Psychological Medicine, 2007, **37**, 935–945.

Testing the self-medication hypothesis of depression and aggression in cannabis-dependent subjects

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ABSTRACT

Background. A self-medication hypothesis has been proposed to explain the association between cannabis use and psychiatric and behavioral problems. However, little is known about the reasons for use and reactions while intoxicated in cannabis users who suffer from depression or problems controlling violent behavior.

Method. We assessed 119 cannabis-dependent subjects using the Schedules of Clinical Assessment in Neuropsychiatry (SCAN), parts of the Addiction Severity Index (ASI), and questionnaires on reasons for cannabis use and reactions to cannabis use while intoxicated. Participants with lifetime depression and problems controlling violent behavior were compared to subjects without such problems. Validity of the groupings was corroborated by use of a psychiatric treatment register, previous use of psychotropic medication and convictions for violence.

Results. Subjects with lifetime depression used cannabis for the same reasons as others. While under the influence of cannabis, they more often experienced depression, sadness, anxiety and paranoia, and they were less likely to report happiness or euphoria. Participants reporting problems controlling violent behavior more often used cannabis to decrease aggression, decrease suspiciousness, and for relaxation; while intoxicated they more often reacted with aggression.

Conclusions. Subjects with prior depression do not use cannabis as a mean of self-medication. They are more likely to experience specific increases of adverse symptoms while under the influence of cannabis, and are less likely to experience specific symptom relief. There is some evidence that cannabis is used as a means of self-medication for problems controlling aggression.

INTRODUCTION

Cannabis use has been linked with increased risk of a range of psychiatric disorders. The reasons for these associations remain controversial. Three main types of explanations have been explored in research on the topic: (1) causal, where cannabis is thought to increase the risk of psychopathology, (2) reverse causation, where psychiatric disorders are a cause of cannabis use, and (3) third factor models, where bias in study design or confounding factors, such as low socio-economic status, other drug use, personality and involvement with drug-using peers, explain the association rather than cannabis *per se* (Johns, 2001; Arseneault *et al.* 2004; Macleod *et al.* 2004).

The possibility that psychiatric disorders may lead to cannabis use has often been discussed in the context of a 'self-medication' hypothesis.

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This model has been advanced to explain drug use not only in relation to psychiatric disorders but also in non-clinical populations (Khantzian, 1985). According to the self-medication hypothesis, individuals who experience negative emotional states seek out specific substances to alleviate specific symptoms (Khantzian, 1985).

In relation to cannabis, the self-medication hypothesis has been most extensively studied in patients suffering from schizophrenia. Some studies have found tentative evidence (Knudsen & Vilmar, 1984; Schneier & Siris, 1987; Dixon *et al.* 1990, 1991; Warner *et al.* 1994; Addington & Duchak, 1997; Ferdinand *et al.* 2005). However, most of these studies are relatively old, and recent reviews agree that there is not much support for the hypothesis that patients suffering from schizophrenia specifically use cannabis to alleviate psychotic symptoms or side-effects of medication (Mueser *et al.* 1998; Smit *et al.* 2004; Spencer, 2004).

A number of studies have documented an association between heavy cannabis use and depression. These studies have been reviewed by Degenhardt *et al.* (2003). Cannabis used as self-medication for depression has been much discussed, but has received little empirical investigation. Some studies have shown that many use the substance to alleviate depressive symptoms (Dixon *et al.* 1990, 1991; Warner *et al.* 1994; Gruber *et al.* 1996, 1997; Ogborne *et al.* 2000). However, it has not been demonstrated that antidepressant effects are specifically sought by cannabis users or that cannabis specifically relieves these problems (Degenhardt *et al.* 2003), or that the risk of cannabis use is higher after the onset of depressive episodes (Bovasso, 2001; Patton *et al.* 2002; Degenhardt *et al.* 2003).

No data exist on cannabis used as self-medication for problems controlling aggression, although cannabis in moderate to high dose appears to suppress aggressive behavior (Myerscough & Taylor, 1985; Hoaken & Stewart, 2003).

We investigated the self-medication hypothesis of depression and aggression in a group of cannabis-dependent subjects. The presence of current or lifetime depression and violent behavior was assessed. We then investigated whether there was any correlation between these psychiatric and behavioral problems and the reasons for cannabis use and reactions during intoxication.

