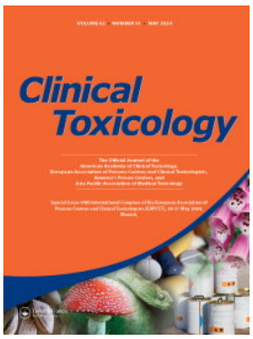

Clinical Toxicology

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/ictx20

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To cite this article: Rachael Wilkes, Darren M. Roberts, Paul Liknaitzky & Jonathan Brett (16 May 2024): The psychedelic call: analysis of Australian Poisons Information Centre calls associated with classic psychedelics, Clinical Toxicology, DOI: 10.1080/15563650.2024.2346612

To link to this article: https://doi.org/10.1080/15563650.2024.2346612

CLINICAL TOXICOLOGY
https://doi.org/10.1080/15563650.2024.2346612

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CLINICAL RESEARCH

The psychedelic call: analysis of Australian Poisons Information Centre calls associated with classic psychedelics

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ABSTRACT

Introduction: The global use of certain classical psychedelics has increased in recent years, but little is known about their spectrum of toxicity within Australia. We aim to describe calls to New South Wales Poisons Information Centre relating to exposures to classical psychedelics including lysergic acid diethylamide, psilocybin, N,N-dimethyltryptamine, ayahuasca, mescaline and ibogaine.

Methods: This is a retrospective observational study of calls to New South Wales Poisons Information Centre between January 2014 and December 2022. We identified exposures to classical psychedelics within New South Wales Poisons Information Centre database and measured the annual number of exposures, source of call (hospital, health care worker, member of the public), co-ingested substances, clinical features and advice given.

Results: There were 737 calls related to relevant psychedelic exposures; 352 (47.8 per cent) to lysergic acid diethylamide, 347 (47.0 per cent) to psilocybin, 28 (3.8 per cent) to N,N-dimethyltryptamine, 4 (0.5 per cent) to ayahuasca, 4 (0.5 per cent) to mescaline and 2 (0.3 per cent) to ibogaine. Cases were predominantly male (77.2 per cent) and aged between 20 and 74 years (65.6 per cent). Psychedelic calls more than doubled from 45 in 2014 to 105 in 2022 and 625 (85 per cent) of all calls were either from or referred to hospital. Co-ingestion of psychedelics with another substance occurred in 249 (33.8 per cent) of calls and the most frequent clinical features related to single substance psychedelic exposures were hallucinations (27.6 per cent), gastrointestinal symptoms (21.7 per cent) and tachycardia (18.1 per cent). Seizures occurred in 2.9 per cent of single substance psychedelic exposures.

Discussion: Increasing incidence of psychedelic exposure calls, including those reporting significant toxicity, likely reflects increasing community use. This may in part be driven by increasing interest in psychedelic assisted psychotherapy trials subsequently increasing public awareness.

Conclusion: Relatively high poisoning severity contrasts with safety within clinical trials of psychedelic assisted psychotherapy that may relate to the uncontrolled nature of community use which is mitigated within clinical trial environments. Education about safe use may be useful.

ARTICLE HISTORY
Received 27 November 2023
Revised 17 April 2024
Accepted 18 April 2024

KEYWORDS
Psychedelics; poisoning; overdose; lysergic acid diethylamide (LSD); psilocybin; N,N-dimethyltryptamine (DMT); ayahuasca; mescaline; ibogaine

Introduction

Worldwide use of certain classical psychedelic compounds, including psilocybin, lysergic acid diethylamide (LSD), N,N-dimethyltryptamine (DMT), mescaline and ibogaine, is now more prevalent than ever before [1]. Beyond the burgeoning field of psychedelic research, and the small group of legalized clinical services, large numbers of people around the world use classic psychedelics in naturalistic (non-experimental) settings for recreational, ceremonial, self-medicating, or other purposes [2]. Australia is no exception to the trend of increasing psychedelic drug use globally, with the most recent National Drug Strategy Household Survey demonstrating an increase in frequency and recent past use [3].

