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Attributes of long-term heavy cannabis users: a case–control study

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ABSTRACT

Background. Although cannabis is the most widely used illicit drug in the United States, few recent American studies have examined the attributes of long-term heavy cannabis users.

Method. Using a case–control design, we obtained psychological and demographic measures on 108 individuals, age 30–55, who had smoked cannabis a mean of 18 000 times and a minimum of 5000 times in their lives. We compared these heavy users to 72 age-matched control subjects who had smoked at least once, but no more than 50 times in their lives.

Results. We found no significant differences between the two groups on reported levels of income and education in their families of origin. However, the heavy users themselves reported significantly lower educational attainment ($P<0{\cdot}001$) and income ($P=0{\cdot}003$) than the controls, even after adjustment for a large number of potentially confounding variables. When asked to rate the subjective effects of cannabis on their cognition, memory, career, social life, physical health and mental health, large majorities of heavy users (66–90%) reported a 'negative effect'. On several measures of quality of life, heavy users also reported significantly lower levels of satisfaction than controls.

Conclusion. Both objective and self-report measures suggest numerous negative features associated with long-term heavy cannabis use. Thus, it seems important to understand why heavy users continue to smoke regularly for years, despite acknowledging these negative effects. Such an understanding may guide the development of strategies to treat cannabis dependence.

INTRODUCTION

Americans who use cannabis typically try the drug for the first time in adolescence (Chen & Kandel, 1995; Monitoring the Future Study). However, most cease cannabis use by their late twenties or early thirties, and only a minority continues regular use into middle age (Kandel & Chen, 2000). What distinguishes long-term heavy users from those who try cannabis only briefly in adolescence or early adulthood?

Several types of studies bear on this question. First, recent evidence suggests an important genetic component in cannabis dependence (Bierut *et al*. 1998; Kendler & Prescott, 1998; True *et al*. 1999). Genetic studies alone, however, provide little information about the demographic and psychological attributes of long-term users. One of the best studies to address this question is a 19-year follow-up of 708 individuals who began using cannabis in adolescence (Chen & Kandel, 1995, 1998; Kandel & Chen, 2000). One analysis of this cohort looked at predictors of cessation of use (Chen & Kandel, 1998); frequent users, those who started use early, and those who used other illicit drugs were less likely to have stopped use on follow-up at age 34–35. Use of cannabis to alter mood decreased the odds of stopping; use for social reasons increased the odds of stopping. In a subsequent study, the same investigators identified four types of

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users via cluster analysis: early-onset heavy use, early-onset light use, mid-onset heavy use, and late-onset light use (Kandel & Chen, 2000). The two heavy-using groups significantly differed from the two light-using groups in being male, using cannabis to enhance positive feelings, having cannabis-using friends in young adulthood, and being delinquent in adolescence.

In addition to these longitudinal data, many studies have provided cross-sectional comparisons of heavy cannabis users *versus* non-users or light users. Most of these studies, however, were performed more than 25 years ago (Brill *et al*. 1971; Mirin *et al*. 1971; Hochman & Brill, 1973; Kupfer *et al*. 1973; Brill & Christie, 1974) or in different cultures, such as Jamaica (Rubin & Comitas, 1975), Costa Rica (Carter *et al*. 1980; Page *et al*. 1988), Nepal (Sharma, 1975), India (Mendhiratta & Wig, 1975; Mendhiratta *et al*. 1978), or Egypt (Soueif, 1975). Thus, their results may not generalize to the contemporary American population. Several additional studies have examined samples in which the majority of subjects were too young to qualify as long-term heavy cannabis users (Hogan *et al*. 1970; Kandel, 1984; Hammer & Vaglum, 1990; Kouri *et al*. 1995). We are aware of only two recent studies that have examined long-term heavy users over the age of 30. Bourque *et al*. (1991) compared 277 heavy users in Los Angeles with 350 subjects from a representative population sample of Los Angeles County residents, matched for age (mean 32, range 24–49), and race (all subjects were Caucasian). However, controls were not assessed for cannabis use; some may perhaps have used cannabis frequently. In comparisons adjusted for gender, heavy users did not differ from controls on completed education, reported health, or use of alcohol and tobacco, but they reported significantly lower incomes, lower marital rates, and higher unemployment rates. Reilly *et al*. (1998) described 268 long-term heavy users in rural Australia with a mean age of 36. Almost all of these individuals reported some negative aspects of cannabis use, but 72% believed that 'the benefits of cannabis outweighed the risks'; 21% reported an 'even balance' and 7% stated that cannabis had 'done them more harm than good'. However, this study lacked a comparison group of non-users or infrequent users.

