Research report on
ICE Induced Psychosis: A Prevalence Study in Local Ice Abusers

Submitted to

Beat Drugs Fund Association

Submitted by

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SARDA Adult Female Rehabilitation Centre;

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Abbreviations

ASI: Addiction Severity Index

BDI: Beck Depression Inventory

BPRS: Brief Psychiatric Rating Scale

CBT: cognitive behavioural therapy

CCPSA: Counseling Centres for Psychotropic Substance Abusers

DSM-V: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

HADSA: Hospital Anxiety Depression Scale

ICE: Methamphetamine

IIP: ICE induced psychosis

NPS: No psychotic symptoms

OCD: Obsessive – compulsive disorder

OR: Odds ratio

PANSS: Positive and Negative Symptoms Scale

PPS: Persistent psychotic symptoms

RAs: Research assistants

SDS: Severity of Dependence Scale

SCID: Structured Clinical Interview for DSM-V

TPS: Transient psychotic symptoms

Background

Methamphetamine (popularly known as ICE) is the most commonly abused psychotropic drug in Hong Kong. ICE is a stimulant most commonly smoked using a meth bong, but it can also be snorted (inhaled via the nose), swallowed, injected or inserted rectally (Trautmann et al., 2013). The consumption rate of ICE varies widely amongst users. A study of Chinese ICE users found minimum and maximum daily doses of 0.1 and 2.0 grams, respectively (He et al., 2013).

ICE produces a rapid feeling of euphoria, a heightened level of alertness and increased energy. A stronger libido and enhanced sexual pleasure have also been reported. Acute subjective effects diminish over 4 hours (Cruickshank & Dyer, 2009). Possible acute psychiatric symptoms following exposure to ICE are anxiety, insomnia, and psychosis (Cruickshank & Dyer, 2009). The chronic use of ICE can result in a wide range of psychiatric symptoms, including anxiety, depression, psychosis, cognitive impairment, suicidal ideation and violent behaviour (Cruickshank & Dyer, 2009; Darke et al., 2008). The preceding states, traits and comorbidities of ICE use include other substance use disorders, attention deficit hyperactivity disorder, antisocial personality disorder and aggressive behaviour (Harro, 2015).

Of the aforementioned comorbidities, psychotic symptoms and psychosis are the most commonly reported. A study of 309 ICE users in Australia found that 60% had experienced increased suspiciousness in the previous year, 56% had hallucinations and 37% had unusual thoughts (McKetin et al., 2006). There is considerable variation in both the dose of ICE

required (55–640 mg) and the onset of psychotic symptoms (7 minutes to 34 hours post-dose). The duration of psychotic symptoms also varies, dissipating within 1 week of abstinence in some cases and persisting indefinitely in others (Cruickshank & Dyer, 2009).

ICE induced psychosis (IIP) refers to paranoid–hallucinatory states induced by ICE, which are largely indistinguishable from acute paranoid schizophrenia. Volitional disturbances (e.g., blunted affect and a loss of spontaneity) have been observed in IIP (Yui et al., 2000). Regular ICE use is also associated with a high incidence of chronic psychotic symptoms. It has been suggested that 26% to 46% of ICE-dependent users develop IIP (Grant et al., 2012). In a community sample of ICE users in Australia, 13% of the subjects appeared to be experiencing psychosis at a structured interview, and 23% had experienced clinically significant symptoms of psychosis (McKetin et al., 2006). According to our own database, among 80 ICE users attending a local substance abuse clinic, 76% had psychosis, 11% had mood disorder and 1% had anxiety disorder (Tang, unpublished). A study of 325 ICE users in Taiwan showed that 21.5% had psychosis (Lin et al., 2004).

The most common signs of IIP are hallucinations, delusions and odd speech. ICE-induced hallucinations are predominantly auditory (experienced in 85% of cases of IIP), visual (46%) and tactile (21%). Delusions of persecution (71%), reference (63%) and ‘mind-reading’ (40%) are also common (Cruickshank & Dyer, 2009). Other characteristics of IIP are rapid onset, the dream-like quality of experiences, brisk emotional reactions (usually in the direction of

anxiety), brevity of psychotic episodes, frequent aggravation and the absence of thought disorders (Yui et al., 2000).

The average difference between the age of onset of ICE use and the onset of psychotic disorders is slightly more than 5 years (Power et al., 2014). Risk factors for IIP include increased duration and frequency of ICE use, early age of onset of drug use, injection use and a personal or family history of psychosis. Environmental stressors such as incarceration, severe insomnia and heavy alcohol consumption may also induce psychotic symptoms in ICE users (Darke et al., 2008; Cruickshank & Dyer, 2009; Marshall & Werb, 2010; Harro et al., 2015).

IIP can run a chronic course. In a sample of 170 Japanese ICE users affected by psychosis, 59% recovered within 30 days, but symptoms persisted for more than 1 month for 41%, including 28% who reported symptoms after more than 6 months of abstinence (Ujike & Sato, 2004). Spontaneous recurrences of IIP (i.e., flashbacks) occasionally occur upon exposure to physical and psychological stress in subjects with a history of the disorder (Yui et al., 2000). A follow-up study of patients in Thailand with IIP revealed that 56% of them had experienced a relapse of psychosis approximately 6 years after the index episode (Kittirattanapaiboon et al., 2010).

Data are lacking on the prevalence, clinical features and risk factors for IIP and other psychiatric disorders in local ICE users. We conducted a large-scale study investigating the prevalence of psychiatric comorbidity in a group of ICE users in Hong Kong. The study's primary objective was to determine the prevalence of IIP and psychotic symptoms in local

users. Secondary objectives included identification of the prevalence of mood and anxiety disorders in local ICE users.

Design

This was a cross-sectional study to investigate the influence of ICE on psychotic symptoms and other mental illnesses by a structured diagnostic interview. Data were collected in face-to-face structured interviews administered by a research assistant or a postgraduate student. Each interview lasted 40–90 minutes. The subjects were compensated with HK$300 supermarket shopping coupons after the interview. This study was approved by the Survey and Behavioural Research Ethics Committee of the Chinese University of Hong Kong.

Participants

Participant recruitment sites

All subjects were recruited from the following Counselling Centres for Psychotropic Substance Abusers (CCPSA) or residential treatment centres:

a. Hong Kong Christian Service PS33
b. Hong Kong Children and Youth Service Sane Centre
c. Caritas HUGS Centre
d. The Evangelical Lutheran Church of Hong Kong Enlighten Centre
e. Hong Kong Sheng Kung Hui Welfare Council Neo-Horizon
f. Hong Kong Lutheran Social Services Cheer Lutheran Centre
g. Barnabas Charitable Service Association
h. Caritas Hong Kong

i. Christian New Being Fellowship

j. Christian New Life Association

k. Christian Zheng Sheng Association

l. Drug Addicts Counselling and Rehabilitation Services

m. The Evangelical Lutheran Church of Hong Kong

n. Hong Kong Christian Service

o. Mission Ark

p. Operation Dawn

q. The Society for the Aid and Rehabilitation of Drug Abusers

r. The Hong Kong Federation of Youth Groups

Inclusion criteria

a. Aged between 18 and 65;

b. ICE use at least 20 times in the past year; and

c. Met the criteria for ICE use disorder in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V, American Psychiatric Association, 2013).

Psychiatric assessment

Demographic information

The interview started by collecting personal information from the subject. Demographic information included:

a. age;

b. sex;

c. level of education;

d. marital status;

e. employment status;

f. monthly income;

g. housing property;

h. smoking history; and

i. psychosis history.

Drug use patterns and severity

To establish the subjects' drug use patterns, the age of initial use, frequency, duration of use and date of last use were collected. Lifetime and current ICE use and the use of other illicit drugs, alcohol and cigarettes were estimated using a semi-structured interview similar to the Lifetime Drinking History interview (Skinner & Sheu, 1982). Current consumption was calculated as the average use in one day in the past month before recruitment.

The SDS (Gossop et al., 1995) is a 5-item self-report scale used to measure the degree of drug dependence in the previous month or the month before abstinence. Each item was scored from 0 to 3 with a higher score indicating increased severity of dependence.

Psychiatric comorbidities

The Structured Clinical Interview (SCID; Kam et al., 2003) was administered to screen for possible Axis-I psychiatric disorders. The SCID is a semi-structured interview that guides the making of DSM-V diagnoses. It takes approximately 30–45 minutes to administer the SCID.

Psychotic disorders were further divided into primary and substance-induced (i.e., IIP). Based on the DSM-V, the criteria for a drug-induced disorder are a) the onset of symptoms within 1 month of drug use, intoxication or withdrawal; b) symptoms that do not persist for more than 1 month after the cessation of drug use; and c) no history of recurrence of non-drug-related episodes.

Based on the pattern of psychotic symptoms, the participants were also divided into the following groups:

a) no psychotic symptoms (NPS);

b) transient psychotic symptoms (TPS), in which the subjects experienced psychotic symptoms during at least one month when they were using methamphetamine, but not during any months when they were not using the drug;

c) persistent psychotic symptoms (PPS), in which the subjects experienced psychotic symptoms during at least one month when they were using methamphetamine and also during at least one month when they were not using the drug;

d) had psychotic symptoms, not yet in detoxification stage;

e) had psychotic symptoms only during months of abstinence from ICE;

f) had psychotic symptoms, followed later by flashbacks, representing a spontaneous recurrence of psychosis even without further use of ICE.

The BPRS (Lukoff et al., 1986), which measures the positive, negative and affective symptoms of an individual with psychotic disorders, schizophrenia in particular, was used to measure the subjects' severity of currently (during the interview) occurring psychotic symptoms and mood conditions (if any). The score ranges from 0 (not assessed) to 7 (extremely severe). The PANSS (Bell et al., 1992) was used to measure the subjects' severity of currently occurring positive and negative symptoms. The score for each item ranges from 1 (absent) to 7 (extreme).

A 21-item version of the BDI (Shek, 1990) was used to measure depressive symptoms 1 week prior to the interview. The BDI has been previously applied in a group of ecstasy users in Hong Kong (Chen et al. 2005b). Total BDI scores can range from 0 to 63. The sensitivity and specificity of BDI are 100% and 82%, respectively (Lee et al., 2001)

The Hospital Anxiety Depression Scale for Anxiety (HADSA, Leung et al., 1993; Spinhoven et al., 1997) was used to measure anxiety symptoms 1 week prior to the interview. The HADSA has 7 items, each graded from 0 to 3. The total score was counted, where a higher score indicates a greater severity of symptoms (Bunevicius et al., 2007).

Statistical method

Data analyses were performed using SPSS 17.0. The independent variables were socio-demographic and drug-use parameters, the primary dependent variable was IIP and psychotic symptoms and the secondary dependent variable was other psychiatric comorbidities.

The frequency distribution of all variables was calculated, with descriptive statistics used to summarise the variables.