Numerous controlled trials performed to date along with studies of addictive potential demonstrate the safety of classic psychedelics in experimental settings [4–6]. Large population surveys of self-reported safety amongst people using classical psychedelics [7] also imply naturalistic use is relatively safe and studies of expert consensus consistently rate classic psychedelics as one of the least harmful recreational drugs to the user and society [8]. In contrast, reports from international poison centres, other health settings and surveys have described a spectrum of toxicity related to naturalistic use of psychedelics [9–12]. While serious clinical consequences were infrequent, they included hyperthermia, seizures, coma, acute kidney injury, and cardiac arrest [10]. This might be explained by co-ingestion of other substances, extremes of dose, or delays in health-seeking for atypical

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/15563650.2024.2346612.

effects. Further, psychological unpreparedness and the uncontrolled nature of settings frequently associated with naturalistic use (including auditory and visual stimuli, environmental temperature, exertion, and hydration) compared to carefully curated experimental settings [13–15].

Clinical trials of psychedelic-assisted psychotherapy are gaining traction in Australia, which has also recently made psilocybin available by prescription (with various constraints) for treatment-resistant depression from 1 July 2023 [16]. Increasing public awareness may further drive naturalistic use. However, the spectrum of toxicity from psychedelic use in naturalistic settings in Australia remains unclear. The aim of this study is to describe calls to New South Wales Poisons Information Centre relating to exposures to LSD, psilocybin, N,N-dimethyltryptamine, ayahuasca, mescaline and ibogaine over 9 years. These classical psychedelics were selected due to their similar mechanisms of action and prevalence of both their use in the community and in psychedelic assisted psychotherapy. Specifically, we will describe the number of exposures and the clinical features of toxicity, including symptoms, signs and severity, and co-ingested substances.

Methods

We performed a retrospective observational study of calls to New South Wales Poisons Information Centre relating to exposures to classical psychedelics between 1st January 2014 and 31st December 2022.

The New South Wales Poisons Information Centre is the largest of four Australian poisons centres, taking nearly 120,000 calls annually, which is approximately 50% of the calls received by all Australian poisons centres. The New South Wales Poisons Information Centre contributes to a national 24/7 service to health-care professionals and members of the public, handling most calls from New South Wales Tasmania and the Australian Capital Territory, and calls from the rest of Australia at other times depending on operating hours of other poisons centres and a national roster. The New South Wales Poisons Information Centre database records information on the sex and age group of the exposed person, the location and identity of the caller, details of poisoning including all associated substances, and advice given to the caller. Most fields contain predefined coded information, with a single free text field for additional details relating to the case. All calls are initially managed by specialists in poisons information who are specially trained pharmacists or pharmacologists, and responsible for entering this data. Each call entry is reviewed by a second specialist in poisons information for quality purposes. Calls relating to complicated exposures or critically ill patients are referred to medically trained clinical toxicologists as required.

A free and coded text search of all fields was performed on the New South Wales Poisons Information Centre database for reported exposures (calls related to enquiries were excluded) to the following classical psychedelic compounds: LSD, psilocybin, N,N-dimethyltryptamine, ayahuasca, mescaline, and ibogaine, including abbreviations or spelling permutations for each substance (see Supplementary material for search strategy). We then manually reviewed the resulting data extract to ensure only exposures to classical psychedelics were included.

We extracted demographic information according to categories available within the poisons centre database, including age group (15–19, 20–74 and 75+ years) and sex (male/female), intentionality (intentional/unintentional), route of administration (ingested/sublingual/other), caller background (hospital/community medical/patient/family or friend), advice to caller (referred to hospital/already in hospital/see general practitioner/stay at home) and whether the call was referred to a clinical toxicologist. All categories included unknown/not recorded. We considered calls from or referrals to hospital and clinical toxicologists as markers of clinical severity of poisoning. We identified other substances documented as being taken at the same time as the classical psychedelic (co-ingestants).

We manually reviewed the free text field for clinical features reported for each exposure and grouped these using previously described clinical features of toxicity of classical psychedelics [10] along with any additional features. In primary analyses, we identified cases in which only a single psychedelic substance was taken to identify the spectrum of toxicity related to individual classical psychedelics. In secondary analyses, we included all cases (both single and multiple substance ingestions). To illustrate the frequency of co-occurring clinical features of toxicity, we plotted the most prevalent combinations of features within an UpSet Plot for both primary and secondary analyses [17].