In summary, despite the many available studies of heavy cannabis users, no recent American study, to our knowledge, compares the attributes of long-term users (mean age >30 years) with non-users or light users. To augment these limited recent data, we obtained demographic and psychological data from 108 long-term heavy users, who had smoked at least 5000 times in their lives, and 72 control subjects who had smoked at least once, but fewer than 50 times in their lives. These subjects, all aged 30–55 years, were recruited in the course of a recent study examining the residual neuropsychological effects of cannabis (Pope *et al*. 2001).

METHOD

Subjects and procedures

We used newspaper advertisements and word-of-mouth to recruit individuals age 30–55 years in three groups: (1) current long-term heavy users who reported at least 5000 lifetime episodes of cannabis use, and who were currently smoking at least seven times per week; (2) former long-term heavy users who also reported at least 5000 lifetime episodes of smoking, but no more than one episode per week during the last 3 months; and (3) control subjects who reported that they had smoked cannabis at least once, but no more than 50 times in their lives. For these purposes, an 'episode' of smoking cannabis was defined as separated by at least one hour from another episode. Thus, an individual with 5000 episodes of smoking would need to have smoked at least once per day for approximately 14 years, or at least twice per day for at least 7 years.

We excluded subjects on telephone screening if they reported: (1) use of any other class of illicit drugs more than 100 times in their lives; (2) evidence to suggest that they had experienced alcohol abuse or dependence; (3) evidence of a current DSM-IV Axis I disorder other than simple phobia or social phobia; (4) a history of head injury with loss of consciousness requiring hospitalization; (5) current use of any psychoactive medications; or (6) evidence of a clinically significant medical or psychiatric condition that might affect cognitive functioning. We did not attempt to match the three groups

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on any variable except gender; since heavy users were disproportionately male, we accepted women into the control group only in proportion to the number of women recruited for the two heavy user groups. Further details of our recruitment procedures, including a flow sheet showing subjects accepted and withdrawn, have been provided elsewhere (Pope *et al*. 2001).

Subjects qualifying on telephone screening were then entered into a 28-day period of supervised abstinence from cannabis, as described in detail previously (Pope *et al*. 2001). A total of 180 subjects – 108 heavy users (63 current and 45 former) and 72 controls – met all entrance criteria and completed the study. On the first day of the study (study day 0), all subjects were seen for a baseline evaluation that included a history of their psychoactive substance use, questions about the chronology of their cannabis use, demographic questions about both themselves and their families, medical history and the Structured Clinical Interview for DSM-IV (SCID) (First *et al*. 1996). For the 108 heavy users, we also elicited 14 additional subjective ratings, using questions of our own design. These included ratings of the effects of cannabis use on six aspects of their lives (see items in Table 2 below) and ratings of 10 aspects of their quality of life (see items in Table 3 below). We also administered two measures of symptoms of childhood attention deficit hyperactivity disorder (ADHD) – the Wender Utah Rating Scale (WURS) (Ward *et al*. 1993) and the ADHD rating scale (DuPaul, 1991), with the latter instrument modified to include 18 questions covering all of the DSM-IV inattention criteria and hyperactivity-impulsivity criteria (Findling *et al*. 1996). However, these two instruments were introduced after the study began and were administered to only 109 of the 180 subjects (33 current users, 31 former users and 45 controls). We calculated a conduct disorder score by adding the scores on four items on the WURS: 'ran away from home'; 'gets into fights'; 'trouble with authorities, trouble with school, visits to the principal's office'; and 'trouble with the police, booked, convicted'. We assessed history of DSM-IV Axis I psychiatric disorders in the subjects' first-degree relatives using semi-structured questions as described previously (Hudson *et al*. 1987).

