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Cross-sectional and prospective relation of cannabis potency, dosing and smoking behaviour with cannabis dependence: an ecological study

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ABSTRACT

Background and Aims Increased delta-9-tetrahydrocannabinol (THC) concentrations in cannabis may lead to higher THC exposure, cannabis dependence and treatment need, but users may also adapt the actual intake of THC through reduced inhalation of THC containing smoke (titration). We investigated whether consumers of stronger cannabis use less cannabis per joint or inhale less smoke than those using less potent cannabis and whether these factors predict cannabis dependence severity. **Methods** Heavy cannabis users ($n = 98$) brought their own cannabis, rolled a joint and smoked it *ad libitum* in a naturalistic setting. We analysed the content of the joint, its association with smoking behaviour and the cross-sectional and prospective (1.5-year follow-up) relations between smoking behaviour and cannabis dependence severity (total number of DSM-IV dependence symptoms). **Results** THC concentration in cannabis (range 1.10–24.70%) was correlated positively with cannabis dose per joint ($b = 0.008$, $P = 0.01$), but the resulting THC concentration per joint (range 0.24–15.72%) was associated negatively with inhalation volume ($b = -0.05$, $P = 0.03$). Smoking behaviour measures (number of puffs, inhaled volume, reduction of puff volume and puff duration while smoking) predicted follow-up dependence severity, independently of baseline dependence severity and monthly THC dose (number of joints × cannabis dose × cannabis THC concentration). Monthly THC dose only predicted follow-up dependence severity when unadjusted for baseline severity. **Conclusions** Cannabis users titrate their delta-9-tetrahydrocannabinol intake by inhaling lower volumes of smoke when smoking strong joints, but this does not fully compensate for the higher cannabis doses per joint when using strong cannabis. Thus, users of more potent cannabis are generally exposed to more delta-9-tetrahydrocannabinol. Smoking behaviour appears to be a stronger predictor for cannabis dependence severity than monthly delta-9-tetrahydrocannabinol dose.

Keywords Dose, exposure, frequent cannabis use, marijuana, smoking topography, THC concentration, titration.

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INTRODUCTION

Although the majority of more than 160 million cannabis users world-wide are recreational and non-problematic users [1], roughly one in 10 users becomes dependent, which poses a serious public health issue [2]. Because frequent users are at higher risk of dependence [3,4], the addiction potential of cannabis has been proposed to be dose-dependent and thus linked to the exposure to delta-9-tetrahydrocannabinol (THC; the primary psychoactive constituent of cannabis). Accordingly, the recent increase of the THC concentration in cannabis [5,6] has been suggested to increase the risk of cannabis dependence and to enhance the demand for cannabis dependence treatment [7]. However, people smoking cannabis with a high THC concentration may reduce the total amount of cannabis that they use or adapt their smoking behaviour to titrate their THC exposure, i.e. smoke until a satisfactory effect is reached. Specifically, a reduction in THC exposure can be attained by reducing the dose (grams) of cannabis per joint/cone or inhalation of a smaller volume of THC containing smoke [8–14]. However, most studies on the risk of cannabis dependence and the need for treatment assess only frequency of

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cannabis use (number of days), and thus the effects of THC concentration, cannabis dose and smoking behaviour on total THC exposure are largely overlooked [15]. Moreover, it remains unknown as to whether and to what extent these THC exposure determinants interact, which is inherent to the concept of titration and may be important to consider when addressing the adverse consequences of cannabis. Moreover, smoking behaviour may also be a risk factor independent of total THC exposure. For example, cannabis smokers who inhale rapidly with short intervals may be at greater risk for dependence than calmer smokers, as has been reported for cigarette smokers and nicotine dependence [16].

