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Université de Lausanne Faculté de biologie et de médecine

Routes of administration of cannabis used for non-medical purposes and associations with patterns of drug use

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Abstract

Purpose. Little is known regarding cannabis administration routes for non-medical use, i.e., its delivery methods (e.g., joints, water pipe or food). Therefore, we have examined the prevalence rates of different cannabis delivery methods and assessed the relationship of the distinct administration routes with problematic drug use. Subgroups of cannabis users were also investigated (i.e. "pure" cannabis users, previously described as a harmless route of administration).

Methods. As part of the Cohort Study on Substance Use Risk Factors, 1,763 cannabis users answered questions concerning their drug use (i.e., routes of administration, problematic cannabis use, other illicit drugs use). Descriptive statistics, latent class analysis (LCA), correlations and t-tests were assessed.

Results. The main administration route was "joints with tobacco", but other routes of administration had prevalence rates going from 23.99% to 38.23%. In addition, increasing the number of administration routes was associated with more problematic cannabis use as well as heavier illicit drug use. Water pipes without tobacco were especially linked to heavy drug use patterns, whereas "pure" cannabis use seemed less harmful.

Conclusions. Our findings highlighted that diversification in routes of administration can be associated with heavier illicit drug use. This was especially true for water pipe users, whereas "pure" cannabis users, who did not mix their cannabis with tobacco, were an exception. Indeed, these results may be useful for future preventive programs, which may need to focus on those who have diversified their routes of administration for cannabis.

Key words. Cannabis administration routes; Patterns of drug use; "Pure" cannabis use; Problematic cannabis use; Water pipe.

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Implications and contributions

This study filled a gap by analyzing cannabis administration routes and its associations with drug use patterns. It showed that diversification in the routes of administration was associated with heavier drug use. This was especially true for water pipe users, but not for "pure" cannabis users.

Introduction

Cannabis is the most used illicit drug worldwide [1, 2], and its use has recently increased in European countries, including Switzerland [3-5]. Many studies have investigated patterns of cannabis use [6-10], especially concerning its relationship with tobacco use [2, 11-17]. However, since most of the studies analyzing cannabis use have not differentiated between the various methods of delivery, little is known regarding distinct administration routes during non-medical use of cannabis or their relationship with drug use patterns.

There are three main routes of administration for cannabis during non-medical use: smoking joints (with or without tobacco), smoking or inhaling with a water pipe (with or without tobacco), and swallowing (i.e., food, tea). Although cannabis is most widely used via joint smoking, other routes of administration appear to be increasingly used among youth [18, 19]. So far, very few studies investigating non-medical use of cannabis have compared the effect of different routes of administration on health [18], whereas studies related to medical use of cannabis have often examined delivery methods [20].

In regards to therapeutic administration, the most common route of administration is smoking [21]; however, alternative delivery methods have been studied in order to minimize respiratory damage [22, 23], while maintaining rapid action [24]. Comparisons of administration routes for medical use have demonstrated that smoked cannabis acts faster than ingested cannabis [25-28]. In fact, the effect of ingested cannabis can be delayed from 15 minutes to one hour, whereas inhaled (smoked) cannabis acts almost immediately [25-27, 29, 30]. However, the effects of ingested cannabis last longer, persisting from three to eight hours depending on the dose

swallowed [25-28]. Nevertheless, the risk of accidental overdose is more prevalent with oral cannabis use because there is not a clear idea of the dose taken [23]. This would be especially true for non-medical users, who may not know the dose of cannabis (or of its principal psychoactive constituent, delta-9-tetrahydrocannabinol [THC]) used in the preparation of food, such as space cakes.

Studies concerning the medical use of cannabis have compared smoking, inhaling and swallowing cannabis. Thereby, they might overlook some important issues associated with nonmedical use of cannabis, such as water pipe use and mix of cannabis with tobacco. Few studies focused on water pipe use. Notably, Chabrol et al. [18] have reported that water pipes have a sharp, quick, and strong effect that is comparable to the effect of "harder" illicit drugs, such as cocaine or heroin. Indeed, water pipes allow the inhalation of more smoke and THC at once, amplifying the effect of cannabis. Moreover, the use of bongs (a special sort of water pipes) is linked to cannabis dependence [19]. On the contrary, "pure" cannabis use and mixed cannabis with tobacco is a well studied topic. Among cannabis users, several studies have reported that non-tobacco smokers showed fewer complications than tobacco smokers, such as problematic polydrug use or illicit drug use [1, 14, 31, 32].

In order to address current gaps in cannabis research, the aim of this study was threefold: 1) to explore the prevalence rates and patterns of use of different cannabis administration routes during non-medical use in Switzerland; 2) to investigate the relationship between the distinct cannabis administration routes and drug use patterns (i.e., associations between routes of administration, problematic cannabis use, use of other illicit drugs); and 3) to compare specific subgroups of cannabis users, described in previous studies to be a harmless route of administration ("pure" cannabis use instead of mixing cannabis with tobacco), and a harmful route of administration (water pipe use).

