluwabusi, O.O., Lobach, L., Akhtar, U., Youngman, B., Ambrosini, P.J., 2012. Synthetic Cannabinoid-Induced psychosis: two adolescent cases. *J. Child Adolesc. Psychopharmacol.* 22 (5), 393–395. <https://doi.org/10.1089/cap.2012.0004>.
- Ozer, U., Ceri, V., Evren, C., 2016. Capgras syndrome after use of synthetic cannabinoids: an adolescent case. *Dusunen Adam J. Psychiatry Neurol. Sci.* 374–378. <https://doi.org/10.5350/DAJPN2016290410>.
- Öznur, T., Öznur, H., Bolu, A., Çelik, C., Zmenler, K.N., 2018. Sociodemographic and clinical features of young adult males using synthetic cannabinoid. In *klinik psikiyatri dergisi*, 21 (1). <https://doi.org/10.5505/kpd.2018.07269>.
- Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., Chou, R., Glanville, J., Grimshaw, J.M., Hróbjartsson, A., Lalu, M.M., Li, T., Loder, E.W., Mayo-Wilson, E., McDonald, S., Moher, D., 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* n71. <https://doi.org/10.1136/bmj.n71>.
- Papanti, D., Schifano, F., Botteon, G., Bertossi, F., Mannix, J., Vidoni, D., Impagnatiello, M., Pascolo-Fabrizi, E., Bonavigo, T., 2013a. Spiceophrenia": a systematic overview of "Spice"-related psychopathological issues and a case report. *Hum. Psychopharmacol. Clin. Exp.* 28 (4), 379–389. <https://doi.org/10.1002/hup.2312>.
- Papanti, D., Schifano, F., Botteon, G., Bertossi, F., Mannix, J., Vidoni, D., Impagnatiello, M., Pascolo-Fabrizi, E., Bonavigo, T., 2013b. Spiceophrenia": a systematic overview of "Spice"-related psychopathological issues and a case report. *Hum. Psychopharmacol. Clin. Exp.* 28 (4), 379–389. <https://doi.org/10.1002/hup.2312>.
- Papaseit, E., Farré, M., Pérez-Mañá, C., Torrens, M., Ventura, M., Pujadas, M., de la Torre, R., González, D., 2018. Acute pharmacological effects of 2C-B in humans: an observational study. *Front. Pharmacol.* 9. <https://doi.org/10.3389/fphar.2018.00206>.
- Papaseit, E., Olesti, E., Pérez-Mañá, C., Torrens, M., Grifell, M., Ventura, M., Pozo, O.J., de Sousa Fernandes Perna, E.B., Ramaekers, J.G., de la Torre, R., Farré, M., 2020. Acute effects of 2C-E in humans: an observational study. *Front. Pharmacol.* 11. <https://doi.org/10.3389/fphar.2020.00233>.
- Paul, L.D., Welter-Luedeker, J., Penzel, S., Zangl, A., Graw, M., 2021. Alpha-Pyrrolidinopentiophenone (α-PVT): a forensic case study including plasma concentrations. *Forensic Sci. Int.* 321, 110721. <https://doi.org/10.1016/j.forsciint.2021.110721>.
- Peglow, S., Buchner, J., Briscoe, G., 2012. Synthetic cannabinoid induced psychosis in a previously nonpsychotic patient. *Am. J. Addict.* 21 (3). <https://doi.org/10.1111/j.1521-0391.2012.00222.x>.
- Peralta, V., Cuesta, M.J., 2023. Schneider's first-rank symptoms have neither diagnostic value for schizophrenia nor higher clinical validity than other delusions and hallucinations in psychotic disorders. *Psychol. Med.* 53 (6). <https://doi.org/10.1017/S0033291720003293>.
- Rahmani, M., Paul, S., Nguyen, M.L., 2014. Treatment of refractory substance-induced psychosis in adolescent males with a genetic predisposition to mental illness. *Int. J. Adolesc. Med. Health* 26 (2), 297–301. <https://doi.org/10.1515/ijamh-2013-0505>.
