Cannabis dimensionality: Dependence, abuse and consumption

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A R T I C L E   I N F O

A B S T R A C T

Aims: Genetic research on substance use disorders usually defines phenotypes as a binary diagnosis, resulting in a loss of information if the disorder is inherently dimensional. The DSM-IV criteria for drug dependence were based on a theoretically dimensional (linear) model. Considerable investigation has been conducted on DSM-IV alcohol criteria, but less is known about the dimensionality of DSM-IV cannabis criteria for abuse and dependence. The aim of this study is to assess whether DSM-IV cannabis dependence (including withdrawal) and abuse criteria fit a linear measure of severity and whether a consumption criterion adds linearly to severity.

Design/setting/participants/measurements: Participants were 8172 in the National Epidemiologic Survey on Alcohol and Related Conditions who had ever used cannabis. Wald statistics were used to test whether categorical, dimensional or hybrid forms best fit the data. We examined the following as criterion sets: (1) dependence; (2) dependence and abuse; and (3) dependence, abuse and frequency of use. Validating variables included family history of drug problems, early onset of cannabis use, and antisocial personality disorder.

Findings: For cannabis dependence, no evidence was found for categorical or hybrid models; Wald tests indicated that models representing the seven DSM-IV dependence criteria as a linear severity measure best described the association between the criteria and validating variables. However, significant differences from linearity occurred after adding the four cannabis abuse criteria ($p = 0.03$) and the use indicator ($p = 0.01$) for family history and antisocial personality disorder.

Conclusion: With ample power to detect non-linearity, cannabis dependence was shown to form an underlying continuum of severity. However, adding abuse criteria, with and without a measure of consumption, resulted in a model that differed significantly from linearity for two of the three validating variables.

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1. Introduction

1.1. Cannabis

Cannabis is the most widely used illegal drug in many countries (Copeland & Swift 2009; Stinson, Ruan, Pickering & Grant, 2006; Hall, Teesson, Lynskey & Degenhardt, 1999). Cannabis use may result in withdrawal (Budney, Hughes, Moore & Vandrey, 2004; Haney et al., 2004; Hasin et al., 2008) and diagnoses of abuse and dependence (American Psychiatric Association, 1994). Since 1994, DSM-IV has provided diagnostic criteria for psychiatric disorders that have been used across mental health disciplines for many purposes. However, research developments and experience with DSM-IV have raised issues now under consideration regarding DSM-V. These include (1) whether diagnoses should have dimensional representations, (2) whether

related disorders should be consolidated into a single category, and (3) whether adding new criteria improves a particular diagnosis.

1.1.1. Issue 1: dimensional representation

The basis of DSM-III-R and DSM-IV substance dependence criteria (Rounsaville, Spitzer & Williams, 1986) was the Dependence Syndrome (Edwards & Gross, 1976; Edwards, Arif & Hadgson, 1981; Edwards, 1986), a construct assumed to be dimensional (i.e., occurring in gradations of severity) that represented impaired control over substance use. The neuroadaptive changes that produce impaired control were hypothesized to be similar across all substances (Koob, 1992; Nestler, Hope & Widnell, 1993; Hasin, Grant, Harford & Endicott, 1988). If the same neuronal systems mediate reinforcement of all addictive drugs, then a similar gradient of clinical manifestations should be seen across all substances. If a given substance disorder is inherently graded, then etiologic research using dichotomized measures (i.e. defining yes/no categories), as is presently the case in DSM-IV, imposes an artificial threshold, which may result in the loss of potentially important information and increased difficulty in identifying etiologic factors. The validity of a

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dimensional representation of substance use disorders (SUDs) is currently under study as a potential addition to DSM-V (Helzer, Bucholz & Gossop, 2007).

1.1.2. Issue 2: combining highly related disorders

DSM-IV operationalized dependence and abuse (consequences) as two separate and hierarchical disorders, with dependence taking precedence over abuse if criteria for both are met. However, questions for DSM-V include the validity of the hierarchical division of SUDs into dependence and abuse, and whether the two disorders should be combined (Hasin, Hatzenbuehler, Keyes & Ogburn, 2006; Schuckit & Saunders, 2006; Saha, Chou & Grant, 2006; Martin, Chung, Kirisci & Langenbucher, 2006).

1.1.3. Issue 3: adding new criteria

A set of diagnostic criteria lacking important elements will be less sensitive or specific than a set incorporating all relevant elements. However, reasons for not adding criteria include (1) keeping criteria sets simpler for clinical use (Hasin et al., 2003), and (2) expanded heterogeneity. Thus, when new criteria are proposed, their effect on the psychometric performance of the entire criteria set requires scrutiny to justify their addition. For current alcohol use disorders, such a proposed criterion is current binge drinking, defined as 5+ drinks per occasion at least weekly for men, and 4+ drinks for women (Saha, Stinson & Grant, 2007; Li, Hewitt & Grant, 2007; Keyes, Geier, Grant & Hasin, 2009). A parallel criterion proposed for cannabis is based on weekly use (Compton, Saha, Conway & Grant, 2009). A second criterion for possible addition to DSM-V is cannabis withdrawal.

1.2. Approaches to investigating abuse and dependence criteria

Latent variable analyses including latent class analyses (LCA), factor analyses and item response theory analyses (IRT) have been used to address the psychometric properties of cannabis abuse and dependence (Helzer et al., 2007). In both population-based (Grant et al., 2006) and treated adolescents, (Chung & Martin, 2005), LCA identified classes of cannabis users based largely on severity. Investigators using data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (Agrawal & Lynskey, 2007), male Virginia twins (Gillespie, Neale, Prescott, Aggen & Kendler, 2007) and the Australian general population (Teesson, Lynskey, Manor & Baillie, 2002) showed that 1- and 2-factor models corresponding to cannabis dependence and abuse fit the data well. However, they chose the 1-factor model due to high factor correlations in the 2-factor model, with two studies (Teesson et al., 2002; Agrawal & Lynskey, 2007) dropping some abuse items to achieve unidimensionality. Using NLAES data (Blanco, Harford, Nunes, Grant & Hasin, 2007), two factors were also found for cannabis abuse and dependence criteria, with a correlation of .77 between the two factors. A criterion for weekly cannabis use fits a one-factor model of current cannabis abuse and dependence criteria in current users in NESARC and showed low severity in an IRT analysis (Compton et al., 2009). Large sample sizes are better at showing smaller effect sizes to be statistically significant, which may favor models showing a greater number of factors (Agrawal & Lynskey, 2007); but this does not explain the significantly better fit of two-factor models in small studies such as Teesson et al., 2002.

