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The detection and prevention of unintentional consumption of DOx and 25x-NBOMe at Portugal's Boom Festival

Running head: DOx and 25x-NBOMe at Boom Festival

Keywords: new psychoactive substances, LSD, DOx, 25x-NBOMe, drug checking

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Abstract

Objective: This paper describes the misrepresentation of LSD at Portugal's Boom Festival 2014 and the prevention of unintentional consumption of DOx and 25x-NBOMe among LSD consumers attending a drug-checking service.

Methods: 245 drug samples expected to contain LSD were submitted to the drug-checking service for chemical analysis. 110 post-test questionnaires were successfully matched with test results.

Results: 67.3% of the alleged LSD samples tested contained only LSD; 0.8% contained LSD combined with adulterants; 24.1% did not contain LSD but did contain another psychoactive substance, including 11.4% that were 2,5-dimethoxyamphetamine derivatives and 9.8% that were *N*-benzyl-2,5-dimethoxyphenethylamine derivatives; and no psychoactive substance was detected in 7.8%. The majority of service users who received unexpected test results regarding their alleged LSD (74.2%) reported that they did not intend to consume the drug. Following dissemination of alerts on Day 2, a larger than expected proportion of all tests conducted were for LSD, when comparing the 2014 festival to 2012, where no such alert was disseminated.

Conclusions: Although these results support the provision of integrated drug checking services in party settings, evidence of their utility and effectiveness would be improved through future research incorporating more robust measures of outcomes following provision of drug-checking results.

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INTRODUCTION

Since the discovery of LSD's (lysergic acid diethylamide) psychoactive effects by Albert Hofmann in 1943, this substance has been widely available as a tool for exploration of the mind, as a potential medicine and as a recreational drug (Hofmann, 1980; Smith, Raswyck, & Davidson, 2014). Despite public perception of LSD as a dangerous psychedelic, from a physiological standpoint it has one of the safest profiles of this drug class (Nichols, 2016). In a recent review, Nichols (2016) stated that there are no known deaths arising from LSD toxicity even in severe intoxications. Indeed, safety protocols have been developed to guide the use of LSD in human trials (Johnson, Richards, & Griffiths, 2008), including for LSD-assisted psychotherapy for patients with life-threatening diseases (Gasser et al., 2014).

Currently, LSD is a prohibited drug according to the UN Conventions (United Nations Office on Drugs and Crime, 2013). As a consequence, the supply of LSD for use as a recreational drug is not subject to manufacturing regulations. In such unregulated markets, the risks of prohibited drugs to human health are amplified: in addition to the risks of consuming a 'standard' dose, additional risks arise from consuming an unexpected hazardous substance or substance combination. The use of blotter paper to distribute LSD limits the possible active substances that can feasibly be used as a substitute to compounds with low threshold dosages. In the 1960s when LSD first appeared in street markets, it remained unique regarding its potency and psychedelic effects. After the discovery of DOM's (2,5-dimethoxy-4-methylamphetamine) effects, and from its homologue halogenated series, with bromine (DOB), chlorine (DOC) and iodine (DOI) in fourth ring position, these highly potent and long lasting psychedelic amphetamines have been intermittently detected in blotter samples sold as LSD (Brown & Malone, 1976; Brunt & Niesink, 2011; Grifell et al., 2015; Renfroe & Messinger, 1985; Snyder, Faillace, & Hollister, 1967).

The level of misrepresentation among alleged LSD samples has been measured over time through community-based drug analysis, testing, or checking programs. In the 1970s and 1980s, US-based testing programs detected that most alleged LSD did contain only the expected substance: 92% of 746 samples (Brown & Malone, 1976) and 88% of 1845 samples (Renfroe & Messinger, 1985). Where unexpected substances were detected, they included phencyclidine (PCP), DOB, DOM, amphetamine and caffeine (Brown & Malone, 1976; Renfroe & Messinger, 1985). In the first decade of 2000s the trends were similar. The Dutch Drug Information and Monitoring Service (DIMS), which includes a drug-checking program,

