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The N-BOMe psychedelic drug series: patterns of use, characteristics of users, and self-reported effects in a large international sample.

Abstract

Background: The N-BOMe compounds are a novel series of psychedelic drugs that have recently become popular in the U.S.A. and elsewhere. They are potent agonists of 5-HT_{2A} receptors, have a very short history of human consumption, and they are available to buy online in most countries.

Objectives: We sought to investigate the patterns of use, characteristics of users and self-reported effects.

Methods: A cross-sectional anonymous online survey of 25B-N-BOMe, 25C-N-BOMe, and 25I-N-BOMe, and comparison hallucinogenic drugs, recruited as part of a larger, international study exploring patterns of drug use was used (n = 22,289).

Results: 2.6% (n = 582) of the total sample reported having ever tried one of the three N-BOMe drugs, with 25I-N-BOMe as the most popular (n = 442, 2.0%). The emergence of these drugs appears to be very recent; the majority (93.5%) of people whose last new drug tried was an N-BOMe drug reported trying it in 2012. People who used an N-BOMe drug within the last year were younger than people who reported use of other hallucinogens (2C drugs, magic mushrooms, or LSD) within the last year (p<0.001). The majority (81.2%) of people whose last new drug tried was an N-BOMe drug either swallowed or dissolved the tab under the tongue or in the mouth, as their route of administration. This same group reported subjective effects that were very similar to the comparison serotonergic hallucinogenic drugs, but with slightly higher 'negative effects while high' and a better 'value for money'. The most common (41.7%) source of the drugs was via a website.

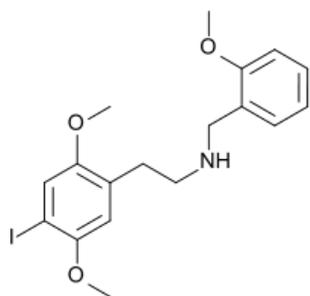
Conclusions: N-BOMe drugs have emerged over the last few years, are frequently bought from the internet and are often taken orally or sublingually/bucally. They have similar effects to other hallucinogenic drugs; however, they may pose larger risks due to the limited knowledge about them, the very small doses required, and their cheapness and availability.

Introduction

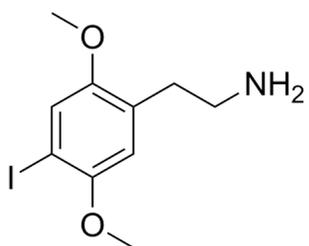
The N-BOMe drug series are n-o-methoxybenzyl analogues of the more well-known 2C-X (e.g. 2C-B) family of phenethylamines (Erowid¹), see figure 1. The N-BOMe series were discovered in the early 2000s and they are psychoactive compounds belonging to the class of ring-substituted phenethylamines, or "classical hallucinogens". These drugs (Ettrup et al., 2011) and other classical hallucinogens, including LSD (Fiorella et al., 1995), magic mushrooms, and the related 2C-X series, are thought to act via agonism of the 5-HT_{2A} receptors.

Figure 1- Molecular diagrams of the 25X-N-BOMe and 2C-X drugs

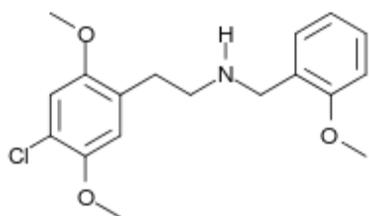
25I-N-BOMe



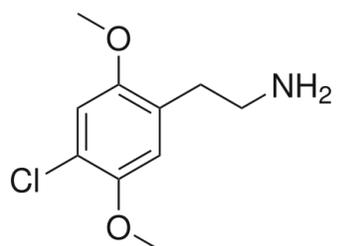
2C-I



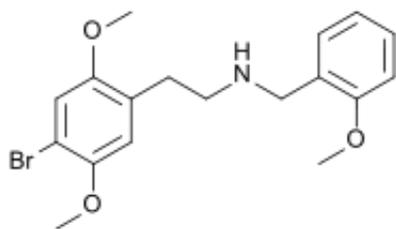
25C-N-BOMe



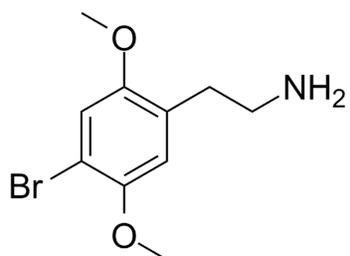
2C-C



25B-N-BOMe



2C-B



Ettrup et al. (2011) demonstrated that a radiolabelled version of 25I-N-BOMe showed high affinity for the 5-HT_{2A} receptor in an ex vivo study in rats and a Positron Emission Tomography study in pigs. Furthermore, they showed that the 25I-N-BOMe molecules were displaceable by the 5-HT_{2A} antagonist ketanserin. These experiments suggest the N-BOMe drugs, like other classical hallucinogens, are agonists of the 5-HT_{2A} receptors.