1.3. Gaps in knowledge

While many investigators have preferred the unidimensional concept of abuse and dependence, the repeated appearance of two factors warrants additional attention. Further, none of the latent variable studies directly test whether a dimensional or binary model fit the data better, whether dimensionality is found only after the DSM-IV diagnostic threshold has been exceeded, or whether the criteria are dimensional in relation to known risk factors for SUDs. We therefore extended a statistical method used previously (Kendler & Gardner, 1998; Kendell & Brockington, 1980; Hasin, Liu, Alderson & Grant, 2006; Hasin & Beseler, 2009), the "discontinuity approach" (Hasin & Beseler, 2009) to examine these issues.

1.4. The discontinuity approach

The discontinuity approach directly incorporates the relationship of an observed criterion set to important external validating variables. Assuming an inherent threshold exists in the diagnostic set, two underlying assumptions hold. (1) After a diagnostic threshold has been met, cases will show a stronger association between the number of criteria and a risk factor than non-cases. (2) The statistical association between the number of criteria and risk factors will be homogeneous within groups of cases and non-cases, i.e., among those designated a 'non-case', there will be no association between risk factors and number of criteria met. A theoretical depiction of these assumptions has been published previously (Hasin & Beseler, 2009). If the criteria are inherently dimensional and no threshold exists, then each additional criterion adds in equal measure to the severity of the disease resulting in a monotonically increasing linear relationship to a validating variable.

With the discontinuity approach focused on alcohol use disorders, we previously examined whether a dimensional representation of a disorder is warranted, whether abuse and dependence should be combined, and whether a new alcohol use criterion should be added to DSM-IV alcohol use disorder criteria. We found that the dependence criteria related to risk factors in a monotonic fashion, with no support for any model of alcohol dependence that included a category (Hasin, Liu, et al., 2006; Hasin & Beseler, 2009). Results did not support the addition of a binge drinking criterion (Hasin & Beseler, 2009). We now extend this approach to study lifetime criteria for cannabis dependence, abuse and use among the lifetime cannabis users from a national representative general population sample. We hypothesized that (1) the alcohol dependence syndrome applies to cannabis; (2) cannabis dependence and abuse criteria, like alcohol criteria, will show a linear relationship with the validating variables; and (3) cannabis use will not fit on a linear continuum with other DSM-IV criteria.

2. Methods

2.1. Sample

Respondents were participants in the NESARC. The full survey included 43,093 respondents, with over-sampling of African-Americans, Hispanics, and young adults (Grant et al., 2004). The NESARC face-to-face survey conducted by NIAAA in 2001–2002 targeted the adult civilian non-institutionalized population residing in the US, the District of Columbia, Alaska and Hawaii. The overall response rate was 81%. The sample analyzed consisted of the 8172 NESARC participants who ever used cannabis during their lifetime. These respondents were 65.4% white, 15.9% black and 14.4% Hispanic, and 54.0% were male. By age, 26.7% were 18–29, 43.4% 30–44, 28.4% 45–64 and 1.5% were 65 or older.

2.2. Measures

2.2.1. DSM-IV diagnostic interview

The structured interview used in NESARC was the Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV) designed for lay interviewers (Grant et al., 2004). Professional interviewers administered the AUDADIS-IV using laptop computer-assisted software with built-in skip logic and consistency checks (Grant et al., 2004). Training and quality control procedures are described elsewhere (Grant et al., 2004; Grant et al.,

2005; Hasin, Stinson, Ogburn & Grant, 2007). The diagnostic measures for the substance use disorders and their reliability and validity have been described extensively (Grant et al., 2003; Grant et al., 2004; Hasin et al., 2007; Compton, Thomas, Stinson & Grant, 2007). Lifetime use of cannabis and age at first use as measured in AUDADIS have good to excellent reliability (Grant, Harford, Dawson, Chou & Pickering, 1995; Hasin, Carpenter, McCloud, Smith & Grant, 1997).

2.2.2. Cannabis abuse, dependence and use

Six DSM-IV criteria for cannabis dependence and four criteria for abuse are measured in the AUDADIS among individuals that ever used cannabis (Grant et al., 1995). The six criteria of cannabis dependence include (1) tolerance; (2) persistent desire or unsuccessful attempts to reduce use; (3) time spent using cannabis or recovering from its effects; (4) giving up or reducing occupational, social and/or recreational activities to use; (5) impaired control; and (6) continued cannabis use despite physical or psychological problems. The four criteria for cannabis abuse included (1) failure to fulfill major role obligations; (2) recurrent physically hazardous use; (3) recurrent substance-related legal problems; and (4) continued substance use despite having persistent social or interpersonal problems related to use. Although cannabis withdrawal was not included in DSM-IV, numerous studies support its addition in DSM-V (Budney et al., 2004; Haney, 2005; Agrawal & Lynskey, 2007; Hasin et al., 2008), therefore, we added a withdrawal criterion to make a set of seven cannabis dependence criteria, analogous to the other substances in DSM-IV. We created the withdrawal variable by requiring two or more out of the following, after reduction or cessation in use: anxiety, insomnia, vivid or unpleasant dreams, hallucinations, restlessness, shaking, depressed mood, hypersomnia, psychomotor retardation, feeling weak or tired, bad headaches, muscle cramps, runny eyes or nose, yawning, nausea, sweating, fever, and seizure, and by requiring that the withdrawal symptoms caused significant distress. The definition of withdrawal was based on a previous report where withdrawal using a cutoff of two criteria, when added to the six DSM-IV dependence criteria, increased the prevalence of cannabis dependence from 16% to 32.3%; a cutoff of three withdrawal criteria resulted in a 30.1% prevalence (Hasin et al., 2008). Further, the two latent factors representing withdrawal were each significantly associated with distress over symptoms. We tested whether requiring two or three criteria resulted in changes in linearity with the six dependence criteria and no significant differences were noted. For these reasons we used a cutoff of two withdrawal criteria and the presence of distress due to experiencing the symptoms.

Cannabis consumption was ascertained from a question asking how often cannabis was used when using the most. Responses were as follows: (1) every day; (2) nearly every day; (3) 3–4 times per week; (4) 1–2 times per week; (5) 2–3 times per month; (6) once a month; (7) 7–11 times per year; (8) 3–6 times per year; (9) 2 times per year; and (10) once a year. Respondents who endorsed using 1–2 times per week or more often were coded as weekly users and zero if less often. This variable was dichotomized (at least weekly vs. less frequently) at the point that corresponded most closely to the binge drinking variable studied previously (Saha et al., 2007; Li et al., 2007; Hasin & Beseler, 2009; Compton et al., 2009).