Titration

Joints consist of plain tobacco to which cannabis is added. Cannabis users have reported to adapt (titrate) the amount of cannabis added per joint according to the strength of the cannabis [9], but experimental data to confirm this behaviour are not available. However, laboratory-based experiments which assess smoking behaviour ('topography') using parameters such as number of puffs, inhalation volume, smoking duration, pattern of inhalation and puff flow velocity support the notion that smokers adapt their smoking behaviour according to the strength of the joint [12,17]. Some cannabis users had shorter puff duration and inhaled lower smoke volumes when joints with a higher THC concentration were used [11–14]. It has been thought that a larger puff volume has been associated with higher post-smoking THC blood levels and higher subjective effects (e.g. 'high') [17]. However, it is unknown how THC exposure determinants (potency–dose–smoking behaviour) interact outside the laboratory in an *ad libitum* and naturalistic setting. On one hand, self-reports of cannabis dose and potency are not very reliable [18], while on the other hand laboratory settings may produce reliable data, but in users who altered their normal smoking behaviour [19]. Moreover, laboratory experiments fix all except one of the variables, precluding investigation of their natural interaction. The only reported naturalistic cannabis smoking topography study investigated the link between cannabis smoking behaviour and withdrawal/craving symptoms during 3 days of abstinence [20]. A positive association between total puff volume and withdrawal/craving was found, indicating that a larger inhaled volume may increase the THC exposure sufficiently to result in significant effects on clinical outcomes. However, this study included only 20 cannabis users smoking 'standard joints'. As user preferences in cannabis dose and potency vary widely [18], the standard joints may have disrupted their natural smoking behaviour. Moreover, the assessment in this study of the unique predictive value of smoking topography considered only cannabis use frequency, but did not include the other exposure determinants (cannabis quantity and potency).

Smoking behaviour

Differences in cannabis smoking behaviour may also represent different risks for cannabis dependence independently of total THC exposure. Similar to cigarette smokers [16,21–24], cannabis smokers typically gradually decrease the puff volume and puff duration during the course of one joint, whereas puff velocity and interpuff interval gradually increase [20]. Interestingly, in a 2-year prospective study, nicotine dependence has been shown to develop more rapidly in tobacco smokers who smoke with stable or increasing puff volume and increasing puff duration ('atypical' smoking) [16]. One interpretation of this finding is that the risk of becoming nicotine-dependent is lower in smokers who reach nicotine saturation before the cigarette is finished and decrease their pace of smoking. If this mechanism also applies to cannabis smoking, one may expect that the risk for and the severity of cannabis dependence is associated with 'atypical' cannabis smoking.

In this study, experienced cannabis users rolled a joint of their own preferred cannabis and smoked it *ad libitum* in a naturalistic setting. Our aims were twofold: first, to investigate whether users titrate their cannabis intake, and secondly to predict cannabis dependence severity using smoking behaviour variables. We hypothesize (i) that strong cannabis (containing a high concentration of THC) is used in lower doses per joint, and that a lower total puff volume is inhaled when joints contain more THC; and (ii) that an (atypical) increase in puff volume and puff duration during the course of smoking a joint is associated with cannabis dependence severity at baseline and predicts dependence severity after 1.5 years, independently of estimated monthly THC exposure and baseline severity.

METHODS

Participants and procedures

Participants were selected from the CanDep study, a prospective cohort study of 600 frequent (dependent and non-dependent) cannabis users [25]. Briefly, Dutch young adult frequent cannabis users (≥3 days use per week for >12 months) were recruited from 'coffee-shops' (where the sale and use of cannabis is condoned) and through chain referral, and monitored with interviews after 1.5 and 3 years. When participants were contacted for the first follow-up interview they were informed about the smoking topography study and checked for eligibility, i.e. past month cannabis use. In the Netherlands, cannabis is smoked almost exclusively in joints mulled with

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tobacco, hence no participants were excluded with other routes of cannabis administration. On a 'first come-first served' principle 70 eligible participants were included. Subsequently, to achieve sufficient variation in cannabis use frequency and cannabis potency preference, recruitment was targeted at under-represented relatively infrequent cannabis users and those with a preference for mild cannabis types, resulting in a total of 106 participants. The final sample included 98 participants because, after the experimental procedure, eight participants had to be excluded: three due to flawed data transmission from the smoking topography device, two because of flawed measurements and three because of follow-up attrition.