Human consumption of the N-BOMe drugs appears to have begun in 2010, when they became available online (Zuba et al., 2013). At the current time the N-BOMe drugs are mostly uncontrolled around the world. However, they are illegal in New Zealand, and Poland (Zuba et al., 2013) and were made temporarily illegal in the U.K. on 10/06/2013 (Home Office₁). The three most available N-BOMe drugs online are 25B-N-BOMe, 25C-N-BOMe, and 25I-N-BOMe (e.g. website₁; website₂), and this article will focus on these three.

No human experimental studies have been undertaken with the N-BOMe drugs. However, anecdotal reports arising from the recreational drug using community suggest that they provoke similar effects to other “classical hallucinogens” (Erowid₂), which would be expected given their 5-HT_{2A} receptor stimulation. People experimenting with these drugs have reported euphoria, visual and auditory hallucinations, extraordinary thoughts, and dissociations with reality (Erowid₂).

N-BOMe drugs are sold on blotter paper or in powder form (Erowid₃) and require very small doses (200-1000µg) (Zuba et al., 2013), with nasal insufflation requiring smaller amounts to sublingual administration (Erowid₁). Given the small dose required and the lack of knowledge about these drugs, it would seem to be very easy for people to potentially take too large a dose. Furthermore, there is growing concern within amongst some hallucinogen users that N-BOMe drugs are being sold as LSD, given that the doses and sublingual route of administration are similar (e.g. Drugs-Forum₁).

There have been various media reports of death following the use of a N-BOMe drug (Erowid₄) and one academic report concerning the hospitalization of an 18-year-old male after consuming 25I-N-BOMe (Rose et al., 2013).

Given that no experimental studies or quantitative analyses of N-BOMe use have taken place, the potential harms of these drugs remains largely unknown. Their extremely recent emergence, their apparent legal status, their potential to be mis-represented as LSD and their availability on the internet also augment the dangers associated with this drug series.

Therefore, this paper sought to investigate the patterns of use of these novel compounds; the characteristics of the users; the drugs’ subjective effects when compared with other hallucinogenic drugs; and the prevalence of use, albeit in a self-nominating sample. We expected subjective effects to be very similar to “classic hallucinogens”, such as LSD, magic mushrooms, and the 2C-X series, and the history of use to be mostly within the last year.

Method

The Global Drug Survey (GDS) conducts annual anonymous online surveys of drug and alcohol use in partnership with global media partners (The Guardian and Mixmag in the UK, and Fairfax Media in Australia) with onward promotion through media partner websites and social networking sites, such as Facebook and Twitter. The research tool and methods are based on previous work by the group conducted over the last decade. Accessing a large sentinel drug using population in this way allows for the rapid assessment and identification of novel drugs of abuse. Our team has successfully used this methodology to identify new drug trends before they reach the wider community (e.g. McCambridge et al., 2005; Winstock et al., 2001). Extensive discussion of the methods used including their utility, validity, and limitations are discussed in previously published articles (Winstock et al., 2001; Winstock et al., 2011; Winstock et al., 2012; Winstock & Barratt 2013).

When compared with traditional epidemiological criteria for public health surveillance, this data-collection method has significant limitations. For instance, it recruits from a self-nominating population and it relies upon self-reported data concerning substances whose true composition is uncertain. Nonetheless, this method is very useful when determining new drug trends and the associated harms and effects.

In this particular study, basic information was collected to identify the demographic using N-BOMe drugs including: age, currency used, and drug use history. We used 'currency used' as a proxy measure of country of residence because a large amount of 'country of residence' data was missing. In order to quantify the subjective effects of the N-BOMe drugs and compare them against similar hallucinogenic drugs, respondents were asked to name the last new drug that they tried and answer questions about their experience. Specifically, they were asked to rate, from 0 to 10: 'the pleasurable high', 'the strength of the effect', 'the negative effects while high', 'the comedown after use', 'the urge to use more of the drugs when using', 'the value-for-money', and 'the risk of harm following a session of use'. Furthermore, they were asked how the drug was administered, how the drug was sourced, how long the effects lasted, how long it took for 'peak effects' to occur after a single dose, and what the 'predominant effect' of the drug was.

In order to assess N-BOMe, and other hallucinogen use, absolute numbers and percentages of people reporting having ever used a drug, use in the last 12 months, and use in the last month were collected. To determine the recency of N-BOMe use, those whose last new drug was an N-BOMe were asked which year they had tried it. Furthermore, the proportion of people who reported ever having used a drug and who stated that drug was their most recently tried new drug was calculated. A chi-square test was used to determine whether there were differences in the proportions of males and females within the N-BOMe user group and a group of comparison hallucinogen users. A t-test was used to test whether there was a significant difference in age between these two groups. Predominant effect, route of administration, duration of effect, time until peak effect, and subjective effects of the N-BOMe drugs were assessed by consideration of absolute numbers and percentages.

Due to the nature of data collection through an online survey, it was inevitable that missing data would occur. The majority of the results are reported simply as absolute numbers and percentages, e.g. W people (X%) stated that N-BOMe was their last new tried drug and Y (Z%) of those tried it in 2012. It was common for people to provide one piece of information, e.g. the last new drug they tried, but not a secondary piece of information, e.g. which year they tried it in. In this situation, we have used 'valid' percentages, that is the proportion of respondents who reported a specific thing out of those who reported something; the percentages do not include those who did not provide specific information. For instance, if someone reported N-BOMe as their last new drug tried but did not report the year they tried it in, they would not contribute to the denominator of the percentage calculation.