2.2.3. Validating variables

The dimensionality of cannabis criteria was tested using three validating variables: family history of drug problems (Milne et al., 2009; Heiman, Ogburn, Gorroochurn, Keyes & Hasin, 2008; Bierut et al., 1998), age of onset of cannabis use (Copeland & Swift, 2009; Swift, Coffey, Carlin, Degenhardt & Patton, 2008) and DSM-IV antisocial personality disorder (ASPD) (Mariani et al., 2008; Compton, Conway, Stinson, Colliver & Grant, 2005; Fu et al., 2002). We considered treatment as a validating variable because we previously showed a strong linear relationship between the alcohol criteria and

seeking treatment for an alcohol use disorder. However, because only 8% of the cannabis users were ever in treatment for their cannabis use, numbers were too small to use treatment as a validating variable. Family history was defined as the proportion of first-degree relatives with a drug problem relative to the total number of first-degree relatives that attained the initial age of risk for first drug use (>10 years of age). Age of onset of cannabis use was dichotomized at 15 years (<15 = 1) from the question asking about age first used cannabis (possible responses, 5–64 years). Fifteen was chosen because analyses in the National Household Survey on Drug Abuse showed an increased risk of cannabis dependence in those who initiated use at 11–15 years of age (Chen, O'Brien & Anthony, 2005) and to be consistent with the previous alcohol dimensionality study (Hasin & Beseler, 2009). Sensitivity analyses dichotomizing at 14 and 16 did not alter the linear relationship between the dependence criteria and early age of onset. ASPD was diagnosed if respondents met full criteria for child conduct disorder as well as the adult symptoms required by DSM-IV. Control variables included sex (Guxens, Nebot & Ariza, 2007), age (a continuous variable) and race (whites compared to all others; Stinson et al., 2006).

2.2.4. Statistical analysis

2.2.4.1. Variables created for analysis

2.2.4.1.1. Dimensional variables. Unidimensionality means that a sloping straight line describes the relationship between the number of DSM-IV criteria met (the X axis on a graph), and the risk for the validating variables (the Y axis on a graph). In our case, we hypothesized that such a line would be found, with its lowest point in the lower left quadrant of the graph, and its highest point at the upper right quadrant of a graph. In this case, each criterion endorsed would add linearly and equally to the shape of the line. We created a dimensional or linear representation (a sum score) by adding up the number of criteria endorsed by each participant. We used the sum score variable in separate regression models (referred to below as $M_{NDimensional}$ where N = 7 dependence criteria, 11 dependence and abuse criteria and 12 dependence, abuse and use criteria depending on the model).

2.2.4.1.2. Dummy variables. We next created a set of dummy variables, each representing one subset of the sample defined by the number of criteria they experienced. Dummy variables were used to avoid advance assumptions about the shape of the relationship between the number of criteria and the risk for the validators, instead allowing the actual relationships to form the shape of the line in regression models (which might have been linear, U-shaped, J-shaped, or without shape at all). For example, a person experiencing one criterion would be coded as positive (= 1) for the dummy variable representing having endorsed one criterion and negative (= 0) for all the rest of the dummy variables. A person who endorsed two criteria would be coded as positive = 1 for the variable representing experiencing two criteria and negative = 0 for all the rest of the dummy variables. Using this procedure, in analyses of dependence criteria, each individual contributed to only one of the seven variables representing one to seven dependence criteria, with similar procedures followed for the 11 dependence and abuse criteria, and the twelve criteria for dependence, abuse and use. The seven (M_{7Dum}), eleven (M_{11Dum}) and twelve (M_{12Dum}) dummy variables representing the various levels of severity were used in regression models.

To test a model in which those below the diagnostic threshold were homogeneous, but those above the threshold represented gradients of severity according to the number of dependence criteria met, we combined the dummy variables for 0 to 2 criteria into a single group representing being below the diagnostic threshold of 3 criteria. The dummy variables representing 3 to 7 criteria were not combined. We used this to create an artificial threshold at three criteria while

allowing for a slope at or above three or more criteria ($M_{7Threshtrend}$). We also created a DSM-IV model by allowing for no slope if fewer than 3 criteria were endorsed, a threshold at three criteria and no slope for three or greater criteria (M_{DSM-IV}). In this way we could impose artificial thresholds and test whether they differed significantly from the model with seven dummy variables (Hasin, Liu, et al., 2006; Hasin & Beseler, 2009).

2.2.4.2. Regression models. Analyses were conducted with three sets of lifetime criteria: (1) cannabis dependence (range, 0–7); (2) cannabis dependence and abuse (range, 0–11); and (3) cannabis dependence, abuse and weekly use (range, 0–12). To determine the association between the criteria set and family history, Poisson regression models were used, with the outcome log $((EY)/N)$, where Y is the count of affected relatives and N is the total number of relatives in each family. Early onset of drinking and ASPD were modeled using logistic regression. Survey Data Analysis software (SUDAAN, RTI International, Research Triangle Park, North Carolina) was used to apply these models because it calculates correct estimates of the standard errors (via Taylor linearization) in complex survey designs such as the NESARC. We tested whether withdrawal fit a linear model in relation to the validating variables when added to the six dependence criteria. We also tested for a threshold at 3, 4 or 5 criteria after combining abuse and dependence criteria. All models were adjusted for age, gender and race.

2.2.4.3. Dimensionality of lifetime cannabis dependence criteria. Following the method we used previously (Hasin, Liu, et al., 2006; Hasin & Beseler, 2009), we began with a dummy variable model (M_{7Dum}) with ten predictors: three control variables (age, gender and race) and seven non-ordered dummy variables to represent the seven levels of severity (1–7) of the cannabis dependence criteria. Participants with no cannabis dependence criteria constituted the reference group. Participants with one dependence criterion were compared to the reference group, as were participants with two dependence criteria, etc., up to participants with seven dependence criteria. Consistently increasing regression coefficients for dummy variables, as indicated by the slope of the regression line, would suggest an underlying dimensional relationship between the criteria and the validating variable. The regression line produced from the dimensional model ($M_{7Dimensional}$) was compared to the line produced by the dummy variable model (M_{7Dum}) to determine whether they differed significantly. In addition to testing a purely linear model ($M_{7Dimensional}$), we compared the $M_{7Threshtrend}$ to M_{7Dum} to determine whether those endorsing 0–2 criteria were homogeneous (slope = 0) but those with three or greater criteria showed an increasing level of dependence (slope > 0). Lastly, we tested whether the DSM-IV categorical model (M_{DSM-IV}) fit the dummy variable model, i.e., those endorsing 0–2 criteria were homogeneous (slope = 0) and those endorsing three or greater criteria were homogeneous (slope = 0), but with the second category showing a greater level of cannabis dependence (a threshold effect).