The study was performed immediately after the first follow-up interview and this assessment is referred to hereafter as 'baseline' assessment. Interview and measurements took place in a natural setting chosen by the participants, such as their home (60.2%), the research institute (21.4%) or a coffee shop (6.1%). Participants had been asked to bring along at least 1 g of their preferred usually smoked cannabis, and to roll a joint in their own habitual manner. The cannabis dose per joint and the THC concentration of the cannabis were measured objectively (see Assessments) and cannabis smoking behaviours (topography) were measured while smoking the self-prepared joint.

All participants gave written informed consent to participate in the study. The study protocol was approved by the medical ethics committee.

Assessments

Cannabis

The cannabis dose per joint (dose in grams) was determined by weighing the cannabis sample before and after preparation of the joint. Cannabis THC concentration (potency in %) was measured in the remaining sample by laboratory analysis using gas chromatography with flame ionization detection [18,26].

To investigate whether subjects titrated their intake according to potency, the total THC concentration of the joints was determined, adjusted for its tobacco content: [cannabis dose per joint (g) × THC concentration of the cannabis (%)]/total weight of the joint (g).

As users who prefer to become more intoxicated may inhale more smoke and use higher dosages, the preferred level of cannabis intoxication was assessed with a visual analogue scale (1, 'light buzz' to 10, 'very stoned/high').

Finally, to investigate whether cannabis smoking topography is a predictor of cannabis dependence severity independent from other exposure determinants, estimated monthly THC exposure (g) was computed as the product of the number of days using cannabis in the past 4 weeks (n) × average number of (whole) joints per day using cannabis (n) × dose per joint (g) × cannabis THC concentration (%).

Figure 1 Topography measurement device

Smoking topography

Smoking topography was measured using portable smoking topography Cress-micro devices® (Plowshare Technologies, Inc., Baltimore, MD, USA) (Fig. 1). Research staff placed the joint in the device and the participant lit the joint, with the first puff registering immediately upon inhalation. Participants were instructed to smoke the joint in their habitual manner, although they were not allowed to share the joint with others. The smoking session was terminated when participants had finished the joint or when they had achieved their desired high and indicated that they would smoke no more within the next half-hour. In addition to the total number of puffs and total session duration (minutes), assessments for every puff included: puff volume (ml), puff duration (seconds), interpuff interval (seconds), average velocity (flow, ml/second), peak flow (ml/second) and time to peak puff velocity (seconds) (Fig. 2). Means were calculated for these variables for each participant and puff volumes for individual puffs were added to obtain a total puff volume (ml). In addition, pace of smoking was expressed as total puff volume divided by total session duration. Finally, to investigate participants' changes in smoking behaviour during the course of a smoking session, changes in topography patterns were represented by calculating the differences between the three first real puffs and final three puffs.* The first 'lighting' puff was excluded, as this puff is atypical, because it is commonly much larger than subsequent puffs [20]. When the average volume of the first puffs was higher than the

*Three subjects took fewer than seven puffs. For them, changes in smoking behaviour during the course of a smoking session were represented by the differences between the second puff (excluding the first lighting puff) and the final puff.

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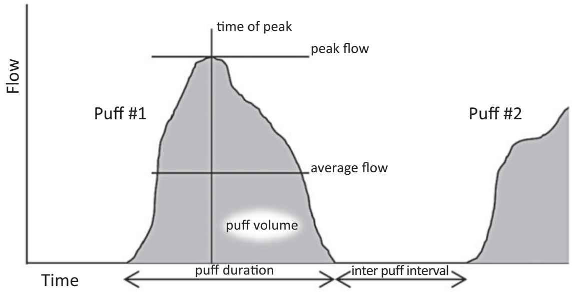

Figure 2 Topography measures

last puffs, the change in volume variable has a positive value, representing a decrease during the course of the joint.

Cannabis dependence severity

Baseline cannabis dependence severity was assessed as the total number of DSM-IV dependence symptoms present between recruitment and baseline interview (approximately 1.5 years) using the Composite International Diagnostic Interview (CIDI) version 3.0 [27]. Follow-up dependence severity was assessed similarly covering the period of 18 months after the baseline interview.

DATA ANALYSES

Titration

The association between cannabis potency and dose was assessed with linear regression analyses, with and without controlling for frequency of cannabis use, preferred level of cannabis intoxication and baseline cannabis dependence severity.