Results

Whole sample demographics

The Global Drug Survey went online in November 2012 and closed in December 2012. A total of 22,289 responses were collected. 7,360 (33.9%) respondents were from the UK, 2,164 (10.0%) were from the Euro-Zone, 3,756 (17.3%) were from the U.S.A., 618 (2.9%) were from Canada, and 7,784 (35.9%) were from Australia (using local currency as a proxy for country).

Most (68.6%) respondents were male and the mean age was 31.4 years (standard deviation (SD) = 12.4, range 16–100). The male age mean was 30.9 (SD = 12.6) and the female age mean was 30.9 (SD = 11.8).

Commented [MJB1]: can't start sentence with a number ☹

Hallucinogenic drug use

The sample consisted of experienced users of hallucinogenic drugs; 39.4% of respondents reported having ever used LSD, 43.1% magic mushrooms, and 26.0% ketamine. Last month use for these three hallucinogenic drugs was similar in the global sample, at around 5%, see table 1 for the prevalence statistics.

582 (2.6%) of respondents reported having ever used any one of the three N-BOMe drugs. The most popular of the three was 25I-N-BOMe (n = 442, 2%), followed by 25B-N-BOMe (n = 267, 1.2%), followed by 25C-N-BOMe (n = 65, 0.8%). Because the separate drugs' effects were similar, their chemical structures alike, and very little is known about them, even as a group of drugs, analysis will continue with them grouped together as N-BOMe drugs.

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Table 1 – Prevalence of hallucinogenic drug use

	Ever used		Last 12 months use		Last month use	
	N	%	N	%	N	%
LSD	8774	39.4	3340	15	1149	5.2
Magic mushrooms	9604	43.1	3587	16.1	1180	5.3
Ketamine	5784	26.0	2505	11.2	1185	5.3
2C-I	1054	4.7	419	1.9	65	0.3
2C-B	1866	8.4	879	3.9	242	1.1
2C-E	777	3.5	338	1.5	58	0.3
2C-C	180	0.8	91	0.4	18	0.1
25B-N-BOMe	65	0.3	47	0.2	24	0.1
25C-N-BOMe	267	1.2	233	1.0	112	0.5
25I-N-BOMe	442	2.0	406	1.8	177	0.8
Any N-BOMe drug	582	2.6	526	2.4	189	0.8
Any 2C-X drug	2526	11.3	1263	5.7	348	1.6

Commented [MJB3]: Consider what this means or whether to use an alternative base sample

OK I'll try and explain what I mean. This table shows prevalence stats for the whole GDS sample. But this sample includes all kinds of people. It's not representative of anything. I don't see that these numbers are useful for anyone or actually help with any of the main points/aims of the paper.

An alternative base sample might be taking all last 12 month illicit drug users and then creating the table from that, i.e. prevalence of hallucinogenic drug use among a sample of recent illicit drug users.

You can leave this as it is... but this would be my criticism as a reviewer of the paper. Our reviewers may not notice or ask... ☺

Adam may see it differently!

Commented [W4]: I will leave it for the moment and then see what Adam says about it...

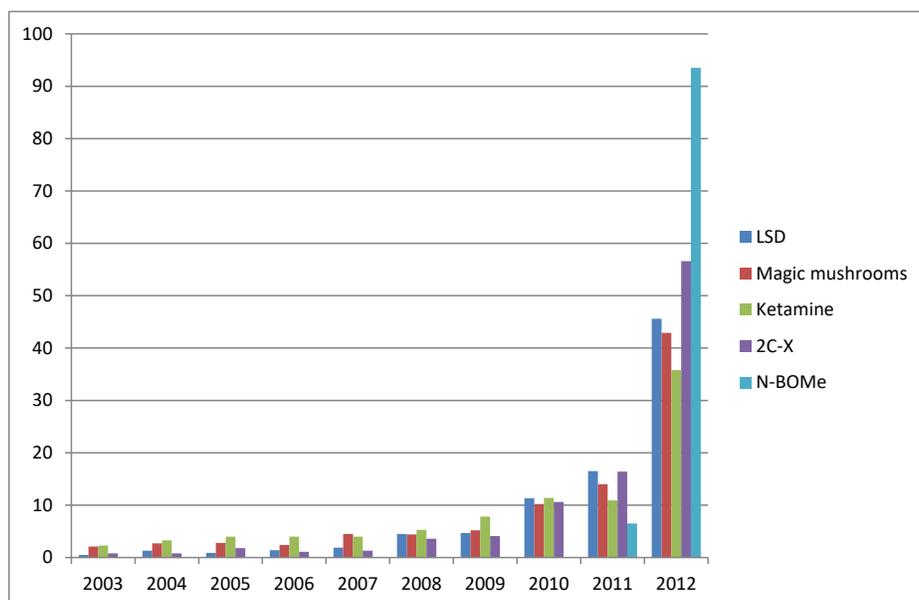
Recent N-BOMe drug use

526 (2.3%) of respondents reported having used any one of the three N-BOMe drugs in the last 12 months and 189 (0.8%) reported having used one in the last month. This former percentage suggests that the majority of people who have ever used this drug have used it in the last 12 months.

