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Effects and Toxicity of Hallucinogenic New Psychoactive Substances From the Perspectives of e-Psychonauts

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Abstract

Hallucinogenic new psychoactive substances have been rapidly emerging due to the increasing use of the Internet as a marketplace and source of information. This study explores hallucinogenic new psychoactive substances' profile, effects and toxicity from the perspectives of e-psychonauts by conducting content analysis of online discussion forums. Qualitative content analysis was applied to threads extracted from online discussion forums. Each thread was coded carefully, and similar codes were grouped into sub-themes and themes respectively. The results showed four main themes related to users' characteristics, hallucinogenic new psychoactive substances profile, effects and toxicity. The majority of users in this study were men in the age range of 18–25 years old. The main effects sought were stimulant/hallucinogenic effects; yet neurological and cardiovascular toxicity were frequently reported. The research found that online discussion forums offered a rich source of information as they provided a safe space for truthful experience reports without fear of legal consequence for e-psychonauts.

Keywords

hallucinogenic, new psychoactive substances, online discussion forums, qualitative content analysis, e-psychonauts

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Introduction

New psychoactive substances (NPS) comprise novel derivatives of classical drugs of abuse that impose a public health threat, and that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances (Shafi et al., 2020). Classical drugs of abuse include the internationally controlled drugs e.g. amfetamine, cocaine and lysergic acid diethylamide (EMCDDA, 2022). Increase in prevalence of NPS has been linked to several factors including low purity of classical drugs and increased use of the Internet. According to the United Nations Office for Drugs and Crime (UNODC), 1230 NPS have been reported in 131 countries as of November 2023 (UNODC, 2023).

Hallucinogenic NPS (HNPS) are synthetically produced substances designed to mimic effects of classic hallucinogens, by interaction with the serotonergic, dopaminergic and adrenergic systems (Nikolaou et al., 2015). They are typically divided into three classes: lysergamides, tryptamines and phenethylamines (Baumeister et al., 2015); where phenethylamines as the most prevalent class (Mallaroni et al., 2022; Palamar et al., 2016; Palamar & Le, 2019). Phenethylamines have both stimulant and hallucinogenic properties (Cocchi et al., 2020; Miliano et al., 2016), and can present different effects based on their structural variations (Halberstadt, 2015; Nelson & Bryant, 2014). Their hallucinogenic action is the result of agonism on specific serotonin receptors (5-$HT_{2A,B,C}$) (Eshleman et al., 2018; Herian et al., 2019).

2C series drugs are ring-substituted phenethylamines that exhibit affinity to serotonin receptors, and act as agonist or antagonists to receptor subtypes (Maurer, 2010; Villalobos et al., 2004). NBOMe and NBOH compounds are both N-benzylated derivatives of the 2C family, with NBOMe drugs bearing a methoxy group and NBOH drugs bearing a hydroxy group (de Barros et al., 2021; Potts et al., 2022; Herian et al., 2019). The addition of an N-benzyl group shows a significant increase affinity to 5-HT2A receptors (Eshleman et al., 2018; Herian et al., 2019, 2020), resulting in NBOMe and NBOH compounds being much more potent than their 2C counterparts.

Recently, Internet forums offered valuable information on individuals' attitude and authentic experience of drugs (Coombs, 2023; Shah et al., 2020). Research have shown that people were more honest on social media and Internet forums where they could voice their opinion (Shah et al., 2020). This made online discussion forums an ideal place to evaluate HNPS use. Previous research has explored the factors surrounding the use of NPS by means of online discussion forums but on a broader scale of all classes of NPS (Rhumorbarbe et al., 2019; Van Hout & Hearne, 2017).

Consequently, this study builds on the findings of previous studies in determining the profile, effects and toxicity of HNPS from online discussion forums via qualitative content analysis. The study used four different online discussion forums to gain perspectives on uses, effects and toxicities linked to HNPS. It enabled gaining insights into e-psychonauts' honest opinions and attitudes towards HNPS.

Methods

Study Design and Settings

The present study involved qualitative retrospective analysis of online discussion forums regarding e-psychonauts experience of hallucinogenic NPS. The retrospective approach enabled understanding the real views of e-psychonauts in non-intrusive settings minimising any ethical implications. Hence, extraction of data was made in a covert way with no intervention from the researcher. In addition, the qualitative analysis allowed in-depth understanding of e-psychonauts' personal insights and perceptions of hallucinogens' use (Moser & Korstjens, 2017). This allowed

the researchers to have access to information regarding authentic experience of the population studies that would otherwise not be accessible due to legal issues surrounding NPS use and stigma against drug users (Soussan et al., 2018). Stigma against NPS users' is consistent across countries regardless of NPS legal status and that also acts as a barrier for individuals sharing information about their drug use (Douglass et al., 2023).

Data Collection

Data were collected between November 2022 and November 2023 from four online discussion forums being: Drug Forum, Hip Forums, Bluelight and Erowid. The forums were open access and did not require membership to view their content. Hence no login was made to any of the forums to extract information.

Search terms used in these forums included: 'e-psychonaut' OR 'e-psychonauts' AND 'synthetic hallucinogen' OR 'hallucinogen new psychoactive substance' OR 'hallucinogen novel psychoactive substance' OR '2C' OR 'NBOME' OR 'NBOH' AND 'experience'.

Using these search terms yielded initially 50,000 results for the forums in total. Search results were organised by relevance. Then, the first 10 pages of each forum were evaluated based on the inclusion and exclusion criteria. Included threads were those that reported experience with using hallucinogenic NPS. There was no limit on the timing the thread was posted. Out of the included studies, studies related to using natural hallucinogenic substances were excluded. This yielded a total of 50 threads that were saved in PDF format (Table 1).