- Ricci, V., Di Salvo, G., Maina, G., 2022. Remission of persistent methamphetamine-induced psychosis after cariprazine therapy: presentation of a case report. *J. Addict. Dis.* 40 (1), 145–148. <https://doi.org/10.1080/10550887.2021.1945398>.
- Roberto, A.J., Lorenzo, A., Li, K.J., Young, J., Mohan, A., Pinnaka, S., Lapidus, K.A.B., 2016. First-Episode of synthetic Cannabinoid-Induced psychosis in a young adult, successfully managed with hospitalization and risperidone. *Case Rep. Psychiatry* 2016, 1–4. <https://doi.org/10.1155/2016/7257489>.
- Roberts, L., Ford, L., Patel, N., Vale, J.A., Bradberry, S.M., 2017. 11 analytically confirmed cases of mephedrone use among polydrug users. *Clin. Toxicol.* 55 (3), 181–186. <https://doi.org/10.1080/15563650.2016.1271424>.
- Robson, H., Braund, R., Glass, M., Ashton, J., Tatley, M., 2021. Synthetic cannabis: adverse events reported to the New Zealand pharmacovigilance centre. *Clin. Toxicol.* 59 (6), 472–479. <https://doi.org/10.1080/15563650.2020.1828592>.
- Rognli, E.B., Heiberg, I.H., Jacobsen, B.K., Høy, A., Branness, J.G., 2023. Transition from Substance-Induced psychosis to schizophrenia spectrum disorder or bipolar disorder. *Am. J. Psychiatry* 180 (6), 437–444. <https://doi.org/10.1176/appi.ajp.22010076>.
- Romanek, K., Stenzel, J., Schmoll, S., Schrettl, V., Geith, S., Eyer, F., Rabe, C., 2017. Synthetic cathinones in Southern Germany – characteristics of users, substance-patterns, co-ingestions, and complications. *Clin. Toxicol.* 55 (6), 573–578. <https://doi.org/10.1080/15563650.2017.1301463>.

- Rose, S.R., Poklis, J.L., Poklis, A., 2013. A case of 25I-NBOMe (25-I) intoxication: a new potent 5-HT_{2A} agonist designer drug. *Clin. Toxicol.* 51 (3), 174–177. <https://doi.org/10.3109/15563650.2013.772191>.
- ROSENBERG, D.E., ISBELL, H., MINER, E.J., LOGAN, C.R., 1964. THE EFFECT OF N,N-DIMETHYLTRYPTAMINE IN HUMAN SUBJECTS TOLERANT TO LYSERGIC ACID DIETHYLAMIDE. *Psychopharmacologia* 5, 217–227. <https://doi.org/10.1007/BF00413244>. PMID: 14138757.
- Satodiya, R., Palekar, N., 2020. Synthetic cannabinoids and its association with persistent negative symptoms of schizophrenia. *Cureus*. <https://doi.org/10.7759/cureus.10329>.
- Schetz, D., Schetz, A., Kocić, I., 2022. A retrospective analysis of the “Neverending Trip” after administration of a potent full agonist of 5-HT_{2A} receptor – 25I-NBOMe. *Biomed. Pharmacother.* 146, 112295. <https://doi.org/10.1016/j.biopha.2021.112295>.
- Schifano, F., Chiappini, S., Corkery, J.M., Scherbaum, N., Guirguis, A., 2021. The e-psychoactive drugs’ psychopharmacology. *Curr. Opin. Pharmacol.* 57, 165–174. <https://doi.org/10.1016/j.coph.2021.02.008>.
- Schifano, F., Orsolini, L., Duccio Papanti, G., Corkery, J.M., 2015. Novel psychoactive substances of interest for psychiatry. *World Psychiatry* 14 (1), 15–26. <https://doi.org/10.1002/wps.20174>.