Associations between the different smoking topography measures, particularly total inhaled volume, and THC concentration of the joints were analysed using linear regression analyses.

Prediction of dependence severity

We examined predictors of concurrent and prospective cannabis dependence severity using linear regression models in three steps:

1. The association between baseline estimated monthly THC exposure and baseline and follow-up cannabis dependence severity were calculated. In addition, the effect of baseline estimated monthly THC exposure on follow-up dependence severity was adjusted for baseline cannabis dependence severity. The log-transformed value of the estimated monthly THC exposure was used in all analyses because of its skewed distribution.
2. Using a series of regression analyses with separate analyses for the different cannabis smoking topography measures, the associations with baseline cannabis dependence severity were assessed. To investigate whether topography measures add to the predictive power of other exposure determinants, associations between the different smoking topography measures and dependence severity were adjusted for estimated past month THC exposure, using *F*-tests to compare adjusted R^2s.
3. Similarly, the different smoking topography measures were used to predict cannabis dependence severity at 1.5-year follow-up, first without any adjustments for other cannabis use variables; analyses were then adjusted for the estimated baseline monthly THC exposure. Finally, they were additionally adjusted for baseline cannabis dependence severity, to establish the contribution of the cannabis use topography measure to future cannabis dependence severity over and above these other predictors.

RESULTS

Sample characteristics

Demographics and cannabis use history

Table 1 shows the demographics and cannabis use history of the sample: 73 of the 98 participants (74.5%) were male, mean age was 23.7 years, and 32 participants (32.7%) met DSM-IV criteria for cannabis dependence at baseline.

Cannabis

Table 2 shows large differences in cannabis use characteristics between users. On average, the cannabis dose per joint was 0.26 g (range 0.07–0.89 g), the THC concentration of cannabis was 12.36% (range 1.10–24.70%) and the weight of the joint was 0.94 g (range 0.56–1.76 g), resulting in a mean THC concentration of the joint of 3.64% (range 0.42–15.72%) and an average monthly exposure to THC of 2.05 g (range 0.02–14.50 g).

Smoking topography

Table 2 shows that cannabis smoking topography measurements also varied considerably between users. For example, the total number of puffs ranged from three to 40 and total puff volume per smoking session varied from 0.15 to 2.54 litres. During the course of smoking the joints, typical changes were observed in the following topography measures: a decrease in average puff volume, puff flow and puff duration (indicated by positive average values of first minus last puffs) and an increase in

Table 1 Sample characteristics.

n = 98	*n* (%)	*Mean (SD)*	*Range*
Male	73 (74.5)		
Age (years)		23.7 (3.01)	19–32
Age of first cannabis use		14.5 (2.32)	10–22
Preferred level of intoxication		5.99 (1.81)	2–10
Days using cannabis in past 4 weeks		21.0 (7.8)	2–28
Baseline number of dependence symptoms		2.03 (1.65)	0–7
Baseline dependence diagnosis	32 (32.7)		
Follow-up number of dependence symptoms		1.94 (1.52)	0–6
Follow-up dependence diagnosis	29 (29.6)		
Non-tobacco smoker[a]	26 (26.5)		

[a]Besides tobacco in joints. SD = standard deviation.

Table 2 Description of cannabis use and topography characteristics.

n = 98	*Mean*	*Min*	*Max*	*SD*
Cannabis use				
Cannabis dose per joint (g)	0.26	0.07	0.89	0.14
[THC] of cannabis (%)[a]	12.36	1.10	24.70	4.38
[THC] of joint (%)[b]	3.64	0.24	15.72	2.51
Last month days of use	20.98	2.00	28.00	7.83
Number of joints per use day	2.48	0.20	8.00	1.71
Monthly THC dose (g)	2.05	0.02	14.50	2.71
Topography				
Puff count	18.98	3.00	40.00	9.45
Puff volume (ml)	56.69	14.98	167.22	21.15
Total puff volume (litres)	1.03	0.15	2.54	0.58
Test time (minutes)[c]	20.06	4.37	45.88	11.30
Pace (l/hour)[c]	3.77	0.42	11.37	2.16
Average flow (ml/second)	34.89	15.81	66.47	7.82
Peak flow (ml/second)	50.00	19.52	87.69	11.84
Puff duration (seconds)	1.68	0.59	4.11	0.54
Interpuff interval (seconds)	54.29	16.53	306.59	42.87
Time of peak (seconds)	0.63	0.21	1.49	0.28
Δ Volume (ml)	14.83	−49.78	103.66	24.05
Δ Average flow (ml/second)	1.82	−23.22	27.54	8.77
Δ Peak flow (ml/second)	3.01	−42.49	35.34	13.31
Δ Puff duration (seconds)	0.29	−5.40	1.80	0.87
Δ Interpuff interval (seconds)	−50.76	−456.57	94.97	85.41