The prevalence of IIP and other psychiatric comorbidities was calculated. Potential associations with IIP were first evaluated using the chi-square test or t-test, as appropriate. Significant associations were subsequently examined in multivariate regression analysis to identify independent predictors of IIP. Statistical significance was set at 0.5 in two-sided tests. The analysis was repeated for the other dependent variables.

Demographics and basic information

Two-hundred and sixty ICE users participated in this study. The majority of the subjects were male (54%) and unemployed (77%), with a mean age of 30 years old (range 18–64) and 10 years of education (range 0–17). A majority of the sample were single (76%) and current smokers (70%). The subjects were recruited from residential centres (58%) or CCPSAs (42%). Sixty per cent of the subjects lived in public housing, 10% had a family history of psychiatric diseases and 38% had religious belief (Table 1).

Table 1. Descriptive statistics of demographic characteristics of the entire sample (N = 260).

Age, mean ± SD	30.3 ± 8.0
Gender (male), n (%)	140 (53.8%)
Education (years), mean ± SD	9.5 ± 2.3
Marital status, n (%)	
Single	197 (75.8%)
Married	50 (19.2%)
Separated	12 (4.6%)
Others	1 (0.4%)
Occupation	
Unemployed, n (%)	201 (77.3%)
Employed, n (%)	59 (22.7%)
Source of referral	
Residential, n (%)	150 (57.7%)
Non-residential, n (%)	110 (42.3%)
Smoking history	
Current, n (%)	183 (70.4%)
Previous, n (%)	58 (22.3%)
Family psychiatric history, n (%)	27 (10.4%)
Has a religious belief, n (%)*	98 (38.1%)
Accommodation	
Public housing, n (%)	157 (60.4%)
Private housing, n (%)	77 (29.6%)
Home Owner Scheme housing, n (%)	22 (8.5%)

ICE use pattern

The mean ages of initiation and duration of ICE use were 22 and 6 years, respectively (Table 2). The average number of days of ICE use in a lifetime, the past 2 years, past 1 year and previous month were 1234, 325, 151 and 3 days, respectively. The subjects' average total ICE consumption in a lifetime, the past 2 years, past 1 year and previous month were 1837, 395, 172 and 2 grams, respectively. Fifty-three subjects were still using ICE in the previous month (Table 2).

Table 2. Descriptive statistics of ICE use patterns of the entire sample (N = 260).

Variables	Mean ± SD, Median (range)
Age of first use	21.6 ± 7.5 20.0 (10 - 51)
Duration of use (years)	5.7 ± 4.1 4.8 (0.4 - 21)
Days of use	
Lifetime	1234.2 ± 1151.4 919.7 (14 - 5551)
Past two years	324.8 ± 229.1 273.0 (1 – 728)
Past one year	150.8 ± 113.0 130.0 (1 - 364)
Past month	2.6 ± 7.4 0.0 (0 - 30)
Lifetime consumption	
Total (grams)	1836.8 ± 5006.4 642.2 (7.8 - 69958.2)
Total / body weight (grams / kilogram)	28.2 ± 68.2 10.9 (0.1 - 905.3)
Consumption in one day (grams)	1.2 ± 1.7 0.9 (0.04 - 22.2)
Consumption in the past two years	
Total (grams)	394.9 ± 601.7 169.0 (0.4 - 6066.7)
Total / body weight (grams / kilogram)	6.4 ± 10.1 2.7 (0.004 - 104.2)
Consumption in one day (grams)	1.0 ± 1.1 0.8 (0.04 - 10.0)
Consumption in the past one year	
Total (grams)	172.0 ± 257.6 80.0 (0.3 - 2426.7)
Total / body weight (grams / kilogram)	2.8 ± 4.3 1.3 (0.003 - 41.7)
Consumption in one day (grams)	1.1 ± 1.1 0.8 (0.04 - 10.0)
Consumption in the previous month	

Variables	Mean ± SD, Median (range)
Total (grams)	2.1 ± 8.8 0.0 (0.0 - 75.8)
Total / body weight (grams / kilogram)	0.03 ± 0.2 0.0 (0.0 - 1.6)
Consumption in one day (grams)	0.1 ± 0.4 0.0 (0.0 - 3.5)
Lifetime dependence, n (%)	236 (90.8%)
Lifetime abuse, n (%)	24 (9.2%)
Current dependence, n (%)	28 (10.8%)
Current abuse, n (%)	26 (10.0%)

Table 3. Daily consumption of ICE by age and duration of use

	All ICE users (N = 230)	Male (N = 127)	Female (N = 103)	p value[a]
Consumption in one day (grams) in past one year, mean ± SD, median (range)	1.1 ± 1.1 0.8 (0.04-10.0)	1.1 ± 1.3 0.7 (0.04-10.0)	1.0 ± 0.8 0.8 (0.1-3.5)	0.555
90th percentile	2.0	2.2	2.0	
95th percentile	3.2	3.5	2.5	
99th percentile	5.8	8.9	3.5	
		Duration of use < 6 years) N = 126	Duration >/= 6 years N = 104	
Consumption in one day (gram) in past one year. mean ± SD, median (range)		1.1 ± 1.2 0.7 (0.04 - 10.0)	1.0 ± 1.0 0.8 (0.2 - 6.0)	0.791
90th percentile		1.8	2.0	
95th percentile		3.3	3.4	
99th percentile		8.7	5.9	

[a] Mann-Whitney test.

Pattern of other drug use

All ICE users reported lifetime and current poly-drug use. The three most commonly used drugs were cannabis, ketamine and cocaine, which were used by 70%, 64% and 53% of all subjects, respectively. The age of first use of other drugs ranged from 18 (ketamine, cannabis, ecstasy and cough medicine) to 21 (cocaine and hypnotics). Mean duration of use varied from 2 (ecstasy) to 5 (cough medicine) years. The average number of days of drug use per month in their period of regular use was between 9 (cannabis) and 21 (cough medicine). The frequency of lifetime dependence for these drugs ranged from common (cocaine, 48%) to rare (cannabis, 8%). Current dependence on these drugs was uncommon (0% to 3.6%) (Table 4).

Table 4. Other drug use.

	Cannabis N = 176	Ketamine N = 151	Cocaine N = 139	Ecstasy N = 124	Hypnotics N = 122	Cough medicine N = 59
Age of first use	18.3 ± 5.3[b]	18.4 ± 6.9[b]	21.4 ± 6.7[b]	17.7± 4.4 [b]	20.8 ± 7.1[b]	17.5 ± 3.8
Duration (years)	3.5 ± 5.7[b]	3.6 ± 4.5[b]	2.7 ± 3.3 [b]	2.6 ± 3.4 [b]	3.2 ± 4.4[b]	4.5 ± 6.3
Days of use per month[a]	8.9 ± 9.9[b]	15.5 ± 11.8[b]	14.6 ± 11.9 [b]	9.9 ± 8.5 [b]	13.3 ± 11.8[b]	21.0 ± 11.3
Consumption in one day[a]	2.0 ± 2.1‡[b]	2.5 ± 3.4¶[b]	4.6 ± 10.8¶ [b]	1.4 ± 1.4† [b]	4.7 ± 8.3‡[b]	1.5 ± 0.8§
Current dependence, n (%)	1 (0.6%)	0 (0.0%)	5 (3.6%)	0 (0.0%)	2 (1.6%)	2 (3.4%)
Lifetime dependence, n (%)	14 (8.0%)	56 (37.1%)	66 (47.5%)	14 (11.3%)	32 (26.2%)	20 (33.9%)

Unit: tab†; piece‡; bottle§; gram¶

[a] During period of regular use

[b] N < 260 due to missing data

Psychotic symptoms

Ninety-one per cent (n = 238) and 31.4% (n = 72) of ICE users had lifetime and current psychotic symptoms, respectively. In terms of the pattern of psychotic symptoms, 126 had TPS, meaning that the psychotic symptoms disappeared 1 to 14 days after their last ICE use in this group. Forty-six (18%) subjects had PPS, and for these subjects the time that elapsed between their last use of ICE and the day of assessment was 146.9 ± 83.7 (range 6–334) days. Sixty-four (25%) had psychotic symptoms and were not yet in the detoxification stage. One subject had flashbacks. No subject had psychotic symptoms only during months of abstinence from ICE.

In terms of subtypes of psychotic symptoms, more than three-quarters of the subjects reported lifetime delusions (76%) and hallucinations (77%). Delusion of reference (65%) was the most common delusion, followed by persecutory delusion (42%). Auditory hallucination was the most common type of hallucination (59%), followed by visual (42%) and tactile (33%) hallucinations. Twenty per cent of the sample reported thought broadcasting. Negative symptoms were rare (Table 5).

Table 5. Frequency of lifetime psychotic symptoms (N = 260).

Variables	Lifetime	Current	Past
Delusion (any type), n (%)	197 (75.8%)	53 (20.4%)	152 (58.5%)
Delusion of reference, n (%)	170 (65.4%)	40 (15.4%)	131(50.4%)
Persecutory delusion, n (%)	109 (41.9%)	23 (8.8%)	87 (33.5%)
Delusion of being controlled, n (%)	37 (14.2%)	9 (3.5%)	28 (10.8%)
Grandiose delusion, n (%)	34 (13.1%)	3 (1.2%)	31 (11.9%)
Somatic delusion, n (%), n (%)	31 (11.9%)	7 (2.7%)	25 (9.6%)
Other delusion, n (%)	5 (1.9%)	1 (0.4%)	5 (1.9%)
Religious delusion, n (%)	2 (0.8%)	1 (0.4%)	2 (0.8%)
Delusion of guilt, n (%)	1 (0.4%)	1 (0.4%)	0 (0.0%)
Jealous delusion, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Erotomanic delusion, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hallucination (any type), n (%)	201 (77.3%)	42 (16.2%)	166 (63.8%)
Auditory hallucination, n (%)	154 (59.2%)	34 (13.1%)	120 (46.2%)
Visual hallucination, n (%)	108 (41.5%)	15 (5.8%)	93 (35.8%)
Tactile hallucination, n (%)	85 (32.7%)	10 (3.8%)	75(28.8%)
Olfactory hallucination, n (%)	33 (12.7%)	4 (1.5%)	29 (11.2%)
Gustatory hallucination, n (%)	21 (8.1%)	1 (0.4%)	20 (7.7%)
Thought broadcasting, n (%)	44 (16.9%)	10 (3.8%)	34 (13.1%)
Thought insertion, n (%)	10 (3.8%)	3 (1.2%)	7 (2.7%)
Thought withdrawal, n (%)	2 0.8%)	0 (0.0%)	2 (0.8%)
Catatonic behavior, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Disorganized speech, n (%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
Crossly disorganized behavior, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Grossly inappropriate affect, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Avolition, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Alogia, n (%)	1 (0.4%)	1 (0.4%)	1 (0.4%)
Affective flattening, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Correlates of presence of psychotic symptoms

In terms of demographics, subjects with psychotic symptoms were more likely to live in public housing (61% vs 52%, p = 0.024) but less likely to be current smokers (70% vs 74%, p = 0.034) (Table 6). With regard to ICE use pattern, subjects with psychotic symptoms had higher lifetime consumption of ICE in one day (1.2 vs 0.6 grams, p = 0.010), total consumption (412 vs 211 grams, p = 0.049), total consumption/body weight (6.7 vs 3.2 grams, p = 0.031) and consumption in one day (1.1 vs 0.6 grams, p = 0.006) in the past 2 years. Finally, the group with psychotic symptoms were more likely to have lifetime ICE dependence (95% vs 48%, p < 0.001) (Table 7).