We expressed categorical variables as counts and percentages, and continuous variables as means and standard deviations when normally distributed, and medians and ranges otherwise. Ethics approval for this study was granted by Sydney Children's Hospitals Network Human Research Ethics Committee (2021/ETH00165). All analyses were performed in Microsoft Excel 2022 and R version 4.1.3 (2022-03-10).

Results

After excluding enquiries not relating to a specific exposure event, a total of 2,987 calls were identified in our poisons information centre database search. Following manual review, we excluded 2,250 calls comprised of 511 recalls (multiple phone calls about the same case) and 1,739 calls not relating to a classical psychedelic, leaving 737 relevant exposures. There were 352 (47.8%) calls relating to LSD exposure, 347 (47.0%) to psilocybin, 28 (3.8%) to N,N-dimethyltryptamine, 4 (0.5%) to ayahuasca, 4 (0.5%) to mescaline and 2 (0.3%) to ibogaine. Overall, patients were predominantly male (77.2%) and adult (65.6% aged between 20 and 74 years) (Table 1). Of all calls, 369 (50.0%) were from New South Wales, followed by Victoria (178 (24.2%)) and then Western Australia (171 (23.2%)).

The total annual number of exposure calls relating to psychedelics increased from 46 in 2014 to 105 in 2022. The annual number of psilocybin exposure-related calls increased between 2014 and 2016 from 22 to 32, decreased in 2018 and then rose steadily to approximately 68 exposure calls/year

Table 1. Gender, age group, intentionality of administration, route of administration, caller background and advice to caller for poisons calls related to classic psychedelics.

	All psychedelics	Psilocybin	LSD*	DMT†	Ayahuasca	Mescaline	Ibogaine
Total number (%) all calls	737	347 (47.1)	352 (47.8)	28 (3.8)	4 (0.5)	4 (0.5)	2 (0.3)
Sex							
Female	160 (21.7)	68 (19.5)	86 (24.4)	3 (10.7)	1 (25)	2 (50)	0
Male	569 (77.2)	275 (79.3)	263 (74.7)	25 (89.3)	3 (75.0)	1 (25)	2 (100)
Unknown	8 (1.1)	4 (1.2)	3 (0.85)	0	0	1 (25)	0
Age group (years)							
15–19	251 (34)	88 (25.4)	156 (44.3)	6 (21.4)	0	1 (25)	0
20–74	483 (65.6)	256 (73.8)	196 (55.7)	22 (78.6)	4 (100)	3 (75)	2 (100)
75+	3 (0.4)	3 (0.8)	0	0	0	0	0
Intentionality							
Intentional	697 (94.6)	323 (93.1)	341 (96.9)	25 (89.3)	3 (75)	3 (75)	2 (100)
Unintentional	30 (4)	19 (5.5)	6 (1.7)	3 (10.7)	1 (25)	1 (25)	0
Unknown	10 (1.4)	5 (1.4)	5 (1.4)	0	0	0	0
Route of use							
Ingestion	677 (91.9)	340 (98)	313 (88.9)	15 (53.6)	3 (75)	4 (100)	2 (100)
Buccal/sublingual	21 (2.8)	1 (0.3)	19 (5.4)	1 (3.6)	0	0	0
Other‡	39 (5.3)	6 (1.7)	20 (5.7)	12 (42.9)	1 (25)	0	0
Caller background							
Hospital	452 (61.3)	189 (54.5)	239 (67.9)	17 (60.7)	2 (50)	3 (75)	2 (100)
Medical in community§	69 (9.4)	36 (10.4)	28 (8)	4 (14.3)	1 (25)	0	0
Patient	87 (11.8)	60 (17.3)	21 (6)	5 (17.9)	1 (25)	0	0
Family or friend	129 (17.5)	62 (17.8)	64 (18.2)	2 (7.1)	0	1 (25)	0
Advice to caller							
Referred to hospital	171 (23.2)	99 (28.6)	64 (18.2)	8 (28.6)	0	0	0
Already in hospital	451 (61.2)	189 (54.5)	239 (67.8)	17 (60.7)	2 (50)	3 (75)	2 (100)
See general practitioner	22 (3)	15 (4.3)	5 (1.4)	0	2 (50)	0	0
Stay home	59 (8)	33 (9.5)	24 (6.8)	1 (3.6)	0	1 (25)	0
Unknown	34 (4.6)	16 (4.6)	16 (4.6)	2 (7.1)	0	0	0

*Lysergic acid diethylamide.
†N,N-Dimethyltryptamine.
‡Includes injected, smoked and nasally insufflated.
§Includes nurses, general practitioners and paramedics.