To compare the models incorporating the weights reflecting the complex sample design, the Wald test was used to test the hypothesis that the slope parameters for the two models were identical. Each model was compared with the dummy variable model in the Wald test. While differences in the fit of nested models are often compared using the likelihood ratio test, this test cannot be used with weighted data. We used the Wald statistic to determine whether alternative parameterizations of the association between the validating variable and the number of dependence criteria produce significantly different estimates between M_{7Dum} and $M_{7Dimensional}$, with a single linear predictor (i.e., $(\beta_1, \beta_2, ..., \beta_7)$ compared with $(1\beta, 2\beta, ..., 7\beta)$). The Wald test statistic is calculated using the squared distance between two vectors of estimated effects in the two nested models. Similar to the likelihood ratio test, it follows a χ^2 distribution with degrees of freedom defined as the difference in the number of parameters in the two nested models. With

large samples such as the NESARC, the likelihood ratio test and Wald test are generally equivalent in testing the hypotheses on model parameters for the pattern in the association between outcome and predictors if no sampling weights applied (Pawitan, 2001). Little or no difference between the dummy variable model and the linear model would support the use of $M_{7Dimensional}$, as it is most parsimonious. Following our previous methods, we considered that the dimensional model 'fit' the pattern in the dummy variable model better if the difference between the dummy and dimensional models were small (non-significant), while the difference between, for example, the dummy and DSM-IV model were not small (e.g. significantly different). For all tests, statistical significance was set at 0.05.

2.2.4.4. Dimensionality of lifetime cannabis dependence and abuse criteria. We analyzed only the dummy variable model with 7 dependence and 4 abuse criteria (M_{11Dum}) and the criteria count variable model ($M_{11Dimensional}$) using the same validating variables because no threshold is defined for the combined criteria. M_{11Dum}, representing levels of severity (range 0–11), was compared with $M_{11Dimensional}$, which used a continuous dimensional measure of criteria (range 0–11).

2.2.4.5. Dimensionality of lifetime cannabis dependence, abuse and use criteria. The variables were generated as described above, using a dummy variable model with 7 dependence, 4 abuse, and a criterion for weekly use. M_{12Dum} contained 12 dummy variables and $M_{12Dimensional}$ contained a single indicator of criteria counts (range 0−12). M_{12Dum} was compared to $M_{12Dimensional}$.

2.2.5. Testing the dummy variable model

Prior to conducting these analyses, we used the Wald statistic to test whether the set of dummy variables in M_{7Dum}, M_{11Dum} and M_{12Dum} were associated with each of the validating variables. For example, the null hypothesis on the parameters of M_{7Dum} was $(\beta_1, \beta_2, ..., \beta_7) = (0, 0, ..., 0)$ for no association between the dependence criteria count and the validating variable, adjusting for age, gender and race. The null hypotheses were rejected (all p-values < 0.0001).

3. Results

3.1. Descriptive results

Table 1 shows the prevalence of dependence, abuse and weekly use criteria among this sample of lifetime cannabis users. Weekly use

Table 1
Weighted prevalence of cannabis abuse and dependence criteria and weekly use in NESARC lifetime cannabis users (N = 8134).

Cannabis criterion	Prevalence
Abuse	
Neglect roles	8.4
Hazardous use	33.7
Legal problems	5.9
Social/interpersonal problems	16.0
Dependence	
Tolerance	10.0
Withdrawal[a]	3.2
Larger/longer	7.9
Quit/control	33.3
Time spent	11.5
Activities given up	5.5
Physical/psychological problems	10.6
Consumption	
Weekly use	45.7

[a] Based on requiring two or more, after reduction or cessation in use: anxiety, insomnia, vivid or unpleasant dreams, hallucinations, restlessness, shaking, depressed mood, hypersomnia, psychomotor retardation, feeling weak or tired, bad headaches, muscle cramps, runny eyes or nose, yawning, nausea, sweating, fever, and seizure, and by requiring that the withdrawal symptoms caused significant distress.

showed the highest prevalence, at 45.7% and withdrawal had the lowest prevalence (3.2%). Approximately 73% of the sample endorsed two or fewer criteria and less than 1% endorsed 10 or more criteria.

3.2. Dimensionality of lifetime cannabis dependence criteria

Using family history of drug problems as the validator, the log proportions for family history plotted against the seven dummy variables representing criterion counts (M_{7Dum}) shows a monotonic, increasing linear relationship between the number of criteria and family history of drug use (Fig. 1). Slope coefficients and their standard errors for the four dependence models are shown in Table 2. Comparing these points to the plotted line representing the continuous dimensional model ($M_{7Dimensional}$) with a slope coefficient of 0.19 (s.e. = 0.02) showed no significant difference between the two parameterizations of the criteria with family history (Wald = 3.97; p = 0.68). However, $M_{Threshtrend}$ and M_{DSM-IV} significantly differed from M_{7Dum} (p < 0.0001). Using early age at onset as the validator, the plot of the log odds ratios for the dummy variable model shows points lying very close to the line representing the dimensional model (Fig. 2). In this model, the $M_{7Dimensional}$ model had a slope coefficient of 0.20 (s.e. = 0.02). No statistically significant differences were observed between M_{7Dum} and $M_{7Dimensional}$ (Wald = 9.84; p = 0.13). However, $M_{Threshtrend}$ and M_{DSM-IV} significantly differed from M_{7Dum} (p < 0.0001). Using ASPD as a validator, the plot shows that the points do not deviate greatly from the line representing the dimensional model (Fig. 2). The slope coefficient for $M_{7Dimensional}$ was 0.37; s.e. = 0.02. No statistically significant differences were observed between M_{7Dum} and $M_{7Dimensional}$ (Wald = 2.80; p = 0.83) but $M_{Threshtrend}$ and M_{DSM-IV} significantly differed from M_{7Dum} (p < 0.0001).