Data Analysis

PDF files were imported into NVivo for Mac software where thematic content analysis was applied. Content analysis allowed to understand patterns and themes among the determined posts (Neuendorf, 2017). The standards for reporting qualitative research (SRQR) were applied (Appendix I). In this respect thread contents were carefully read and re-read by two independent researchers (RM and SA), explained then coded into subthemes. Related subthemes were then grouped into themes and the end point of the study was determined when no further themes emerged and thus saturation was reached. Then both researchers compared their coding, and any disagreement was resolved via discussion. Post analysis, themes, sub-themes and quotations were organised into four overarching themes related to users' characteristics, hallucinogenic NPS profile, desired effects and toxicity. The threads that were coded under these themes were re-read several times to make sure nothing was missed. Then codes were summarised in tables for each subtheme.

Data Validation

For determining inter-rater reliability, threads were sent to a third researcher (AA) who evaluated them. High level of agreement was achieved with inter-rater rater reliability of 95%. The minor disagreement obtained (below 5%) was resolved by discussion among the three researchers. Moreover, the information in the threads were validated by matching the findings against clinical reviews on hallucinogenic NPS and that confirmed the accuracy of the findings.

Results

Thematic analysis yielded 50 relevant threads with 132 subthreads. These threads/subthreads were posted between 2000 and 2023. In this respect, 35 threads were posted over one year only, and 15 threads were posted over multiple years (Table 1). The latter 15 included threads published over

Table 1. Threads Included in the Present Study.

TN	Discussion forum	Year(s) posted
TN1	Drugs forum	2009
TN2	Drugs forum	2007–2016
TN3	Drugs forum	2007–2013
TN4	Drugs forum	2014–2015
TN5	Drugs forum	2014
TN6	Drugs forum	2005–2010
TN7	Drugs forum	2005–2010
TN8	Drugs forum	2005–2010
TN9	Drugs forum	2010–2015
TN10	Drugs forum	2005
TN11	Hip forums	2010
TN12	Hip forums	2011
TN13	Hip forums	2011
TN14	Hip forums	2009
TN15	Hip forums	2010–2012
TN16	Hip forums	2010
TN17	Hip forums	2010
TN18	Hip forums	2008
TN19	Hip forums	2009–2010
TN20	Bluelight	2022
TN21	Bluelight	2014–2018
TN22	Bluelight	2020–2023
TN23	Bluelight	2005
TN24	Bluelight	2013–2015
TN25	Bluelight	2004
TN26	Bluelight	2010
TN27	Bluelight	2010–2023
TN28	Bluelight	2015
TN29	Bluelight	2008–2018
TN30	Bluelight	2004–2017
TN31	Erowid	2011
TN32	Erowid	2015
TN33	Erowid	2018
TN34	Erowid	2013
TN35	Erowid	2017
TN36	Erowid	2019
TN37	Erowid	2014
TN38	Erowid	2017
TN39	Erowid	2011
TN40	Erowid	2022
TN41	Erowid	2018
TN42	Erowid	2014
TN43	Erowid	2013
TN44	Erowid	2013
TN45	Erowid	2000
TN46	Erowid	2019

(continued)

Table 1. (continued)

TN	Discussion forum	Year(s) posted
TN47	Erowid	2010
TN48	Erowid	2005
TN49	Erowid	2009
TN50	Erowid	2006

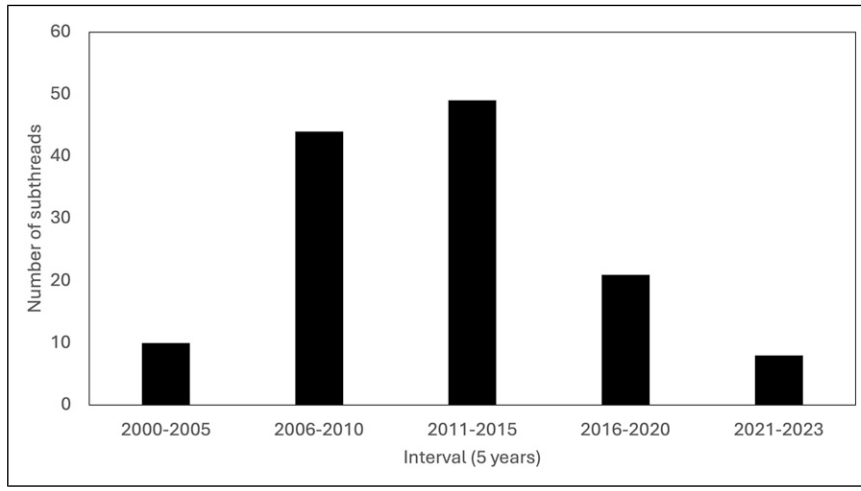

Figure 1. Number of subthreads posted between 2000 and 2023.

two years (TN4 and TN19), three years (TN15), five years (TN21), six years (TN6, TN7, TN8 and TN9), seven years (TN3), 10 years (TN2), 11 years (TN29) and 14 years (TN27 and TN30). When the years subthreads posted were evaluated, the time frame of 2011–2015 ($n = 49$) had the highest number of posts followed by 2006–2010 ($n = 44$) (Figure 1). Yet this number decreased from 2016 onwards where 2016 was the year of introduction of the NPS Act. It is worthmentioning that this number expressed the degree e-psychonauts have posted on the evaluated discussion forum and did not reflect drug use among e-psychonauts. This could be linked to the stigma associated with using illegal drugs from 2016 onwards that held e-psychonauts from reported drug use.

From these threads/subthreads, four main themes were reported by 837 e-psychonauts and included: HNPS prevalence; modalities of intake; pharmacological effects and toxicity.