- Schloermerkemper, N., 2018. Psychotic due to bath salts and methamphetamines: emergency cesarean section under general anesthesia. *J. Biomed. Res.* 32 (4), 311. <https://doi.org/10.7555/JBR.32.20180023>.
- Schneider, K., 1959. *Clin. Psychopathol.*
- Simmons, J., Cookman, L., Kang, C., Skinner, C., 2011. Three cases of “spice” exposure. *Clin. Toxicol.* 49 (5), 431–433. <https://doi.org/10.3109/15563650.2011.584316>.
- Simonato, P., Bulsli, L., Negri, A., Bansal, G.K., Pessa, G., Mioni, D., Borgherini, G., Martiniotti, G., Schifano, F., Perini, G., Corazza, G., 2018. Marvin, the paranoid Android”: the case of an Alpha-PVP user in the expanding galaxy of NPS. *J. Psychoact. Drugs* 50 (4), 306–313. <https://doi.org/10.1080/02791072.2018.1447172>.
- Skryabin, V.Y., Vinnikova, M.A., 2019. Psychotic disorders in patients who use synthetic cannabinoids. *J. Psychiatr. Pract.* 25 (6). <https://doi.org/10.1097/PRA.0000000000000429>.
- Skryabin, V., Yu, Vinnikova, M.A., 2018. Clinical characteristics of synthetic cannabinoid-induced psychotic disorders: a single-center analysis of hospitalized patients. *J. Addict. Dis.* 37 (3–4), 135–141. <https://doi.org/10.1080/10550887.2019.1627635>.
- Soares-Weiser, K., Maayan, N., Bergman, H., Davenport, C., Kirkham, A.J., Grabowski, S., Adams, C.E., 2015. First rank symptoms for schizophrenia. *Cochrane Database Syst. Rev.* (Vol. 2017 Issue 6). <https://doi.org/10.1002/14651858.CD010653.pub2>.
- Sönmez, I., Köşger, F., 2016. Psychotic disorder associated with synthetic cannabinoid receptor agonists: a case report. *Türk. Psikiyatr. Derg.* 27 (1). <https://doi.org/10.5080/u10109>.
- Sterne, J.A., Hernán, M.A., Reeves, B.C., Savović, J., Berkman, N.D., Viswanathan, M., Henry, D., Altman, D.G., Ansari, M.T., Boutron, I., Carpenter, J.R., Chan, A.W., Churchill, R., Deeks, J.J., Hróbjartsson, A., Kirkham, J., Jüni, P., Loke, Y.K., Pigott, T.D., Ramsay, C.R., Regidor, D., Rothstein, H.R., Sandhu, L., Santaguida, P.L., Schünemann, H.J., Shea, B., Shrier, I., Tugwell, P., Turner, L., Valentine, J.C., Waddington, H., Waters, E., Wells, G.A., Whiting, P.F., Higgins, J.P., 2016. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *Oct 12 BMJ* 355, i4919. <https://doi.org/10.1136/bmj.i4919>. PMID: 27733354; PMCID: PMC5062054.
- Stevenson, R., Tuddenham, L., 2014. Novel psychoactive substance intoxication resulting in attempted murder. *J. Forensic Leg. Med.* 25, 60–61. <https://doi.org/10.1016/j.jflm.2014.04.007>.
- Stoller, A., Dolder, P.C., Bodmer, M., Hammann, F., Rentsch, K.M., Exadaktylos, A.K., Liechti, M.E., Liakoni, E., 2017. Mistaking 2C-P for 2C-B: what a difference a letter makes. *J. Anal. Toxicol.* 41 (1), 77–79. <https://doi.org/10.1093/jat/bkw108>.
- Sweet, G., Kim, S., Martin, S., Washington, N.B., Brahm, N., 2017. Psychiatric symptoms and synthetic cannabinoid use: information for clinicians. *Ment. Health Clin.* 7 (4). <https://doi.org/10.9740/mhc.2017.07.156>.