[THC] = THC concentration; Δ = mean of topography parameter of the first three puffs minus mean of the last three puffs (excluding the first 'lighting' puff).* [a](g THC/g cannabis). [b](g THC/g joint). [c]*n* = 97. SD = standard deviation; THC = delta-9-tetrahydrocannabinol.

interpuff interval. However, the minimum values below zero (>0 maximum interpuff interval) indicate atypical smoking patterns, i.e. more intense smoking later in the smoking session.

Dependence severity

Table 1 shows the average number of dependence symptoms at baseline and at 1.5-year follow-up. Between assessments, the number of symptoms remained stable for a third of the participants (30.6%), decreased in a third (35.7%) and increased in a third (33.7%) of the participants.

Titration

Titration was addressed by investigating the associations between cannabis dose and potency, and between smoking topography and THC concentration of the joints. Contrary to our hypothesis, the amount of cannabis per joint (dose) was associated positively with the THC concentration in the cannabis ($b = 0.008$, $P = 0.01$). This indicates that a 1% increase in THC concentration in cannabis is associated with a dose increase per joint of 0.008 g. This association remained positive after adjustment for frequency of use, preferred level of intoxication and baseline dependence ($b = 0.007$, $P = 0.02$).

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Table 3 Smoking behaviour titration: associations between delta-9-tetrahydrocannabinol (THC) concentration in joints and smoking topography measures.

	THC concentration[a]	
	b	*P*
Puff count	−0.36	0.35
Test time (minutes)[b]	−0.19	0.68
Total puff volume (litre)	**−0.05**	**0.03**
Pace (l/hour)[b]	**−0.19**	**0.03**
Volume (ml)	−1.48	0.08
Average flow (ml/second)	−0.47	0.14
Peak flow (ml/second)	−0.44	0.36
Puff duration (seconds)	−0.02	0.43
Interpuff interval (seconds)	−0.41	0.82
Time of peak (seconds)	−0.01	0.21
Δ Volume (ml)	−0.02	0.98
Δ Average flow (ml/second)	−0.04	0.91
Δ Peak flow (ml/second)	−0.14	0.80
Δ Puff duration (seconds)	0.00	0.97
Δ Interpuff interval (seconds)	−1.07	0.76

[a]THC concentration = (dose × THC% cannabis)/total weight joint. All analyses are bivariate linear regressions; *b* = linear regression coefficient. Every % THC increase results in '*b*' increase in topography measure. Δ = mean of topography parameter of the first three puffs minus mean of the last three puffs (excluding the first 'lighting' puff).* [b]*n* = 97. Shown in bold type: $P < 0.05$.

Table 3 shows that participants who smoked joints with a high THC concentration inhaled a lower total volume ($b = -0.05$ litre, $P = 0.03$) indicating that a 1% increase in THC concentration per joint is associated with a decrease of inhalation volume of 0.05 litres (50 millilitres). Moreover, dividing total volume by session duration showed that these subjects also smoked at a slower pace ($b = -0.19$ litres/hour, $P = 0.03$).

To gain a better understanding of the net results of these opposing processes we compared the average cannabis users with the one that uses cannabis with the highest THC concentration. Compared to the average user, who inhales 1.03 litres of smoke of 3.64% THC in the joint, the user with the maximum THC concentration in the joint (15.72%; i.e. 12.08% higher than average) inhales 1.03 litres – (12.08% × 0.05 litres) = 0.43 litres. Thus, although the THC percentage in the joint quadrupled, inhalation only halved.