Users' Characteristics

Characteristics reported by e-psychonauts were age, gender and location (Table 2). Out of the 837 e-psychonauts, only 239 (28.6%) reported their age. The median age was 24 years old (IQR 20–30). Out of the 239 e-psychonauts, 229 (95.8%) were in the age range of 18–84 years old. The most common age range reported was 18–25 years old and was reported by 130 (56.8%) e-psychonauts. This was followed by the ranges of 26–34 and 36–44 years old that were reported by 61 (26.6%) and 21 (9.17%) participants respectively. Nonetheless, only 8 (3.49%) and 9 (3.93%) e-psychonauts reported their ages in the range of 45–50 and 50–84 years old respectively. In addition, only 10 (4.18%) e-psychonauts were in the range of 15–17 years old.

Table 2. Reported Characteristics of e-Psychonauts Included in the Study.

Characteristic	Description	*N* (%)
Age (years)	<18	10 (4.2)
	18–25	130 (54.4)
	26–34	61 (25.5)
	35–44	21 (8.78)
	45-50 8 3.34	8 (3.34)
	>50	9 (3.76)
Gender	Men	358 (88.6)
	Women	36 (8.91)
Location	US	241 (61.9)
	UK	52 (13.1)
	Canada	23 (5.91)
	Netherlands	17 (4.31)
	Australia	15 (3.95)
	Germany and Zimbabwe each	5 (1.28)
	Poland and European country (unspecified) each	4 (1.02)
	Afghanistan, Argentina, Andorra, Bermuda, Denmark, Finland each	2 (0.51)
	Belgium, Greece, Israel, Italy, Norway, Romania, Russia, Slovenia, South America, Spain, Sweden each	1 (0.25)

Regarding gender, 358 (90.9%) out of the 839 e-psychonauts reported their gender as men, 36 (9.13%) reported their gender as women and the remaining 475 (56.6%) did not report their gender. The median (IQR) age of the men and women who reported their gender were 25 (20–32) and 24 (21–27) respectively.

Regarding location, 389 (46.5%) of the 839 e-psychonauts reported their location with the US being the most reported location and was reported by 241 (61.9%) of e-psychonauts. This was followed by the UK, Canada, Netherland and Australia that were reported by 51 (13.1%), 23 (5.91%), 17 (4.37%) and 15 (3.86%) respectively. Only five (1.28%) individuals reported their location in each of Germany and Zimbabwe. Four were reported in each of Poland or Europe (unspecified country). In addition, two e-psychonauts were reported in each of Afghanistan, Argentina, Andorra, Bermuda, Denmark or Finland. Moreover, only one e-psychonaut was reported in each of the following countries: Belgium, Greece, Israel, Italy, Norway, Russia, Slovenia, South American, Spain and Sweden.

Profile of HNPS

HNPS reported were all phenethylamine derivatives and include three types of derivatives: 2C-series, NBOMe and NBOH derivatives. In this sense, four sub-themes emerged and were HNPS type, modality of intake, dose and multidrug use.

Three types of derivatives of HNPS were reported by e-psychonauts on 1,241 occasions and included: 2C-series ($n = 1016$); NBOME ($n = 211$) and NBOHE ($n = 13$) derivatives (Table 3). In this respect, it is worthnoting that the three classes are derivatives of phenethylamines; but NBOME and NBOHE are newer derivatives than 2C series (Cassiano et al., 2023; Dean et al., 2013; Zawilska et al., 2020). Derivatives of the three classes cause hallucinogenic and stimulant effects.

For 2C-series derivatives ($n = 13$), 2C-E was the most popular derivative reported on 262 (25.8%) occasions. This was followed by 2C-I, 2C-B and 2C-C that were reported by 231

Table 3. HNPS Derivatives Reported in the Study.

Drug	Class	Chemical name	*N* (%)
2C-E	2C-series	2,5-Dimethoxy-4-ethylphenethylamine	262 (21.1)
2C-I	2C-series	4-Iodo-2,5-dimethoxyphenethylamine	231 (18.6)
2C-B	2C-series	4-Bromo-2, 5-dimethoxyphenethylamine	198 (15.9)
25I-NBOMe	NBOMe derivative	4-Iodo-2,5-dimethoxy-N-(2-methoxybenzyl) phenethylamine	114 (9.18)
2C-C	2C-series	2,5-dimethoxy-4-chlorophenethylamine	94 (7.57)
25C-NBOMe	NBOMe derivative	2-(4-chloro-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl) methyl]ethanamine	73 (5.88)
2C-T-7	2C-series	2,5-dimethoxy-4- (n)-propylthiophenethylamine	69 (5.56)
2C-D	2C-series	2,5-dimethoxy-4-methylphenethylamine	56 (4.51)
2C-P	2C-series	2-(2,5-Dimethoxy-4-(n)-propylphenyl) ethanamine	38 (3.06)
2C-T-2	2C-series	2,5-dimethoxy-4-ethylthiophenethylamine	35 (2.82)
2C-T-4	2C-series	2,5-dimethoxy-4-isopropylthiophenethylamine	23 (1.85)
25B-NBOMe	NBOMe derivative	4-Bromo-2,5-dimethoxy-N-(2-methoxybenzyl) phenethylamine	14 (1.12)
25D-NBOMe	NBOMe derivative	2-(2,5-dimethoxy-4-methylphenyl)-N-(2-methoxybenzyl) ethanamine	9 (0.72)
25I-NBOH	NBOH derivative	2-(((4-iodo-2,5-dimethoxyphenethyl)amino)methyl)phenol	5 (0.4)
2C-T-21	2C series	4-(2-fluoroethylthio)-2,5-dimethoxyphenethylamine	5 (0.4)
25B-NBOH	NBOH derivative	2-(((4-bromo-2,5-dimethoxyphenethyl)amino)methyl)phenol	3 (0.24)
25C-NBOH	NBOH derivative	2-({[2-(4-chloro-2,5-dimethoxyphenyl)ethyl]amino}methyl) phenol	3 (0.24)
2C-B-FLY	2C-series	2-(8-bromo-2,3,6,7-tetrahydrofuro [2,3-f] [1] benzofuran-4-yl) ethanamine	3 (0.24)
25E-NBOH	NBOH derivative	2-(((4-ethyl-2,5-dimethoxyphenethyl)amino)methyl)phenol	2 (0.16)
25E-NBOMe	NBOMe derivative	2-(4-ethyl-2,5-dimethoxyphenyl)-N-(2-methoxybenzyl) ethanamine	1 (0.08)
2C-H	2C-series	2,5-dimethoxyphenethylamine	1 (0.08)
2C-N	2C-series	5-dimethoxy-4-nitro-dimethoxy-β-phenethylamine	1 (0.08)