With regard to use of other substances, subjects with psychotic symptoms were more likely to have lifetime use of cannabis (71% vs 39%, p=0.003) and cocaine (56% vs 26%, p=0.005) (Table 8). In the logistic regression, lifetime ICE dependence was found to be an independent predictor of psychotic symptoms (OR = 12.818, 95% CI 3.804 – 43.188, p < 0.001) (Table 9).

Table 6. Demographic characteristics of subjects with or without psychotic symptoms.

	With psychotic symptoms N = 237	Without psychotic symptoms N = 23	p value
Age	30.1 ± 8.2	32.1 ± 5.9	0.089[a]
Gender (male), n (%)	126 (53.2%)	14 (60.9%)	0.314[b]
Education (years)	9.6 ± 2.3	9.0 ± 2.3	0.492[a]
Marital status, n (%)			0.007[c]
Single	181 (76.4%)	16 (69.6%)	
Married	44 (18.6%)	6 (26.1%)	
Separated	12 (5.1%)	0 (0.0%)	
Others	0 (0.0%)	1 (4.3%)	
Occupation, n (%)			
Employed	52 (21.9%)	7 (30.4%)	0.245[b]
Unemployed	185 (78.1%)	16 (69.6%)	
Source of referral, n (%)			
Non-residential	98 (41.4%)	12 (52.2%)	0.216[b]
Residential	139 (58.6%)	11 (47.8%)	
Smoking history, n (%)			
Current	166 (70.0%)	17 (73.9%)	0.341[c]
Previous	55 (23.2%)	3 (13.0%)	
Family psychiatric history, n (%)	25 (10.5%)	2 (8.7%)	0.564[b]
Has a religious belief, n (%)[*]	88 (37.4%)	10 (43.5%)	0.872[c]
Accommodation, n (%)			
Public housing	145 (61.2%)	12 (52.2%)	0.024[c]
Private housing	71 (30.0%)	6 (26.1%)	
Home Owner Scheme housing	19 (8.0%)	3 (13.0%)	

[a]Mann-Whitney test; [b]Fisher Exact test; [c]Chi-square test.

Table 7. ICE use patterns in subjects with or without psychotic symptoms.

Variables	With psychotic symptoms N = 237 Mean ± SD, Median (range)	Without psychotic symptoms N = 23 Mean ± SD, Median (range)	P value
Age of first use	21.4 ± 7.5 20.0 (10 - 51)	23.2 ± 8.1 22.0 (12 - 37)	0.352[a]
Duration of Ice use (years)	5.7 ± 4.0 4.9 (0.4 - 21)	5.6 ± 4.7 4.7 (0.5 - 16)	0.459[a]
Days of use			
Lifetime	1241.5 ± 1145.0 931.5 (18 - 5551)	1160.2 ± 1239.3 884.0 (14 - 3943)	0.421[a]
Past two years	329.0 ± 228.0 273.0 (1 - 728)	281.3 ± 241.5 202.6 (14 - 698)	0.296[a]
Past one year	152.4 ± 111.4 136.5 (1 - 364)	133.1 ± 130.5 75.8 (2 - 364)	0.274[a]
Past month	2.5 ± 7.4 0.0 (0 - 30)	3.2 ± 8.0 0.0 (0 - 30)	0.927[a]
Lifetime Consumption			
Total (grams)	1911.6 ± 5213.8 646.1 (7.8 - 69958.2)	1040.4 ± 1415.3 374.4 (13.9 - 5053.5)	0.184[a]
Total / body weight (grams/kilogram)	29.4 ± 70.8 11.3 (0.1 - 905.34)	15.4 ± 22.4 5.4 (0.2 - 81.5)	0.118[a]
Consumption in one day (grams)	1.2 ± 1.7 0.9 (0.04 - 22.2)	0.6 ± 0.4 0.5 (0.1 - 1.5)	0.010[a]
Ice consumption in past two years			
Total (grams)	412.0 ± 621.1 182.0 (0.4 - 6066.7)	210.6 ± 271.8 86.1 (9.5 - 976.7)	0.049[a]
Total / body weight (grams/kilogram)	6.7 ± 10.4 3.0 (0.04 - 104.2)	3.2 ± 4.3 1.4 (0.1 - 15.8)	0.031[a]
Consumption in one day (grams)	1.1 ± 1.1 0.8 (0.04 - 10.0)	0.6 ± 0.4 0.4 (0.1 - 1.5)	0.006[a]
Consumption in the past one year			

Variables	With psychotic symptoms N = 237 Mean ± SD, Median (range)	Without psychotic symptoms N = 23 Mean ± SD, Median (range)	P value
Total (grams)	178.5 ± 266.0 84.3 (0.4 - 2426.7)	104.5 ± 128.2 45.0 (0.3 - 467.1)	0.090[a]
Total / body weight (grams/kilogram)	2.9 ± 4.5 1.3 (0.004 - 41.7)	1.6 ± 2.1 0.6 (0.003 - 7.5)	0.062[a]
Consumption in one day (grams)	1.1 ± 1.1 0.8 (0.04 - 10.0)	0.7 ± 0.5 0.5 (0.1 - 1.5)	0.050[a]
Consumption in the previous month			
Total (grams)	2.1 ± 9.1 0.0 (0.0 - 75.8)	2.0± 5.5 0.0 (0.0 - 21.7)	0.951[a]
Total / body weight (grams/kilogram)	0.03 ± 0.2 0.0 (0.0 - 1.6)	0.04 ± 0.1 0.0 (0.0 - 0.4)	0.955[a]
Consumption in one day (grams)	0.1 ± 0.4 0.0 (0.0 - 3.5)	0.1 ± 0.3 0.0 (0.0 - 1.0)	0.851[a]
Current dependence, n (%)	27 (11.4%)	1 (4.3%)	0.250[b]
Current abuse, n (%)	21 (8.9%)	5 (21.7%)	0.067[b]
Lifetime dependence, n (%)	224 (94.5%)	12 (52.2%)	<0.001[b]
Lifetime abuse, n (%)	13 (5.5%)	11 (47.8%)	<0.001[b]

[a] Mann-Whitney; [b] Fisher's exact test

Table 8. Other drug use in subjects with and without psychotic symptoms.

Lifetime use	With psychotic symptoms N=237	Without psychotic symptoms N=23	p value[a]
Cannabis	167 (70.5%)	9 (39.1%)	0.003
Cocaine	133 (56.1%)	6 (26.1%)	0.005
Ketamine	138 (58.2%)	13 (56.5%)	0.521
Ecstasy	114 (48.1%)	10 (43.5%)	0.413
Hypnotics	112 (47.3%)	10 (43.5%)	0.451
Cough medicine	55 (23.2%)	4 (17.4%)	0.368

[a] Fisher's exact test

Table 9. Logistic regression model of predictors of psychotic symptoms.

		95% Cl for OR		
Variable	OR	Lower	Upper	P value
Lifetime ICE dependence	12.818	3.804	43.188	<0.001
Lifetime cocaine use	3.055	0.987	9.454	0.053
Lifetime cannabis use	-	-	-	-
Marital Status	-	-	-	-
Accommodation	-	-	-	-
Lifetime ICE consumption				
Consumption in one day	-	-	-	-
ICE consumption in past two years				
Total grams	-	-	-	-
Total grams / body weight	-	-	-	-
Consumption in one day	-	-	-	-
ICE consumption in past one year				
Consumption in one day	-	-	-	-

Correlates of PPS

Subjects with PPS and TPS did not differ in terms of demographics (Table 10). In terms of ICE use pattern, the PPS group had higher total consumption (754 vs 383 grams, p = 0.005), consumption per body weight (12.0 vs 6.4 grams/kilogram, p=0.016) and consumption in 1 day (1.8 vs 1.0 grams, p = 0.013) in the past 2 years, as well as consumption in one day in the past one year (1.8 vs 1.1 grams, p=0.036) (Table 11). The PPS group were more likely to report lifetime cannabis use (81% vs 64%, p=0.024) (Table 12). In the logistic regression model, ICE consumption in one day in the past two years (OR = 1.777, 95% CI 1.206 – 8.390, p < 0.004) and lifetime cannabis use (OR = 2.938, 95% CI 1.029 – 8.390, p = 0.044) were predictors of PPS (Table 13).

Table 10. Demographic characteristics of subjects with TPS and PPS.

	PPS N=43	TPS N=125	TPS vs PPS (p value)
Age	29.0±7.9	29.5±7.9	0.702[a]
Gender (male), n (%)	24 (55.8%)	65(52.0%)	0.400[b]
Education (years)	9.4±1.6	9.8±2.5	0.358[a]
Marital status, n (%)			
Single	35 (81.4%)	91 (72.8%)	0.441[c]
Married	7 (16.3%)	26 (20.8%)	
Separated	1 (2.3%)	8 (6.4%)	
Others	0 (0.0%)	0 (0.0%)	
Occupation, n (%)			
Employed,	8 (18.6%)	18 (14.4%)	0.332[b]
Unemployed	35 (81.4%)	107 (85.6%)	
Source of referral, n (%)			
Non-residential)	13 (30.2%)	29 (23.2%)	0.235[b]
Residential	30 (69.8%)	96 (76.8%)	
Smoking history, n (%)			
Current	32 (74.4%)	78 (62.4%)	0.279[c]
Previous	10 (23.3%)	38 (30.4%)	
Family psychiatric history, n (%)	5 (11.6%)	10 (8.0%)	0.329[b]
Has a religious belief, n (%)	17 (39.5%)	52 (42.6%)	0.368[c]
Accommodation, n (%)			
Public housing	23 (53.5%)	75 (60.0%)	0.695[c]
Private housing	16 (37.2%)	38 (30.4%)	
Home Owner Scheme housing	3 (7.0%)	11 (8.8%)	

[a] Mann-Whitney; [b] Fisher's Exact Test; [c] Chi-square test.
TPS: Transient psychotic symptoms; PPS: Persistent psychotic symptoms.

Table 11 Descriptive statistics of ICE use patterns.