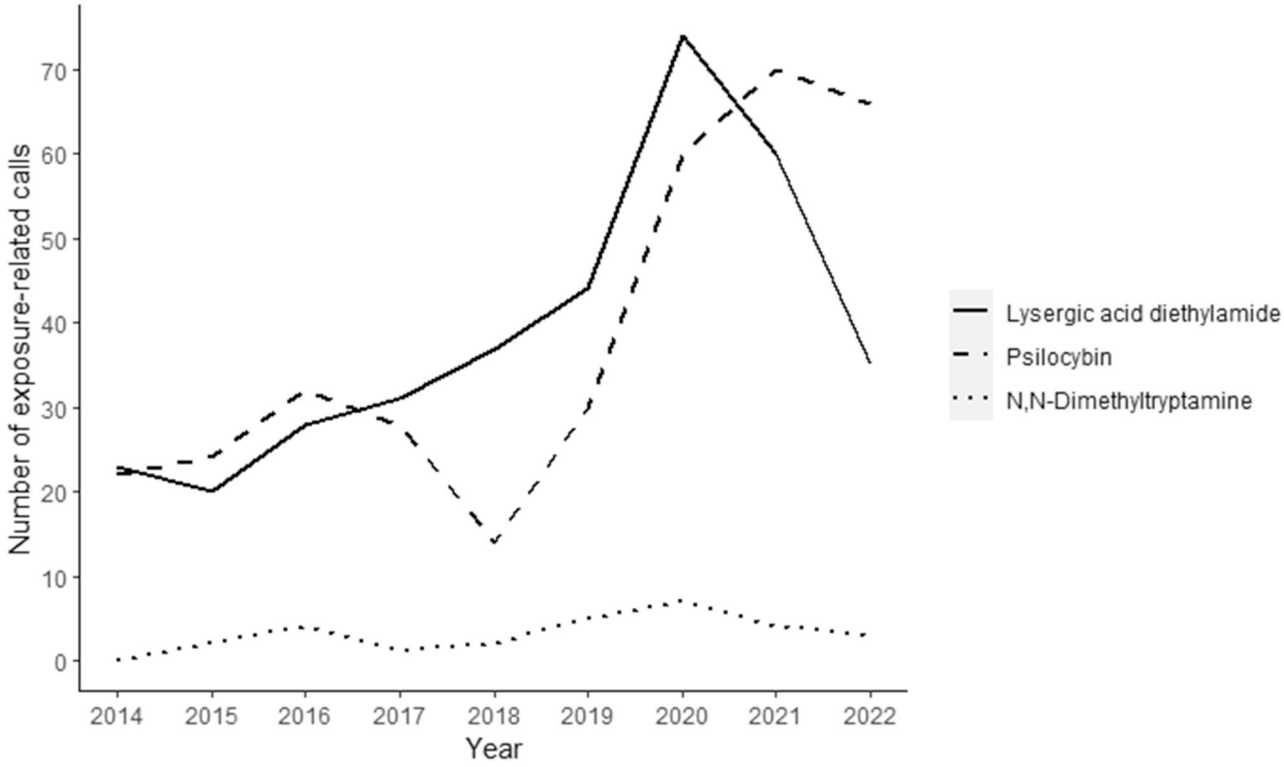

Figure 1. Psilocybin, lysergic acid diethylamide or N,N-dimethyltryptamine exposure-related cases from 2014 to 2022 reported to the New South Wales Poisons Information Centre. Number of cases relating to mescaline, ayahuasca, and ibogaine are small and not shown.

in 2021 and 2022 (Figure 1). Similar trends were seen when annual number of calls relating to these psychedelics were expressed as a rate per 10,000 total exposure related calls to any substance (Supplementary Figure 1). The number of LSD exposure-related calls gradually rose from 23 in 2014 to a peak of 74 in 2020 followed by a decline to 35 in 2022.

N,N-dimethyltryptamine exposure-related calls remained stable throughout the study period between two and seven per year. There were between zero and three calls relating to ayahuasca, mescaline and ibogaine each year.