This is corroborated by the data concerning which drug was tried for the first time most recently and which year it was tried in, see figure 2. Almost all (93.5%) people whose most recently tried new drug was an N-BOMe drug had tried it in 2012, whereas 56.6% of people whose most recently tried new drug was a 2C-X drug had tried it in 2012, and the percentages were smaller still for LSD (45.6%), magic mushrooms (42.9%), and ketamine (35.8%).

Furthermore, the percentage of lifetime N-BOMe users for whom an N-BOMe drug was also their most recently tried new drug was high (40.9%), and higher than that for LSD (14.3%), magic mushrooms (13.5%), ketamine (18.9%) and the 2C-X drugs (26%) These results strongly suggest that N-BOMe drugs have recently become available and are attracting a larger proportion of new users, compared to lifetime users, than other similar hallucinogenic substances.

Figure 2 - The year in which the last new drug was tried.



Demographics of N-BOMe users

A 'user' is defined as anyone who has used a drug in the last 12 months. A majority (n = 296; 56.7%) of N-BOMe users used U.S.A. dollars and were therefore likely to come from the U.S.A. 21.3% (n = 111) of users used British Pounds, 10.2% (n = 53) used Euros, 9.8% (n = 51) used Australian Dollars, and 2.1% (n = 11) used Canadian Dollars. This distribution was significantly different from that of non-N-BOMe-users ($\chi^2_{(4)} = 606.99, p < 0.001$); however due to the self-nominating sample, this result should be considered with caution (see discussion). The distribution of currencies was similar for LSD users and magic mushroom users, where the largest portion of users used U.S. dollars (36.8% and 43.4% respectively). However, for the 2C-

X drugs and ketamine, the largest proportion of users used Pounds (46.1% and 62.2% respectively).

To compare the gender ratio and age of N-BOMe users with other drug users, two groups were analysed: people who reported using an N-BOMe drug but not a 2C-X drug, LSD or magic mushrooms (classic hallucinogen group) in the last year ($n = 77$) and people who reported using a 2C-X drug, LSD or magic mushrooms but not an N-BOMe drug in the last year ($n = 4954$). Most respondents who reported using an N-BOMe drug in the last year had also used a classic hallucinogen in the last year ($n = 449$).

Commented [MJB5]: Provide the n's for each group.

The proportion of males in the N-BOMe group (95.9%) was significantly larger than in the classic hallucinogen group (77.5%) ($\chi^2_{(1)} = 14.079, p < 0.001$). The average age of the N-BOMe user group was 21.5 (SD = 5.3) and the average age of the classic hallucinogen group was 26.2 (SD = 8.7). Without assuming equal variances in the groups, as Levene's test was significant, these ages were significantly different ($t_{(80.540)} = 5.908, p < 0.001, r = 0.550$).

Commented [MJB6]: Provide the percentage male for each group as well.

Commented [MJB7]: I like what you've done with this!

Description by those whom an N-BOMe drug was 'the last new drug tried'

In order to produce abuse liability ratings and subjective effects of various drugs, respondents were asked to name the last new drug that they tried and were asked about the effects of it. Therefore, this allows a comparison of the effects of N-BOMe drugs against other similar hallucinogens' (LSD, magic mushrooms, ketamine, and any 2C-X) effects to be made, all of which were described by people where that drug was the last new drug they had tried.

The following results are from a subpopulation of the sample who gave information on their last new drug tried and who listed it as an N-BOMe drug ($n = 233, 1.3\%$), LSD ($n = 1130, 6.5\%$), magic mushrooms ($n = 1157, 6.6\%$), ketamine ($n = 993, 5.7\%$), or a 2C-X drug ($n = 615, 3.5\%$) when completing this survey.

The prevalence of lifetime hallucinogenic drug use within the N-BOMe as last new drug tried group was large. Most (72.2%, $n = 169$) of them had used LSD, 65.4% ($n = 153$) magic mushrooms, 45.2% ($n = 108$) any 2C-X drug, and 33.8% ($n = 79$) ketamine. In fact, 88.9% ($n = 208$) of this group had tried at least one of these other hallucinogenic drugs. This experience with hallucinogenic drugs makes their ratings of N-BOMe drugs somewhat more trustworthy, as their ratings will be made with the knowledge of what other hallucinogenic drugs feel like.

The amount of experience of hallucinogenic drugs and MDMA was different between the last new drug tried groups. The last new drug as an N-BOMe drug or a 2C-X drug groups appeared to have increased experience of hallucinogens, including more obscure drugs, compared with the other groups. As seen above, most of the N-BOMe group had tried the other hallucinogens investigated and 64.1% ($n = 150$) had tried MDMA in their lifetime, while 70.6% ($n = 434$), 65.4% ($n = 464$), 63.6% ($n = 391$), and 84.4% ($n = 519$) of the 2C-X group had tried LSD, magic

mushrooms, and ketamine respectively. These groups both had over 4% of group members reporting 4-ACO-DMT and 5-MEO-DMT lifetime use, which represents more obscure hallucinogenic drug use.