Variables	PPS N=43 Mean ± SD, Median (range)	TPS N=125 Mean ± SD, Median (range)	TPS vs PPS (p value)
Age of first use	20.3 ± 6.8 19.0 (12 - 44)	21.1 ± 6.9 19.0 (10 - 51)	0.371[a]
Duration of use (years)	5.6 ± 4.2 4.7 (0.4 - 18)	5.7 ± 4.2 4.9 (0.4 - 21)	0.847[a]
Days of use			
Lifetime	1396.4 ± 1231.0 977.2 (76 - 5551)	1260.2 ± 1141.5 936.0 (18 - 5395)	0.456[a]
Past two years	386.6 ± 195.2 394.3 (20 – 728)	317.7 ± 222.0 266.5 (1 - 728)	0.064[a]
Past one year	163.1 ± 94.0 173.3 (15 - 364)	144.6 ± 101.8 130.0 (1 - 364)	0.235[a]
Lifetime consumption			
Total (grams)	2818.8 ± 3320.9 1582.8 (24.9 - 12740.0)	1534.0 ± 2110.1 743.2 (7.8 - 11466.0)	0.093[a]
Total / body weight (grams/kilogram)	44.2 ± 54.8 20.9 (0.2 - 231.6)	24.0 ± 30.6 12.6 (0.1 - 145..1)	0.177[a]
Consumption in one day (grams)	1.6 ± 1.4 1.2 (0.1 - 6.8)	1.1 ± 0.8 0.9 (0.04 - 4.8)	0.055[a]
Consumption in the past two years			
Total (grams)	753.5 ± 1061.1 336.7 (10.0 - 6066.7)	382.8 ± 493.0 170.1 (0.4 - 3025.8)	0.005[a]
Total / body weight (grams/kilogram)	12.0 ± 18.5 5.0 (0.2 - 104.2)	6.4 ± 8.2 3.1 (0.004 - 42.7)	0.016[a]
Consumption in one day (grams)	1.8 ± 1.9 1.1 (0.1 - 10.0)	1.0 ± 0.8 0.9 (0.04 - 5.3)	0.013[a]
Consumption in the past one year			
Total (grams); Mean ± SD, Median (range)	293.6 ± 448.0 122.6 (10.0 - 2426.7)	170.2 ± 212.6 91.0 (0.4 - 1114.8)	0.056[a]

Variables	PPS N=43 Mean ± SD, Median (range)	TPS N=125 Mean ± SD, Median (range)	TPS vs PPS (p value)
Total / body weight (grams/kilogram)	4.7 ± 7.8 2.0 (0.1 - 41.7)	2.9 ± 3.6 1.4 (0.004 - 19.3)	0.175[a]
Consumption in one day (grams)	1.8 ± 1.9 1.0 (0.1 - 10.0)	1.1 ± 0.9 0.9 (0.04 - 5.3)	0.036[a]
Lifetime dependence, n (%)	42 (97.7%)	120 (96.0%)	0.518[b]
Lifetime abuse, n (%)	1 (2.3%)	5 (4.0%)	0.518[b]

[a] Mann-Whitney; [b] Fisher's Exact test.
TPS: Transient psychotic symptoms; PPS: Persistent psychotic symptoms.

Table 12. Other drug use in the TPS and PPS group.

Lifetime use	PPS N=43	TPS N=125	p value[a]
Cannabis use	35 (81.4%)	80 (64.0%)	0.024
Cough medicine use	12 (27.9%)	21 (16.8%)	0.089
Cocaine use	27 (62.8%)	70 (56.0%)	0.276
Ketamine use	24 (55.8%)	71 (56.8%)	0.525
Ecstasy use	20 (46.5%)	57 (45.6%)	0.528
Hypnotics use	20 (46.5%)	54 (43.2%)	0.420

[a] Fisher's Exact test

Table 13. Logistic regression model of predictors of PPS.

		95% Cl for OR		
Variable	OR	Lower	Upper	P value
ICE consumption in past two years				
Consumption in one day	1.777	1.206	2.617	0.004
Total grams	-	-	-	-
Total grams / body weight	-	-	-	-
ICE consumption in past one year				
Consumption in one day	-	-	-	-
Lifetime cannabis use	2.938	1.029	8.390	0.044

Psychiatric diagnoses

The pattern of psychiatric disorders is shown in Table 14. Approximately three-quarters of the subjects had lifetime IIP. A small proportion of the subjects had other psychoses, namely schizophrenia or delusional disorder. Lifetime substance-induced mood disorder was also common, being found in 59% of the subjects. The predominant presentation was depressive episodes. The prevalence of lifetime diagnosis of major depressive disorder and bipolar disorder was 8% and 10%, respectively. Lifetime substance-induced anxiety disorder was found in approximately 60% of the subjects. Obsessive compulsive features were the most common presentation, affecting more than half of the subjects, followed by phobic symptoms. In contrast, non-substance-related anxiety disorders were uncommon.

Table 14. Pattern of psychiatric diagnoses.

Variables, n (%)	All users N = 260 lifetime	Current	Past
Any psychotic disorders	230 (88.5%)	67 (25.8%)	163 (62.7%)
ICE induced psychotic disorder (IIP)	197 (75.8%)	38 (14.6%)	159 (61.2%)
Psychotic not otherwise specified	12 (4.6%)	12 (4.6%)	0 (0.0%)
Delusional disorder	7 (2.7%)	7 (2.7%)	0 (0.0%)
Schizophrenia / schizophreniform disorder	14 (5.4%)	10 (3.8%)	4 (1.5%)
Any mood disorders	193 (74.2%)	48 (18.5%)	165 (63.5%)
Substance-induced mood disorder	152 (58.5%)	20 (7.7%)	146 (56.2%)
Depressive episodes	101 (38.8%)	13 (5.0%)	97 (37.3%)
Manic / hypomanic episodes	8 (3.1%)	4 (1.5%)	7 (2.7%)
Mixed episodes	43 (16.5%)	3 (1.2%)	42 (16.2%)
Major depressive disorder	26 (10.0%)	14 (5.4%)	12 (4.6%)
Bipolar I or II disorder	21 (8.1%)	14 (5.4%)	7 (2.7%)
Any anxiety disorders	175 (67.3%)	-	-
Substance-induced anxiety disorder (any type)	160 (61.5%)	-	-
With obsessive compulsive symptoms	143 (55.0%)	-	-
With phobic features	61 (23.5%)	-	-
With panic attacks	24 (9.2%)	-	-
With generalized anxiety symptoms	14 (5.4%)	-	-
Specific phobia	9 (3.5%)	-	-
Panic disorder	2 (0.8%)	-	-
Generalized Anxiety Disorder	2 (0.8%)	-	-
Obsessive Compulsive Disorder	1 (0.4%)	-	-

Correlates of lifetime ICE induced psychotic disorder (IIP)

There were no associations between IIP and socio-demographic variables, except type of housing (Table 15). In terms of ICE use, IIP was related to a more frequent use ($p = 0.005$) and higher total consumption ($p = 0.007$) of ICE in the previous month. Current and lifetime ICE dependence were also related to IIP (Table 16). Other drug use was not related to IIP (Table 17). In the logistic regression, both current (OR = 7.987) and lifetime (OR = 3.255) dependence on ICE were predictors of IIP (Table 18).

Table 15. Demographic characteristics of subject with or without lifetime substance-induced psychotic disorders.

	With substance-induced psychotic disorders N = 197	Without substance-induced psychotic disorders N = 63	P-values
Age	30.5 ± 8.4	29.6 ± 6.9	0.747[a]
Gender (female), n (%)	95 (48.2%)	25 (39.7%)	0.149[b]
Education (years)	9.7 ± 2.5	9.2 ± 1.9	0.497[a]
Marital status (single), n (%)			
Single	148 (75.1%)	49 (77.8%)	0.185[c]
Married	38 (19.3%)	12 (19.0%)	
Separated	11 (5.6%)	1 (1.6%)	
Others	0 (0.0%)	1 (1.6%)	
Occupation, n (%)			
Employed	45 (22.8%)	14 (22.2%)	0.535[b]
Unemployed	152 (77.2%)	49 (77.8%)	
Source of referral, n (%)			
Non-residential	87 (44.2%)	23 (36.5%)	0.178[b]
Residential	110 (55.8%)	40 (63.5%)	
Smoking history, n (%)			
Current	137 (69.5%)	46 (73.0%)	0.865[c]
Previous	45 (22.8%)	13 (20.6%)	
Family psychiatric history, n (%)	23 (11.7%)	4 (6.3%)	0.167[b]
Has a religious belief, n (%)[*]	74 (38.1%)	24 (38.1%)	0.661[c]
Accommodation*, n (%)*			
Public housing	125 (63.5%)	32 (50.8%)	0.041[c]
Private housing	54 (27.4%)	23 (36.5%)	
Home Owner Scheme housing	17 (8.6%)	5 (7.9%)	

[a] Mann-Whitney Test; [b] Fisher's Exact Test; [c] Pearson Chi-Square test.

Table 16. ICE use patterns in subjects' with or without lifetime substance-induced psychotic disorders.

Variables	With substance-induced psychotic disorders N = 197 Mean ± SD, Median (range)	Without substance-induced psychotic disorders N = 63 Mean ± SD, Median (range)	P-values[a]
Age of first use	21.7 ± 7.7 20.0 (10.0 - 51)	21.2 ± 6.9 21.0 (12.0 - 37)	0.748
Duration of Ice use (years)	5.8 ± 4.1 5.0 (0.4 - 21)	5.5 ± 4.2 4.0 (0.4 - 17)	0.362
Days of use			
Lifetime	1221.7 ± 1162.5 900.0 (18 - 5551)	1273.6 ± 1124.2 938.2 (14 - 4312)	0.639
Past two years	320.1 ± 233.5 260.0 (1 - 728)	339.6 ± 216.0 323.5 (14 – 728)	0.469
Past one year	151.8 ± 114.6 130.0 (1 - 364)	147.5 ± 108.6 130.0 (2 - 364)	0.916
Previous month	3.0 ± 8.0 0.0 (0 - 30)	1.2 ± 5.1 0.0 (0 - 30)	0.005
Lifetime consumption			
Total (grams)	1748.5 ± 5492.3 634.4 (7.8 - 69958.2)	2129.6 ± 2879.5 980.7 (13.9 - 12740.0)	0.324
Total / body weight (grams/kilogram)	27.0 ± 73.4 10.1 (0.1 - 905.3)	32.4 ± 47.0 12.7 (0.2 - 231.6)	0.683
Consumption in one day (grams)	1.1 ± 1.8 0.8 (0.04 - 22.2)	1.3 ± 1.3 0.9 (0.2 - 6.8)	0.538
Consumption in the past two years			
Total (grams)	341.1 ± 445.1 161.5 (0.4 - 3025.8)	570.7 ± 933.1 209.3 (9.5 - 6066.7)	0.209
Total / body weight (grams/kilogram)	5.7 ± 7.3 2.7 (0.004 - 42.7)	8.9 ± 16.0 2.7 (0.1 - 104.2)	0.380
Consumption in one day (grams)	0.9 ± 0.8 0.7 (0.04 - 5.3)	1.4 ± 1.7 0.9 (0.1 - 10.0)	0.359
Consumption in the past one			