Prediction of dependence severity

Baseline THC exposure estimates and the different smoking topography measures were associated with dependence severity at baseline and 1.5-year follow-up, adjusted for several potential confounders, as follows.

Monthly THC dose and cannabis dependence severity

The estimated baseline monthly THC exposure (range 0.02–14.50 g) was associated with baseline dependence severity ($b = 0.27$, $P = 0.03$, adjusted $R^2 = 0.04$). Due to the natural log transformation, this regression coefficient *b* can be interpreted as an odds ratio: participants who use 1 g more THC per month showed on average 27% more baseline dependence symptoms.

Baseline estimated monthly THC exposure also predicted dependence severity at 1.5-year follow-up ($b = 0.29$ $P = 0.01$, adjusted $R^2 = 0.06$), but this effect was no longer statistically significant after adjustment for baseline severity ($b = 0.13$ $P = 0.13$).

Topography and baseline cannabis dependence severity

Table 4 shows the results of the regression analyses for the different smoking topography measures. Total puff number ($b = 0.05$, $P = 0.008$) and a decrease in puff volume during the course of smoking joints ($b = 0.02$, $P = 0.01$) at baseline were associated positively with baseline cannabis dependence severity. Thus (on average) a user had one more dependence symptom with every 20 puffs, or every 50-ml decrease between first and last puff volume. Similar results were obtained after adjustment for total THC exposure. However, mean puff volume became correlated negatively with baseline dependence severity ($b = -0.02$, $P = 0.03$).

Baseline topography and cannabis dependence severity at follow-up

Table 4 also shows that, like dependence severity at baseline, dependence severity at follow-up was also predicted by total puff number ($b = 0.04$, $P = 0.02$) and a decrease in puff volume during the course of smoking joints ($b = 0.02$, $P < 0.001$). Cannabis dependence severity at follow-up was also predicted by total inhaled volume ($b = 0.73$, $P = 0.006$) and a decrease in puff duration during the course of smoking joints ($b = 0.61$, $P < 0.001$). Again, adjustment for monthly baseline THC exposure did not affect these associations. Added baseline topography variables to baseline THC exposure improved the prediction of cannabis dependence severity significantly at follow-up (*F*-tests: all $P < 0.03$). None the less, the explained variance of these models remained low (all adjusted $R^2 < 0.17$).

Progression of cannabis dependence (i.e. severity of follow-up dependence adjusted for baseline severity and THC exposure) was predicted by total puff volume, decrease in puff volume and decrease in puff duration during the course of smoking joints, but not by total puff number. Finally, pace of smoking and mean puff volume were also significant predictors after adjustment for baseline severity (Table 4). In a series of sensitivity analyses (see Supporting information), the results remained similar (a) for males only, (b) when using the dichotomous dependence diagnosis, (c) after additional adjustment for

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Table 4 Prediction of dependence severity: associations between smoking topography and baseline and follow-up dependence severity.