3.3. Dimensionality of lifetime cannabis dependence and abuse criteria

We next examined the combination of cannabis dependence and abuse criteria. The slope coefficient for $M_{11Dimensional}$ was 0.14 (s.e. = 0.01) for family history, 0.17 (s.e. = 0.02) for age of onset, and 0.27 (s.e. = 0.02) for ASPD (Table 3). In contrast to the results for cannabis using only the dependence criteria, the addition of four cannabis abuse criteria resulted in significant deviations from linearity in relation to the validating variables family history (Wald = 20.1, p = 0.03) and ASPD (Wald = 20.0, p = 0.03), but not early age of onset (Wald = 15.2, p = 0.12) (Table 3 and Fig. 2). Thus, when the cannabis abuse criteria were added to the dependence criteria, a single continuum of severity was no longer found for two of the three validating variables. Further, there was no evidence for a threshold at endorsement of 3, 4 or 5 cannabis dependence and abuse criteria (results not shown).

3.4. Dimensionality of lifetime cannabis dependence, abuse and use criteria

Finally, we examined the combination of cannabis dependence and abuse criteria with the addition of cannabis use. The slope coefficient for $M_{12Dimensional}$ was 0.14 (s.e. 0.01) for family history, 0.18 (s.e. 0.01) for age of onset, and 0.25 (s.e. 0.01) for ASPD (Table 4 and Fig. 3). M_{12Dum} and $M_{12Dimensional}$ differed significantly for family history (Wald = 26.7, p = 0.01) and ASPD (Wald = 24.5, p = 0.01), but not for early age of onset (Wald = 19.2, p = 0.06) (Table 4 and Fig. 3). Thus, when cannabis abuse criteria and a consumption measure were added to the dependence criteria, a single continuum of severity was not found for family history or ASPD.

4. Discussion

Lifetime cannabis dependence criteria represented a continuum of severity in those who ever used cannabis in relation to family history of drug use, early age of onset and ASPD. No support was found for a
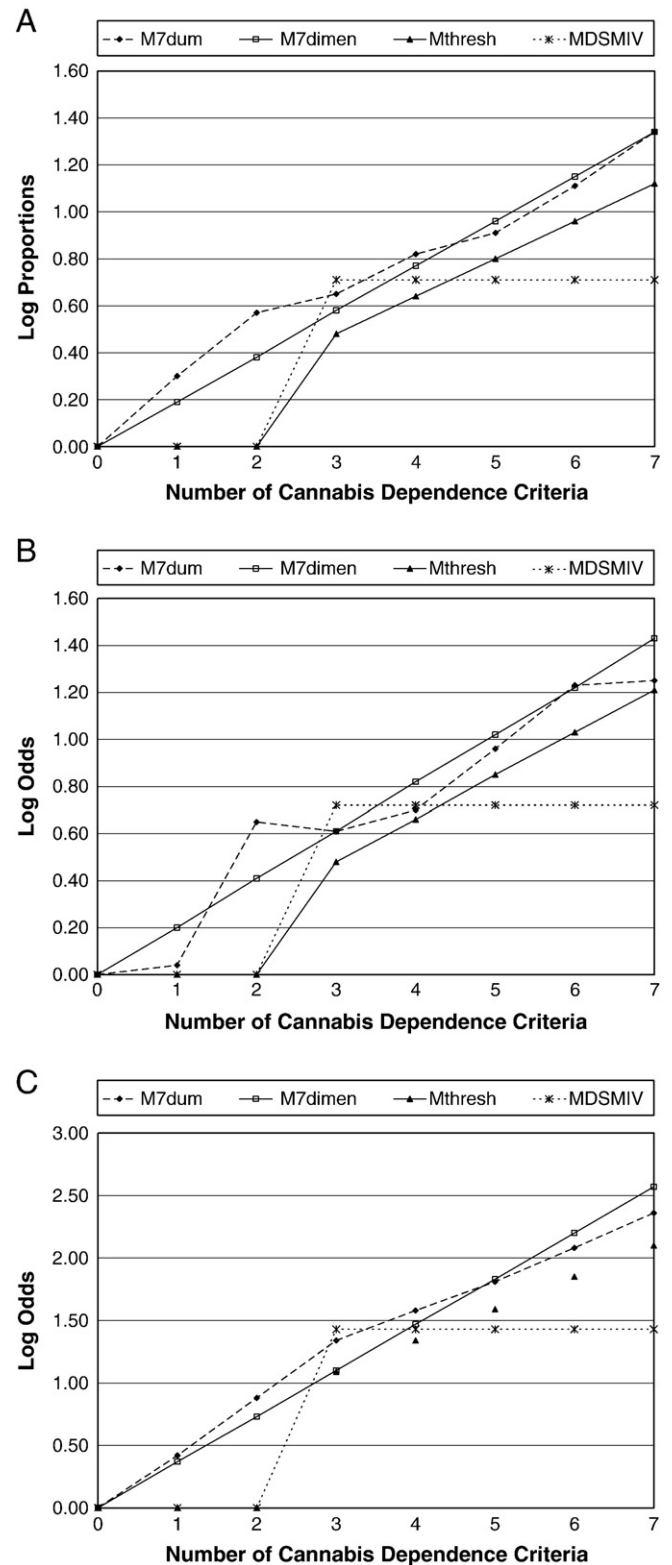

Fig. 1. a. Family history. b. Age of onset. c. Antisocial personality disorder.

model including categories either below the DSM-IV diagnostic threshold for cannabis dependence, at the present DSM-IV threshold, or at any of several thresholds. Therefore, results for cannabis dependence criteria supported the dimensional construct underlying the Dependence Syndrome (Edwards & Gross, 1976). Our results are

Table 2
Comparison of five models[a] representing cannabis dependence criteria in different forms: NESARC (N = 8172).