reported that 85% of the 638 alleged LSD samples from 1999 to 2010 contained only the expected substance. The year 2002 was an exception, where among 40 alleged LSD samples, only 10 contained LSD, with many of the remainder containing DOB (Brunt, 2016; Brunt & Niesink, 2011). Between 2009-2013 in Portugal, drug-checking services tested 105 alleged LSD samples, finding 91% contained only LSD, and the remainder containing psychedelic amphetamines such as DOI and DOB (Martins, Valente, & Pires, 2015). Since 2012, a newer phenethylamine series (*N*-benzylphenethylamine - 25x-NBOMe) has been repeatedly detected in expected LSD samples (Caldicott, Bright, & Barratt, 2013; Vidal-Giné, Fornís-Espinosa, & Ventura-Vilamala, 2014). While the overall proportion of alleged LSD samples that contain these unexpected substances remains low, drug-checking service data where DOx and 25x-NBOMe are detected show that these drugs are sold as LSD. For example, in Spain from 2012-2015, 25I-NBOMe was detected in 56 samples, 43% of which were alleged to be LSD (Ezquiaga et al., 2016). In the same Spanish service from 2009-2014, DOC was detected in 41 samples, 42% of which were alleged to be LSD (Grifell, et al., 2015).

Unintentional consumption of DOx and 25x-NBOMe may pose a high risk of acute toxicity or even death (Nichols, 2016). There are several reports of both acute and fatal intoxication after consumption of some of these compounds (Balikova, 2005; Barnett et al., 2014; Burish, Thoren, Madou, Toossi, & Shah, 2015; Hill et al., 2013; Nikolaou, Papoutsis, Stefanidou, Spiliopoulou, & Athanaselis, 2015). Recently, a review of intoxication cases associated with *N*-benzylphenethylamine derivatives was published (Suzuki et al., 2015). From the 20 cases studied, seizures were reported in 8 cases and 3 cases resulted in death. At this moment there is not robust data to conclude if reported deaths related to consumption of DOx and 25x-NBOMe resulted from lethal amounts of the pure substance or an inherent toxicity, regardless of dose (Nichols, 2016). However, compared with LSD toxicological data of almost 70 years of medical and recreational use, at least it can be reasonably argued that their consumption is associated with greater risk.

As shown in the above review of LSD misrepresentation, drug-checking services provide information useful for drug market monitoring. This information is unique because such services can access a different and arguable wider range of drug samples to those accessed through police seizures (Camilleri & Caldicott, 2005), and they provide information about the nature and size of the discrepancy between alleged and actual chemical content of drugs (Barratt & Ezard, 2016). In the last decade, with the increased availability of new psychoactive substances (NPS) (European Monitoring Centre for Drugs and Drug Addiction,

2016), the provision of mechanisms to screen and identify these substances is of utmost importance. In addition to their use in monitoring drug trends, drug-checking services can also change consumer behaviour at point of consumption (i.e., when the consumer is confronted with an unexpected test result, see Benschop, Rabes, & Korf, 2002; Sage, 2015), inform clinical management at the point of intervention (Butterfield, Barratt, Ezard, & Day, 2016), and facilitate brief intervention and referral to services (Hungerbuehler, Buecheli, & Schaub, 2011).

Aims

The aims of this paper were to use the data generated by a drug-checking service to:

1. Describe rates of misrepresentation of LSD at Portugal's Boom Festival 2014,
2. Evaluate the prevention of unintentional consumption of DOx and 25x-NBOMe among potential LSD consumers, and
3. Evaluate the effect of dissemination of alerts designed to increase use of the service among potential LSD consumers over the 5-day intervention at the festival event.

METHODS

Setting

The data presented in this paper was collected at the 2014 Boom Festival, held in Idanha-a-Nova, Portugal. For comparative purposes, some data from the previous Boom Festival (2012) is also presented. Boom is biennial festival of psychedelic culture and in 2014 gathered almost 40,000 people from 150 different countries. Known and marked by its ecological and social awareness, Boom Festival organisers make significant investments in comprehensive prevention and harm reduction interventions that include, but not limited to, psychological crises intervention (Carvalho et al., 2014), harm reduction information booths, and integrated drug-checking services (Martins, et al., 2015).

Procedure

A team of four laboratory technicians ran a small mobile laboratory inside a container, positioned near the dance floor. Other two technicians worked in collaboration with the harm reduction information team collecting samples and giving users detailed information on their results. Drug-checking users were asked to answer a pre- and post-test questionnaire. In the

pre-test questionnaire, socio-demographic data were collected alongside the service user's expectation of the chemical content of the sample. The post-test questionnaire asked service users to report their intended behaviours, following provision of the test result. By the second day, several detections of alleged LSD containing other psychoactive substances had occurred. On this day, the drug-checking service distributed alerts within the festival grounds with messages about these specific results, urging festival-goers to use the service.