	Baseline dependence severity				*Follow-up dependence severity*					
n = 98	*b*	*P*	$b1_{adjusted}$	*P*	*b*	*P*	$b1_{adjusted}$	*P*	$b2_{adjusted}$	*P*
Puff count	**0.05**	**0.008**	**0.04**	**0.01**[b]	**0.04**	**0.02**	**0.03**	**0.03**[e]	0.01	0.47
Puff volume (ml)	−0.02	0.06	**−0.02**	**0.03**[c]	0.00	0.73	0.00	0.97	**0.01**	**0.05**
Total puff volume (litres)	0.44	0.14	0.31	0.28	**0.73**	**0.006**	**0.61**	**0.02**[f]	**0.43**	**0.04**
Test time (minutes)[a]	0.01	0.72	0.00	0.80	−0.01	0.31	−0.02	0.24	−0.02	0.08
Pace (l/hour)[a]	−0.03	0.67	−0.05	0.56	0.13	0.08	0.11	0.10	**0.14**	**0.008**
Average flow (ml/second)	−0.03	0.15	−0.03	0.12	0.01	0.72	0.01	0.79	0.03	0.10
Peak flow (ml/second)	−0.02	0.23	−0.02	0.16	0.00	0.82	0.00	0.96	0.01	0.22
Puff duration (seconds)	−0.34	0.28	−0.41	0.19	−0.17	0.57	−0.23	0.40	0.03	1.00
Interpuff interval (seconds)	0.00	0.51	0.00	0.49	−0.01	0.17	−0.01	0.14	0.00	0.19
Time of peak (seconds)	−0.87	0.15	−0.86	0.15	−0.39	0.49	−0.38	0.48	0.12	0.78
Δ Volume (ml)	**0.02**	**0.01**	**0.02**	**0.03**[d]	**0.02**	**<0.001**	**0.02**	**<0.001**[g]	**0.01**	**0.006**
Δ Average flow (m/second)	0.01	0.72	0.01	0.61	0.01	0.55	0.01	0.44	0.01	0.56
Δ Peak flow (ml/second)	0.01	0.64	0.01	0.55	0.01	0.37	0.01	0.28	0.01	0.38
Δ Puff duration (seconds)	0.37	0.06	0.31	0.11	**0.61**	**<0.001**	**0.55**	**0.001**[h]	**0.38**	**0.004**
Δ Interpuff interval (seconds)	0.00	0.83	0.00	0.78	0.00	0.15	0.00	0.16	**0.00**	**0.04**

Δ = mean of topography parameter of the first three puffs minus mean of the last three puffs (excluding the first 'lighting' puff).* [a]*n*= 97. Unadjusted analyses are bivariate linear regressions for each topography measure (*b* = linear regression coefficient). These regressions are subsequently adjusted for baseline (log-tranformed) total estimated monthly delta-9-tetrahydrocannabinol (THC) exposure (g) ($b1_{adjusted}$) and for baseline dependence severity + (log-tranformed) baseline total monthly THC exposure (g) ($b2_{adjusted}$). [b]$R^2_{adjusted}$ = 0.09; [c]$R^2_{adjusted}$ = 0.08; [d]$R^2_{adjusted}$ = 0.08; [e]$R^2_{adjusted}$ = 0.09; [f]$R^2_{adjusted}$ = 0.10; [g]$R^2_{adjusted}$ = 0.17; [h]$R^2_{adjusted}$ = 0.15. Shown in bold type: $P < 0.05$.

preferred level of intoxication and (d) after additional adjustment for percentage of the joint smoked. Independent predictors were identified using stepwise backwards regression ($P < 0.10$).

DISCUSSION

This study among 98 experienced cannabis smokers is the first naturalistic study to examine whether users of cannabis with high THC concentration titrate the psychoactive effects by using lower doses and/or by reduced inhalation, and whether cannabis smoking behaviour (topography) predicts cannabis dependence severity independently of total THC exposure.

In contrast to our hypothesis, there was a positive association between cannabis THC concentration and cannabis dose, indicating that users of stronger cannabis generally used larger amounts of cannabis to prepare their regular joint. However, in line with our hypothesis, the negative association between THC concentration of joints and total inhaled smoke volume indicates that users of stronger joints inhaled smaller smoke volumes, thus resulting in partial titration of the total THC exposure. Overall, as exemplified by the comparison of the average user with the user with the maximum THC concentration, users of high-potency cannabis will generally be exposed to higher total doses of THC (at least in this sample). This is in line with Cappell *et al.*'s observations through a one-way mirror experiment in 1973 where users only partly adapted their intake [14]. Indeed, increased THC concentrations of cannabis have recently been linked to increased internal THC exposure assessed in blood [28].

THC concentration of the participants' preferred cannabis samples and the self-prepared joints varied markedly, highlighting the importance of our naturalistic approach. Nevertheless, the average THC concentration of the participants' joints (3.64%) was similar to the stronger variants used in previous studies [12–14,17,20]. Similarly, the estimated baseline monthly THC dose ranged largely from 0.02 to 14.50 g THC, and was associated with cannabis dependence severity. It also predicted cannabis dependence severity at follow-up, but not independently of baseline severity. Thus, THC exposure does not add to the prediction of future cannabis dependence severity over and above baseline cannabis dependence severity. This corresponds with the limited role we observed for self-reported cannabis exposure in the incidence and persistence of cannabis dependence in the full CanDep cohort [29, Van der Pol *et al.*, 2014 (Unpublished)]. However, baseline smoking topography measures predicted future cannabis dependence severity independently of estimated baseline monthly THC exposure. Given the limited role of total monthly exposure predicting dependence severity, the added predictive value of the total number of puffs and puff volume is probably not caused by its associated effect on total THC exposure, but rather marks compulsive use that is presumably related to (lack of) THC saturation during the session.