Outcome	Criterion count (K)	M_{7Dum} estimate	$M_{7dimensiona}$ estimate[b]	$M_{threshtrend}$ estimate[b]	M_{DSM-IV} estimate[b]
Log P(K)/P(0)					
Family history	1	0.30 (0.08)	0.19 (0.02)	0.00 (0.00)	0.00 (0.00)
	2	0.57 (0.13)	0.38 (0.04)	0.00 (0.00)	0.00 (0.00)
	3	0.65 (0.14)	0.58 (0.05)	0.48 (0.31)	0.71 (0.09)
	4	0.82 (0.18)	0.77 (0.07)	0.64 (0.34)	0.71 (0.09)
	5	0.91 (0.18)	0.96 (0.09)	0.80 (0.38)	0.71 (0.09)
	6	1.11 (0.20)	1.15 (0.11)	0.96 (0.42)	0.71 (0.09)
	7	1.34 (0.21)	1.34 (0.13)	1.12 (0.47)	0.71 (0.09)
P-value for test of difference with M_{7Dum}			0.68	0.00	0.00
Log (Odds(K)/Odds(0))					
Age of onset	1	0.04 (0.10)	0.20 (0.02)	0.00 (0.00)	0.00 (0.00)
	2	0.64 (0.14)	0.41 (0.05)	0.00 (0.00)	0.00 (0.00)
	3	0.61 (0.16)	0.61 (0.07)	0.48 (0.39)	0.72 (0.10)
	4	0.70 (0.20)	0.82 (0.10)	0.66 (0.43)	0.72 (0.10)
	5	0.96 (0.23)	1.02 (0.12)	0.85 (0.49)	0.72 (0.10)
	6	1.23 (0.25)	1.22 (0.14)	1.03 (0.54)	0.72 (0.10)
	7	1.25 (0.39)	1.43 (0.17)	1.21 (0.60)	0.72 (0.10)
P-value for test of difference with M_{7Dum}			0.13	0.00	0.00
Log (Odds(K)/Odds(0))					
Antisocial personality	1	0.42 (0.12)	0.37 (0.02)	0.00 (0.00)	0.00 (0.00)
	2	0.88 (0.15)	0.73 (0.05)	0.00 (0.00)	0.00 (0.00)
	3	1.34 (0.22)	1.10 (0.07)	1.09 (0.48)	1.43 (0.11)
	4	1.58 (0.21)	1.47 (0.09)	1.34 (0.53)	1.43 (0.11)
	5	1.81 (0.21)	1.83 (0.11)	1.59 (0.58)	1.43 (0.11)
	6	2.08 (0.23)	2.20 (0.14)	1.85 (0.64)	1.43 (0.11)
	7	2.36 (0.33)	2.57 (0.16)	2.10 (0.71)	1.43 (0.11)
P-value for test of difference with M_{7Dum}			0.83	0.00	0.00

[a] Adjusted for age (continuous), gender (0 = female, 1 = male) and race (white = 1, others = 0).
[b] K represents number of criteria present compared to the reference group with 0 criteria.

consistent with previous analyses showing that cannabis dependence criteria share an underlying construct (Swift, Hall & Teesson, 2001; Nelson, Rehm, Ustun, Grant & Chatterji, 1999; Feingold & Rounsaville, 1995; Denson & Earleywine, 2006). The findings on cannabis dependence criteria, including withdrawal, contribute to the existing literature showing that cannabis dependence is a unidimensional construct by relating this continuum to validating variables with well-established relationships to a cannabis use disorder. These results are in agreement with our previous studies on the unidimensionality of alcohol dependence using family history and age of onset as validating variables (Hasin, Liu, et al., 2006; Hasin & Beseler, 2009).

In contrast, when cannabis dependence and abuse criteria were combined, they no longer showed a linear relationship to family history or ASPD, although a linear relationship was still seen for age of onset of cannabis use. The non-linearity of family history to the combined criteria suggests that caution should be taken when combining cannabis dependence and abuse criteria to create a phenotypic quantitative variable in genetics studies, as doing so may introduce heterogeneity.

To explore heterogeneity in the family history models, which have direct implications for genetic research, we removed each abuse criterion one at a time. We ran the models with three abuse criteria; two abuse criteria; and, finally, only one abuse criterion to identify which criterion or criteria were creating the non-linearity in the relationship to the validating variables. The family history model became linear in relation to the cannabis criteria after excluding legal problems and hazardous use. Addition of a consumption variable resulted in greater deviations from linearity, representing increased heterogeneity.

Combining cannabis dependence and abuse criteria in DSM-V requires that the question of a diagnostic threshold be addressed. We tested for a discontinuity at endorsing 3, 4 and 5 dependence and abuse criteria and found no evidence for a threshold. The lack of evidence for a diagnostic threshold indicates that a decision regarding a threshold for DSM-V will require taking into account considerations other than empirical evidence for a natural threshold or division between cases and non-cases.

The discontinuity approach differs from CFA, LCA and IRT model analysis in important ways. These differences may account for some of the discrepant results between the present report and the IRT approach where cannabis use was found to fit a single factor and fall on a spectrum of severity in the current timeframe in NESARC (Compton et al., 2009). First, the discontinuity approach is based on the number of criteria endorsed and not on the properties of the individual items. Second, the approach directly incorporates validation of the criteria set through their relationship to key risk factors. Third, the approach allows for adjustment for important covariates such as gender and age, a feature not available in IRT analysis. Fourth, the method addresses observed rather than latent variables, which are the "variables" actually used in clinical practice. Further, the discontinuity approach has been described as advantageous since it avoids the assumptions required of LCA and IRT that are not always met in practice (Helzer et al., 2007). Thus, while latent variable approaches have contributed important information that has greatly informed discussions about the structure of substance diagnoses, the discontinuity approach offers the advantage of an additional methodology in evaluating alterations to existing sets of diagnostic criteria.