Variables	With substance-induced psychotic disorders N = 197 Mean ± SD, Median (range)	Without substance-induced psychotic disorders N = 63 Mean ± SD, Median (range)	P-values[a]
year			
Total (grams)	153.5 ± 196.5 75.8 (0.4 - 1114.8)	230.9 ± 390.4 100.1 (0.3 - 2426.7)	0.483
Total / body weight (grams/kilogram)	2.6 ± 3.2 1.3 (0.005 - 19.3)	3.6 ± 6.7 1.2 (0.003 - 41.7)	0.847
Consumption in one day (grams)	0.9 ± 0.8 0.7 (0.04 - 5.3)	1.4 ± 1.7 0.9 (0.1 - 10.0)	0.219
Ice consumption in the previous month			
Total (grams); Mean ± SD	2.6 ± 9.9 0.0 (0.0 - 75.8)	0.8 ± 3.5 0.0 (0.0 - 21.7)	0.007
Total / body weight (grams/kilogram)	0.04 ± 0.2 0.0 (0.0 - 1.6)	0.01 ± 0.1 0.0 (0.0 - 0.4)	0.007
Consumption in one day (grams)	0.2 ± 0.5 0.0 (0.0 - 3.5)	0.04 ± 0.2 0.0 (0.0 - 1.0)	0.005
Current dependence, n (%)	27 (13.7%)	1 (1.6%)	0.003[b]
Current abuse, n (%)	22 (11.2%)	4 (6.3%)	0.198[b]
Lifetime dependence, n (%)	185 (93.9%)	51 (81.0%)	0.004[b]
Lifetime abuse, n (%)	12 (6.1%)	12 (19.0%)	0.004[b]

[a] Mann-Whitney Test; [b] Fisher's Exact Test

Table 17. Other drug use in subjects with and without substance-induced psychotic disorders

Lifetime use	With substance-induced psychotic disorders N = 197	Without substance-induced psychotic disorders N = 63	p value[a]
Cannabis use	134 (68.0%)	42 (66.7%)	0.478
Cocaine use	107 (54.3%)	32 (50.8%)	0.365
Ketamine use	115 (58.4%)	36 (57.1%)	0.488
Ecstasy use	94 (47.7%)	30 (47.6%)	0.539
Hypnotics use	94 (47.7%)	28 (44.4%)	0.380
Cough medicine use	43 (21.8%)	16 (25.4%)	0.334

[a] fisher's exact test.

Table 18. Logistic regression model of predictors of lifetime substance-induced psychotic disorders.

		95% Cl for OR		
Variable	OR	Lower	Upper	p value
Current dependence of ICE	7.987	1.055	60.441	0.044
Lifetime dependence of ICE	3.255	1.327	7.986	0.010
Accommodation	-	-	-	-
ICE consumption in the previous month				
Total grams	-	-	-	-
Total grams / body weight	-	-	-	-
Consumption in one day	-	-	-	-
Days of ICE use				
Previous month	-	-	-	-

Correlates of lifetime substance-induced mood disorders

Subjects with lifetime substance-induced mood disorders were older ($p = 0.037$) and more likely to be referred from non-residential centres (Table 19). In terms of ICE use pattern, subjects with mood disorders had a higher number of days of ICE use ($p < 0.035$). In addition, they were more likely to have lifetime ICE dependence ($p = 0.008$) (Table 20). Lifetime cannabis ($p = 0.001$), cocaine ($p = 0.019$) or ecstasy use ($p = 0.044$) were related to substance-induced mood disorder (Table 21). In the logistic regression model, lifetime ICE dependence (OR = 3.176), cannabis use (OR = 2.483) and age (OR = 1.041) were significant predictors (Table 22).

Table 19. Demographic characteristics of subject with or without lifetime substance-induced mood disorders.

	With substance-induced mood disorders N = 152	Without substance-induced mood disorders N = 108	P-values
Age	31.4 ± 8.6	28.8 ± 6.9	0.037[a]
Gender (female), n (%)	71 (46.7%)	49 (45.4%)	0.465[b]
Education (years)	9.7 ± 2.3	9.3 ± 2.4	0.189[a]
Marital status (single), n (%)			
Single	115 (75.7%)	82 (75.9%)	0.627[c]
Married	29 (19.1%)	21 (19.4%)	
Separated	8 (5.3%)	4 (3.7%)	
Others	0 (0.0%)	1 (0.9%)	
Occupation, n (%)			
Employed	36 (23.7%)	23 (21.3%)	0.383[b]
Unemployed	116 (76.3%)	85 (78.7%)	
Source of referral, n (%)			
Non-residential	72 (47.4%)	38 (35.2%)	0.033[b]
Residential	80 (52.6%)	70 (64.8%)	
Smoking history, n (%)			
Current	106 (69.7%)	77 (71.3%)	0.435[c]
Previous	37 (24.3%)	21 (19.4%)	
Family psychiatric history, n (%)	17 (11.2%)	10 (9.3%)	0.388[b]
Has a religious belief, n (%)[*]	60 (40.0%)	38 (35.5%)	0.512[c]
Accommodation*, n (%)*			
Public housing	92 (60.5%)	65 (60.2%)	0.937[c]
Private housing	44 (28.9%)	33 (30.6%)	
Home Owner Scheme housing	14 (9.2%)	8 (7.4%)	

[a] Mann-Whitney Test; [b] Fisher's Exact Test; [c] Pearson Chi-Square test.

Table 20. ICE use patterns in subjects' with or without lifetime substance-induced mood disorders.

Variables	With substance-induced mood disorders N = 152 Mean ± SD, Median (range)	Without substance-induced mood disorders N = 108 Mean ± SD, Median (range)	P-values [a]
Age of first use	22.1 ± 8.1 20.0 (10 - 51)	20.9 ± 6.6 20.0 (12 - 40)	0.399
Duration of Ice use (years)	6.0 ± 4.2 5.0 (0.7 - 21)	5.3 ± 3.9 4.3 (0.4 - 18)	0.166
Days of use			
Lifetime	1328.2 ± 1193.0 988.0 (20 - 5395)	1104.5 ± 1083.6 854.1 (14 - 5551)	0.089
Past two years	346.8 ± 225.7 283.0 (2 - 728)	294.3 ± 231.3 218.8 (1 - 728)	0.035
Past one year	162.5 ± 113.8 147.3 (1 - 364)	134.4 ± 110.4 104.0 (1 - 364)	0.055
Previous month	3.1 ± 8.3 0.0 (0 - 30)	1.8 ± 6.0 0.0 (0 - 30)	0.369
Lifetime consumption			
Total (grams)	1712.0 ± 2329.7 700.4 (19.7 - 11466.0)	2005.8 ± 7205.6 540.0 (7.8 - 69958.2)	0.178
Total / body weight (grams/kilogram)	26.7 ± 34.5 11.5 (0.2 - 145.1)	30.4 ± 97.8 10.1 (0.1 - 905.3)	0.267
Consumption in one day (grams)	1.1 ± 0.9 0.9 (0.04- 6.8)	1.2 ± 2.3 0.8 (0.1 - 22.2)	0.687
Consumption in the past two years			
Total (grams)	445.6 ± 688.0 182.0 (0.4 - 6066.7)	326.3 ± 454.6 156.0 (0.5 - 3609.7)	0.073
Total / body weight (grams/kilogram)	7.2 ± 11.5 3.2 (0.005 - 104.2)	5.2 ± 7.6 2.5 (0.008 - 42.5)	0.071
Consumption in one day (grams)	1.1 ± 1.2 0.8 (0.04 - 10.0)	1.0 ± 0.9 0.7 (0.1 - 6.0)	0.470
Consumption in the past one year			

Variables	With substance-induced mood disorders N = 152 Mean ± SD, Median (range)	Without substance-induced mood disorders N = 108 Mean ± SD, Median (range)	P-values [a]
Total (grams)	192.1 ± 284.2 104.0 (0.3 - 2426.7)	145.0 ± 215.2 66.6 (0.5 - 1092.0)	0.096
Total / body weight (grams/kilogram)	3.1 ± 4.8 1.7 (0.003 - 41.7)	2.4 ± 3.6 1.1 (0.008 - 19.3)	0.177
Consumption in one day (grams)	1.1 ± 1.2 0.8 (0.04 - 10.0)	1.0 ± 0.9 0.6 (0.1 - 6.0)	0.533
Ice consumption in the previous month			
Total (grams); Mean ± SD	2.9 ± 11.1 0.0 (0.0 - 75.8)	1.1 ± 3.6 0.0 (0.0 - 21.7)	0.414
Total / body weight (grams/kilogram)	0.05 ± 0.2 0.0 (0.0 - 1.6)	0.02 ± 0.1 0.0 (0.0 - 0.4)	0.432
Consumption in one day (grams)	0.2 ± 0.5 0.0 (0.0 - 3.5)	0.1 ± 0.3 0.0 (0.0 - 1.0)	0.468
Current dependence, n (%)	19 (12.5%)	9 (8.3%)	0.193[b]
Current abuse, n (%)	15 (9.9%)	11 (10.2%)	0.550[b]
Lifetime dependence, n (%)	144 (94.7%)	92 (85.2%)	0.008[b]
Lifetime abuse, n (%)	8 (5.3%)	16 (14.8%)	0.008[b]

[a] Mann-Whitney Test; [b] Fisher's Exact Test.

Table 21. Other drug use in subjects with or without lifetime substance-induced mood disorders.

Life time use	With substance-induced mood disorders N = 152	Without substance-induced mood disorders N = 108	p value[a]
Cannabis use	115 (75.7%)	61 (56.5%)	0.001
Cocaine use	90 (59.2%)	49 (45.4%)	0.019
Ecstasy use	80 (52.6%)	44 (40.7%)	0.044
Ketamine use	93 (61.2%)	58 (53.7%)	0.141
Hypnotics use	76 (50.0%)	46 (42.6%)	0.146
Cough medicine use	31 (20.4%)	28 (25.9%)	0.184

[a] fisher's exact test.

Table 22. Logistic regression model of predictors of lifetime substance-induced mood disorders.

		95% Cl for OR		
Variable	OR	Lower	Upper	P value
Age	1.041	1.004	1.080	0.031
Sources of referral	1.764	1.001	3.110	0.050
Lifetime dependence of ICE	3.176	1.150	8.766	0.026
Lifetime cannabis use	2.483	1.404	4.391	0.002
Days of ICE use				
Past two years	-	-	-	-
Lifetime Cocaine use	-	-	-	-
Lifetime Ecstasy use	-	-	-	-

Correlates of lifetime substance-induced anxiety disorders

Subjects with lifetime substance-induced anxiety disorders were more likely to be female ($p = 0.007$) and unemployed ($p = 0.020$) (Table 23). In terms of ICE use pattern, subjects with anxiety disorders had younger age of initiation ($p = 0.009$) and longer duration of ICE use ($p = 0.024$). They were more likely to have lifetime ICE dependence ($p = 0.001$) (Table 24). Lifetime cocaine ($p = 0.021$) and ketamine use ($p = 0.045$) were related to anxiety disorders (Table 25). In the logistic regression model, lifetime ICE dependence (OR = 4.815) and female gender (OR = 2.062) were independent predictors (Table 26).

Table 23. Demographic characteristics of subject with or without lifetime substance-induced anxiety disorders.