Statistical analysis

We first compared the current heavy users versus the former heavy users on all variables assessed (i.e. each of the demographic items and all items in Tables 1–3 below, plus ADHD and conduct disorder scores), using Fisher's exact test for unordered categorical variables, a non-parametric trend test for $2 \times K$ ordered categories (Cuzick, 1985), and the t test for continuous variables. In virtually all cases, we found no statistically significant difference between these two groups. This finding was not surprising, since the current and former heavy users differed only modestly in their usage patterns. By definition, all subjects in both groups had smoked >5000 times; all of the 63 current heavy users and 36 (80%) of the 45 former heavy users had smoked daily or near-daily to at least the age of 30. In the occasional instances where we found a significant difference between the current and former heavy users, it is indicated in the text.

In Tables 1–3 below, we have shown values for current and former heavy users separately for the interested reader, but we found no significant differences between these groups on any of the variables. Therefore, for statistical comparison with the control subjects, we pooled the two user groups into a single 'heavy user' group and performed two-way comparisons of all heavy users *versus* controls, adjusting for variables that might confound the association between group and attribute measures, using the method of propensity scores analysis (Rosenbaum & Rubin, 1993; Rubin, 1997). This method generalizes the technique of stratification and thereby reduces dependence on modelling assumptions. It also permits adjustment for a large number of covariates with only a small number of parameters in the final model. To estimate scores for the propensity to be a heavy user, we performed logistic regression with heavy user as the outcome variable and a set of predictor variables, chosen from available baseline demographic measures that could not reasonably be considered consequences of cannabis use: sex; age; mother's and father's educational level; parents' income; region in which the subject grew up (urban *v*. suburban or rural); the subject's reported sexual orientation; and the presence of (*a*) a mood disorder,

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Table 1. *Features of long-term heavy users* v. *control subjects*

Demographic features	Heavy users: Current ($N=63$)	Heavy users: Former ($N=45$)	Heavy users: All ($N=108$)	Controls ($N=72$)	P unadjusted	OR	Adjusted* 95% CI	P
At least one parent graduated college	32 (57·1)[a]	26 (57·8)[c]	58 (58·0)[e]	36 (51·4)[h]	0·65			
Subject graduated college	21 (33·3)	26 (50·8)	47 (43·5)	56 (77·8)	<0·001	0·21	0·10, 0·45	<0·001
Income								
Family <$30 000	17 (27·4)[b]	10 (22·7)[c]	27 (25·5)[f]	13 (18·1)	0·28			
Subject's Household <$30 000	31 (49·2)	24 (53·3)	55 (50·9)	19 (26·4)	0·001	0·32	0·15, 0·68	0·003
Family history								
Any Axis I disorder	37 (59·7)[b]	21 (48·8)[d]	58 (55·2)[g]	26 (37·1)[h]	0·02			
Substance abuse or dependence	31 (50·0)[b]	20 (46·5)[d]	51 (48·6)[g]	20 (28·6)[h]	0·01			

Due to missing data; [a]$N=56$; [b]$N=62$; [c]$N=44$; [d]$N=43$; [e]$N=100$; [f]$N=106$; [g]$N=105$; [h]$N=70$.
* Adjusted for propensity score analysis. Family-of-origin variables are unadjusted because these variables were used to calculate propensity score; see text.

Table 2. *Subjective effects of cannabis*

Variable	Effect: Positive N (%)	Effect: None N (%)	Effect: Negative N (%)
Current heavy cannabis users ($N=63$)			
What effect has marijuana had on your …			
Cognition	1 (1·6)	5 (7·9)	57 (90·5)
Memory	0 (0·0)	6 (7·9)	57 (90·5)
Career	0 (0·0)	13 (20·6)	50 (79·4)
Social life	3 (4·8)	16 (25·4)	44 (69·8)
Physical health	0 (0·0)	12 (19·0)	51 (81·0)
Mental health	15 (23·8)	10 (15·9)	38 (60·3)
Former heavy cannabis users ($N=45$)			
What effect has marijuana had on your …			
Cognition	1 (2·2)	4 (8·9)	40 (88·9)
Memory	1 (2·2)	4 (8·9)	40 (88·9)
Career	0 (0·0)	6 (13·3)	39 (86·7)
Social life	3 (6·7)	7 (15·6)	35 (77·8)
Physical health	1 (2·2)	12 (26·7)	32 (71·1)
Mental health	5 (11·1)	7 (15·6)	33 (73·3)