(22.7%), 198 (19.5%) and 94 (9.25%) respectively. In addition, 2C-T-7 was stated on 69 (6.79%) occasions, followed by 2C-D ($n = 56$, 5.51%) and 2C-P ($n = 38$, 3.74%). Also, 35 (3.44%) reports were made of 2C-T-2 and 23 (2.26%) made of 2C-T-4.

Five NBOMe series derivatives were identified through 211 reports. 25I-NBOMe was the most prominent, with 114 (54.0%) mentions, followed by 25C-NBOMe ($n = 73$, 34.6%) and 25B-NBOMe ($n = 14$, 6.64%). In addition, 25D-NBOMe was mentioned nine times and 25E-NBOMe was only mentioned once.

Four NBOH series derivatives were reported on 13 occasions of which 25I-NBOH was reported by five (38.5%) individuals. 25B-NBOH and 25C-NBOH were both reported by three (23.1%) individuals, while only two (15.4%) reported 25E-NBOH.

For modality of intake, the main sub-themes that emerged were related to route of administration ($n = 491$), dosage ($n = 913$) and multi-drug use ($n = 304$). The route of administration was reported by 491 (58.7%) of the 837 e-psychonauts. Out of these 491, 166 (33.8%) reported insufflation, 150 (30.5%) reported oral intake and 56 (11.4%) reported rectal intake. Other routes

of intake were less often reported. These included sublingual, buccal, smoking, intravenous and intramuscular, and were reported by 49 (9.97%), 31 (6.31%), 24 (4.88%), 11 (2.24%) and 4 (0.81%) respectively (Figure 2).

Insufflation was described as "snorting" or "sniffing" for liquids (in water or alcohol) and as "lines" or "bumps" for solids (powders). Insufflation was predominantly reported by users of 2C series of drugs ($n = 123$, 74.1%). In this respect, users have chosen this route as it gave faster onset and increased intensity of effects when compared to other routes of administration. One user reported:

> "Snorting it makes it hit you quicker and harder. The peak is way more intense than eating it."

Likewise, the oral route was most commonly reported for 2C-series and less common for NBOMe and NBOH series. Oral route intake involved either dissolving the drug in liquid prior to intake, wrapping the drug in a paper prior to swallowing or direct swallowing of the capsule or tablet. 2C-E, 2C-D and 2C-I were the most popular drugs taken via rectal route and were reported by 30 users. Nonetheless, 25C-NBOMe ($n = 18$, 36.78%) and 25I-NBOMe ($n = 14$, 28.6%) were the most predominant drugs taken sublingually. Sublingual doses ranged from 200 µg to 2500 µg. In addition, inhalation/smoking was reported for 2C-E ($n = 8$, 33.3%) and 25E-NBOH that were inhaled using a pipe or foil or wrapped in cigarette paper prior to smoking. 25I-NBOMe ($n = 5$, 45.5%) and 2C-B ($n = 4$, 36.3%) were also stated as taken intravenously by users; however, only 2C-I was reported as take intramuscular.

Regarding the dosage of drugs reported, 913 doses were reported by 837 e-psychonauts and that indicated that certain e-psychonauts reported more than one dose of a drug. In this sense, 76 e-psychonauts reported multiple doses. For instance, one e-psychonaut reported different doses for 2C-series:

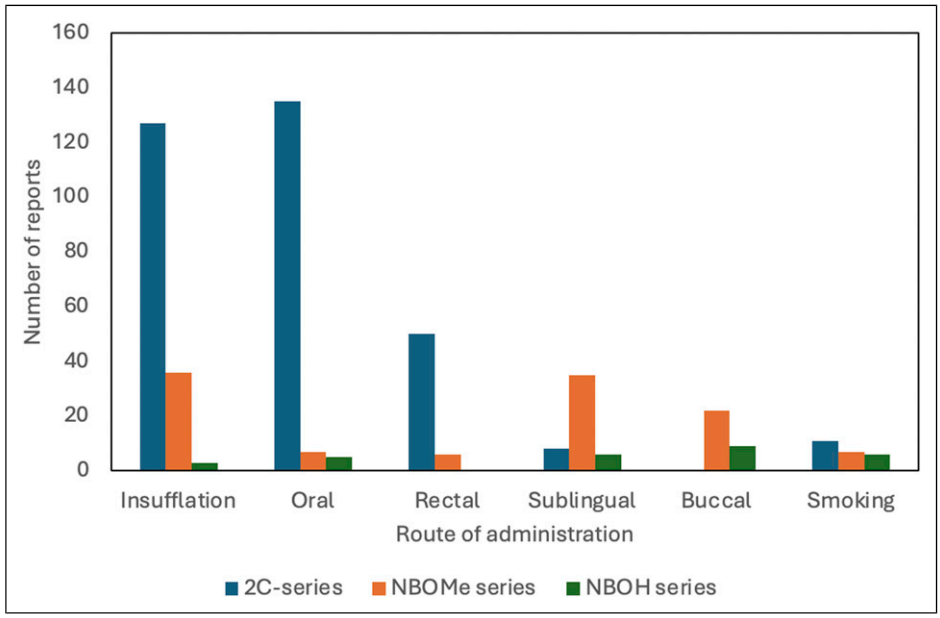

Figure 2. Number of derivatives reported for each route of administration.