Study strengths and limitations are noted. First, dependence and abuse symptoms were measured via retrospective structured self-report rather than observation, as was family history, early drinking onset and ASPD However, all variables had good to excellent test–retest reliability and the measures of substance use disorders have been validated in many paradigms. Second, the study was cross-sectional. A prospective study is needed to confirm these relationships. Third, cannabis, as an illicit substance, may be associated with ASPD through disinhibitory personality traits and not directly related to cannabis use in some people. Fourth, it would have been
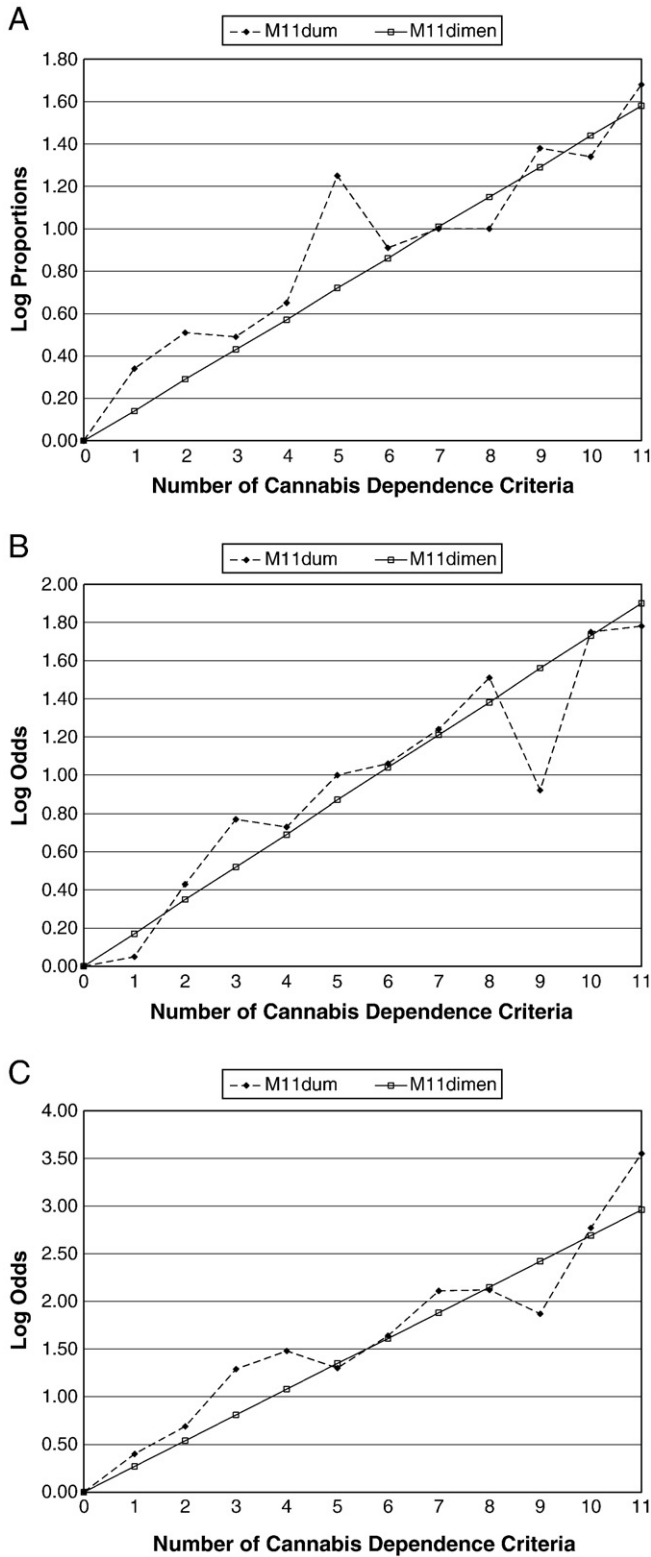
A

B

C

Fig. 2. a. Family history. b. Age of onset. c. Antisocial personality disorder.

of interest to conduct this research with additional substances, but the number of participants using other substances was too limited. Other strengths of the work include a focus on lifetime rather than current variables, a timeframe that is important for epidemiologic and genetic studies.

Table 3
Comparison of the dummy variable model M_{11Dum} to the dimensional model $M_{11dimensional}$, representing 11 cannabis dependence and abuse criteria in NESARC participants (N = 8172).[a]

Outcome	Criterion count (K)	M_{11Dum} estimate	$M_{11dimensional}$ estimate[b]
Log P(K)/P(0)			
Family history	1	0.34 (0.09)	0.14 (0.01)
	2	0.51 (0.11)	0.29 (0.02)
	3	0.49 (0.15)	0.43 (0.03)
	4	0.65 (0.15)	0.57 (0.05)
	5	1.25 (0.15)	0.72 (0.06)
	6	0.91 (0.19)	0.86 (0.07)
	7	1.00 (0.27)	1.01 (0.08)
	8	1.00 (0.20)	1.15 (0.09)
	9	1.38 (0.21)	1.29 (0.10)
	10	1.34 (0.31)	1.44 (0.11)
	11	1.68 (0.31)	1.58 (0.12)
P-value for test of difference with M_{11Dum}			0.03
Log (Odds(K)/Odds(0))			
Age of onset	1	0.05 (0.12)	0.17 (0.02)
	2	0.43 (0.14)	0.35 (0.03)
	3	0.77 (0.15)	0.52 (0.05)
	4	0.73 (0.17)	0.69 (0.06)
	5	1.00 (0.19)	0.87 (0.08)
	6	1.06 (0.24)	1.04 (0.09)
	7	1.24 (0.27)	1.21 (0.11)
	8	1.51 (0.27)	1.38 (0.12)
	9	0.92 (0.30)	1.56 (0.14)
	10	1.75 (0.37)	1.73 (0.15)
	11	1.78 (0.51)	1.90 (0.17)
P-value for test of difference with M_{11Dum}			0.12
Log (Odds(K)/Odds(0))			
Antisocial personality	1	0.40 (0.14)	0.27 (0.02)
	2	0.69 (0.16)	0.54 (0.03)
	3	1.29 (0.19)	0.81 (0.05)
	4	1.48 (0.20)	1.08 (0.06)
	5	1.30 (0.23)	1.35 (0.08)
	6	1.64 (0.25)	1.61 (0.09)
	7	2.11 (0.25)	1.88 (0.11)
	8	2.12 (0.25)	2.15 (0.12)
	9	1.87 (0.28)	2.42 (0.14)
	10	2.77 (0.32)	2.69 (0.15)
	11	3.55 (0.52)	2.96 (0.17)
P-value for test of difference with M_{11Dum}			0.03

[a] Adjusted for age (continuous), gender (0 = female, 1 = male) and race (white = 1, others = 0).
[b] K represents number of criteria present compared to the reference group with 0 criteria.

5. Conclusion

Our study evaluated the dimensionality of lifetime cannabis abuse and dependence criteria to provide information for DSM-V, to identify the set of criteria that best discriminates problem cannabis users and facilitates treatment decisions and for refining variables used in genetic and epidemiological studies. Using a method that connects the criteria to established severity indicators, we showed that combining abuse and dependence can introduce heterogeneity that may be unwanted for some genetic and epidemiological purposes. A useful quantitative phenotype should be correlated with diagnosis and also represent severity of a disease (Almasy, 2003). Using validating variables such as family history, age of onset, or ASPD gives meaningful context because these variables reflect susceptibility (Almasy, 2003). Finally, the results contribute information about the performance of cannabis abuse, dependence and consumption as criteria for cannabis use disorders in DSM-V based on a different approach from that provided by CFA, IRT and LCA. These findings are clinically useful for identifying the set of criteria that best discriminates problem cannabis users and facilitates treatment decisions. The results are timely as they contribute to a convergent picture for the DSM-V Substance Use Disorders Workgroup.