Comparatively, 35.9% (n = 415), 22.7% (n = 263), and 40.4% (n = 468) of the magic mushroom group had tried LSD, ketamine, and MDMA respectively. The percentages for the LSD and ketamine groups were similar to the magic mushroom group. Furthermore, these groups all had less than 1.5% of group members reporting 4-ACO-DMT and 5-MEO-DMT lifetime use.

All five groups had a similar age of first use for these drugs. For instance, all groups had a mean age of first use of MDMA between 19 and 21.

Almost all (93.5%) respondents whose last new drug tried was an N-BOME drug stated that its 'predominant effect' was 'psychedelic: LSD or ketamine-like', while 2.2% described it as 'empathogen: MDMA-like', 1.3% 'stimulant: cocaine-like' and 0.4% 'cannabis-like'. A further 2.6% of this group described it as 'other', in that they thought its predominant effect could not be described by these categories.

When asked about route of administration for N-BOME drugs, the majority (n = 190; 81.2%) of the group reported 'swallowed' or 'other'. When investigating what 'other' referred to, all of the responses were 'sublingual', 'buccal' (between the gum and cheek), 'tab on tongue', or something very similar. Therefore, it can be concluded that putting a tab (a small piece of paper with a drop of liquid drug on it) in the mouth, below the tongue, or swallowed, is the most common route of administration. However, a minority (17.9%) of people reported snorting the drug.

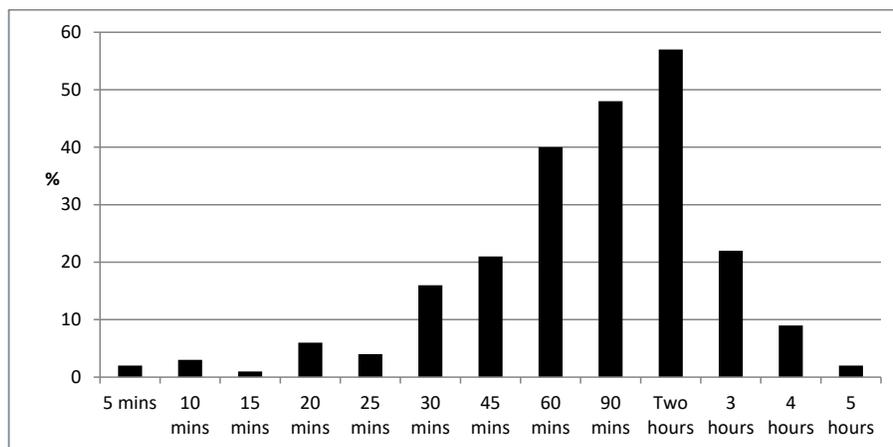
The most common source of N-BOME drugs was from a website (n = 99, 41.7%). The second most common source was a friend (n = 92, 39.7%), and the third most common from a 'dealer' (n = 37, 15.9%).

The variation in time to peak effect was large, see figure 3. Two people reported a peak effect with 5 minutes and two people reported a peak effect within 5 hours. The modal time to reach peak effect was two hours (n = 57, 24.7%), which was the same for LSD (n = 264; 23.9%). However, the 2C-X drugs had a faster modal onset of 90 minutes (n = 115, 19.1%). Magic mushrooms had a modal onset of 60 minutes (n = 261; 23.3%) and ketamine had a modal onset of 5 minutes (n = 204; 21.3%). Those who snorted the N-BOME drug appeared to have a smaller time to peak effect, with a modal time of 45 minutes (n = 9, 21.4%), than those who swallowed it or took it sublingually, with a modal time of 2 hours (n = 52, 27.5%). Furthermore, 19.0% (n = 8) of those who snorted it reported a peak effect by 20 minutes or less, which was significantly larger than the 2.1% (n = 4) of those who swallowed or took it sublingually ($\chi^2_{(1)} = 19.874$, $p < .001$).

Commented [W8]: I put this in so I could discuss the differences in drug experience between the groups that might be important in subjective ratings. However, I realise that it is quite long and clumpy. I didn't include the ketamine, LSD groups because it would have got even longer. And a table including all of this information would have 32 rows! Could we just sum up without reporting all of the data?

Commented [MJB9]: removing spaces between stats is a good way to reduce the word count...

Figure 3- Time to reach peak effect with N-BOME drugs

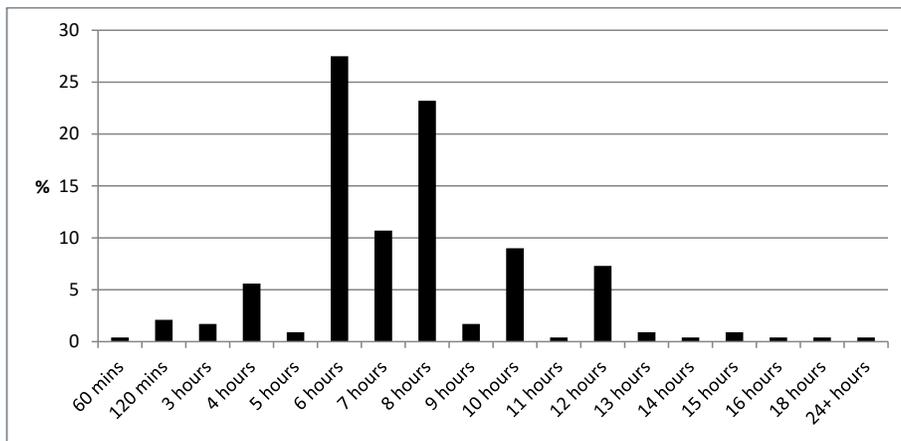


Commented [MJB10]: change “% of people” to “%”