"I've tried 30, 20, and 5 mg doses" (Thread 18 Page 2)

The most frequently reported doses were reported for 2C-series derivatives and were 20 mg (n = 74, 8.1%); followed by 25 mg (n = 59, 6.46%) and 10 mg (n = 55, 6.02%) respectively. Moreover, 15 mg and 30 mg doses were reported by 43 (4.7%) and 42 (4.6%) e-psychonauts using 2C-series. On the other hand, doses for NBOMe and NBOHe derivatives were under-reported and where reported around 0.1–0.3 mg were stated.

Multidrug use was reported when hallucinogenic NPS intake was combined with other drugs. The topic five drugs/drug classes used in combination with hallucinogenic NPS were cannabis/cannabinoids, alcohol, MDMA, ketamine and LSD, and were reported by 117 (38.7%), 32 (10.6%), 20 (6.62%), 13 (4.31%) and 11 (3.64%) respectively. All the remaining drugs were reported by less than 10% of e-psychonauts.

Desired Effects of Hallucinogenic NPS

Five sub-themes emerged under the desired effects of hallucinogenic NPS and included: hallucinogenic (n = 1169, 52%), stimulant (n = 536, 23.9%), psychological (n = 363, 16.2%), other effects (n = 278, 7.92%).

Reported hallucinogenic effects included open eye visuals (n = 794), closed eye visuals (n = 125), altered headspace (n = 108), colour enhancement (n = 80) and auditory hallucinations (n = 62). Auditory hallucinations changed users' perceptions and were described as unique:

"I call this the 'life drug'. It's quite hard to put into words, but it's very unique. Everything is different. It makes me see the world in a different way, but I feel like it simply opens doors in your brain." (Thread 18 Page 1)

Stimulant effects reported were not specified on 211 instances; but where specified the following effects were described: euphoria (n = 163), music appreciation (n = 121), increased sociability (n = 32) and increased creativity (n = 9).

Psychological effects reported were elevated mood (n = 119, 32.8%), introspection (n = 86, 23.7%), empathogenic qualities (n = 65, 17.9%), contentment (n = 36, 9.91), entheogen (n = 26, 7.16%), synthesesia (n = 22, 6.06%), confidence (n = 4, 1.1%), mysticism (n = 3, 0.82%) and hedonism (n = 2, 0.55%).

Other effects reported were enhanced sensory perception (n = 87, 31.3%), aphrodisiac (n = 74, 26.6%), afterglow (n = 8, 2.87%), sedation (n = 6, 2.16%), analgesia (n = 2, 0.72%) and coenesthesia (n = 1, 0.36%).

Toxicity Linked to Hallucinogenic NPS

Sub-themes under toxicity of HNPS were 1794 reports and comprised: neurological (n = 1566), gastrointestinal (GIT) (n = 89), cardiovascular (n = 70), respiratory (n = 16), renal (n = 6) and others (n = 47) (Table 4).

Neurological Effects. Neurological effects reported included general neurological effects (n = 618, 39.5%), cognitive effects (n = 201, 12.8%), altered perceptions (n = 223, 14.3%), muscular effects (n = 128, 8.18%), motor function (n = 73, 4.66%), mental illness (n = 83, 5.3%), visual effects (n = 141, 9.01%), auditory effects (n = 29, 1.85%), altered personality (n = 19, 1.21%) and appetite suppression (n = 11, 0.7%). The highest stated general neurological effect reported was nausea (n = 123, 19.9%) instances. This was followed by negative body load, homeostasis and headache that were reported by 83 (13.4%), 57 (9.22%) and 54 (8.74%) respectively. In addition, headache, fear/panic, insomnia,

Table 4. Reported Toxicity Linked to Hallucinogenic NPS.