Table 4
Comparison of the dummy variable model M_{12Dum} to the dimensional model $M_{12dimensional}$ representing 12 cannabis dependence, abuse and weekly consumption criteria in NESARC participants (N = 8172).[a]

Outcome	Criterion count (K)	M_{12Dum} estimate	$M_{12dimensional}$ estimate[b]
Log P(K)/P(0)			
Family history	1	0.33 (0.09)	0.14 (0.01)
	2	0.60 (0.11)	0.27 (0.02)
	3	0.67 (0.12)	0.41 (0.03)
	4	0.64 (0.15)	0.54 (0.04)
	5	0.70 (0.17)	0.68 (0.05)
	6	1.35 (0.15)	0.82 (0.06)
	7	1.04 (0.18)	0.95 (0.07)
	8	1.13 (0.31)	1.09 (0.08)
	9	1.12 (0.20)	1.22 (0.09)
	10	1.57 (0.20)	1.36 (0.10)
	11	1.25 (0.34)	1.50 (0.11)
	12	1.84 (0.31)	1.63 (0.12)
P-value for test of difference with M_{12Dum}			0.01
Log (Odds(K)/Odds(0))			
Age of onset	1	0.42 (0.15)	0.18 (0.01)
	2	0.73 (0.15)	0.36 (0.03)
	3	0.99 (0.16)	0.53 (0.04)
	4	1.27 (0.18)	0.71 (0.06)
	5	1.17 (0.20)	0.89 (0.07)
	6	1.33 (0.22)	1.07 (0.08)
	7	1.46 (0.24)	1.25 (0.10)
	8	1.79 (0.27)	1.42 (0.11)
	9	1.88 (0.31)	1.60 (0.13)
	10	1.44 (0.30)	1.78 (0.14)
	11	2.11 (0.39)	1.96 (0.15)
	12	2.10 (0.54)	2.13 (0.17)
P-value for test of difference with M_{12Dum}			0.06
Log (Odds(K)/Odds(0))			
Antisocial personality	1	0.40 (0.15)	0.25 (0.01)
	2	0.86 (0.16)	0.51 (0.03)
	3	0.92 (0.18)	0.76 (0.04)
	4	1.59 (0.19)	1.02 (0.06)
	5	1.64 (0.21)	1.27 (0.07)
	6	1.51 (0.24)	1.53 (0.08)
	7	1.79 (0.24)	1.78 (0.10)
	8	2.42 (0.24)	2.04 (0.11)
	9	2.27 (0.26)	2.29 (0.13)
	10	2.14 (0.28)	2.55 (0.14)
	11	2.90 (0.34)	2.80 (0.16)
	12	3.66 (0.54)	3.06 (0.17)
P-value for test of difference with M_{12Dum}			0.01

[a] Adjusted for age (continuous), gender (0 = female, 1 = male) and race (white = 1, others = 0).
[b] K represents number of criteria present compared to the reference group with 0 criteria.
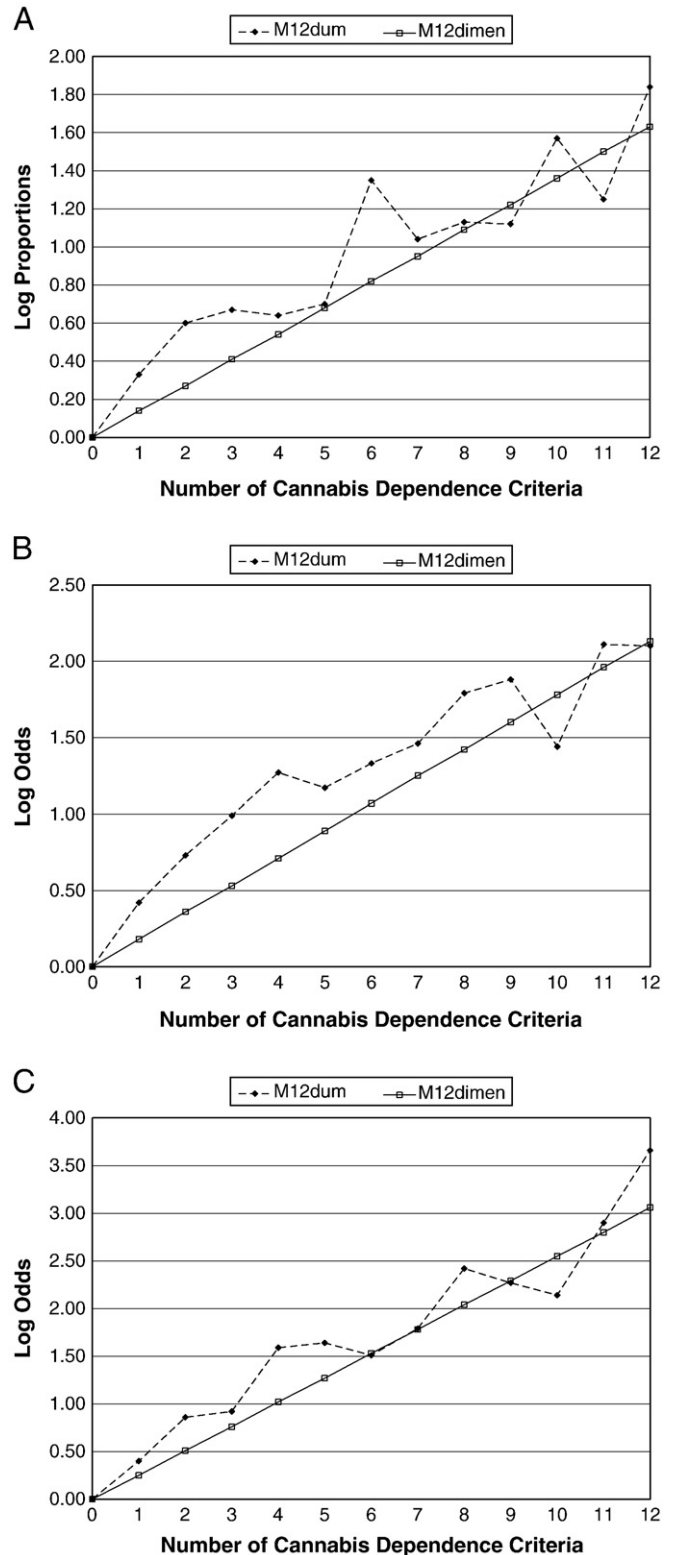
Fig. 3. a. Family history. b. Age of onset. c. Antisocial personality disorder.

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