	With substance-induced anxiety disorders N = 160	Without substance-induced anxiety disorders N = 100	P-values
Age	29.8 ± 8.4	31.2 ± 7.4	0.061[a]
Gender (female), n (%)	84 (52.5%)	36 (36.0%)	0.007[b]
Education (years)	9.5 ± 2.3	9.7 ± 2.4	0.366[a]
Marital status, n (%)			
Single	125 (78.1%)	72 (72.0%)	0.522
Married	28 (17.5%)	22 (22.0%)	
Separated	6 (3.8%)	6 (6.0%)	
Other	1 (0.6%)	0 (0.0%)	
Occupation, n (%)			
Unemployed	131 (81.9%)	70 (70.0%)	0.020[b]
Employed	29 (18.1%)	30 (30.0%)	
Source of referral, n (%)			
Non-residential	62 (38.8%)	48 (48.0%)	0.090[b]
Residential	98 (61.3%)	52 (52.0%)	
Smoking history, n (%)			
Current	111 (69.4%)	72 (72.0%)	0.800[c]
Previous	36 (22.5%)	22 (22.0%)	
Family psychiatric history, n (%)	20 (12.5%)	7 (7.0%)	0.113[b]
Has a religious belief, n (%)	64 (40.5%)	34 (34.0%)	0.449[c]
Accommodation, n (%)			
Public housing	103 (64.4%)	54 (54.0%)	0.065[c]
Private housing	47 (29.4%)	30 (30.0%)	
Home Owner Scheme housing	8 (5.0%)	14 (14.0%)	

[a] Mann-Whitney Test; [b] Fisher's Exact Test; [c] Pearson Chi-Square test.

Table 24. ICE use pattern in subjects with or without lifetime substance-induced anxiety disorders.

Variables	With substance-induced anxiety disorders N = 160 Mean ± SD, Median (range)	Without substance-induced anxiety disorders N = 100 Mean ± SD, Median (range)	P-values [a]
Age of first use	20.8 ± 7.3 18.5 (10 - 50)	22.9 ± 7.7 21.0 (12 - 51)	0.009
Duration of Ice use (years)	6.2 ± 4.3 5.0 (0.4 - 21)	5.0 ± 3.6 3.9 (0.4 - 15)	0.024
Days of use			
Lifetime	1304.4 ± 1186.9 976.1 (18 - 5551)	1122.2 ± 1088.8 731.0 (14 - 4671)	0.135
Past two years	326.4 ± 226.2 275.2 (2 - 728)	322.2 ± 234.7 256.8 (1 - 728)	0.895
Past one year	145.1 ± 106.8 125.7 (1 - 364)	159.8 ± 122.2 143.0 (1 - 364)	0.490
Previous month	2.1 ± 6.7 0.0 (0 - 30)	3.3 ± 8.4 0.0 (0 - 30)	0.494
Lifetime consumption			
Total (grams)	1799.8 ± 2576.1 688.7 (8.8 - 12740.0)	1897.8 ± 7473.1 453.4 (7.8 - 69958.2)	0.104
Total / body weight (grams/kilogram)	28.2 ± 39.0 11.8 (0.1-231.6)	28.3 ± 100.2 7.1 (0.2-905.3)	0.079
Consumption in one day (grams)	1.1 ± 1.0 0.9 (0.1-6.8)	1.2 ± 2.4 0.7 (0.04-22.2)	0.281
Consumption in the past two years			
Total (grams)	454.7 ± 689.3 182.0 (0.4 - 6066.7)	298.6 ± 409.6 167.4 (0.5 - 3025.8)	0.249
Total / body weight (grams/kilogram)	7.5 ± 11.7 3.2 (0.004 - 104.4)	4.6 ± 6.1 2.4 (0.008 - 42.7)	0.195
Consumption in one day (grams)	1.2 ± 1.2 0.8 (0.1 - 10.0)	0.9 ± 0.8 0.6 (0.04 - 5.3)	0.077
Consumption in the past one year			

Variables	With substance-induced anxiety disorders N = 160 Mean ± SD, Median (range)	Without substance-induced anxiety disorders N = 100 Mean ± SD, Median (range)	P-values [a]
Total (grams)	187.3 ± 292.2 86.7 (0.3 - 2426.7)	146.8 ± 186.4 75.8 (0.5 - 1114.8)	0.430
Total / body weight (grams/kilogram)	3.1 ± 5.0 1.3 (0.003 - 41.7)	2.3 ± 2.9 1.1 (0.008 - 15.7)	0.333
Consumption in one day (grams)	1.1 ± 1.2 0.8 (0.1 - 10.0)	0.9 ± 0.9 0.6 (0.04 - 5.3)	0.120
Ice consumption in the previous month			
Total (grams)	2.4 ± 10.6 0.0 (0.0 - 75.8)	1.7 ± 4.5 0.0 (0.0 - 21.7)	0.524
Total / body weight (grams/kilogram)	0.04 ± 0.2 0.0 (0.0 - 1.6)	0.03 ± 0.1 0.0 (0.0 - 0.4)	0.532
Consumption in one day (grams)	0.2 ± 0.5 0.0 (0.0 - 3.5)	0.1 ± 0.3 0.0 (0.0 - 1.0)	0.579
Current dependence, n (%)	17 (10.6%)	11 (11.0%)	0.538[b]
Current abuse, n (%)	15 (9.4%)	11 (11.0%)	0.397[b]
Lifetime dependence, n (%)	153 (95.6%)	83 (83.0%)	0.001[b]
Lifetime abuse, n (%)	7 (4.4%)	17 (17.0%)	0.001[b]

[a] Mann-Whitney Test; [b] Fisher's Exact Test

Table 25. Other drug use in subjects with or without lifetime substance-induced anxiety disorders.

Lifetime use	With substance-induced anxiety disorders N = 160	Without substance-induced anxiety disorders N = 100	p value[a]
Cocaine use	94 (58.8%)	45 (45.0%)	0.021
Ketamine use	100 (62.5%)	51 (51.0%)	0.045
Hypnotics use	69 (43.1%)	53 (53.0%)	0.077
Cannabis use	114 (71.3%)	62 (62%)	0.079
Ecstasy use	74 (46.36%)	50 (50.0%)	0.339
Cough medicine use	32 (20.0%)	27 (27.0%)	0.124

[a] fisher's exact test.

Table 26. Logistic regression of predictors of lifetime substance-induced anxiety disorders.

Variable	OR	95% Cl for OR Lower	Upper	P value
Female gender	2.062	1.214	3.501	0.007
Lifetime dependence of ICE	4.815	1.887	12.290	0.001
Occupation	-	-	-	-
First age of ICE use	-	-	-	-
ICE use duration	-	-	-	-
Lifetime cocaine use	-	-	-	-
Lifetime ketamine use	-	-	-	-

Severity and correlates of psychiatric symptoms

The mean BDI, HADSA and SDS score of all subjects were 16.0 ± 11.7, 5.8 ± 4.8 and 7.7 ± 3.3 respectively. The mean BPRS score was 20.2 ± 4.4, and 1.5% of the sample were rated as mildly to moderately ill (score = 31–41), while only 0.4% of the sample were rated as markedly ill (score above 53) (Leucht et al., 2018). The mean total score of PANSS was 32.6 ± 5.7. The positive, negative and general psychopathology items in the PANSS scores were 7.5 ± 2.2, 7.8 ± 2.7 and 17.2 ± 2.6, respectively. None of the subjects scored higher than 95 (markedly ill) in PANSS, one subject scored more than 75 (moderately ill) and another scored 58 (mildly ill) (Leucht et al., 2005).

The correlations between psychiatric symptoms and demographic characteristics and the patterns of ICE and other drug use are shown in Table 27–29. The subsequent linear regression models are shown in Table 30–34. Days of ICE use in current month (beta = 0.434, $p < 0.001$) and lifetime ICE dependence (beta = 5.580, $p < 0.001$) predicted BDI score (beta = 0.435, $p < 0.001$). Current (beta = 2.262, $p = 0.028$) and lifetime (beta = 2.289, $p = 0.046$) ICE dependence, ICE consumption in one day in the past two years (beta = 0.729, $p = 0.009$) and days of ICE use in the past one year (beta = 0.006, $p = 0.023$) were predictors of HADSA score. Finally, marital status predicted PANSS positive score (beta = -0.315, $p = 0.048$), lifetime ICE dependence predicted SDS score (beta = 3.098, $p <0.001$), no significant predictor of BPRS found.

Table 27. Correlations between psychiatric symptoms and demographic characteristics.

Variables[a]	BDI	HADSA	BPRS	PANSS	PANSS positive	PANSS negative	PANSS GP	SDS
Age [b]	0.070	-0.088	-0.021	-0.017	0.042	-0.029	-0.041	-0.092
Gender	0.083	-0.026	-0.073	-0.068	0.004	-0.119	-0.018	-0.014
Education [b]	-0.097	0.085	-0.045	-0.041	-0.046	-0.035	-0.015	0.120
Marital Status	-0.041	0.006	-0.103	-0.116	-0.129*	-0.071	-0.119	-0.040
Occupation	0.006	0.107	0.050	0.032	0.095	0.010	0.036	-0.046
Sources of referral	0.147*	0.153*	0.071	0.050	0.135*	0.069	-0.002	-0.096
Smoking history	-0.105	-0.092	-0.133*	-0.114	-0.073	-0.129*	-0.078	0.028
Family psychiatry history	0.021	0.078	0.072	0.047	0.080	-0.023	0.092	0.029
Has a Religious belief	0.113	-0.002	0.063	0.095	0.026	0.103	0.082	-0.083
Accommodation	-0.078	-0.055	-0.075	-0.089	-0.094	-0.060	-0.059	-0.112

*$p < 0.05$.

[a] Spearman correlation; [b] Pearson correlation.

Table 28. Correlations between psychiatric symptoms and ICE use pattern.

