Short report

Psychopharm

Journal of Psychopharmacology
19(1) (2005) 67–70

ISSN 0269-8811
SAGE Publications Ltd, London, Thousand Oaks, CA and New Delhi
10.1177/0269881105048898

Preliminary evidence of the cardiovascular effects of polysubstance misuse in nightclubs

J. C. Cole *Psychology Department, Liverpool University, Liverpool, UK.*
H. R. Sumnall *Centre for Public Health, Liverpool John Moores University, Libverpool, UK.*
G. W. Smith *Psychology Department, Liverpool University, Liverpool, UK.*
A. Rostami-Hodjegan *Molecular Pharmacology and Pharmacogenetics Unit, University of Sheffield, Sheffield, UK.*

Abstract

Adverse reactions to polysubstance misuse are common in nightclubs, yet little is known of the physiological effects of polysubstance misuse in this environment. This study examined the heart rate, blood pressure and oral temperature of 50 participants recruited in a nightclub on four separate nights. In addition, the increase in environmental temperature was recorded throughout each night. There were no differences in oral temperature between polysubstance misusers (i.e. those who used Ecstasy, amphetamine, cocaine, alcohol and cannabis) and alcohol/cannabis misusers. On the other hand, there were significant differences in both heart rate and blood pressure between the two groups. These data suggest that polysubstance misusers may be at risk from cardio- and cerebrovascular toxicity. Further field/on-site work is clearly needed to investigate the effects of polysubstance misuse.

Keywords

alcohol, blood pressure, cannabis, cocaine, Ecstasy, heart rate, night-clubs, temperature

Introduction

Nightclubs are one of the commonest public venues for the illegal use of controlled drugs, in particular Ecstasy and other psychostimulants (Deehan and Saville, 2003). There are numerous reports of acute adverse reactions to the use of these controlled drugs in this type of setting (Williamson *et al*., 1997; Cole and Sumnall, 2003). As a consequence it is widely believed that there is an interaction between the nightclub environment and these adverse reactions. For example, when 3,4-methylenedioxymethamphetamine (MDMA) is administered to human volunteers under controlled laboratory/clinical conditions, there is no significant rise in core temperature (Liechti and Vollenweider, 2000), although (very infrequent) adverse hyperthermic reactions to MDMA used in nightclubs are well documented (Cole and Sumnall, 2003). In the laboratory, the majority of substances misused in nightclubs produce profound effects on the cardiovascular and cerebrovascular systems (Chang *et al*., 2000; Ghuran and Nolan, 2000; Liechti and Vollenweider, 2000; Kaufman *et al*., 2001) but there are no data available to indicate whether this occurs when these substances are misused in nightclubs. In addition, the majority of (pre-)clinical studies involve the study of a single substance whereas polysubstance misuse is the norm in the nightclub setting. Overall, this indicates that there is a lack of data on the effects of polysubstance misuse in the nightclub setting and this study aimed to provide some preliminary data.

Methods

Participants

Fifty participants were recruited on four different nights from a popular Merseyside nightclub (capacity of approximately 600). Sixty percent of the samples were male and were aged (mean ± SD) 23.0 ± 5.0 years (range 18.0–43.0 years). The study proceeded with the agreement and assistance of club management and staff and was conducted in the 'chill out' room provided by the nightclub for customers to rest after periods of dancing. Participants were randomly recruited over the course of the evening by the field researcher (G.W.S.), informed of the nature of the study, and asked to sign a consent form. As it was anticipated that many subjects would be intoxicated at the time of giving consent, a telephone number was provided to them if they wished to retrospectively withdraw from the study over the following days. The study

Corresponding author: Dr Jon Cole, Psychology Department, Liverpool University, Liverpool L69 7ZA, UK. *Email*: joncole@liv.ac.uk

was given ethical approval by Liverpool University Psychology Department's ethics committee.

Procedure

The participants were initially asked to provide a saliva sample using the Omni-SAL collection device (SDS Inc., New York, NY, USA). Subsequently, their oral temperature and heart rate were measured with commercially available electronic equipment (obtained from Boots The Chemist). A short structured interview was then used to ascertain their drug use over the preceding 24 h. The participants were informed that the saliva sample would be used to objectively verify these self reports. Approximately 10 min after the first measurements were taken, oral temperature, heart rate and blood pressure were measured. Unfortunately, the saliva collection devices were lost in transit and it was not possible to objectively verify the drug intake of the participants. However, their use probably ensured the veracity of self-report, and there is no reason to suspect that subjects would consciously falsify data. Finally, the ambient temperature of three different areas of the nightclub was measured at hourly intervals throughout the night.