The mobile laboratory was equipped with one colorimetric reagent station and three different thin-layer chromatography (TLC) solvent systems. The colorimetric reagents Marquis, Mecke, Mandelin and p-DMAB-TS were prepared as reported in literature (O'Neal, Crouch, & Fatah, 2000) and used for preliminary screening. The TLC aluminium plates pre-coated with silica gel 60F-254 (Merck) were used as stationary phase. In LSD and phenethylamines samples analysis, the development of plates was carried out in a glass chambers saturated with the mobile phase methanol/25% ammonia (100:1.5). Obtained chromatograms were revealed under ultraviolet (UV) light of wavelength of 254 nm and/or 366 nm. Further confirmation was obtained from application of the Marquis reagent and p-DMAB over the developed plates.

Selected samples were analysed by GC-MS to confirm TLC results. Sample preliminary identification was performed by GC/MS at the IMIM facilities using an Agilent 7890B gas Chromatograph, coupled to a 5977A quadrupole mass spectrometer detector (Agilent; Santa Clara, CA, USA). The gas chromatograph was fitted with G4513A auto sampler injector. Insert liners packed with silanized glasswool were used, and the injector and the interface were operated at 280 °C. Samples were injected in split mode into a 30 m 0.25 mm i.d., 0.25 µm film thickness 5% phenylmethylsilicone column (HP-5MS, Agilent Technologies). Helium was used as carrier gas at a flow rate of 1 mL/min. The oven temperature was initially maintained at 90 °C for 2 min and programmed to reach 320 °C at 20 °C per min. It was finally maintained at 320 °C for 9.5 min (total run time was 21.5 min). The mass spectrometer was operated in electron impact ionization mode at 70 eV. In order to confirm the mass spectra, four libraries were used: the Searchable Mass Spectral Library NIST/EPA/NIH Mass Spectral Library, Data Version: NIST 14; Searchable Mass Spectral Library Version 2.3 (<http://www.swgdrug.org/ms.htm>), Searchable Mass Spectral Library Cayman Spectral Library (CSL) (<https://www.caymanchem.com/app/template/SpectralLibrary.vm>), and the Energy Control's Mass Spectral library for internal use.

Analysis

During the 5-day intervention at the festival in 2014, 625 suspected drug samples were submitted to the drug-checking service for chemical analysis. In the current study data concerning only the samples which were expected to contain LSD (N=245) are presented. While all 245 individuals who submitted samples expected to be LSD completed the pre- and post-questionnaire, only 110 were able to be successfully matched. The treatment of data regarding the results of analysis was accomplished using MS Excel. All the statistics and questionnaire data treatment was carried out in SPSS. Pearson's chi-square tests were used to test differences between categorical groups. The alpha level was set to $p=.05$. When testing the effect of the service alert in 2014, the proportion of samples submitted for testing on each day that were alleged LSD was calculated and compared between 2014 and 2012.

RESULTS

The chemical composition of alleged LSD

Two thirds (67.3%; $n=165$) of the 245 alleged LSD samples did in fact contain only LSD. An additional 2 samples (0.8%) contained LSD combined with adulterants or synthesis residues. One quarter (24.1%; $n = 59$) of the alleged LSD samples did not contain any LSD, but did contain another psychoactive substance. Of these, 28 samples (11.4%) contained a compound from the DOx family (2,5-dimethoxyamphetamine derivatives, $x=Br, I, Cl$ or CH_3), 24 samples (9.8%) contained a compound from the 25x-NBOMe family (*N*-benzyl-2,5-dimethoxyphenethylamine derivatives, $x=Br, I,$ or Cl), and in the remaining 7 samples (2.9%), other psychoactive substances were detected but their identification was not possible. In 19 samples (7.8%) no psychoactive substance was detected.

Behavioural intentions following drug-checking

The 110 drug-checking service users who submitted alleged LSD samples and were matched to post-test questionnaire are analysed here. The sample had a mean age of 27.1 years ($SD = 5.7$; range 18 to 40) and the majority (78.2%) of the sample were male. Service users were residents of 27 countries, mainly from Europe, with higher frequencies in Germany (14), Sweden (12) and Portugal (11).