METHOD

Participants

One hundred and nineteen subjects were recruited from 19 different treatment centers for substance dependence in Jutland and Funen, Denmark, between 2002 and 2004. The mean age of the subjects was 22·3 years (S.D. = 3·2, range 16–30, median 22); 99 (83·2%) were males. The average time from start of treatment to the assessment interview was 5 months (S.D. = 5·2, range 0–24, median 3). Forty-eight per cent had used cannabis after the start of treatment.

In a previous study, over 75% of the subjects seeking treatment for cannabis dependence in Denmark were less than 30 years of age (Arendt & Munk-Jørgensen, 2004). Consequently, subjects over 30 years of age were excluded in this study to avoid possible cohort effects and to get a homogeneous sample. In addition, the subjects had to be fluent in Danish, and they had to fulfill ICD-10 criteria (WHO, 1992*a*) for cannabis dependence. Subjects were excluded if there was any doubt whether cannabis dependence was the main reason for entering treatment. This was determined initially by the referring institutions, and subsequently by the interviewer. Daily use of any substance other than cannabis at the time of the interview led to exclusion. Subjects were also excluded if the time-line follow-back method revealed no evidence of cannabis abuse without co-morbid abuse of alcohol or other substances. Subjects suffering from neurological disorders were also excluded.

A total of 146 subjects were approached for screening. Five refused to participate, and one was excluded because of severe epilepsy. Nine subjects were excluded because it could not be ascertained that cannabis was the primary substance of abuse. Twelve subjects were excluded because they were over 30 years of age. All subjects gave written informed consent as required by the Danish Scientific Ethical Committee, who approved the study.

Measures

Lifetime and current psychiatric disorders were assessed through the administration of the Schedules of Clinical Assessment in Neuropsychiatry – computerized version (SCAN; WHO, 1992*b*). Both 'present state' and 'lifetime before' were assessed using the cut-off criteria for affective disorders. If a subject screened positive, the worst episode of the disorder was evaluated further. SCAN was administered by either a clinical psychologist (J.B. or M.A.) or a medical doctor (L.F.). Meetings to discuss ratings to ensure reliability were attended by all interviewers and took place throughout the study period under the supervision of the Danish WHO Collaborating Center for Research and Training in Mental Health.

The 21-item version of the Beck Depression Inventory (BDI-II; Beck *et al*. 1996) was used to validate the presence of current affective symptoms. Sections of the Addiction Severity Index (ASI; McLellan *et al*. 1980) were used to determine levels of drug and alcohol use for both the preceding month and lifetime. Items on substance dependence from the Composite International Diagnostic Interview (CIDI; WHO, 1997) were used to ascertain that subjects fulfilled diagnostic criteria for cannabis dependence according to ICD-10. Subjects were asked to estimate the total number of separate occasions of cannabis use (+5000 times and +10 000 times). In accordance with the Danish Board of Health, we defined alcohol misuse as a prolonged period of more than 21 units of alcohol intake per week for males and 14 units for females, or recurring drinking binges. Follow-back time-lines (Sobell *et al*. 1979), from early adolescence to the day of the interview, were used prior to the structured interview and psychiatric assessment to establish psychopathology and substance use patterns. After the interview these time-lines were adjusted if new information appeared.

Demographic characteristics and problems controlling violent behavior were assessed through a series of closed questions. Violent behavior was defined as recurrent tendencies to initiate fights or harm other people physically. As estimation of such behavior is subjective, we also asked if the participants had ever been convicted of violence, and made separate analyses for this measure. Information on problems controlling violent behavior was missing for four subjects, and therefore analyses of these problems are based on 115 subjects.

Reasons for cannabis use and reactions while intoxicated were assessed by use of two questionnaires administered by the investigators. Reasons for cannabis use were given in response to the question: 'Why do you use cannabis?' The subjects were asked to choose their answers from a number of different possibilities. To determine the reactions to cannabis use the subjects were asked the question: 'How often have you experienced the following reactions to cannabis use, while "high" or under the influence of the substance?' The same five-point Likert scale was used for both of these questionnaires. The scale consists of the categories: 1 = never, 2 = rarely, 3 = sometimes, 4 = often, 5 = always. The items in the two scales are partly based on similar questionnaires used by Dixon *et al*. (1991) and Addington and Duchak (1997) in investigations of reasons for cannabis use and reactions to cannabis in patients with schizophrenia. We eliminated some categories pertaining specifically to psychotic symptoms and sexuality and added questions on aggression. The psychiatric assessment and the questionnaires on reasons for use and reactions to cannabis use were administered at different times during the interview, and the subjects were not informed that these data would be combined.