There was a large variation in the duration of effect from a single dose of an N-BOME drug, with a range from 60 minutes to more than 24 hours, see fig 4. The modal duration was 6 hours ($n = 64, 27.5\%$) and 95% of the respondents reported a duration of effect between 3 hours and 13 hours. Those who snorted the drug and those who swallowed it or took it sublingually also showed modal durations of 6 hours ($n = 13, 31\%$ and $n = 51, 26.7\%$ respectively). However, 21.4% ($n = 9$) of those who snorted it reported a duration of effect of less than 6 hours; which was more than the 15.7% ($n = 30$) of those who swallowed it or took it sublingually, but not significantly so ($\chi^2_{(1)} = 0.809, p = 0.368$).

Comparatively, the modal duration reported by those whose last new drug was LSD was 8 hours ($n = 214, 19.1\%$), for magic mushrooms it was 6 hours ($n = 268, 23.5\%$), for any 2C-X drug it was 6 hours ($n = 121, 19.9\%$), and for ketamine it was 60 minutes ($n = 24.1, 24.9\%$).

Figure 4 – Duration of effect of N-BOMe drugs



Commented [MJB11]: change “% of people” to “%”

Table 2 contains the ratings concerning the subjective effects of N-BOMe drugs, 2C-X drugs, LSD, magic mushrooms and ketamine.

The N-BOMe drugs were rated as giving the third most pleasurable high with 6.5 (SD = 2.0). LSD was rated as giving the most pleasurable high with 7.4 (SD = 2.3). 55.6% and 46.4% of people rating LSD and magic mushrooms rated them as giving a pleasurable high between 8 and 10, respectively. Whereas, 32.5% of people rating the N-BOMe drugs gave scores between 8 and 10. Ketamine had the lowest pleasurable high with 5.27 (SD = 2.7) and only 20.1% of people gave it a score between 8 and 10.

The N-BOME drugs were rated as having the second strongest effect with 7.2 (SD = 2), after LSD with 7.6 (SD = 2.1). However, LSD (59.7%), magic mushrooms (49.7%), and ketamine (50.2%) all had higher proportions of people giving them a strength of effect between 8 and 10 than the N-BOME drugs (47.0%). The 2C-X drugs had the lowest proportion of people rating the strength between 8 and 10 with 42.5%. Unsurprisingly, those who administered an N-BOME drug by snorting it reported a significantly stronger effect of 7.9 (SD = 1.8) than those who administered by swallowing it or taking it sublingually with 7.1 (SD = 2.1) ($t = 2.434, p < 0.05, r = 0.16$).

In terms of value for money, the N-BOME drugs were rated the best with 7.9 (SD = 2.4). Furthermore, they had the largest proportion of people rating them as having a value of money between 8 and 10 with 65.1%.

However, the N-BOME drugs were rated as having the second greatest negative effects while high with 3.5 (SD = 2.4); ketamine was rated worse with 3.7 (SD = 2.9) and the three classical hallucinogens were rated as least negative. The N-BOME drugs also had the smallest proportion of people giving a rating of 0 and 0 – 3 for negative effects while high with 11.7% and 52.8%, respectively.

Furthermore, the N-BOME drugs were rated as having the second worst comedown with 2.7 (SD = 2.3); LSD was rated as worse with 3.2 (SD = 2.8). These two also had the smallest proportions of people giving a rating of 0 for the subsequent comedown: LSD with 20.6% and the N-BOME drugs with 20.8%. Magic mushrooms had the least bad comedown with a score of 2.1 (SD = 2.2).

The N-BOME drugs were also rated as having the second highest risk of harm following a session of use with 2.5 (SD = 2.6); ketamine was rated as the worst with 3.3 (SD = 3.0). Magic mushrooms were rated as producing the least harm following use with 1.8 (SD = 2.4).

On the other hand, the N-BOME drugs and magic mushrooms shared the lowest rating for urge to use more, with 1.3 (SD = 2.6, N-BOME; SD = 2.2, magic mushrooms). These two also had the largest proportion of people rating their urge to use more as 0 with 56.0%, for the N-BOME drugs, and 59.5%, for magic mushrooms.

Table 2- Subjective effects of the last new drug tried

Commented [MJB12]: This is a very interesting table!