Figure 1 shows the self-reported intentions of drug-checking service users presented by checking result. When the drug-checking result provided confirmation of the expected substance (LSD), the majority reported an intention to consume the substance. However, if testing indicated that the alleged LSD contained an unexpected substance, most would not consume it: two-thirds would not consume an unexpected substance that they had information on and three-quarters would not consume an unexpected substance that they did not have information on. Combining data from both groups who received a test result indicating an unexpected substance, 74.2% reported that they would not consume it (n=31). There was a statistically significant association between behavioural intentions and drug-checking result ($\chi^2(3) = 59.67$ p < .001).

[Insert Figure 1 about here]

When asked about the reasons for intending to consume the substance (N=78; multiple responses possible) 78% said “it’s only the expected substance”; 36% said “it’s a substance I am familiar with”; 14% said “it’s new and I want to try it”; 4% said “it’s adulterated but non-toxic” and only 3% of the sample said “don’t know this substance, but I’ll take it anyway”. We also asked people who intended to consume the substance about their behaviour when they take it: 44% said they “just take the drug”; 30% said “they don’t mix with other substances”, 8% “search for more information about the substance or adulterants” and 13% “take a smaller dose”. From the respondents stating they wouldn’t take the substance (N=29; multiple responses possible): 50% said it was because they “didn’t know the substance”; 36% said “I know this substance and don’t like it”; 21% said “it’s toxic or adulterated” and 18% said “maybe take it later, when I have more information about it”. Of respondents stating they wouldn’t take the substance, 50% also said they would “look for another substance to use”; 43% would “change dealer” and 14% would “search for more information about the substance or adulterant”.

We also asked respondents what type of methods they use to assess the quality of their substances when they don’t have a drug-checking service available (N=107; multiple responses possible). 61% of the respondents rely on the opinion of other people that have tried the substance; 41% “start with a small amount”, 33% “ask their dealer”; 31% “just use it”, 29% of users state they “look on the internet”, 16% base their decision on the “outside aspect, e.g. logo” of the substance; 7% use a test kit and 3% base their decisions on price.

The effect of distributing warning alerts on-site

Figure 2 compares the percentage of samples tested per day that were alleged to be LSD at Boom Festival 2014, compared with the previous event in 2012. In 2014, the drug-checking service distributed alerts about the detection of DOx and 25x-NBOMe in alleged LSD, while no such alerts were distributed in 2012. Figure 2 supports the conclusion that these alerts raised interest among LSD users and prompted them to analyze their samples in the following days. Indeed, more than half (59.1%) of the samples tested on Day 3 in 2014, following the distribution of alerts, were alleged to be LSD.

[Insert Figure 2 about here]

DISCUSSION

Only two thirds of the 245 alleged LSD samples tested at Portugal's Boom Festival 2014 contained only LSD. Dutch data spanning the 2000s averaged 85% of alleged LSD samples containing only LSD (Brunt, 2016; Brunt & Niesink, 2011), and recent Portuguese data gave an even higher number of LSD samples containing only LSD (91%) (Martins, et al., 2015). Thus, the rates of LSD misrepresentation reported here are greater than would be expected. The unexpected drugs detected in alleged LSD samples included DOx and 25x-NBOMe. The DOx series have been historically misrepresented as LSD (Brown & Malone, 1976; Renfroe & Messinger, 1985), with the NBOMe series more recently being detected as an LSD substitute (Caldicott, et al., 2013; Vidal-Giné, et al., 2014). The misrepresentation of DOx and 25x-NBOMe as LSD introduces additional risks for LSD consumers, as DOx and 25x-NBOMe are arguably more likely to cause harm and a subset of these harms are not normally associated with LSD consumption (Nichols, 2016).

The majority of drug-checking service users who received unexpected test results regarding their alleged LSD (74.2%) reported that they did not intend to consume the drug. In this way, assuming service users' intentions matched their subsequent behaviour, drug-checking services worked to prevent the unintentional consumption of DOx and 25x-NBOMe at Boom Festival 2014. A body of research where party drug users have been asked to comment on the hypothetical situation of finding out that their drugs contained unexpected, suspicious or more dangerous substances has found similarly high levels of intentions not to consume the drug (Benschop, et al., 2002; Johnston et al., 2006; Wiese & Verthein, 2014); however, it is

unclear whether reported intentions in the hypothetical scenario will predict actual behaviour in the party setting. A recent Canadian study reported on the discard rates at their drug-checking service, finding that out of 1900 drug-checking service encounters, 31% of those whose results indicated highly hazardous substances including PMA/PMMA, 25x-NBOMe or 2C-T-7 discarded the drugs, compared to 4% for other drugs (Sage, 2015). They also note that using the discard rate at the service may hide the true prevention effect of testing, because some substance may be discarded at other locations or returned to the supplier (Sage, 2015).