Register

Information was retrieved from The Danish Psychiatric Case Register (DPCR; Munk-Jørgensen & Mortensen, 1997) to further validate lifetime diagnoses of psychiatric disorders. This register contains information on admissions to Danish psychiatric hospitals and departments since 1970. Out-patient treatment provided by psychiatric hospitals has been registered since 1995. We retrieved information on all patients from the time they were born until 1 February 2006. The register therefore captures all psychiatric treatment in Denmark provided by hospitals and out-patient clinics.

Groupings and validation of diagnoses

Group 1: *Depression*

Evidence of either dysthymia or at least one depressive episode in the absence of substance intoxication or withdrawal was assessed through the use of SCAN. Fifty-five subjects had experienced at least one depressive episode or suffered from dysthymia, according to ICD-10 criteria, and they were compared with the remaining 64 subjects. Sixty-two per cent of the subjects in the 'depression group' had received antidepressant medication. Data from the DPCR revealed that 18 subjects (33%) had been admitted to, or received out-patient treatment at, a psychiatric hospital for depression or adjustment disorder before or after our assessment. One subject was registered with depression before our assessment, without being included in our depression group.

Group 2: *Violent behavior*

Subjects who answered 'yes' to the question: 'Have you ever experienced problems controlling violent behavior?', as defined above, were included in this group. The 58 subjects with a history of such problems were compared with the remaining 57 subjects. The subgroup who answered 'yes' to the question: 'Have you ever been convicted of violence?' were analyzed separately. Twenty-three subjects had received a sentence for violence, and they were compared with the 57 subjects with no history of problems controlling violent behavior.

Twenty-four subjects (41%) in the 'violent behavior group' were also in the 'depression group', and being in one group was not associated with being in the other ($\chi^2 = 1{\cdot}46$, $p = 0{\cdot}23$). Three subjects fulfilled lifetime criteria for a schizophrenia spectrum disorder (F20 schizophrenia, F21 schizotypal disorder, or F25 schizo-affective disorder). All of these subjects were included in the group with prior depressive episodes. None of them had received a sentence for violence, and one reported problems controlling violent behavior. The diagnostic information was confirmed by use of the DPCR. One additional patient was registered with a schizophrenia diagnosis in the DPCR without being diagnosed with lifetime schizophrenia during the SCAN interview. This patient was included in the group with no lifetime depression. None of the subjects fulfilled lifetime criteria for manic episodes or bipolar affective disorder. This was consistent with register data.

Statistics

The analyses consist of comparisons between the groups described above ('depression group' compared with 'no depression group', and 'violent behavior' group compared with 'no violent behavior group'). χ^2 tests were used for comparisons on categorical variables. The Mann–Whitney rank-sum test was used for comparisons of age and average scores on the BDI. Items from the questionnaires 'reasons for cannabis use' and 'reactions to cannabis use' were used as outcome measures for all group comparisons. Logistic regression models for ordinal outcomes, specifically proportional-odds models (McCullagh & Nelder, 1989), were used for these analyses. It was decided in advance to adjust for possible gender differences in these analyses, as the prevalence rate for depression differs between the two genders and there are no previously published data on gender differences in relation to these outcomes. Overall, we performed 74 comparisons with 'reasons for cannabis use' or 'effects of cannabis use while intoxicated' as outcomes. Because of the exploratory nature of the study, p values $<0{\cdot}05$ are reported. Two-sided tests were applied for all analyses. SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) and Stata Statistical Software release 9.2 (Stata Corporation, College Station, TX, USA) were used for the statistical analyses.