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Although, overall, the 'typical' changes in puffing during the course of the joint smoking session were observed (e.g. average decreased puff volume and puff duration over time [20]), 'typical' rather than 'atypical' topographies predicted dependence severity, which is in contrast with the tobacco literature [16]. Possibly, more subtle effects of saturation on smoking behaviour were concealed by two characteristics that are specific for cannabis users. First, unlike most cigarette smokers, cannabis users do not always finish their joint in one session. Secondly, joints were usually made with a rolled-up piece of paper instead of a (cellulose) cigarette filter, which may cause the last puffs of the joint to be hot, and therefore smaller and shorter. As this occurs only in those finishing the joint in one session (without having reached their desired 'high'), these may be more tolerant and more severely dependent users. *Post-hoc* analyses indeed showed that the percentage of the joint smoked during the session was associated with follow-up dependence severity. However, all topography predictors except total puff volume remained significant after additional adjustment for the percentage of the joint smoked (see Supporting information). Nevertheless, percentage of the joint smoked may be a simple proxy for risky smoking behaviour.

Strengths and limitations

The main strengths of the current study are the sample size, the ecological context and the availability of follow-up data. The study also has some limitations. First, the current study only allowed investigation of overall (between-subject) correlations rather than individual (within-subject) adaptations. In particular, while our data suggest that potent cannabis is generally not used in lower doses, this may be associated with tolerance to the effect of THC in chronic heavy users. Further, despite adjustment for baseline dependence severity and estimated monthly THC dose, tolerance may still contribute to the relatively low explained variance of the predictive models. Therefore, future studies should also assess whether individual users adapt their dose to the cannabis potency they expect, although it should be noted that users' estimates of cannabis potency are quite unreliable [18]. Similarly, adaptation of smoking behaviour to changing levels of THC concentration of joints should be investigated by comparing smoking topography using self-prepared joints with standard joints. Secondly, although the cannabis dose and potency were measured objectively, we relied upon self-report for the preferred type of cannabis and for the estimated monthly total THC dose (frequency and joints per day). In addition, sharing a joint with others could not be simulated, while 65.3% reported to often share their joint with one or more others. However, sharing was approximated by asking participants to smoke until they achieved their desired 'high'. Thirdly, the use of tobacco in joints may interfere with our results, as tobacco dependence may also influence (cannabis) smoking topography. However, *post-hoc* analyses showed unchanged results when adjusted for a proxy measure of nicotine dependence [30]. None the less, extrapolation to other consumption methods may be problematic.

CONCLUSIONS

Although experienced young adult cannabis users with a preference for stronger joints titrated their THC exposure to some extent by inhaling less smoke, in general more potent cannabis was used in higher dosages leading to a higher THC exposure compared to users preferring lower potency cannabis. None the less, in our population of frequent cannabis users, total THC exposure was only a weak predictor of dependence severity, and did not remain significant after adjustment for baseline dependence severity. However, cannabis smoking behaviours predicted cannabis dependence severity independently of baseline THC exposure and baseline cannabis dependence severity. As the amount of explained variance was low, due possibly to the multifactorial aetiology of dependence, future studies should include other predictors, such as genetic variations, early traumatic experiences and—most importantly—time-dependent variables representing the dynamic nature of personal and dependence development. Meanwhile, smoking variables, such as smoking topography and completely finishing high-dose/high-potent joints in one smoking session, may be helpful to identify people at risk of escalating cannabis dependence severity.

Declaration of interests

None.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher’s web-site:

Online Supplement Sensitivity analyses of the relation of cannabis potency, dosing and smoking behaviour with cannabis dependence: an ecological study.

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