Variables[a]	BDI	HADSA	BPRS	PANSS	PANSS positive	PANSS negative	PANSS GP	SDS
Onset Age	0.032	-0.033	0.064	0.053	0.103	0.008	0.020	-0.063
Duration	-0.003	-0.025	-0.074	-0.083	-0.085	-0.064	-0.044	-0.058
Days of ICE use								
Lifetime	0.039	0.045	-0.080	-0.098	-0.079	-0.114	-0.026	0.034
Past two years	0.085	0.103	-0.074	-0.098	-0.057	-0.094	-0.065	0.090
Past one year	0.159*	0.187**	-0.035	-0.044	-0.003	-0.037	-0.054	0.134*
Previous month	0.275**	0.216**	0.073	0.061	0.051	0.073	0.014	0.011
Lifetime consumption								
Total	-0.020	-0.007	-0.055	-0.061	-0.053	-0.058	-0.031	-0.004
Total / body weight	-0.004	0.011	-0.060	-0.066	-0.060	-0.064	-0.029	-0.003
Consumption in one day	-0.013	0.008	-0.051	-0.047	-0.032	-0.053	-0.023	0.033
Consumption in the past two years								
Total	0.067	0.147*	-0.066	-0.069	-0.066	-0.064	-0.030	0.125
Total / body weight	0.064	0.154*	-0.081	-0.085	-0.069	-0.070	-0.055	0.111
Consumption in one day	0.063	0.141*	-0.022	-0.022	-0.031	-0.040	0.018	0.162*
Consumption in the past one year								
Total	0.098	0.175**	-0.037	-0.028	-0.020	-0.038	-0.007	0.166*
Total / body weight	0.091	0.171*	-0.048	-0.040	-0.026	-0.041	-0.025	0.144*
Consumption in one day	0.056	0.146*	-0.040	-0.044	-0.034	-0.066	-0.003	0.162*
Previous month								
Total	0.214**	0.156*	0.020	0.009	-0.024	0.033	0.001	-0.009
Total / body weight	0.202**	0.150*	0.003	-0.007	-0.022	0.014	-0.014	-0.015
Consumption in one day	0.231**	0.171**	0.028	0.027	-0.019	0.049	0.020	-0.047
Current dependence [b]	0.253**	0.225**	0.019	0.028	-0.042	0.045	-0.003	0.044
Current abuse [b]	0.051	0.034	0.092	0.087	0.117	0.060	0.055	-0.183**
Lifetime dependence [b]	0.176**	.236**	0.055	0.078	0.115	0.008	0.073	0.302**
Lifetime abuse [b]	-0.176**	-0.236**	-0.055	-0.078	-0.115	-0.008	-0.073	-0.302**

**$p < 0.01$.

*$p < 0.05$.

[a] Pearson correlation; [b] Spearman correlation.

BDI: Beck Depression Inventory; HADSA: Hospital Anxiety Depression Scale; PBRS: Brief Psychiatric Rating Scale; PANSS: Positive and Negative Syndrome Scale; GP: General psychopathology; SDS: Severity of Dependence Scale.

Table 29. Correlations between psychiatric symptoms and other drug use.

Variables [a]	BDI	HADSA	BPRS	PANSS	PANSS positive	PANSS negative	PANSS GP	SDS
Lifetime use								
Hypnotics	0.057	0.048	0.103	0.078	-0.012	-0.004	0.098	0.027
Cannabis	0.060	0.117	0.019	0.009	-0.028	-0.037	0.034	0.132*
Cough medicine	0.086	0.062	0.061	0.045	-0.019	0.028	0.047	0.109
Cocaine	0.011	0.045	0.011	-0.024	-0.072	-0.032	0.038	0.180**
Eactasy	-0.102	0.016	0.010	-0.046	-0.029	-0.076	-0.040	-0.024
Ketamine	-0.079	-0.028	0.044	0.017	-0.030	0.017	0.049	0.048

**$p < 0.01$.
*$p < 0.05$.
[a] Pearson correlation; [b] Spearman correlation
BDI: Beck Depression Inventory; HADSA: Hospital Anxiety Depression Scale; PBRS: Brief Psychiatric Rating Scale; PANSS: Positive and Negative Syndrome Scale; GP: General psychopathology; SDS: Severity of Dependence Scale.

Table 30. Linear regression of BDI scores.

Variable	Unstandardized beta	95% Cl for OR Lower	Upper	p value
Days of ICE use				
Previous month	0.435	0.248	0.621	<0.001
Sources of referral	-	-	-	-
Has a religious belief	-	-	-	-
ICE consumption in the previous month				
Total grams	-	-	-	-
Total grams / body weight	-	-	-	-
Consumption in one day	-	-	-	-
Lifetime ICE dependence	5.580	0.464	10.697	0.033

Table 31. Linear regression of HADSA scores.

Variable	Unstandardized beta	95% Cl for OR Lower	Upper	P value
Sources of referral	1.431	0.112	2.751	0.034
Day of ICE use				
Past one year	0.006	0.001	0.012	0.023
Previous month	-	-	-	-
ICE consumption in the past two years				
Total	-	-	-	-
Total/body weight	-	-	-	-
Consumption in one day	0.729	0.181	1.277	0.009
ICE consumption in the past one year				
Total	-	-	-	-
Total/body weight	-	-	-	-
Consumption in one day	-	-	-	-
ICE consumption in the previous month				
Total	-	-	-	-
Total/body weight	-	-	-	-
Consumption in one day	-	-	-	-
Current ICE dependence	2.262	0.243	4.280	0.028
Lifetime ICE dependence	2.289	0.037	4.541	0.046

Table 32. Linear regression of BPRS scores.

Variable	Unstandardized beta	95% Cl for OR Lower	Upper	P value
Smoking history	-	-	-	-

Table 33. Linear regression of PANSS scores.

	PANSS				PANSS Positive				PANSS Negative				PANSS GP			
		95% Cl for OR				95% Cl for OR				95% Cl for OR				95% Cl for OR		
Variable	B	Lower	Upper	P value	B	Lower	Upper	P value	B	Lower	Upper	P value	B	Lower	Upper	P value
Marital status					-0.315	-0.626	-0.003	0.048								
Sources of referral					-	-	-	-								
Smoking history									-	-	-	-				

B = Unstandardized beta

Table 34. Linear regression of SDS scores.

Variable	Unstandardized beta	95% Cl for OR Lower	Upper	P value
Days of ICE use				
Past one year	-	-	-	-
ICE consumption in the past two years				
Consumption in one day	-	-	-	-
ICE consumption in the past one year				
Total	-	-	-	-
Total / body weight	-	-	-	-
Consumption in one day	-	-	-	-
Current ICE abuse	-	-	-	-
Lifetime ICE dependence	3.098	1.460	4.736	<0.001
Lifetime ICE abuse	-	-	-	-
Lifetime cannabis use	-	-	-	-
Lifetime cocaine use	-	-	-	-

Characteristics of the sample

The subjects recruited in the study were either young or middle-aged adults. They had received 10 years of education on average, and less than one-third were employed. The majority were single, living in public housing and current smokers. These characteristics are comparable to those reported amongst local drug users (Narcotics Division, 2018). The subjects began to use ICE in their early twenties and the average duration of use was 6 years. More than 90% of the subjects had lifetime ICE dependence. On average, they used ICE for 150 days in 1 year and consumed approximately 1 gram of ICE in 1 day. Hence, the sample consisted of chronic regular heavy users with ICE dependence. Approximately one-fifth were current ICE users. Apart from ICE, cannabis, ketamine and cocaine were the three most commonly used drugs. According to the latest statistics of the Hong Kong Narcotics Division, ICE was the most popular drug in the first half of 2019 followed by cocaine and cannabis, while ketamine ranked fourth.

ICE induced psychotic disorder (IIP)

The majority (75.8%) of the subjects had a lifetime diagnosis of IIP. In a recent review, the figures for lifetime IIP prevalence ranged from 16% (Hides et al., 2015) to 64% (McKetin et al., 2016), with a median of 42% (Tang et al., in press). The relatively high prevalence of IIP in the present study could be due to the pattern of ice use of the sample, namely, long-term, regular and heavy users.

Only 15% of the sample in our study had current IIP. The previously reported prevalence of current IIP has varied from 13% (Sulaiman et al., 2014) to 25% (Hides et al., 2015). In the present study, only 20% of the sample were current ice users, which might explained the low rate of current IIP.

In the univariate analysis, the presence of IIP was related to type of housing, more frequent ICE use and higher ICE consumption, as well as ICE dependence. In the subsequent multivariate analysis, only current and lifetime ICE dependence remained significant. Previous studies suggest that risk factors for IIP/psychotic symptoms can be broadly classified into four groups based on demographics, characteristics of ICE use, personal history of psychological or psychiatric problems and family history of psychiatric illness. The risk of IIP is dependent on dose and, inversely, on the age of onset of ICE use (Harro 2015). Apart from the chronicity, pattern, severity and route of drug administration, psychological vulnerability predisposes some individuals to develop acute psychotic symptoms and syndromes in response to ICE use. IIP has been reported to be more common in subjects with male or, conversely, female gender, older age, schizotypal or schizoid traits, affective disorders, antisocial personality disorder or poly-drug use and in subjects with a family history of psychotic disorders. Sleep deprivation, which is commonly associated with ICE binge episodes, has also been cited as a putative contributory factor in IIP (Glasner-Edwards & Mooney 2014).

It is likely that IIP is a complex disease in which environmental factors interact with multiple polymorphic genes to influence susceptibility (Grant et al., 2012). Lines of evidence support the notion that ICE abuse leads to neurodegeneration and, as such, may be a component of IIP pathobiology. Grey and white matter deficits have been found in IIP, including reduced amygdala and hippocampal volumes. Reduced regional activation and dopamine transporter density and changes in metabolite concentrations have also been reported. Together, these findings suggest that subcortical pathology and a reduction in dopamine receptors following ICE use may contribute to the development of IIP (Gururajan et al., 2012). There is evidence that increased dopamine release and noradrenergic hyperactivity may be important in the susceptibility to subsequent spontaneous recurrence of IIP (Fiorentini et al., 2011).

The pharmacological treatment of acute IIP may include the use of antipsychotic medications as well as benzodiazepines, although symptoms may resolve without pharmacological treatment if the user is able to achieve a period of abstinence from ICE. Importantly, psychosocial treatment for ICE dependence has a

strong evidence base and is the optimal first-line treatment approach to reducing rates of psychosis among individuals who use ICE. Prevention of ICE relapse is the most direct means of preventing recurrence of psychotic symptoms and syndromes. Long-term management of individuals presenting with recurrent and persistent psychosis, even in the absence of ICE use, may include both behavioural treatment to prevent resumption of ICE use and pharmacological treatment targeting psychotic symptoms. In addition, treatment of co-occurring psychiatric disorders including depression and anxiety is an important means of preventing relapse to ICE use, which is often triggered by associated symptoms (Glasner-Edwards & Mooney, 2014).

Data on the individual treatment methods of IIP are very limited. Iwanami et al. (1994) examined 104 patients with IIP recruited from a university medical centre and found that all of them had been treated with antipsychotic medications. A few studies have investigated the efficacy of antipsychotic medications in IIP. In these studies, aripiprazole was more effective than a placebo (Sulaiman et al., 2013); risperidone, quetiapine and haloperidol were similarly effective (Verachai et al., 2014; Samiei et al., 2016); and risperidone was more effective for positive symptoms whereas aripiprazole was more effective for negative symptoms (Farnia et al., 2014). A small-scale clinical trial suggested that electroconvulsive therapy may not be useful in treatment-resistant IIP (Ziaaddini et al., 2015). Two case reports found olanzapine and clozapine to be effective in treating IIP and treatment-resistant IIP, respectively (Seddigh et al., 2014). In a naturalistic study of 152 inpatients with IIP, 46% were treated with risperidone and 38% with olanzapine (Misra et al., 2000; Zarrabi et al., 2016).