Statistical analysis

All data were statistically analysed using the software package SPSS for Windows (version 12.0; SPSS Inc., Chicago, IL, USA). Normally distributed data were examined using *t*-tests; additional Mann-Whitney tests were performed for diastolic pressure, heart rate change over the 10-min assessment period, and the second oral temperature reading. Sex distribution of the derived groups was examined using the chi-square test. The effects of time and club area on ambient temperature across the five time points was analysed using two-way repeated measures analysis of variance (ANOVA). Significant treatment-related interactions and effects were further analysed using planned comparisons. Finally, non-parametric data were transformed, and forward stepwise linear regression analyses undertaken to investigate which (if any) drug use parameters predicted physiological measures. $p < 0.05$ was considered statistically significant for all tests.

Results

Subjects were initially grouped on the basis of self-reported psychostimulant use (Table 1). Because the majority of subjects reported polysubstance use, the psychostimulant group also included individuals reporting alcohol and cannabis. This reflects the ubiquity of alcohol use in social settings. Of those subjects reporting alcohol use, 21 (44.7%; 39.1% of alcohol/cannabis users, 44.4% of psychostimulant users) were binge drinking at the time of assessment, as defined as ingesting twice the recommended daily alcohol intake in a single episode (Prime Minister's Strategy Unit, 2004).

At the time of assessment both systolic ($p < 0.001$) and diastolic ($p < 0.01$) blood pressure were significantly higher in psychostimulant users, and heart rate was elevated at both time points ($p < 0.05$ and $p < 0.01$, respectively). The overall change in heart rate was significantly different between the two groups across the two time points [$F(1,48) = 7.064$, $p < 0.05$]. By contrast, there were

Table 1 Characteristics, drug use and physiological measurements in two groups of night club attendees

Measure	Alcohol/cannabis (n = 23)	Psychostimulants (n = 27)	$t/U/\chi^2/F$
Age	21.8 ± 3.4	24.1 ± 5.9	1.62
% Male	52.2	66.7	1.09
Drug use on night; no. reporting use/'units'(range)			
Alcohol	20/7.8 ± 4.3 (2.0–15.0)	27/8.0 ± 5.3 (2.0–20.0)	0.03
Amphetamines	0/–	3/0.3 ± 0.2 (0.1–0.5)	1.41
Cannabis	7/4.6 ± 3.9 (1.0–12.0)	13/3.5 ± 3.1 (0.5–10.0)	0.30
Cocaine	0/–	4/1.6 ± 1.6 (0.0–3.0)	1.44
Ecstasy	0/–	22/1.8 ± 0.9 (0.5–3.0)	6.52***
Systolic pressure (mmHg)	132.4 ± 24.6	155.9 ± 23.2	4.08***
Diastolic pressure (mmHg)	85.2 ± 14.8	111.7 ± 34.5	141.5**
Percentage body fat	17.5 ± 8.1	14.6 ± 6.0	1.29
HR_1 (b.p.m.)	88.5 ± 13.2	97.2 ± 13.0	2.13*
HR_2 (b.p.m.)	89.0 ± 14.0	101.9 ± 14.7	2.89**
HR difference	0.4 ± 5.0	4.8 ± 2.0	7.064*
$T°C_1$	36.4 ± 0.7	36.5 ± 0.6	0.76
$T°C_2$	36.6 ± 0.5	36.7 ± 0.5	546.5
T°C difference	0.2 ± 0.6	0.14 ± 0.5	0.319

Data are mean ± SD, with associated *t*, Mann–Whitney, or chi-square tests. Drug units represent number of alcohol units, 'joints', tablets and grams in those individuals reporting use. HR_1 and HR_2, heart rate recorded at an interval of 10 min; $T°C_1$ and $T°C_2$, oral temperature recorded at an interval of 10 min. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$, significant difference between groups. *t*-tests performed for all variables, except Mann–Whitney test performed for diastolic pressure, HR difference and $T°C_2$, and chi-square test for sex distribution. Two-way repeated measures ANOVA were used to compare differences in HR and T°C across the two time points.