(*b*) a substance use disorder, or (*c*) another psychiatric disorder in at least one first-degree relative of the subject. The median value for the total sample was assigned to missing observations for predictors. In most cases these imputed values represented <5% of all values, except for parental education, where 5–10% of subjects lacked information on at least one parent. We did not include ethnicity because of the collinearity of this variable with other predictor variables in the propensity score model. After determining the propensity score for each subject, we created five ordered categories based on quintile of propensity score. We entered indicator variables for these categories into the regression model above to adjust for propensity for heavy cannabis use. In the regression model for each outcome, we first tested for an interaction between heavy use and propensity score category. In the absence of a significant interaction, we used the regression model above as our final model for the mean value of the outcome variable, adjusted for the predictors that went into determining the propensity score.

We also fitted a model that included terms for ADHD rating scale scores (DuPaul, 1991) and the conduct disorder scores calculated as described above. This was a secondary analysis because these data were limited to 109 subjects.

We used STATA 6.0 software (StataCorp, 1999) for all analyses. All tests were two-tailed, alpha was 0·05.

RESULTS

Basic demographic characteristics

The 63 current heavy users had used cannabis a mean (S.D.) of 20 700 (11 300) times, the 45 former users 14 200 (10 450) times, and the 72 controls only 17 (15) times ($P<0·001$ for all differences between groups). By definition, no subjects had a history of any non-cannabis substance use disorder or any current Axis I disorder other than simple or social phobia. The groups were closely matched on age (mean for all 108 heavy users: 39·2 (6·9) years; controls 39·8 (7·2); $t=0·56$; df$=178$; $P=0·58$), gender (85 (79%) *v.* 61 (85%) men; $P=0·34$) and ethnicity (93 (86%) *v.* 60 (83%) Caucasian; $P=0·67$). Among the heavy users, current users were slightly younger than former users

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Table 3. *Features of long-term heavy users* v. *control subjects*

Subjective ratings*	Heavy Users: Current ($N=63$)	Heavy Users: Former ($N=45$)	Heavy Users: All ($N=108$)	Controls ($N=72$)	P unadjusted	OR	Adjusted† 95% CI	P
Quality of diet	17 (27·0)	16 (35·6)	33 (30·6)	42 (58·3)	<0·001	0·38	0·19, 0·77	0·007
Quality of exercise	19 (30·2)	11 (24·4)	30 (27·8)	38 (52·8)	<0·001	0·43	0·22, 0·87	0·019
Quality of spiritual life	12 (19·0)	16 (35·6)	28 (25·9)	35 (48·6)	0·002	0·45	0·22, 0·92	0·029
Overall satisfaction with self & life	22 (34·9)	15 (33·3)	37 (34·3)	38 (52·8)	0·02	0·67	0·33, 1·30	0·25
Satisfaction with work	20 (31·7)	11 (24·4)	31 (28·7)	34 (47·2)	0·02	0·55	0·27, 1·10	0·091
Quality of recreational activities	23 (36·5)	10 (22·2)	33 (30·6)	34 (47·2)	0·03	0·64	0·32, 1·29	0·21
General happiness level	30 (47·6)	21 (46·7)	51 (47·2)	43 (59·7)	0·13	0·85	0·43, 1·70	0·65
Satisfaction with intimate relationships	21 (33·3)	17 (37·8)	38 (35·2)	33 (45·8)	0·16	0·87	0·43, 1·80	0·71
Quality of sleep	19 (30·2)	16 (35·6)	35 (32·4)	28 (38·9)	0·34	1	0·50, 2·00	0·99
Quality of general health	45 (71·4)	31 (68·9)	76 (70·4)	55 (76·4)	0·4	1·3	0·58, 2·90	0·58

* Number of subjects responding 'good' as opposed to 'fair' or 'poor'.
† Adjusted using propensity score analysis; see text.