Pattern of psychotic symptoms

More than 90% of the subjects had lifetime psychotic symptoms. In terms of subtypes of psychotic symptoms, more than three-quarters of the subjects reported lifetime delusions and hallucinations. Delusion of reference was the most common delusion, followed by persecutory delusion. Auditory hallucination was

the most frequent type of hallucination, followed by visual and tactile hallucinations. Thought broadcasting was uncommon and negative symptoms were rare. In a recent review, the frequency of any psychotic symptoms in ICE users ranged from 16% to 81%, with a median of 78%. The frequency of persecutory delusion ranged from 29% to 77%, with a median of 34%. Hallucinations are also frequent, with 47% to 57% of users reporting them. The reported frequency of auditory hallucination ranged from 52% to 59%, with a median of 55%. The frequency of visual hallucination ranged from 7% to 54%, with a median of 32%. Other types of hallucination, including somatic and olfactory, are less common (Tang et al., in press).

PPS

In univariate analysis, PPS was related to higher total consumption, consumption per body weight and consumption in 1 day of ICE in the past 2 years, consumption in one day in the past one year and lifetime cannabis use. In multivariate analysis, only consumption in 1 day in the past two years and lifetime cannabis use predicted PPS. Lecomte et al. (2013) reported that correlates of persistent IIP included older age, longer duration of ICE use, longer duration of regular alcohol use, comorbid antisocial personality disorder and depressive symptoms. There is evidence that both ICE and cannabis play a role in psychosis. The effects of ICE on people with psychosis may be different from or additive to those of cannabis. However, majority of persons who use stimulants have also used cannabis. Even very large studies of young people with psychosis have not had sufficient power to examine the correlates of stimulant disorders and to assess whether they differ from those of cannabis disorders (Sara et al., 2013).

Some patients with IIP can recover within 1 week, whereas others do not remit for weeks or months, exhibiting the so-called ‘prolonged type’ of IIP (Harro, 2015). Even if symptoms abate with abstinence, in 25% to 38% of ICE users, IIP can re-emerge with repeated use or under stressful situations. If relapse to psychosis follows ICE use, it typically occurs promptly, with 60% of ICE users relapsing in less than 1 week

and 80% relapsing within 1 month (Grant et al., 2012). Identified triggers of recurrence of IIP include the resumption of ICE use, even in relatively small amounts, following protracted abstinence, other substance use including heavy alcohol use, sleep deprivation and psychosocial stressors (Glasner-Edwards & Mooney 2014). The propensity for ICE use to trigger psychosis among individuals who have previously experienced psychotic symptoms can persist for years, and has been described as 'ICE sensitisation' (Glasner-Edwards & Mooney 2014). Once developed, IIP is predictive of poor outcomes. More than half of those who could be reached at follow-up approximately 6 years after the index IIP episode had experienced a relapse of psychosis or had current alcohol use disorder (Harro 2015).

Several theories may explain the finding that psychosis can become chronic and persistent among ICE users. Pre-existing schizophrenia may be unmasked or triggered by ICE use, IIP may share a very similar clinical course to that of schizophrenia, or IIP and primary psychosis may not be distinct diagnostic entities, but rather fall along a continuum of psychosis (Glasner-Edwards & Mooney 2014). Indeed, persistent IIP may have similar vulnerability biomarkers as schizophrenia. In a study on exploratory eye movements (EEM), the response search score (a measure of EEM) in IIP patients of the persistent type was lowest, significantly lower than those of the transient type and the healthy controls. It did not differ from that of the subjects with schizophrenia (Mikami et al., 2003).

Bramness et al. (2012) hypothesised a paradigm of vulnerability to stress paradigm to explain the relationship between IIP and psychosis. Exposure to ICE should be viewed as a stressor in the acute phase for the vulnerable individual. For individuals with lower vulnerability, higher doses of ICE are needed, whereas individuals with higher vulnerability require lower doses to precipitate acute psychosis. In addition, due to its sensitising effects, ICE may play a role in the development of vulnerability to psychosis. Repeated use of ICE could increase vulnerability, thereby increasing the chances of developing psychotic symptoms even in the absence of acute exposure to ICE.

Mood disorders

In this study, 59% of the subjects had lifetime substance-induced mood disorder. The predominant presentation was depressive episodes. Previous studies also reported that mood disorders were common amongst ICE users. In an epidemiologic study of amphetamine dependence, 51% had lifetime depression and 23.5% had lifetime dysthymia (Conway et al., 2006). In a group of 526 subjects with ICE dependence, 15% had major depressive disorder (Glasner-Edwards et al., 2008). In a third study of 67 incarcerated women with ICE dependence, 64% had a lifetime mood disorder (Peter 2007). In a fourth study of 286 ICE-using men who have sex with men, 36% reported current major depressive episodes (Fletcher et al., 2018). Finally, in a forensic sample of 170 subjects with ICE dependence, 57% reported experiencing depression during the past year (Kalechstein et al., 2000).

In this study, lifetime ICE dependence and cannabis use were significant predictors of substance-induced mood disorder. The association between ICE dependence and depression and suicide has been reported previously (Darke et al., 2008; Glasner-Edwards et al., 2008). Other putative predictors have included female gender, higher consumption, longer use career, injecting ICE, and previous alcohol treatment (Darke et al., 2008; Glasner-Edwards et al., 2008). A few studies suggested a dose–response between the level of cannabis use and risk of depression or depressive symptoms. The link between cannabis use and depression can be explained by psychosocial mechanisms—for example, the adoption of a counter-cultural lifestyle—possibly underlie the association. Social consequences of frequent use include educational failure, dropout, unemployment, and crime— all factors that may lead to higher rates of mental disorders. Because risks seem confined largely to daily users, however, the question about a direct pharmaco-logical effect remains (Patton et al., 2002). Cannabinoid receptors are found widely in the central nervous system, with a distribution that is consistent with effects on a wide range of brain functions including memory, emotion, cognition, and movement (Ameri et al., 1999).

The mechanism underlying the association between depression symptoms and ICE dependence is complex. It was postulated that the neurotoxicity induced by ICE was associated with mood disturbance (Carvalho et al., 2012). Previous research in humans has demonstrated that the dopamine and dopamine transporter levels in the striatum and prefrontal cortex, as well as the global serotonin transporter density, all of which are theorised to be associated with depression, were reduced in patients with ICE dependence (Sekine et al., 2006), even after ICE abstinence (Sekine et al., 2001). Additionally, studies in rodents have revealed that ICE can lead to substantial decreases in dopamine, 5-hydroxytryptamine (serotonin) and other depression-associated markers of the monoaminergic system in various brain regions (Graham et al., 2008).

In terms of treatment, a systematic review suggests that exercise is effective in reducing depression in previous ICE users (Morris et al., 2018). A small-scale clinical trial suggested that cognitive behavioural therapy reduced depressive symptoms in ICE users (Pirnia et al., 2019). Another trial found that electro-acupuncture helps to improve symptoms of depression in ICE users during abstinence (Zeng et al., 2018). Two studies have examined the benefits of nutritional supplements. An open label trial found that creatine treatment may be a promising therapeutic approach for women with depression and comorbid ICE dependence (Hellem et al., 2015). Another trial in 60 subjects with depression and ICE dependence suggested that citicoline might have antidepressant properties in this population (Brown & Gabrielson et al., 2012).

Anxiety disorders

In this study, lifetime substance-induced anxiety disorder was found in approximately 60% of the subjects. Obsessive compulsive features were the most frequent presentation, affecting more than half of the subjects, followed by phobic symptoms. The prevalence of anxiety disorders in previous studies amongst ICE/amphetamine users ranged from 30% to 51%. In an epidemiologic study of subjects with amphetamine dependence, the lifetime prevalence of anxiety disorders was 50%. In another study of 526 subjects with ICE dependence, 23% had current and 8% had past anxiety disorders (Glasner-Edward et al., 2010). In a

third study of 67 incarcerated women with ICE dependence, 51% had lifetime anxiety disorder (Peter 2007). In a fourth study of 400 subjects with ICE dependence, 30% to 42% of them had a history of anxiety problems (Mcketin 2008). The existing literature suggests that a quarter of ICE users have OCD. In a study of 245 ICE-using HIV-positive men, 26% had OCD (Semple et al., 2011). In another study of 286 ICE-using men who had sex with men, 23% had OCD (Fletcher et al., 2018). In a third study of 121 patients with ICE induced psychosis, 25% had OCD (Eslami-Shahrbabaki et al., 2015).

In this study, predictors of substance-induced anxiety disorders were lifetime ICE dependence and female gender. Anxiety disorders have been shown to be associated with longer use careers, more frequent use, dependence and injecting (Darke et al., 2008). OCD was reportedly associated with greater frequency of ICE use and more depressive symptoms (Semple et al., 2011).

Only two published studies have examined treatment of anxiety disorders in ICE users. Rawson et al. (2015) conducted a trial of exercise versus cognitive behavioural therapy (CBT). Exercises were scheduled 3 days per week for 8 weeks. The level of anxiety in the exercise group was significantly lower ($p = 0.001$) at the 8-week follow-up compared with the CBT group. The exercise group's anxiety scores changed from 17 to 2 at the 8-week follow-up, while those of the CBT group changed from 12 to 5. Another trial found that electro-acupuncture helped to improve symptoms of anxiety in ICE users during abstinence (Zeng et al., 2018).

Limitations

First, the route of ICE administration was not assessed. Although Mcketin et al. (2008) reported that ICE injectors and smokers had similar levels of poor mental health and psychosis, according to Grant et al. (2012), ICE injection was associated with more severe psychotic symptoms. Second, because most of the ICE users had also abused or were dependent on other illicit substances, these substances might have

contributed to the development of psychotic symptoms. Third, this study aimed to quantify the subjects' lifetime consumption of ICE. Reliance on the subjects' ability to recall ICE use patterns of a longer duration may have reduced the reporting accuracy due to memory deficits or impairment among ICE dependent users (Chang et al, 2002). Fourth, some potential confounders were not assessed, such as childhood adversity, schizotypal personality or antisocial personality. Fifth, the study subjects were all recruited from various treatment facilities, hence the findings may not be applicable to non-treatment-seeking ICE users. Sixth, no urine testing was performed to confirm recent use of ICE.

Future research directions

In terms of study design, a long-term prospective study may provide further insight into the complex inter-play between ICE use and IIP. A large population-based sample and an enriched sample with equal proportions of men and women with minimal concurrent use of other illicit substances would increase the generalisability of the findings. Healthy controls should be recruited as well. It would be ideal to confirm recent ICE use by means of urine tests. Detailed measurements of possible confounders, such as childhood and adolescent adversity, premorbid intelligence, learning disabilities, personality disorders or a family history of psychosis, would also strengthen any future studies.

Conclusions

IIP was found to be very common in local ICE users, and ICE dependence increased the risk of IIP. Psychotic symptoms, such as delusions and hallucinations, were also very frequent in this population. One-fifth of users had persistent psychotic symptoms. The amount of ICE consumption was a risk factor for persistent psychotic symptoms. Lifetime mood and anxiety disorders were frequent as well. The predominant presentations were depressive episodes and obsessive compulsive features. Risk factors for mood and anxiety disorders were ICE dependence, age and female gender.

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