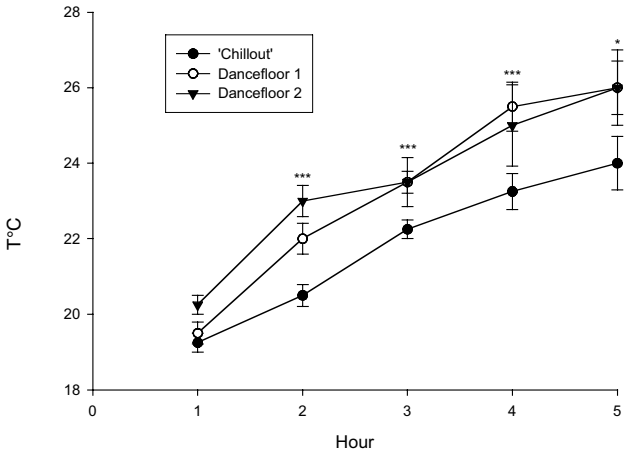

Figure 1 Change in room temperature in three areas within the night club. Ambient temperature increased as a function of time (see text). There was a trend towards lower 'chill out' room temperature compared to the two dancefloors at all testing times, although the change across the evening was not significantly different between areas. *$p < 0.05$, ***$p < 0.001$, significant hourly increase in ambient temperature compared to hour 1 and each preceding hour

no differences in oral temperature and in the change in temperature across the two time points between groups [$F(1,47) = 0.319$, NS]. Using a forwards stepwise linear regression model, it was found that systolic and diastolic blood pressure were predicted by the number of Ecstasy tablets ($t = 2.80$, $p < 0.01$, $\beta = 0.36$; $t = 3.78$, $p < 0.001$, $\beta = 0.42$, respectively) and grams of cocaine consumed ($t = 3.63$, $p < 0.01$, $\beta = 0.46$; $t = 5.62$, $p < 0.001$, $\beta = 0.62$, respectively). Both HR_1 and HR_2 were also predicted by the amount of cocaine consumed ($t = 3.51$, $p < 0.01$, $\beta = 0.45$; $t = 3.64$, $p < 0.01$, $\beta = 0.46$, respectively). Oral temperature at the end of the assessment ($T°C_2$) was significantly predicted by the number of cannabis joints smoked ($t = 2.69$, $p < 0.05$, $\beta = 0.36$). Examining those individuals who reported using cocaine, higher diastolic (135.0 ± 49.1 mmHg) and systolic blood pressures (173.0 ± 25.9 mmHg) and heart rates (HR_1 = 106.5 ± 23.4 b.p.m.; HR_2 = 120.8 ± 16.0 b.p.m.) were recorded compared to control subjects and other types of psychostimulant user. However, because relatively few individuals reported the use of this drug ($n = 4$), these data must be interpreted cautiously.

Repeated measures ANOVA showed that there was a significant increase in mean ambient temperature across the course of the evening(s) [$F(4,36) = 83.69$, $p < 0.001$] (Fig. 1), although this was independent of the area (two dance floors, 'chill out' room) in which it was recorded. There was a significant hourly increase compared to temperature at the beginning of the evening, and compared to each preceding hour ($p < 0.001$, except hour 5 versus hour 4, $p < 0.05$).

Discussion

These data demonstrate that compared to non-users, Ecstasy and other psychostimulant users have normal oral temperatures despite increases in environmental temperature and periods of dancing. This is in sharp contrast to the current perception of the effects of Ecstasy use in nightclubs (e.g. Parrott, 2002). In addition, the preclinical data indicate that hyperthermia is necessary for, and lowering body temperature prevents, MDMA-induced serotonergic neurotoxicity (Green *et al*., 2003), suggesting that the risk to Ecstasy users may be lower than currently believed. However, these preliminary data require replication before either of these issues can be discussed further.

However, the cardiovascular effects of polysubstance misuse were marked, which suggests that users are at risk of cardio- and cerebrovascular toxicity. Recent studies in rats (Badon *et al*., 2002; Hicks *et al*., 2003) have shown that the pattern of frequent binge administrations of psychostimulants followed by a period of abstinence can significantly alter cardiovascular function and produce cardiac toxicity. Acute administration of MDMA has also been shown to cause cerebrovascular dysfunction in the CYP2D2 deficient Dark Agouti rat, which may generalize to abnormalities in humans with latent congenital conditions; particularly those with the analogous CYP2D6 mutation (Quate *et al*., 2004). It has been demonstrated that amphetamine, cocaine and Ecstasy users have both altered cardio- and cerebrovascular function (Bolla *et al*., 1998; Brody *et al*., 1998; Chang *et al*., 2000; Gatley and Volkow, 1998). This suggests that there may be a common mechanism for the neuropsychological deficits observed in amphetamine, cocaine and Ecstasy users.