RESULTS

Demographics and substance use

A summary of the demographic characteristics and substance use patterns is presented in Table 1. The average age at first cannabis use was 14·1 years (S.D. = 1·8, range 10–18, median 14). All subjects had a history of daily cannabis use, and the average age for first daily use was 15·5 years (S.D. = 2·0, range 11–21, median 15). The average duration of daily use was 71 months (S.D. = 36, range 2–180, median 63). Nearly all subjects (92·2%) had used cannabis more than 5000 times and 66·4% had used cannabis on more than 10 000 separate

Table 1. *Demographic characteristics and co-morbid substance use*

	All subjects ($n=119$)	No depression ($n=64$) *versus* depression ($n=55$)	No violent behavior ($n=57$) *versus* violent behavior ($n=58$)
Age (years)	22·3	21·3 *v.* 23·4***	22·9 *v.* 21·7
Male gender (%)	83·2	92·2 *v.* 72·7**	77·2 *v.* 87·9
No education beyond elementary school (%)	73·1	81·3 *v.* 63·6*	71·9 *v.* 74·1
State subsidies are primary source of income (%)	76·5	68·8 *v.* 85·5*	73·7 *v.* 77·6
Age at first cannabis use (years)	14·1	13·8 *v.* 14·4	14·5 *v.* 13·7*
Age at first daily cannabis use (years)	15·5	15·1 *v.* 15·9	16·1 *v.* 15·0*
Heavy use of opioids (%)	4·2	3·1 *v.* 5·5	1·8 *v.* 5·2
Heavy use of stimulants (%)	47·9	51·6 *v.* 43·6	29·8 *v.* 65·5***
Heavy use of hallucinogens (%)	21·0	20·3 *v.* 21·8	7·0 *v.* 36·2***
Heavy use of alcohol (%)	29·4	23·4 *v.* 36·4	21·1 *v.* 36·2
Average BDI score (mean)	14·3	12·1 *v.* 17·1*	13·9 *v.* 14·4

BDI, Beck Depression Inventory.
* $p<0·05$, ** $p<0·01$, *** $p<0·001$.

occasions. The majority (82·4%) reported hashish as the most frequently used type of cannabis, while all the remaining subjects, except one, used a combination of pot/marijuana, skunk and hashish.

Almost all subjects had used other substances at some time. Lifetime use of heroin (20%), morphine (33%), methadone (7%), amphetamine (95%), cocaine (74%), ecstasy (71%), LSD/mushrooms (72%) and benzodiazepines (52%) was reported. Misuse of alcohol over an extended time period was reported by 29%. Heavy use of other substances, defined as use on at least 100 separate occasions, was reported by 48% for stimulants (amphetamine or cocaine), 21% for hallucinogens (ecstasy or LSD/mushrooms), and 4% for opioids (heroin, morphine or methadone) (see Table 1). The subjects describing problems controlling violent behavior more often reported heavy use of both stimulants ($\chi^2=14·7$, $p<0·001$) and hallucinogens ($\chi^2=14·4$, $p<0·001$).

Reasons for cannabis use

In Table 2 the reasons for cannabis use are ranked. The most frequently reported reasons were relaxation, pleasure seeking and the experience of being 'high'. Other common reasons were to relieve unwanted emotions such as depression and aggression. Cannabis was often used to go along with the group, but rarely to make the subjects more outgoing. Some apparently used it for inspirational purposes, such as getting more thoughts or interests, but these reasons were less often reported. Cannabis was not used to increase energy, decrease tiredness or improve concentration. There were also some gender differences. Women less frequently used cannabis for relaxation [odds ratio (OR) 0·3, 95% confidence interval (CI) 0·1–0·8, $p<0·05$], to 'get high' (OR 0·2, 95% CI 0·1–0·5, $p<0·01$) or to go along with the group (OR 0·3, 95% CI 0·1–0·7, $p<0·01$).

There were no differences in reasons for cannabis use between subjects with a history of depression compared with others, after adjustment for the potential influence of gender (see Table 2). Those who had problems controlling violent behavior more frequently reported using cannabis to decrease aggression (OR 4·5, 95% CI 2·2–9·1, $p<0·0001$). This group also used the substance for relaxation (OR 2·1, 95% CI 1·0–4·4, $p<0·05$) and to decrease suspiciousness (OR 2·4, 95% CI 1·2–5·0, $p<0·05$) more than other users. The subgroup with a conviction for violence ($n=23$) more often used cannabis to decrease aggression (OR 6·3, 95% CI 2·4–16·9, $p<0·001$) and to relieve depression (OR 2·7, 95% CI 1·0–7·0, $p<0·05$) (results not shown).