Theme	Subtheme	Common effects	*N*	Example quotation
Neurological/ psychological	General effects	Nausea	123	I Do often get nauseous on psychedelics
		Negative body load	83	I Found the 2C-x compounds have a significant body load
		Homeostasis	57	There is a change in the perception of temperature
		Headache	54	I had a major headache when I woke up the next day
		Fear/Panic	47	I was confused and scared
		Insomnia	47	I tried to sleep but didn't till late in the morning
		Anxiety	45	Anxiety start to creep into the experience
		Exhaustion	30	I was mentally and physically exhausted
		Hangover/Come Down	28	I ask myself oh god, why did I take this s*** again. Oh yeah, brutal hangovers
		Sweating	23	I was drenched in sweat
		Lack of focus	15	Headspace is generally positive, but gets increasingly disjointed and unfocused as dosage rises
		Shivering	13	Mild to moderate tremors and shivers ran through my legs and torso
		Numbness	11	My arms would increasing grow numb with the waves as well as my face
		Dysphoria	9	I was propelled into a confusing and dysphoric trip
		Dehydration	8	I usually get a UTI the day after from all the dehydration
		Sedation	7	It (2C-C) seemed quite heavily sedating
		Dizziness	5	2C-E is a bit dizzying and uncomfortable
		Polydipsia	5	I was very thirsty and kept drinking
		Tachyphylaxis	4	NBOMe type drugs cause a lot of tachyphylaxis… very quick and strong tolerance which I think is seen in hyper-potent drugs and which may also be a factor in the very strong tolerance effects
	Cognitive	Altered Thought Process	69	I got caught in the first thought/time loop of the trip. Trying to act ok, trying to grip onto what was actually happening, trying to calm myself down and doing separate things for each of these
		Confusion	48	The overwhelming feelings and extreme confusion come in waves
		Aphasia	38	I lost the ability to talk at all and just sat there
		Memory loss	25	You lose a lot of coherence, attentiveness and memory of the experience
		Paranoia	23	The next day I realised that I was just in the throws of extreme paranoia
		Disorientation	17	I started to experience severe disorientation, the floor was rolling violently, creating large lumps in the carpet as the walls swayed and rocked in unison
		Agnosia	15	It took me like five minutes of staring at them to realise they were just hoola-hooping
		Decreased Intelligence	2	It got harder and harder to concentrate on my music work since my brain somehow got 'dumb'
	Altered perception	Altered Perception dissociation	171	I had absolutely no control over myself or my actions the trip completely took over
		Tachypsychia	48	This is where person has very little memory and no perception of time
	Muscular	Muscular Tension	34	Tension that encompasses the whole body, that forces me to stay tense and move, even when I am exhausted, in an ""itchy"" way if it makes sense
		Bruxism	25	Signs of bruxism were evident
		Muscular Spasms	23	I am still being bothered with some physical discomfort but I am mostly ignoring it now except for some muscle spasms
		Tingling	13	The air around me envelopes my skin causing a tingly sensation
		Tremors	11	I Found it to consist of major tremors in calf muscles
		Muscular Pain	10	I was in pain and just wanted to come down
		Cramping	5	I Cramp up strongly
		Aching	4	Had weird overall body aches
	Motor function	Lack of Motor Coordination	34	I would lose some motor skill in my hands and my face movement
		Restlessness	21	Restlessness ensues and we cannot sit in any place for longer than a few
		Shaking	8	It made me involuntarily shaky
		Paralysis	5	I Could not move I felt paralysed
		Seizure	4	Psychedelics can make seizures more likely to occur in people who are susceptible to them
	Mental illness	Psychosis	41	Late night tripping often gets me close to psychosis
		HPPD	24	That gave me massive HPPD for a long time About a year and a half. Only drug that has given me lasting effects. I am talking about persistent HPPD too, not flashbacks
		Depression	15	I Felt a bit stressed and depressed the next day
	Visual	Visual Hallucinations	90	So many visuals I cannot tell what I am seeing
		Mydriasis	23	I've been tripping for eight hours now and my pupils are still huge
		Visual Distortions	21	I had faint visual distortions
		Nystagmus	6	My eyeballs wiggling so much that I couldn't see anything
	Auditory	Auditory Hallucinations	14	The sound of the siren in my mind continued on and I started to have headache
		Auditory Distortions	12	The music sounded like it was coming from everywhere (surround sound)
	Altered perception	Altered Personality agitation	11	Had agitation, 20 minutes post-arrival...Severe agitation, screaming
		Frustration	4	I was getting frustrated with myself
		Permanent Alterations	4	He tried and tried to get back to feeling normal but really struggled
	Appetite	Decreased Appetite	11	My appetite is still suppressed

(continued)

Table 4. (continued)

Theme	Subtheme	Common effects	N	Example quotation
GIT	Vomiting	-	44	I don't enjoy sweating and repeatedly projectile vomiting
	Stomach discomfort	-	18	Felt some stomach discomfort throughout and the need to defecate but no substance to excrete
	Diarrhoea	-	8	I had slight diarrhoea (not uncommon for female on phenethylamines)
	Stomach pain	-	9	The pain in my stomach and really entire torso prevailed throughout the day
Cardiovascular	tachycardia	-	35	I had to pay attention to my heart, which at one point was beating quite fast and hard. Enough to cause a small amount of concern
	vasoconstriction	-	25	The only side effect was vasoconstriction on the comedown
Respiratory	Dyspnoea		6	There was a serious upset in my breathing, for starters. I simply could not t enough air. Very shallow breathing, and I could not control it. It was VERY scary
Kidney	urinary incontinence	-	6	"I had incontinence which is a fairly common thing for some people on psychedelics
Other	Death	-	8	The deaths associated with 2C-T-7 and 2C-T-21 were enough to scare me away
	OD	-	7	People have overdosed and died doing this
	hospitalisation	-	2	I was in the hospital because of an OD from 25I-NBOH (1.5 mg) and 25C-NBOH (3.5 mg)

2C-C: 2,5-dimethoxy-4-chlorophenethylamine; 2C-E: 2,5-Dimethoxy-4-ethylphenethylamine; 2C-T-7: 2,5-dimethoxy-4-(*n*)-propylthiophenethylamine; 2C-T-21: 4-(2-fluoroethylthio)-2,5-dimethoxyphenethylamine; 25I-NBOH: 2-(((4-iodo-2,5-dimethoxyphenethyl)amino)methyl)phenol; 25C-NBOH: 2-({[2-(4-chloro-2,5-dimethoxyphenyl)ethyl]amino}methyl) phenol; GIT: Gastrointestinal; HPPD: Hallucinogen Persistent Perception Disorder; N: number; OD: overdose; UTI: Urinary Tract Infection.

anxiety and exhausted were reported between 30-50 times. Neurological effects reported between 15 - 30 times hangover/come down, sweating and lack of focus. Neurological effects stated less than 15 times included shivering, numbness, dysphoria, dehydration, sedation, dizziness, polydipsia, tachyphylaxis, sialorrhoea, dry mouth and excessive yawning.

Cognitive effects were the second most common neurological toxicity, with 239 (15.2%) reports. Altered thoughts were discussed by 69 (28.9%) individuals, confusion by 48 (20.1%) and aphasia by 38 (15.9%). 25 reports were made of memory loss (10.5%), 23 of paranoia (9.62%), 17 of disorientation (7.11%) and 15 of agnosia (6.27%). Less frequented cognitive effects included decreased intelligence, ataxia and decreased libido.