Similar to all studies involving the study of polysubstance misusers, there were numerous methodological limitations. First and foremost is the quantification of the substances ingested. We tried to overcome this with the use of the saliva samples, which were unfortunately lost in transit and thus unavailable for analysis. However, their use probably ensured that responses to the self-report items were as honest as could be expected from an intoxicated respondent. In addition, the physiological data indicated that individuals who reported using Ecstasy, cocaine and amphetamine had ingested stimulant substances. The self-report data were brief as the quantification of substance use was meant to replace them. This meant that we were unable to perform many analyses. Similarly, data on the physiology of all subjects across the night would have been preferable. However, in the context of intoxicated people enjoying themselves, it is probably impractical to obtain these data (i.e. repeat testing). Therefore, it is important that caution is taken in interpreting these findings until they can be replicated.

Current harm reduction advice has focussed on the symptoms of hyperthermia and recent Government Guidelines on safer clubbing have suggested methods of assisting temperature reduction (Webster *et al*., 2002). Although rises in body temperature are simple to detect, these drug users and those around them were unaware of any cardiovascular changes. These preliminary data suggest that the risk of potential cardio- and cerebrovascular toxicity caused by polysubstance misuse in nightclubs may be greater than that of hyperthermia. Furthermore, there is a clear need to investigate the effects of simultaneous polysubstance misuse, particularly regarding pharmacokinetic interactions and their resulting physiological effects.

Acknowledgements

This study received no external funding.

References

Badon L A, Hicks A, Lord K, Ogden B A, Meleg-Smith S, Varner K J (2002) Changes in cardiovascular responsiveness and cardiotoxicity elicited during binge administration of ecstasy. J Pharmacol Exp Therapeut *302*: 898–907

Bolla K L, Cadet J-L, London E D (1998) The neuropsychiatry of chronic cocaine abuse. J Neuropsychiatry Clin Neurosci *10*: 280–289

Brody S, Krause C, Veit R, Rau H (1998) Cardiovascular autonomic dysregulation in users of MDMA ('ecstasy'). Psychopharmacology *136*: 390–393

Chang L, Grob C S, Ernst T, Itti L, Mishkin F S, Jose-Melchor R, Poland R E (2000) Effect of ecstasy [3,4-methylenedioxymethamphetamine (MDMA)] on cerebral blood flow: a co-registered SPECT and MRI study. Psychiatry Res Neuroimag *98*: 15–28

Cole J C, Sumnall H R (2003) Altered states: the clinical effects of 'Ecstasy'. Pharmacol Therapeut *93*: 35–58

Deehan A, Saville E (2003) Calculating the risk: recreational drug use among clubbers in the South East of England. Home Office Online Report *43*: 03

Gatley S J, Volkow N D (1998) Addiction and imaging of the living human brain. Drug Alcohol Depend *51*: 97–108

Ghuran A, Nolan J (2000) Recreational drug misuse: issues for the cardiologist. Heart *83*: 627–633

Green A R, Mechan A O, Elliott J M, O'Shea E, Colado M I (2003) The pharmacology and clinical pharmacology of 3, 4-methylenedioxymethamphetamine (MDMA, 'ecstasy'). Pharmacol Rev *55*: 463–508

Hicks A R, Ogden B A, Varner K J (2003) Cardiovascular responses elicited during binge administration of cocaine. Physiol Behav *80*: 115–122

Kaufman M J, Levin J M, Maas L C, Kukes T J, Villafuerte R A, Dostal K, Lukas S E, Mendelson J H, Cohen B M, Renshaw P F (2001) Cocaine-induced cerebral vasoconstriction differs as a function of sex and menstrual cycle phase. Biol Psychiatry *49*: 774–781

Liechti M E, Vollenweider F X (2000) Acute psychological and physiological effects of MDMA ('Ecstasy') after haloperidol pretreatment in healthy humans. Eur Neuropsychopharmacol *10*: 289–295

Parrott A C (2002) Recreational ecstasy/MDMA, the serotonin syndrome, and serotonergic neurotoxicity. Pharmacol Biochem Behav *71*: 837–844

Prime Minister's Strategy Unit (2004) Alcohol Harm Reduction Strategy for England. Cabinet Office, London, UK

Quate L, McBean D E, Ritchie I M, Olverman H J, Kelly P A T (2004) Acute methylenedioxymethamphetamine administration: effects on local cerebral blood flow and glucose utilisation in the dark agouti rat. Psychopharmacology *173*: 287–295

Webster R, Goodman M, Whalley G (2002) Safer Clubbing: Guide for Licensing Authorities, Club Management, and Promoters. Home Office, London

Williamson S, Gossop M, Powis B, Griffiths P, Fountain J, Strang J (1997) Adverse effects of stimulant drugs in a community sample of drug users. Drug Alcohol Depend *44*: 87–94