As is evident from Table 1, co-morbid heavy use of both stimulants and ecstasy was associated with problems controlling aggression. To control for possible confounding, we performed two additional regression analyses. In the first, we entered heavy use of stimulants, hallucinogens and problems controlling violent behavior, along with gender, as covariates explaining the outcome of using cannabis to decrease aggression. In the second analysis, conviction for

Table 2. *Reasons for cannabis use*

Reason for use	All subjects ($n=119$) Average ('often' or 'always' %)	No depression ($n=64$) *versus* depression ($n=55$)	No violent behavior ($n=57$) *versus* violent behavior ($n=58$)
To relax	4·39 (85·7)	4·42 *v.* 4·35	4·26 *v.* 4·53*
To 'get high'	4·39 (82·4)	4·53 *v.* 4·22	4·33 *v.* 4·41
To increase pleasure	4·29 (81·5)	4·36 *v.* 4·20	4·26 *v.* 4·31
To relieve depression	3·62 (56·3)	3·67 *v.* 3·56	3·46 *v.* 3·74
To go along with the group	3·48 (56·8)	3·60 *v.* 3·35	3·21 *v.* 3·77
To decrease aggression	3·13 (48·8)	3·17 *v.* 3·09	2·51 *v.* 3·74****
To give one more thoughts	2·41 (27·7)	2·28 *v.* 2·56	2·46 *v.* 2·41
To become more outgoing	2·33 (22·7)	2·44 *v.* 2·20	2·28 *v.* 2·36
To give one more interests	2·32 (21·2)	2·33 *v.* 2·31	2·42 *v.* 2·21
To feel more emotions	2·24 (17·6)	2·16 *v.* 2·35	2·18 *v.* 2·26
To concentrate better	2·10 (15·1)	2·19 *v.* 2·00	2·09 *v.* 2·16
To decrease suspiciousness	2·08 (20·5)	2·10 *v.* 2·06	1·77 *v.* 2·44*
To increase energy levels	1·82 (11·8)	1·95 *v.* 1·65	1·88 *v.* 1·76
To decrease tiredness	1·64 (5·0)	1·64 *v.* 1·64	1·54 *v.* 1·72

Average scores are reported on a Likert scale with values: 1 = never, 2 = rarely, 3 = sometimes, 4 = often, 5 = always.
All comparisons are adjusted for gender.
* $p<0·05$, **** $p<0·0001$.

violence was entered instead of problems controlling violent behavior in the same model. The association between problems controlling violent behavior (OR 5·0, 95% CI 2·3–10·8, $p<0·0001$), convictions for violence (OR 6·9, 95% CI 2·3–20·8, $p<0·001$) and using cannabis to decrease aggression remained.

Effects of cannabis use

Positive effects such as relaxation, happiness and euphoria were very common while under the influence of cannabis (Table 3). Changes in cognition such as altered visual, auditory or temporal perception and a sense that thoughts slow down were also frequent. Adverse effects were less pronounced but still frequent; delusions and paranoia were the most commonly reported. Depression and anxiety were relatively rare experiences, while anger and aggression were among the least likely reactions. The majority (69%) had never experienced auditory or visual hallucinations while using cannabis, and very few (5%) reported that such symptoms occurred 'often' or 'always'. There were also some gender differences. Women were less likely to report relaxation while being intoxicated (OR 0·4, 95% CI 0·1–0·9, $p<0·05$), but this was still their most common reaction. They were more likely to experience sadness (OR 5·3, 95% CI 2·0–13·5, $p<0·001$) and depression (OR 2·4, 95% CI 1·0–5·8, $p<0·05$) than men.

The subjects who had experienced at least one episode of depression differed from the rest of the sample in their pattern of reactions to cannabis (see Table 3). After adjustment for potential gender differences, they were more likely to experience sadness (OR 3·5, 95% CI 1·7–7·2, $p<0·001$), depression (OR 3·7, 95% CI 1·8–7·5, $p<0·001$), paranoia (OR 3·1 95% CI 1·5–6·2, $p<0·01$) and anxiety (OR 3·9, 95% CI 1·9–8·0, $p<0·001$) and less likely to report happiness (OR 0·5, 95% CI 0·2–0·9, $p<0·05$) and euphoria (OR 0·5, 95% CI 0·2–0·9, $p<0·05$). Because 22 subjects (40%) in the 'depression group' also fulfilled criteria for an anxiety disorder at some point, we compared the subjects with depression only to those with a history of depression and co-morbid anxiety on all outcome measures included in Tables 2 and 3. The only significant difference was that those with a co-morbid anxiety disorder at some point were more likely than those with depression only to react with anxiety while intoxicated (OR 3·1, 95% CI 1·1–9·0, $p<0·05$). Consequently, we compared the subjects with depression only to the subjects without a history of depression in a regression analysis adjusted for gender. Even after exclusion of those with co-morbid anxiety, the subjects in the depression alone subgroup were more likely than subjects without a history of depression to react with anxiety while intoxicated (OR 3·0, 95% CI 1·3–7·0, $p<0·01$).