The third type of neurological effects were cognitive effects of which the top five were altered thought process, confusion, aphasia, memory loss and paranoia, and were reported by 69 (28.9%), 48 (20.1%), 38 (15.9%), 25 (10.5%) and 23 (9.62%) respectively. The remaining cognitive effects were reported less than 20 times and included: disorientation, agnosia and decreased intelligence.

Muscular neurological effects were reported on 128 instances and included muscular tension (n = 34, 26.6%), bruxism (n = 25, 19.5%), muscular spasms (n = 23, 17.9%), tingling (n = 13, 10.2%) and tremors (n = 11, 8.6%). One user of 25I-NBOMe reported experiencing tension, bruxism and spasms simultaneously:

> "*** began gurning his f*****g face off. The most uncontrollable gurn that he has ever experienced in his life. This tension also occurred in the leg muscles and in the eyes. When I would tense any of these areas, they would uncontrollably spasm." (Thread 37 Page 1)

Lack of motor coordination (n = 34, 46.6%) was the most frequent motor function effect (n = 73, 4.66%), followed by restlessness (n = 21, 28.8%). One user who reported restlessness also reported experiencing muscular effects and anxiety:

> "I started to get some muscle spasms and tremors, which were annoying as hell, and which also contributed to me having some anxiety. When I closed my eyes and tried to ignore them, I found I could not keep my legs still." Thread 50 Page 1)

Less frequent effects included shaking (n = 8, 10.9%), paralysis (5, 6.84%), seizures (n = 4, 11.8%) and balance impairment (n = 1, 2.94%).

Seven variations of mental illnesses were stated on 85 (5.42%) occasions. Of these 85, 41 (48.2%) were reports of psychosis. The next most common mental illnesses were HPPD (n = 24, 27.9%) and depression (n = 15, 17.6%). 2 respondents (2.35%) stated that they faced problems with addiction, both of whom were consuming 2C-B. Mental breakdowns, schizophrenia, and serotonin syndrome were all discussed by one person each.

Furthermore, 29 reports were made for auditory effects, with 26 (89.7%) relating to auditory hallucinations (n = 14, 48.2%) or distortions (n = 12, 41.3%). Three reports were made for effects on ear pressure (10.3%). Agitation (n = 11, 57.9%) was the predominant subcategory under altered personality, which 19 respondents (1.21%) reported. Four people each (21.1%) stated that they experienced frustration or long lasting/permanent alterations to their personality. The least frequent neurological effect was a decreased appetite, which was only reported by 11 (0.70%) of users.

Gastrointestinal Effects. GIT effects were stated 89 (4.96%) times of which vomiting was the most frequent and was reported 44 (49.4%) times. Vomiting was described as potentiator of the visual effects (Thread 10 Page 5). Other GIT effects included stomach discomfort, diarrhoea, stomach pain, bloating, stomach cramps, heartburn, and indigestion.

Cardiovascular Effects. Cardiovascular effects were discussed on 74 (4.12%) different occasions. The most stated effects were tachycardia (n = 35, 47.3%) and vasoconstriction (n = 25, 33.8%). NBOMe and NBOH series drugs were indicated as the most likely to cause such effects, with one user of both 25I-NBOMe and 25C-NBOMe together reporting experiencing both:

> "Things led me to believe that the dangerous heart rate combined with limb coldness were the signs of a minor phenethylamine overdose (CNS overstimulation, vasoconstriction, and inability to think straight), which made me about 50% sure I was going to die." (Thread 43 Page 1)

Less frequented effects included angina, arrhythmia, chest pain, circulation, dysrhythmia and hypertension.

Respiratory Effects. Adverse respiratory effects emerged on 7 (0.39%) occasions. Dyspnoea was reported six (85.7%) times and one (14.3%) report was made complaining of a sore throat.

Renal Effects. Kidney toxicity was narrated six times (0.33%). Two people each (33.3%) told of experiencing incontinence or increased urination, whilst one person each (16.6%) experienced discoloured urine or kidney pain:

> "My urine was also quite dark orange for a day or two after the trip." (Thread 9 Page 3)

Other Effects. A total of 47 (2.62%) effects were not specific to any organ system or affected multiple organ systems. These included death, overdose, hospitalisation and multiple organ failure that were reported by 8 (17%), 7 (87.5%), 2 (4.26%) and 30 (63.8%) e-psychonauts respectively.

Discussion

This study determined e-psychonauts' perspectives linked to using HNPS via online discussion forums. Online discussion forums allowed e-psychonauts to post their experience and drug issues

in a blame free environment without worrying about legal consequences (Véliz, 2019). In this respect recent studies have reported understanding toxicity linked to NPS from online discussion forums (Coombs, 2023; Holm et al., 2023; Schifano et al., 2023; Shafi et al., 2020). Yet, these studies either included numerous NPS classes not specifying hallucinogenic NPS derivatives (Coombs, 2023; Schifano et al., 2023; Shafi et al., 2020), or have focused on hallucinogenic NPS derivatives in a single country (Holm et al., 2023).

Hence, this study complemented the previous studies by focusing on e-psychonaut experience from discussion forums with no limit on country or age group. In this respect, the present study highlighted the authentic experience of e-psychonauts in terms of the desired effects and toxicity encountered with classical phenethylamine hallucinogens and HNPS. Understanding authentic perspectives of e-psychonauts among healthcare practitioners is important in designing a harm reduction approach. The qualitative analysis in the study yielded four major themes linked to users' characteristics, profile of HNPS, desired effects and toxicity.