A second way that the checking service prevented the unintentional consumption of DOx and 25x-NBOMe was by disseminating alerts designed to increase use of the service among potential LSD consumers, following the initial detection of these substances in alleged LSD. Following dissemination of alerts on Day 2, a larger than expected proportion of all tests conducted were for alleged LSD, when comparing the 2014 festival to 2012, where no such alert was disseminated.

Limitations

Concerning the most used analytical technique in this study, TLC, a commentary must be made. An intervention with a high sample throughput as presented here (125 samples/day) requires a technique that has the ability to separate compounds simultaneously in parallel lanes, is not dependent on complex sample preparation, and can produce final results rapidly. A balance between reliability, time of analysis and costs of equipment and maintenance is required within this setting. Comparing with other available techniques, TLC fulfils all these requirements and is considered a good option. The literature on TLC performance and reliability is vast, and it has been reportedly used for decades on detection and identification of psychoactive drugs (Gough & Baker, 1982; Niwaguchi & Inoue, 1976; Sherma & Fried, 2003). The use of TLC in conjunction with the spraying of colorimetric reagents (eg. p-DMAB) over the plates for spot confirmation can increase performance and accuracy of identification (Svendsen & Verpoorte, 1983). In the moment that the result is communicated the accuracy limits of the technique are discussed with the service user. In addition to these limitations, of 245 alleged LSD tests, only 110 (45%) service users who completed the post-test questionnaire were able to be matched to test results. The high influx of users attending the service and a reduced number of volunteers to apply the evaluation tools resulted in a high number of self-filled post-questionnaires that were unable to be matched with the

respective pre-questionnaire. The timing of the post-test questionnaire – completed just after receiving the drug-checking result – meant that we could only ask questions about people’s intended behaviours following drug-checking. These measures are limited in that intentions may not match the actions then taken. Studies that report discard rates at the service and include follow-up periods over days or weeks should be implemented in future work to enabling self-report about actual behaviour of drug-checking service users. It should also be noted that the monitoring capacity of drug-checking services is limited by the sampling biases of voluntarily delivered samples: that is, people are more likely to bring samples to a checking service if they have reason to believe the substance is suspect. Therefore the levels of adulteration found in drug-checking monitoring may be greater than in the general population.

Conclusion

Drugs that contain unexpected and in some cases, significantly more dangerous substances than they are represented to be continue to circulate in illegal drug markets. Drug checking can be an effective tool to deal with these drug market adulterations and help users to better manage their drug use. Our results show that most consumers, when given accurate information about their drug content, report they will implement actions to protect their health: to avoid the unexpected substance, as well as to seek more information. Additionally, the drug checking results allowed the service to adapt its intervention and the type of information provided to clients, potentiating its effectiveness. That is, if the harm reduction technicians didn’t have drug checking available, the information and counselling they would provide to users would be based only on the users’ self-reported information about the substance they wanted to use which was LSD. Instead, drug checking provided them with specific information and harm reduction strategies for the true content of their drug samples. Even for the small group who reported an intention to consume the DOx or 25x-NBOMe detected in their ‘LSD’, drug-checking services integrated with harm reduction counselling provided the most relevant information to guide this (admittedly more dangerous) choice. Although the current results support the provision of integrated drug checking services in party settings, evidence of their utility and effectiveness would be improved through future research incorporating more robust measures of outcomes following provision of drug checking results.

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Declarations of interest

The authors declare that there are no conflicts of interest.

Author contributions

D.M. performed all analytical work, designed the data collection tools, interpreted the results and wrote the manuscript. M.J.B. interpreted the results, wrote and critically revised the manuscript. C.V.P. and H.C. contributed in data acquisition and analysis. M.V.V. and I.F.E. performed all the GC-MS analysis. H.V. supervised all the field intervention, designed the data collection tools, interpreted the results and wrote the manuscript. All authors have read and agreed to this manuscript.

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