Drug	The pleasurable high		Strength of the effect		Negative effects when high		Comedown after use		Value for money		Risk of harm following a session of use		Urge to use more of the drugs when using	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
N-BOMe	6.5	2.0	7.2	2.1	3.5	2.4	2.7	2.3	7.9	2.6	2.5	2.1	1.3	2.4
2C- X	6.3	2.3	6.9	2.1	2.8	2.7	2.5	2.2	6.8	2.2	1.8	2.3	1.6	2.6
LSD	7.4	2.3	7.6	2.1	2.8	2.7	3.2	2.8	7.7	2.6	2.0	2.3	1.5	2.6
Magic Mushrooms	6.8	2.5	7.1	2.3	2.9	2.8	2.1	2.4	7.3	2.4	1.8	2.2	1.3	2.7
Ketamine	5.3	2.7	7.2	2.2	3.7	2.9	2.6	2.5	5.6	3.0	3.3	3.0	2.9	2.9
N-BOMe (never tried hallucinogens)	6.2	2.3	7.7	2.0	4.2	2.2	3.2	2.6	7.6	2.3	2.9	2.6	1.2	1.9
N-BOMe (tried other hallucinogens)	6.5	2.0	7.2	2.1	3.5	2.4	2.7	2.3	7.9	2.5	2.4	2.6	1.3	2.1

Discussion

This is the first report on patterns of use and associated psychological effects of the highly novel N-BOMe drug series in a human population. We surveyed 582 people who reported having ever used one of the three N-BOMe drugs, with 25I-N-BOMe the most popular (n = 442). The popularity of these drugs is a very recent phenomenon, with 93.5% of those whose last new drug tried was an N-BOMe drug tried it in 2012. Furthermore, people who had used an N-BOMe drug but not a classical hallucinogen in the last year were younger and more likely to be male than people who had used a classical hallucinogen but not an N-BOMe drug in the last year. N-BOMe drugs were mostly swallowed or taken sublingually/bucally (81.2%), though a minority (17.9%) snorted them.

In terms of subjective effects, 93.5% of the N-BOMe as last new drug tried group described its predominant effect as 'psychedelic'. Furthermore, their 'pleasurable high', 'strength of effect', 'comedown after use', and 'urge to use more' ratings were very similar to the serotonergic hallucinogenic drugs. However, their 'negative effects while high' and 'risk of harm following use' ratings were higher than those of the serotonergic hallucinogens and were more similar to the glutamatergic hallucinogen ketamine. Interestingly, the N-BOMe drugs were rated as the best value for money.

Our finding that the N-BOMe as last new drug tried group mostly tried it in 2012 supports the information on Erowid, which holds reports of N-BOMe use from 2011 onwards (Erowid₁). 40.9% of lifetime users, who did report a last new drug tried, reported an N-BOMe drug as their last new drug tried. It is possible, though unlikely, that the 59.1% of them who didn't report an N-BOMe drug as their last new drug tried could have tried it before 2011. This study implies that the N-BOMe drugs have emerged very recently and rapidly.

The geographical distribution of N-BOMe users, using currency as a proxy, should be interpreted cautiously. Although we found there were significantly more N-BOMe users from the U.S.A. than in the non-N-BOMe user group, this may well be due to the different ways of recruiting respondents from different countries. Across the whole survey, the mean age of respondents from the U.S.A. was much lower than the mean age of respondents from Australia. Hence, this difference could have driven the different proportions of N-BOMe users from these countries. Further investigation of N-BOMe users is needed to confirm these findings.

Nearly half of the N-BOMe as last drug group sourced their drug from a website. This is unsurprising given their apparent legality, as websites can legally advertise the drugs as 'not for human consumption' chemicals (e.g. website₁). This widespread availability on the internet and easy transportation, given the small doses required, may result in a simple transaction, which could be preferable to buying drugs from a traditional dealer for some drug users. Furthermore, this availability could be involved in the claims that N-BOMe drugs are being sold as LSD (Drugs-Forum₁), as dealers could potentially buy N-BOMe drugs cheaply and easily from the internet and make profits marketing it as LSD.

Commented [MJB13]: I've removed this reference to Silk Road – paper still needs to be submitted and reviewed. Can't really cite it yet.

The fact that a large majority of people reported 'swallow' or 'other' (which equated to 'sublingual', 'buccal', or something very similar) as their route of administration for N-BOMe drugs is likely a result of their most common form being tabs. Alternatively, users could wrap up powder form N-BOMe drugs and swallow them, but our data does not permit us to differentiate these different routes of administration within the 'swallow' category. A minority of people reported 'snorting' as the way they consumed the drug. As with many other drugs, the desired effects of N-BOMe drugs require smaller doses using this route of administration (Erowid₁) and therefore the danger of over-dosing is higher, and should potentially be advised against.

The variability in the time to reach peak effect reported by the N-BOMe as last new drug group was large, ranging between 5 minutes to 5 hours. This is probably a consequence of some people

snorting the drug, which led to a quicker onset and others administering it sublingually, or a similar route, which led to a slower onset. The modal time to reach peak effect was 2 hours, which was the same for LSD, demonstrating the similar mechanism of action and sublingual route of administration.

The modal duration of effect from a single dose for any N-BOMe drug was 6 hours, which was the same as for magic mushrooms and the 2C-X drugs. These durations were slightly smaller than that for LSD, which had a modal duration of 8 hours and has been found to produce effects for over 24 hours at large doses (Klee et al., 1961). Those who snorted an N-BOMe drug appeared to have a shorter duration than those who swallowed it or took it sublingually, though there was no significant difference between the proportions that reported a duration of less than 6 hours.