For users' characteristics, age, gender and location were reported, and the three characteristics confirmed the findings in previous literature. The median age was 24 years, which was close to median age reported by Soussan & Kjellgren (2016) and Carhart-Harris & Nutt (2010). This could be due to young adults having an increased rate of internet usage (Office for National Statistics, 2020). Above 90% of users in this study were men. This latter study agreed with other studies that stated men were more likely to engage in and discuss drug use openly than women (Chiauzzi et al., 2013; Deligianni et al., 2017; Soussan & Kjellgren, 2016). Most users reported locations as US, UK, Canada, Netherlands or Australia; and that supported previous findings (Soussan & Kjellgren, 2016; Wood et al., 2014). Yet, there were reports from other countries and that could be related to phenethylamine popularity globally (UNODC World Drug Report, 2023).

Regarding HNPS use, it is worthnoting that the NPS/drugs reported in this study were not all novel drug derivatives that emerged in the market post 2007 as per the UNODC. On the other hand, reported HNPS on the discussion forums included in the study comprised a mixture of classical hallucinogen and HNPS. For instance, 2C-series, that were classical hallucinogenic drugs, were the most reported derivatives and their use outweighed HNPS (that were NBOME and NBOH series) (Hondebrink et al., 2019; Palamar & Le, 2019). This could be related to NBOME and NBOH being newer derivatives than 2C-series. NBOME and NBOH derivatives did not gain popularity on the NPS drug market until 2013 (Halberstadt, 2017; Coelho Neto et al., 2017; Poklis et al., 2015; Yoon et al., 2022; Zuba et al., 2013). The most common routes of administration of HNPS were nasal insufflation followed by oral route that have been reported in previous literature (Musselman & Hampton, 2014). Insufflation was a preferred route in some instances due to having faster onset and more intense effects (Musselman & Hampton, 2014). Where used in combination with other drugs, cannabis/synthetic cannabinoids were the most frequent drugs taken with HNPS and this was seen in previous studies (Kuc et al., 2022). Such combinations have been claimed to maximise the desired effects and minimise adverse events (Kuc et al., 2022).

Desired effects of HNPS by users were hallucinogenic and stimulant effects that were correlated to psychoactive phenethylamines binding affinity to α-adrenergic and 5-HT_2 receptors (Eshleman et al., 2018; Herian et al., 2019). Differences between effects seen by users of 2C series, NBOMe and NBOH drugs could be explained by the structural variations between them altering their pharmacological effects (Cocchi et al., 2020). Different 2C-series drugs have variable affinity at 5-HT2 receptor subtypes and that indicated that their pharmacological effects are dependent on the individual compound (Luethi & Liechti, 2020). NBOMe drugs' prevalence over 2C-drugs for certain hallucinogenic effects could be explained due to the addition of N-benzyl groups to 2C-compounds leading to increased affinity to 5-HT_2 receptors (Halberstadt, 2017).

Yet, the toxicity related to HNPS use outweighed its desired effects and was reported for multiple organ systems including neurological, GIT, CV, respiratory and renal systems. Main

neurological toxicity symptoms were altered thoughts and perception that were also seen in previous literature (Zawilska et al., 2020). It is worthnoting that other studies additionally found prolonged mental illness and psychosis for NBOMe derivatives (Nikolaou et al., 2015); but this has not been identified in this study. GIT toxicity reported included nausea and vomiting and that could be attributed to the elevated level of serotonin in the gut (Calina et al., 2021). Reported CV toxicity included mainly tachycardia and vasoconstriction and that have been reported in previous studies (Shanks et al., 2015; Wood et al., 2015). Respiratory toxicity was less frequently reported than CV toxicity and included chest pain and dyspnoea that were often related to increased panic and anxiety related to increased panic and anxiety related to hallucinogenic effects rather than direct effects of the drug (Mowry et al., 2003). Moreover, overdoses, hospitalisation and lethal effects were stated mainly for NBOMe drugs that had more potency over 2C-series contributing to accidental overdose (Bersani et al., 2014).

Strengths and Limitations

This study demonstrated the benefits of using online discussion forums as a source of rich information regarding uses of HNPS. It contributed to the body of pre-existing knowledge on these drugs from users' perspective in a blame free environment. Such environment prompts truthful, unrestricted experiences from users. This is beneficial for people working in the field, such as drug counsellors and doctors, as it provides further insight into how and why these drugs are used, as well as who they are predominantly used by and the effects that they cause.

As the study was retrospective, limitations arose with missing gaps in data due to certain information, such as age or location, being unobtainable. The information that was provided could not be verified through personal identifications or toxicological analysis. Furthermore, due to the anonymity of the discussion forums it was not possible to ask questions without breaching ethics. Moreover, there was no way to verify drug use by chemical means or other means. Hence, the HNPS reported included what e-psychonauts shared over discussion forums and did not necessarily reflect drug use among e-psychonauts. However, the discussion provided rich content and in-depth understanding of users' experience until saturation was achieved.

Conclusion

This study provided in-depth understanding on the experiences of e-psychonauts with HNPS. The findings of the study contributed to the literature regarding HNPS use, effects and toxicity. In this respect, were predominantly used by men in the age range of 18–25 years old. Insufflation was the most frequent route of administration used, with 2C-derivatives being the most used. The desired effects of HNPS were mainly stimulant/hallucinogenic; however, many adverse events were encountered and were related to multiple organs. Future research would benefit from accessing other social media platforms to have better understanding from wider population and different demographics. Moreover, application of machine learning algorithms offers further insights regarding HNPS use.

Author Contributions

Abdullah Al Hamid: Conceptualisation, Methodology, Validation, Writing-Original Draft. Rebecca McGuinness: Conceptualisation, Methodology, Formal Analysis, Writing- Review and Edit. Dhiya Al-Jumeily OBE: Validation, Writing- Review and Edit. Sulaf Assi: Conceptualisation, Validation, Writing-Original Draft.

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Ethical Statement

Ethical Approval

The study did not require full ethical approval as it involved no participants as recommended by the institutional ethics committee.

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Data Availability Statement

Relevant data to the study have been included in the manuscript.

Supplemental Material

Supplemental material for this article is available online.

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