Table 3. *Effects of cannabis use while intoxicated*

Experience while under the influence of cannabis	All subjects ($n=119$) Average ('often' or 'always' %)	No depression ($n=64$) *versus* depression ($n=55$)	No violent behavior ($n=57$) *versus* violent behavior ($n=58$)
Relaxed	4·49 (89·1)	4·52 *v.* 4·45	4·35 *v.* 4·59
Memory impairment	3·99 (73·9)	4·03 *v.* 3·95	3·82 *v.* 4·12
Happy	3·67 (58·0)	3·88 *v.* 3·44*	3·54 *v.* 3·72
Change in time perception	3·45 (50·4)	3·45 *v.* 3·45	3·33 *v.* 3·55
Changed perception	3·42 (55·1)	3·51 *v.* 3·31	3·53 *v.* 3·32
Thoughts slow down	3·42 (47·1)	3·45 *v.* 3·38	3·35 *v.* 3·47
Delusional	3·35 (44·5)	3·38 *v.* 3·33	3·21 *v.* 3·48
Slower movements	3·31 (45·8)	3·25 *v.* 3·38	3·32 *v.* 3·35
Euphoric	3·18 (48·3)	3·43 *v.* 2·89*	3·05 *v.* 3·34
Confused	2·99 (31·1)	2·95 *v.* 3·04	3·00 *v.* 2·98
Empty inside	2·80 (35·6)	2·73 *v.* 2·87	2·67 *v.* 2·98
Outgoing	2·66 (23·5)	2·73 *v.* 2·56	2·72 *v.* 2·64
Suspicious/paranoid	2·61 (24·4)	2·31 *v.* 2·96**	2·60 *v.* 2·66
Restless	2·45 (20·2)	2·39 *v.* 2·51	2·47 *v.* 2·45
Nervous	2·45 (16·0)	2·30 *v.* 2·64	2·44 *v.* 2·47
Anxious	2·22 (10·9)	1·88 *v.* 2·62***	2·30 *v.* 2·17
Sad	2·19 (9·3)	1·86 *v.* 2·56***	2·21 *v.* 2·17
Depressed	2·16 (10·9)	1·80 *v.* 2·58***	2·11 *v.* 2·26
Increased energy	2·02 (9·2)	2·08 *v.* 1·95	1·93 *v.* 2·10
Depersonalization	1·81 (11·8)	1·66 *v.* 1·98	1·82 *v.* 1·83
Angry	1·74 (3·4)	1·86 *v.* 1·60	1·58 *v.* 1·88
Aggressive	1·50 (3·4)	1·56 *v.* 1·42	1·21 *v.* 1·79***
Auditory or visual hallucinations	1·47 (5·0)	1·52 *v.* 1·42	1·49 *v.* 1·45

Average scores are reported on a Likert scale with values: 1 = never, 2 = rarely, 3 = sometimes, 4 = often, 5 = always.
All comparisons are adjusted for gender.
* $p<0·05$, ** $p<0·01$, *** $p<0·001$.

The subjects who reported difficulties controlling violent behavior were more likely to react with aggression (OR 4·4, 95% CI 1·9–10·2, $p<0·001$) than the rest of the sample. However, even in this group aggression was one of the least likely reactions. The subgroup with convictions for violence ($n=23$) were more likely to report increased aggression (OR 11·9, 95% CI 3·8–37·8, $p<0·0001$) and feeling empty inside (OR 4·6, 95% CI 1·8–12·2, $p<0·01$), and less likely to experience changed perception (OR 0·3, 95% CI 0·1–0·8, $p<0·05$) or be more outgoing (OR 0·4, 95% CI 0·2–1·0, $p<0·05$) (results not included).