Most exposure-related calls for classical psychedelics (94.6%) were related to intentional exposures and ingestion was the preferred route of administration (92%) (Table 1). Inhalation was more common with N,N-dimethyltryptamine and buccal/sublingual administration with LSD. Calls were most frequently received from healthcare professionals in hospital (452 [61.3%]). Of the 285 calls from the community, 171 (60.0%) were referred to hospital. A clinical toxicologist was consulted for 65 (8.8%) of all calls.

Co-ingestion of another substance with the psychedelic occurred in 249 (33.8%) of psychedelic exposure-related calls; one co-ingestant in 139 (19.1%) and two co-ingestants in 62 (8.6%) of calls (Supplementary Table 1). The most common co-ingestant was alcohol, which accounted for 102 (13.9%) calls, followed by cannabis in 79 (10.4%) calls, and 'ecstasy' in 57 (7.7%) calls (Supplementary Table 2). Twelve (1.6%) calls involved exposure to multiple psychedelics, with ten of these being combinations of psilocybin and LSD.

Single substance ingestions of psychedelics accounted for 261/347 (75.2%) of psilocybin calls and 189/352 (53.7%) of LSD calls. Clinical features were documented in 329 (69.2%) of all single substance calls. The most common clinical features reported were hallucinations (27.6%), gastrointestinal symptoms (including nausea, vomiting and abdominal pain) (21.7%), tachycardia (18.1%), and agitation (14.5%) (Supplementary Table 3). For psilocybin specifically, the most common clinical features were hallucinations (31.4% psilocybin calls) and gastrointestinal symptoms (30.7% psilocybin calls); for LSD, the most common clinical features were tachycardia (22.2% LSD calls) and agitation (21.2% LSD calls) (Supplementary Table 3). Seizures, while infrequent, occurred in 14/475 (2.9%) of all calls related to single psychedelic exposures; 9/189 (4.8%) for LSD, 3/261 (1.0%) for psilocybin, 1/17 for N,N-dimethyltryptamine and 1/3 calls for ayahuasca. According to UpSet analysis the most common recorded combination of clinical features for single ingestion was hallucinations and gastrointestinal symptoms in 18 (3.8%) calls, followed by tachycardia and hypertension in eight (1.7%) calls (Figure 2). Like all calls, calls relating to single substance ingestions were most frequently received from healthcare professionals in hospital (256 (53.9% of single substance ingestions)). Of the 219 calls from the community regarding single substance ingestions, 121 (55.3%) were referred to hospital. A clinical toxicologist was consulted for 39 (8.2%) single substance ingestions.

In secondary analyses of all calls (not limited to single substance ingestions), clinical features were documented in 513 (69.6.%) of the 737 total calls. The clinical features of toxicity occurred at similar frequencies to those with single substance ingestions, except for tachycardia which was more common than gastrointestinal symptoms (Supplementary Table 4 and Figure 2).

Discussion

In this study of classical psychedelic exposures reported to the poison centre, most exposure calls (97%) were related to LSD and psilocybin, and calls related to psilocybin, LSD and