- Szara, S., Rockland, L.H., Rosenthal, D., Handlon, J.H., 1966. Psychological effects and metabolism of N,N-diethyltryptamine in man. *Arch. Gen. Psychiatry* 15 (3). <https://doi.org/10.1001/archpsyc.1966.01730150096014>.
- Täljemark, J., Johansson, B.A., 2012. Drug-induced acute psychosis in an adolescent first-time user of 4-HO-MET. *Eur. Child Adolesc. Psychiatry* 21 (9), 527–528. <https://doi.org/10.1007/s00787-012-0282-9>.
- Tancer, M.E., Johanson, C.E., 2001. The subjective effects of MDMA and mCPP in moderate MDMA users. *Drug Alcohol Depend.* 65 (1). [https://doi.org/10.1016/S0376-8716\(01\)00146-6](https://doi.org/10.1016/S0376-8716(01)00146-6).
- Theunissen, E.L., Hutten, N.R.P.W., Mason, N.L., Toennes, S.W., Kuypers, K.P.C., Ramaekers, J.G., 2019. Neurocognition and subjective experience following acute doses of the synthetic cannabinoid JWH-018: responders versus nonresponders. *Cannabis Cannabinoid Res.* 4 (1). <https://doi.org/10.1089/can.2018.0047>.
- Theunissen, E.L., Reckweg, J.T., Hutten, N.R.P.W., Kuypers, K.P.C., Toennes, S.W., Neukamm, M.A., Halter, S., Ramaekers, J.G., 2022. Psychotomimetic symptoms after a moderate dose of a synthetic cannabinoid (JWH-018): implications for psychosis. *Psychopharmacology* 239 (5). <https://doi.org/10.1007/s00213-021-05768-0>.
- Thompson, I., Williams, G., Caldwell, B., Aldington, S., Dickson, S., Lucas, N., McDowall, J., Weatherall, M., Robinson, G., Beasley, R., 2010. Randomised double-blind, placebo-controlled trial of the effects of the ‘party pills’ BZP/TFMPP alone and in combination with alcohol. *J. Psychopharmacol.* 24 (9). <https://doi.org/10.1177/0269881109102608>.
- Tofighi, B., Lee, J.D., 2012. Internet highs-seizures after consumption of synthetic cannabinoids purchased online. *J. Addict. Med.* 6 (3). <https://doi.org/10.1097/ADM.0b013e3182619004>.
- Truscott, S.M., Crittenden, N.E., Shaw, M.A., Middleberg, R.A., Jortani, S.A., 2013. Violent behavior and hallucination in a 32-year-old patient. *Clin. Chem.* 59 (4). <https://doi.org/10.1373/clinchem.2011.179507>.
- Tung, C.K., Chiang, T.P., Lam, M., 2012. Acute mental disturbance caused by synthetic cannabinoid: a potential emerging substance of abuse in Hong Kong. *East Asian Arch. Psychiatry* 22 (1).
- Udow, S.J., Freitas, M.E., Fox, S.H., Lang, A.E., 2018. Exacerbation of psychosis triggered by a synthetic cannabinoid in a 70-year-old woman with parkinson disease. *Can. Med. Assoc. J.* 190 (2), E50–E52. <https://doi.org/10.1503/cmaj.170361>.
- Umebachi, R., Aoki, H., Sugita, M., Taira, T., Wakai, S., Saito, T., Inokuchi, S., 2016. Clinical characteristics of α -pyrrolidinovanilone (α-PVP) poisoning. *Clin. Toxicol.* 54 (7), 563–567. <https://doi.org/10.3109/15563650.2016.1166508>.
- UNODC (United Nations Office on Drugs and Crime). (2020). *World Drug Report 2020*.
- UNODC (United Nations Office on Drugs and Crime). (2024). New psychoactive substances: Data visualisations.
- van Amsterdam, J., Brunt, T., van den Brink, W., 2015. The adverse health effects of synthetic cannabinoids with emphasis on psychosis-like effects. *J. Psychopharmacol.* 29 (3), 254–263. <https://doi.org/10.1177/0269881114565142>.