DISCUSSION

This study demonstrates that subjects with a history of depression use cannabis for the same reasons as others, that is to relax, 'get high' and increase pleasure, but also to relieve depression or aggressive impulses. Accordingly, it could not be demonstrated that cannabis is used specifically to self-medicate for depression. Those who reported problems controlling violent behavior more often used cannabis for relaxation and to decrease suspiciousness, and they were much more likely to use cannabis to decrease aggression. This could indicate that cannabis is used as a means of self-medication in this respect. An interesting pattern emerged from the analyses of reactions to cannabis while intoxicated. Depressive symptoms and aggression were significantly more common in users with a lifetime history of such problems, rather than vice versa. Furthermore, there was a trend for those with prior depression to report less positive consequences, such as happiness and euphoria, while under the influence of cannabis.

Mueser *et al.* (1998) have argued that convincing evidence for the concept of self-medication might include (*a*) self-report studies in which patients describe particular substances alleviating specific symptoms of mental illness, (*b*) epidemiological studies showing that patients with particular diagnoses select specific substances, and (*c*) studies showing that

specific substances are used in response to specific symptoms of mental illness. Little is known about the first and third of these points concerning cannabis. It has been shown that heavy cannabis users seeking substance abuse treatment have elevated levels of depression, and behavioral problems (Stephens *et al*. 1993; Budney *et al*. 2000; Copeland *et al*. 2001; Grella *et al*. 2001; Stephens *et al*. 2002; Tims *et al*. 2002; Arendt & Munk-Jørgensen, 2004). Epidemiological studies have also shown an association between cannabis use disorders and affective disorders (e.g. Conway *et al*. 2006). The self-medication hypothesis has been proposed as an explanation of this fact, mainly based on studies showing that regular cannabis users often report using the substance to relieve depression and anxiety (Gruber *et al*. 1996, 1997; Reilly *et al*. 1998; Ogborne *et al*. 2000).

The subjective experiences of cannabis intoxication and the reasons for cannabis use have been investigated in non-clinical samples (Johnson & O'Malley, 1986; Thomas, 1996; Atha & Blanchard, 1997; Gruber *et al*. 1997; Lyons *et al*. 1997; Reilly *et al*. 1998), in patients suffering from schizophrenia (Knudsen & Vilmar, 1984; Negrete *et al*. 1986; Dixon *et al*. 1991; Warner *et al*. 1994; Addington & Duchak, 1997) and in placebo-controlled medical trials (Tramer *et al*. 2001). However, very few studies have emphasized the interplay between psychopathology and reasons for use and reactions while intoxicated. Only two studies report detailed data on reasons for cannabis use and symptoms while intoxicated among subjects with specific psychiatric disorders or behavioral problems. Both of these are concerned with cannabis-using patients suffering from schizophrenia (Dixon *et al*. 1991; Addington & Duchak, 1997). There are also some problems in previous studies concerning reasons for cannabis use and reactions to the substance. Most involve infrequent cannabis users. In addition, few studies have systematically asked about a range of possible self-perceived reasons for use, or symptoms while under the influence of cannabis. This is the first study to correlate a history of depression and violent behavior with reasons for use and reactions while intoxicated. A major advantage is the use of a sample of long-term heavy cannabis users with a high level of co-morbid psychiatric disorders, and the use of a comprehensive questionnaire to evaluate the reasons for use and the subjective reactions to the substance.

We found no evidence of specific self-medication for depression. A central point of disagreement seems to be one of specificity – whether subjects specifically use cannabis to counteract depressive symptoms. Generally there has not been much support for such a proposal, either in the cannabis literature or in studies concerning other drugs (Mueser *et al*. 1998). For example, Spencer (2004) points out that cannabis is used by patients with schizophrenia for the same reasons as other users, and that other substances, such as alcohol, are used to achieve the same effects. Similarly, in a study on the association between depression and opioid or cocaine addiction, Weiss *et al*. (1992) found that all patients experienced mood elevation, regardless of drug of choice. However, this is the first study to demonstrate this lack of specificity between reasons for regular cannabis use and depression. If anything, it seems that subjects with prior depression are more likely to experience specific increases of adverse symptoms while under the influence of cannabis, and less likely to experience specific symptom relief. There are other ways of approaching the self-medication hypothesis, including sequential timing of onset of depression and substance use disorders (Mueser *et al*. 1998). These approaches have led to the same negative conclusions as those found in this paper (Degenhardt *et al*. 2003).