As predicted, the N-BOMe drugs have a very similar profile of subjective effects compared with the classical hallucinogens of LSD and magic mushrooms, with some less attractive aspects. The vast majority of people reported a predominant effect that was 'psychedelic', which was expected given the N-BOMe drugs' agonism of the 5-HT_{2A} receptors (Ettrup et al., 2011) and the well-substantiated claim that hallucinogenic effects are mediated through activity at these receptors (e.g. Marek & Aghajanian, 1996). Furthermore, the 'pleasurable high', 'strength of effect', 'comedown after use', and 'urge to use more' ratings were similar for the four serotonergic hallucinogens compared in this study. This conforms to the idea that serotonergic hallucinogenic drugs have low abuse liabilities (Morgenstern et al., 1994), with very little urge to use more. On the other hand, ketamine, primarily a glutamatergic drug, had higher 'urge to use more' ratings, which is concordant with reports of dependence (Morgan & Curran, 2012). Additionally, the 'comedown after use' ratings were low for all of the hallucinogenic drugs investigated, which could also play into their low abuse liabilities, as the desire to escape unpleasant after-effects would be minimal.

However, N-BOMe drugs did have a higher rating for 'negative effects while high' in comparison to the other serotonergic hallucinogenic drugs, and the rating was more similar to that of ketamine. The reasons for these larger negative effects are not known. However, along with the very important fact that these drugs are highly novel and their harms have not been documented yet, this information could be used to dissuade people from using them instead of other traditional hallucinogens, such as LSD and magic mushrooms, where the harms are thought to be relatively small (Nutt et al., 2010).

One alternative explanation for this higher 'negative effects while high' rating for N-BOMe drugs could be a difference between those rating N-BOMe drugs and those rating other hallucinogenic drugs. It is likely that those whose last new drug tried was an N-BOMe drug are more experimental drug users than those whose last new drug tried was a traditional drug, like magic mushrooms was found that those whose last new drug tried was an N-BOMe drug were more experienced with a variety of hallucinogenic drugs than those whose last new drug tried was magic mushrooms, LSD or ketamine. With heavier and more experimental drug use, one might expect different ratings, for instance more positive ratings because heavier users might

generally enjoy drug use more. This was somewhat substantiated in that those whose last new drug was an N-BOMe and had tried one of the other comparison hallucinogens rated the N-BOMe drugs slightly more pleasurable and with a slightly smaller negative effect while high. However, this effect is very small, so it is unlikely that a difference in previous drug use experience could account for the differences in ratings of the hallucinogens investigated here.

Commented [MJB14]: this is very interesting – NBOMe last time users might be more experimental or more experienced. But we can test for this can't we... e.g. compare number of different drugs tried by last use NBOMe versus the others, also age of first use?

Interestingly, the N-BOMe drugs were rated as the best value for money amongst the hallucinogenic drugs investigated. This is probably a consequence of their apparent legal status and availability online, where prohibition is thought to drive the price of an illegal drug up (Schulhofer et al., 1994). This price situation is somewhat undesirable given that it would probably be less harmful for people to take traditional hallucinogens than these relatively poorly understood N-BOMe drugs.

This study found a relatively low prevalence of N-BOMe use in comparison with other classic hallucinogens. However, due to the self-nominating sample used, one cannot draw conclusions about prevalence in the population. With the temporary ban in the U.K., a fall in use and a rise in price may be expected. Freeman et al. (2012) found that 80% of mephedrone users used less after its ban in the U.K. and 95% reported an increase in price. However, Winstock et al. (2010) reported that soon after the ban, use remained stable but the price had increased. Hence, the temporary illegality's effect on N-BOMe use in the U.K. is unclear. The 2014 Global Drug Survey will provide data concerning the differential trends of N-BOMe use in countries that illegalised the drugs and those that didn't.

Limitations

This is the first, and relatively large, quantitative study of N-BOMe drug use ever conducted. However, the respondents in this survey may not be representative of N-BOMe drug users as a whole, given that the sample was self-nominating. And as always, the findings are limited by the self-reported nature of the data and the fact that there is no way to confirm the true composition of the substance consumed. Furthermore, high-levels of poly-drug use is expected and no data concerning the dose of the drug consumed or setting during the experience was collected. These limitations and others have been discussed more fully elsewhere (e.g. e.g. McCambridge et al., 2005; Winstock et al., 2001; Winstock et al., 2011). However, this group has previously shown that self-report studies in this population can be a valid and effective tool for describing the effects and emergence of novel drugs (e.g. Winstock et al., 2011).

Conclusions

The rapid, yet limited, emergence of N-BOMe drugs around the world, and especially in the U.S.A., is very likely a consequence of the ease of availability provided by the internet. These drugs seem to have a very similar profile of effects to other serotonergic hallucinogenic drugs and are most frequently consumed sublingually or via a similar method.

N-BOMe drugs have an extremely short history of human consumption, have been linked to deaths (Erowid₅) and hospitalizations (Rose et al., 2013), and have a higher rating for 'negative effects while high' than similar drugs. Therefore, people should be dissuaded from using these drugs until further evidence has been accrued, and information about the relative safety of traditional, and purportedly more enjoyable, serotonergic hallucinogenic drugs should be disseminated.

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