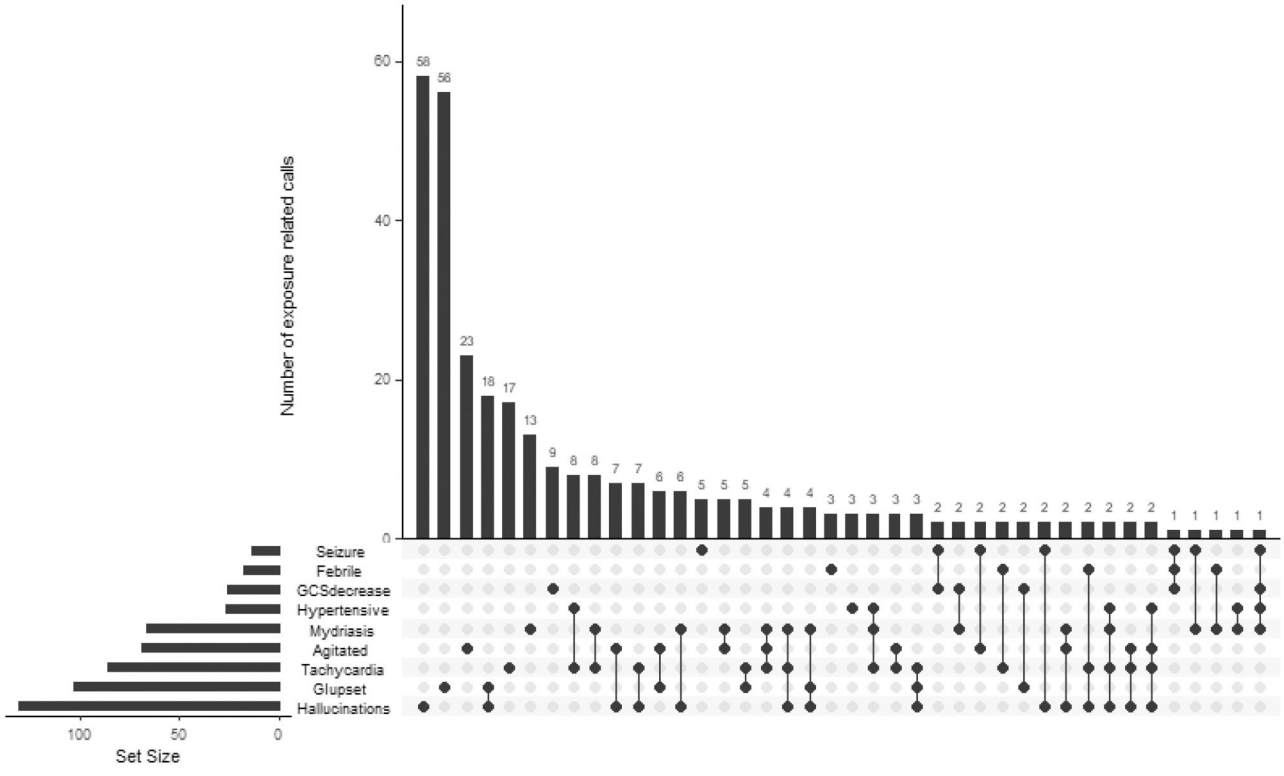

Figure 2. Upset plot of the clinical spectrum of toxicity of single psychedelic showing cases with one, two, three or four clinical features. GCS: Glasgow Coma Scale; GI: Gastrointestinal.

N,N-dimethyltryptamine more than doubled between 2014 and 2020 followed by a plateau or decline to 2022. Consistent with prior reports of use from global surveys and overdoses reported to United States (US) poison centres, there was nearly four times as many male to female exposures [10,18]. While 84.5% and 8.8% of calls in this series were in hospital or referred to hospital and referred to a clinical toxicologist respectively, this was the case for only 43.6% and 2.4% of total poison centre calls in 2022 [19], implying that toxicity from classic psychedelics is of some concern. This may relate to toxicity that is severe or unusual, or possibly comfort with specialists in poison information and other healthcare workers in managing such calls. Co-ingestion of substances along with psychedelics occurred in around one third of calls; the most common being alcohol, cannabis, and ecstasy, indicating the likely recreational intent of these exposures.

The re-emerging interest in psychedelics alongside psychotherapy as treatments for psychiatric and substance use disorders and subsequently increasing public awareness may be important drivers of increasing naturalistic use and calls to New South Wales Poisons Information Centre over the past few years. The Australian National Drug Strategy Household Survey reported a substantial increase in prior 12-month psychedelic use from 1.0% in 2016 to 1.6% in 2019, driven mostly by people in their twenties. Frequency of use also increased in this period and most people using psychedelics reported using LSD (73%) or psilocybin containing mushrooms (61%) in 2019 [3]. An Australian sample of people regularly using ecstasy and related drugs between 2010 and 2020 reported use of LSD in the prior 6 months increased from around 40% in the first half of the decade to 50% in the second. Recent use of natural products (psilocybin, mescaline and ayahuasca) fluctuated between 20% to 30% over the same period [20]. These Australian findings are consistent with a global survey across more than 25 countries indicating increasing psychedelic use; between 2016 and 2021, the number of global respondents reporting prior 12 month use increased from 12.9 to 21% for LSD, 11.8% to 16.1% for psilocybin and 2.2% to 4.8% for N,N-dimethyltryptamine [1]. Of those completing this global survey, over half reported the primary reason for taking LSD or psilocybin was to enhance wellbeing and 37.4% and 18.4% reported self-medication for depression and anxiety as motivators for use [1].