On the contrary, lowering of aggression proved to be one of the main reasons for cannabis use among subjects with difficulties controlling violent behavior, and among those with prior convictions for violence. While under the influence of cannabis these subjects were also more likely to react with aggression. No previous study has included data on decreased aggression/anger as a reason for cannabis use, and only one prior investigation showed that anger is an infrequent consequence while intoxicated (Addington & Duchak, 1997). The fact that cannabis could be used as a mean of self-medication in this respect is in line with previous research showing that cannabis intoxicated subjects are less likely to react aggressively (Hoaken & Stewart, 2003), and also with

the fact that relaxation is found to be the most common reason for use and effect while intoxicated. However, we used a crude measure of problems controlling violent behavior. The results need to be replicated in future studies using a more sophisticated assessment of impulsivity, aggression proneness or personality factors.

There are some limitations to the study. The evaluations of depressive episodes and violent behavior were retrospective, and consequently there is risk of recall bias. However, the diagnostic data were corroborated by more objective measures such as previous use of antidepressant medication and convictions for violence, as well as register data. In addition, the prevalence of depression is in line with findings from other investigations on treatment-seeking cannabis users (Budney *et al*. 2000; Copeland *et al*. 2001; Stephens *et al*. 2002; Dennis *et al*. 2004), as well as daily cannabis users from the general population (Patton *et al*. 2002).

It is possible that the higher level of depressive symptoms while intoxicated, among those with lifetime depression, might be explained by report bias (e.g. a tendency to report higher levels of depressive symptoms, or current depressive symptoms leading to a mood-congruent memory bias). However, although the BDI scores differed significantly between the groups, they were only marginally higher in the lifetime depression group compared with the rest of the sample. In addition, if report bias was the explanation, it should also pertain to the results on reasons for cannabis use, and on this measure the subjects in the lifetime depression group were similar to the comparison group.

We assessed reactions to cannabis shortly after the subjects entered treatment. This may lead to recall bias. Such bias can only be avoided by gathering information while the subjects are under the influence of cannabis, and this was not possible for ethical reasons and because the subjects were recruited from treatment settings. It would also have been preferable to assess reasons for use while the subjects were experiencing symptoms of depression or elevated aggression. It is possible that during depressive episodes, individuals may use cannabis for different reasons than during remission. It might be hypothesized that the subjects were aware that the questions on reasons for cannabis use and effects while intoxicated, on the one hand, and depression and aggression, on the other, would be correlated, and that they adjusted their answers accordingly. However, this is unlikely because the questions on cannabis use were posed in the beginning of the interview while the psychiatric evaluation and the questions on history of aggressive behavior were at the very end. Additionally, the subjects were not informed that the concept of self-medication would be explored, and two of the three interviewers were unaware of this aim of the study.

In some cases it was difficult to determine whether the symptoms of depression and problems controlling violent behavior were substance induced, even though the subjects were asked to dismiss symptoms occurring while intoxicated or in a withdrawal state. Despite much effort by the data collectors, many of the subjects had been using cannabis or other drugs with minimal abstinence periods since childhood or early adolescence. However, the subjects did display a rate of co-morbid substance use similar to that reported in other studies on cannabis users in substance abuse treatment (e.g. Stephens *et al*. 1993; Copeland *et al*. 2001; Urbanoski *et al*. 2005).

The study includes a large number of comparisons. We chose not to adjust for this, and the issue of Type I error is therefore of concern. This is especially important to consider when evaluating findings that are significant at a modest level. However, it should be evident that the majority of the findings were significant even at conservative significance levels. Only 20 females were included in the study and therefore results regarding this subgroup may not be accurate.

The concentrations and relative contents of Δ^9-tetrahydrocannabinol (THC) and cannabidiol (CBD) vary in different preparations of cannabis (ElSohly, 2000). Furthermore, the psychological effects of THC and CBD differ and are dose dependent (Ashton *et al*. 2005). It is therefore possible that subjects who primarily use marijuana seek other effects than those who use hashish. However, we were unable to address this issue because our subjects predominantly used hashish, either alone or in combination. Furthermore, we were not able to assess the exact dose that the subjects were typically using.

ACKNOWLEDGMENTS

We thank Aksel Bertelsen from the Danish WHO Collaborating Center, and all the 19 substance abuse treatment centers for their co-operation. The study received internal funding from the Center for Basic Psychiatric Research, Aarhus University Hospital.

DECLARATION OF INTEREST

None.

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