- van Dam, D.S., Korver-Nieberg, N., Velthorst, E., Meijer, C.J., de Haan, L., 2014. Childhood maltreatment, adult attachment and psychotic symptomatology: a study in patients, siblings and controls. *Soc. Psychiatry Psychiatr. Epidemiol.* 49 (11), 1759–1767. <https://doi.org/10.1007/s00127-014-0894-0>.
- Voce, A., Calabria, B., Burns, R., Castle, D., McKetin, R., 2019. A systematic review of the symptom profile and course of Methamphetamine-Associated psychosis. *Subst. Use Misuse* 54 (4), 549–559. <https://doi.org/10.1080/10826084.2018.1521430>.
- Waugh, J., Najafi, J., Hawkins, L., Hill, S.L., Eddleston, M., Vale, J.A., Thompson, J.P., Thomas, S.H.L., 2016. Epidemiology and clinical features of toxicity following recreational use of synthetic cannabinoid receptor agonists: a report from the United Kingdom national poisons information service. *Clin. Toxicol.* 54 (6), 512–518. <https://doi.org/10.3109/15563650.2016.1171329>.
- Welter, S., Lücke, C., Lam, A.P., Custal, C., Moeller, S., Sörös, P., Thiel, C.M., Philippen, A., Müller, H.H.O., 2017. Synthetic cannabinoid use in a psychiatric patient population: a pilot study. *Eur. Addict. Res.* 23 (4), 182–193. <https://doi.org/10.1159/000479554>.
- White, J.C., Wood, D.M., Hill, S.L., Eddleston, M., Officer, J., Dargan, P.I., Dunn, M., Thomas, S.H.L., 2019. Acute toxicity following analytically confirmed use of the novel psychoactive substance (NPS) methiopropamine. A report from the identification of novel psychoactive substances (IONA) study. *Clin. Toxicol.* 57 (7), 663–667. <https://doi.org/10.1080/15563650.2018.1538519>.
- Whitley, R., 2008. Postmodernity and mental health. *Harv. Rev. Psychiatry* 16 (6), 352–364. <https://doi.org/10.1080/10673220802564186>.
- Wilcox, J., 2012. Psychoactive properties of alpha-methyltryptamine: analysis from self reports of users. *J. Psychoact. Drugs* 44 (3). <https://doi.org/10.1080/02791072.2012.704592>.
- Wilkins, C., Girling, M., Sweetsur, P., 2007. The prevalence of use, dependency and harms of legal ‘party pills’ containing benzylpiperazine (BZP) and trifluorophenylmethylpiperazine (TFMPP) in New Zealand. *J. Subst. Use* 12 (3). <https://doi.org/10.1080/14659890701288945>.
- WILLIAMS, E.G., HIMMELSBACH, C.K., 1846. *Studies on marihuana and pyrahexyl compound*. *Public Health Rep.* 61, 1059–1083 (1896). PMID: 20992145.
- Wilson, L., Szigei, A., Kearney, A., Clarke, M., 2018. Clinical characteristics of primary psychotic disorders with concurrent substance abuse and substance-induced psychotic disorders: a systematic review. *Schizophr. Res.* 197, 78–86. <https://doi.org/10.1016/j.schres.2017.11.001>.
- Yazici, A.B., Yazici, E., Erol, A., 2017. Delirium and High Creatine Kinase and Myoglobin Levels Related to Synthetic Cannabinoid Withdrawal. *Case Rep. Med.*, 3894749. <https://doi.org/10.1155/2017/3894749>. Epub 2017 Apr 10. PMID: 28487743; PMCID: PMC5402247.
- Zidkova, M., Hložek, T., Balik, M., Kopecky, O., Tesinsky, P., Svanda, J., Balikova, M.A., 2017. Two cases of Non-fatal intoxication with a novel street hallucinogen: 3-Methoxy-Phencyclidine. *J. Anal. Toxicol.* 41 (4), 350–354. <https://doi.org/10.1093/jat/bkx009>.