The increase and then decrease or plateau in exposure calls after 2020 was likely associated with COVID-19 related restrictions on population movement, social gatherings, and international border closures between March 2020 and October 2021. This pattern is consistent with international surveys of psychedelic use during the peak of the COVID-19 pandemic restrictions, and likely related to changes in the frequency, motivations, and context of use during this time [21].

Irrespective of whether they were single or multiple substance ingestions, clinical features were described in two thirds of psychedelic exposure-related calls, consistent with a similar prior US poison centre study [10]. In a global survey of recreational psilocybin-containing mushroom and LSD use, the commonest reported symptoms amongst those requiring emergency medical treatment were anxiety/panic, paranoia, confusion and hallucinations [14,15].

Seizures following only LSD ingestion were found in 2.9% of exposures in our study compared to 4.8% in a study of US poison centres [10]. However, greater seizure rates (12.7%) following LSD use were self-reported in the 2017 Global Drug Survey [14]. In our study, co-ingestants were associated with almost half the exposure calls where seizures were reported, including ethanol, cannabis and 2,3 methylenedioxymethamfetamine (MDMA). Seizures have previously been associated with the co-ingestion of psychedelics and other psychoactive drugs [22].

While the denominator of people taking psychedelics in naturalistic settings in Australia is unclear, the spectrum of toxicity associated with psychedelics taken in uncontrolled settings described here, contrasts with the paucity of severe toxicities seen in clinical trial settings. This may be related to numerous factors commonly associated with naturalistic use, including the lack of professional support before and during use of the psychedelic, inadequate psychological preparation, high and uncontrolled stimulus environments, unknown doses and purity of the substance, and co-ingestion of other substances that may enhance toxicity. This suggests that professional support and an appropriate context may have substantially mitigated these issues within clinical trials. Moreover, clinical trials have strict eligibility criteria, excluding certain pre-existing medical or psychiatric conditions, and many medications [13].

Several key limitations of this retrospective study based on clinical documentation should be considered. Substance use was based on history and not confirmed by analytical testing. These data do not permit attribution of causality associated with a psychedelic substance, as numerous measured and unmeasured factors may have contributed to these events, including other concomitant medications, pre-conditions, and contextual and behavioural factors. As this study relates to exposure calls to the New South Wales Poisons Information Centre, findings reported here may not generalise to other geographical regions that are predominantly served by another poisons information centre. In addition, not all community exposures to psychedelics will result in a call to the poisons information centre because not all cases in hospital will be referred to a poison centre, and so cases described here are very likely to represent more severe toxicity. Also, it is likely that only the most salient clinical features of toxicity have been recorded within the Poisons Information Centre database, and we were unable to determine the severity of these symptoms. We were unable to determine the motivation for use, age was defined in wide range categories, and the context of exposure was not reliably captured. Neither were we able to perform follow up on all calls to determine clinical outcomes. Finally, this study was conducting during the COVID pandemic which is likely to have impacted on the prevalence of classical psychedelic use in the community.

Conclusion

The increasing incidence of calls to a poison centre reporting toxicity from psychedelics over the past nine years may be

related to an increasing prevalence of naturalistic use which appears to be of higher than the average severity of New South Wales Poisons Information Centre calls. These data support the importance of harm reduction approaches to psychedelic use in naturalistic contexts [23].

Acknowledgements

We would like to acknowledge Jared Brown for assisting with data retrieval.

Disclosure statement

Liknaitzky has received research funding from Incannex Healthcare Ltd, the Multidisciplinary Association for Psychedelic Studies, and Beckley Psytech, is a member of the Medical Advisory Board of Incannex Healthcare Ltd, and the Scientific Advisory Board of The MIND Foundation. He is a co-founder and Director of the Clarion Clinics. These organisations were not involved in any aspect of this paper, including the decision to write it, drafting the paper, or its publication.

Funding

JB is supported by the National Health and Medical Research Council (NHMRC) Centre of Research Excellence in Medications Intelligence [ID: 1196900] and an NHMRC Investigator Grant [ID: 1196560].

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Data availability statement

Data not available due to ethical restrictions.

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