(37·4 (6·2) *v.* 41·7 (7·0) years; $t=3·4$, df = 106, $P=0·001$) and included more men (55 (87%) *v.* 30 (67%); $P=0·02$). The three groups did not differ significantly from one another ($P>0·1$, unadjusted) on childhood residence (urban, suburban, rural), marital status, number of children, living situation, or religious affiliations and political orientations of the subjects or the subjects' parents. However, heavy users reported significantly higher rates of substance abuse and other Axis I disorders in their first-degree relatives (Table 1).

Despite these demographic similarities, however, heavy cannabis users and controls differed strikingly on other measures. The groups of subjects differed markedly on various measures of life accomplishment, even after adjustment for the pre-exposure variables as described above. For example, despite similar education and income in their families of origin, the subjects themselves differed significantly on education and income (Table 1).

Subjective ratings

Turning from demographic to self-rated measures, we asked the heavy users specific questions about the effects of cannabis on six aspects of functioning (Table 2). When given a choice of 'positive effect', 'no effect', or 'negative effect', substantial majorities of the heavy users reported negative effects on every index; interestingly, the percentage of subjects reporting negative effects was just as great among current heavy users as among former users (see Table 2). Similarly, on 10 measures of quality of life, where subjects rated their satisfaction as poor, fair, or good, we found that both current and former heavy users consistently reported lower levels of satisfaction than the controls, with these differences reaching significance in the case of diet, exercise and quality of spiritual life (Table 3).

Additional analyses

We found no significant differences among the groups in baseline ADHD scores (mean (S.D.) for 64 heavy users *v.* 45 controls: 11·3 (8·1) *v.* 9·9 (7·0); $t=0·94$, df = 107, $P=0·35$) or conduct disorder scores (1·9 (2·1) *v.* 1·2 (2·4); $t=1·61$, df = 107, $P=0·11$) in the subsample receiving these measures. We then compared the groups on the variables in Tables 1 to 3 while adjusting for ADHD rating scale scores and conduct disorder scores. We found that the parameter estimates were only minimally affected (less then 15% change in estimate for almost all measures), and that in no instance was there a change in the qualitative finding (i.e. significant *v.* not significant) of the analysis.

DISCUSSION

Using a case–control design, we examined 108 individuals, age 30–55, who had smoked cannabis a mean of 18 000 times and a minimum of 5000 times in their lives. We compared the attributes of these heavy users to those of control subjects who had smoked at least once, but no more than 50 times. By design, none of the subjects in either group reported lifetime use of another illicit drug more than 100 times, a history of alcohol abuse or dependence, current

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use of a psychoactive medication, or a current DSM-IV Axis I disorder other than social phobia or simple phobia. Thus, the study offered an opportunity to compare relatively 'pure' long-term heavy cannabis users (e.g. individuals with little evidence of any additional psychiatric or substance use disorders) with individuals who had used the drug only briefly.

The study produced two principal findings. First, we found little difference between the heavy users and controls on measures of family background, but striking differences on many of the same measures in the subjects themselves. Most notably, heavy users and controls reported similar levels of education and income in their families of origin, but the users themselves reported significantly lower levels of educational attainment and income than controls. These findings resemble those of Bourque *et al.* (1991) with regard to income but not education. Our findings regarding decreased education and income are also consistent with several studies of cannabis use in adolescents and young adults, which have found that cannabis users are more likely than non-users to drop out of high school and to be unemployed (Kandel & Chen, 1984; Brook *et al.* 1999; Bray *et al.* 2000).

Secondly, the heavy users acknowledged numerous negative effects of their drug use, and reported lower levels of satisfaction than controls on several measures of quality of life. Some of the specific negative effects reported by our heavy users resemble those reported by Australian heavy users in the study of Reilly *et al.* 1998). However, when asked about the overall influence of cannabis on various aspects of their lives (Table 3), the heavy users in our sample appeared to see cannabis much more negatively than their rural Australian counterparts. Our observations in this regard appear consistent with several American studies (Roffman & Barnhart, 1987; Stephens *et al.* 1993, 1994, 2000; Budney *et al.* 1998, 2000) suggesting that many adults desire treatment for cannabis dependence. Indeed, the United States Substance Abuse and Health Services Administration reported 208 000 admissions in 1998 for treatment of marijuana/hashish as a primary drug of abuse, or about 13% of all substance abuse admissions nationally (Substance Abuse and Mental Health Services Association Office of Applied Studies, 1992–1998).

Why did the current heavy users continue to use cannabis, despite consistently reporting negative effects and frequently desiring treatment? One known factor is genetic predisposition to cannabis dependence (Bierut *et al.* 1998; Kendler & Prescott, 1998; True *et al.* 1999). A second factor may be physical dependence and withdrawal symptoms associated with cannabis use (Anthony *et al.* 1994; Rodriguez deFonesca *et al.* 1997; Diana *et al.* 1998; Grant & Pickering, 1998). Although cannabis withdrawal is less severe than opioid or alcohol withdrawal, our subjects frequently reported prominent withdrawal symptoms (Kouri & Pope, 2000), as have subjects in other studies (Jones *et al.* 1981; Wiesbeck *et al.* 1996; Budney *et al.* 1999, 2001; Haney *et al.* 1999).

Given the cross-sectional design of the study, it is unclear whether the differences between heavy users and controls were effects of long-term heavy cannabis use, or whether they may have been attributable to unmeasured confounders, such as differences in pre-morbid functioning between the heavy users and controls. For example, the heavy users might have exhibited lower educational attainment because chronic cannabis intoxication seriously compromised their academic functioning. Alternatively, pre-morbid traits, such as limited career aspirations, might predispose individuals both to lower educational attainment and separately to heavy cannabis use. We cannot easily distinguish between such possibilities, especially in the absence of formal measures of pre-morbid levels of functioning. However, substantial differences between groups remained on many measures even after adjustment for the pre-morbid variables that we were able to assess.

The principal methodological limitation of the study is the problem of selection bias. For example, our threshold of 5000 lifetime episodes of use might identify a group with different attributes than would be found in a study using a higher or lower threshold. Furthermore, individuals willing to enrol on a 28-day study, requiring daily or every-other-day visits to our laboratory, may have differed from the overall population of long-term cannabis users in various respects. On the one hand, long-term heavy cannabis users who were particularly worried about their cognitive abilities, or users who were unemployed and eager to obtain compensation

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for the study, might have been particularly likely to enrol – potentially biasing the sample towards lower-functioning heavy users. However, the same biases would presumably affect the control group as well. Conversely, our study selection criteria – excluding heavy cannabis users who reported substantial use of other illicit drugs, a history of alcohol abuse or dependence, or evidence of a current Axis I disorder – would likely produce a bias towards healthier heavy cannabis users. This bias might cause our results to represent an overly conservative estimate of the negative effects and morbidity that would be found in an unrestricted group of long-term cannabis users.

Another limitation of the study is that we relied on self-report for most of our measures. However, previous studies have suggested that self-reports of use of cannabis and other drugs are valid (Rouse *et al*. 1985; Brown *et al*. 1992; Harrison *et al*. 1993). On other variables, any mismeasurement in self-reports would likely affect both groups similarly; such non-differential measurement error would seem unlikely to create major spurious differences between the groups. Finally, the heavy users might introduce response bias by emphasizing the positive aspects and minimizing the negative aspects of their use – but if so, this bias would again only render our findings too conservative.

In summary, our findings combine with those of previous investigations (Bourque *et al*. 1991; Chen & Kandel, 1995, 1998; Reilly *et al*. 1998; Kandel & Chen, 2000) to suggest that long-term heavy cannabis use is associated with many negative attributes on both objective measures and self-ratings of health and life satisfaction, at least among American users. It is not clear, however, whether our findings would generalize to other cultures, where patterns of cannabis use and associated behaviors may be very different (Mendhiratta & Wig, 1975; Rubin & Comitas, 1975; Sharma, 1975; Soueif, 1975; Mendhiratata *et al*. 1978; Carter *et al*. 1980; Page *et al*. 1988). Further studies are needed to better understand the direction of causality in these associations, since this information will be important for developing better strategies to treat cannabis dependence.

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