Methods

Participants and procedure

The data presented here were part of the baseline information collected for the Cohort Study on Substance Use Risk Factors (C-SURF), which was a longitudinal study assessing substance use patterns and related consequences in young Swiss men. Participants were enrolled between August 23, 2010 and November 15, 2011 at three out of six army recruitment centers located in Lausanne (French-speaking), Windisch (German-speaking), and Mels (German-speaking). Notably, these three centers cover 21 of 26 cantons in Switzerland, including all French-speaking cantons. Also, since army recruitment is mandatory in Switzerland, the sample is highly representative of young Swiss men. It is important to note that the recruitment centres were used only to enroll participants. Assessment was done outside the army environment and independent of army service, civil service or no service.

Of the 13,245 conscripts informed of the study, 7,563 gave written consent to participate, and 5,990 completed the baseline questionnaire. Specifically, the current study focused on the 1,841 participants who used cannabis during the past 12 months (30.7% of the sample). Missing values were deleted listwise, ultimately resulting in a total of 1,763 participants included in the study (95.8% of the sample of cannabis users). This subsample displayed a similar age range to that of the overall sample (12 past months cannabis users: 20.03 ± 1.23 ; overall sample: 20.01 ± 1.25).

More information on sampling and non-responders can be found in Studer et al. [33]. In brief, non-responders were more often substance users; however, there were only small differences between respondents and non-respondents, which could likely be attributed to the large sample size.

Measures

Routes of administration of cannabis

We measured the frequency of cannabis use in the previous 12 months. First of all, we asked whether use had occurred in the past 12 months, and then we inquired about the frequency of use (with a scale ranging from 0 when it was used "monthly or less" to 4 when it was used "every day or almost every day"). The main routes of cannabis administration were also assessed: joint of cannabis with tobacco, joint of cannabis without tobacco, water pipe with tobacco, water pipe without tobacco, or cannabis mixed with food. In addition, another option was added, "other ways". The answers were collected on a five-point scale, including "never", "seldom", "sometimes", "often", and "always", which were coded from 0 (never) to 4 (always).

Subgroups were created based on the specific kinds of cannabis use in order to investigate patterns of drug use: (i) "pure" cannabis use: "pure" cannabis users, who used cannabis exclusively without tobacco (i.e., no joints with tobacco or water pipes with tobacco) vs. non "pure" cannabis users; (ii) water pipe use: water pipe users, who used water pipes with and/or without tobacco versus non-water pipe users, who did not use water pipes with or without tobacco.

Problematic cannabis use

Participants were asked about their problematic use of cannabis during the past 12 months utilizing the Cannabis Use Disorder Identification Test, CUDIT [34], a 10 item assessment tool for evaluating cannabis misuse. Seven items were coded on a 5-point scale from 0 to 4, and three items were coded 0 or 4. A total score was computed, which goes from 0 to 40. Example items included "how often have you failed to do what was normally expected from you because of using cannabis?" (coded on a 5-point scale), "how often have you felt guilty or remorseful after using cannabis?" (coded on a 5-point scale) or "have you or someone else been injured as a result of your use of cannabis over the past 12 months?" (coded 0 "no" or 4 "yes").

Illicit drug use

The use of illicit drugs during the past 12 months was measured through fifteen categories, which were answered as either "used" (coded 1) or "non-used" (coded 0). Substances included were as follows: 1) hallucinogens, magic mushrooms, psilocybin, peyote, mescaline; 2) other hallucinogens (LSD, PCP/Angel Dust, 2-CB, 2-CI); 3) salvia divinorum; 4) speed; 5) amphetamine, methamphetamine, amphetaminsulfate (e.g., Dexedrine, Benzedrine); 6) crystal meth (Ice); 7) poppers (Amylnitrit, Butylnitrit); 8) solvent sniffing (e.g., glue, solvent and gases, such as benzin, ether, toulol, trichloroethylene, nitrous oxide); 9) ecstasy, MDMA; 10) cocaine, crack, freebase; 11) heroin; 12) ketamine (Special K), DXM; 13) GHB/GBL/I-4 Butandiol (BDB); 14) research chemicals (e.g., mephedrone, butylone, and methedrone) and 15) spices or similar substances (synthetic cannabis). Finally, a total score relating to the substances used during the past 12 months was computed (from 0 to 15).

Statistical analyses. The three main purposes of the study were investigated as follow. Descriptive statistics first provided information regarding prevalence rates of the different administration routes and related drug use patterns (i.e., problematic cannabis use and illicit drug use) (purpose 1). The patterns of use of routes of administration were also investigated with latent class analysis (LCA) [35, 36] was performed to determine whether there were in fact distinct groups of cannabis users based on routes of administration. In LCA, the categorical classes correspond to latent variables, and posterior probabilities are used to assign each participant to the most likely latent class. Since the number of classes is unknown, the optimal number of latent classes is determined using fit indices for various models. The Lo-Mendel-Rubin likelihood ratio test (LMR LRT) was conducted to examine whether a model with k-class was better than a model with k-1-class [37]. In this test, a low p-value indicates that the model with k-1-class is rejected in favor of a model with k-class. This analysis was performed using Mplus 6 [38]. Descriptive statistics were then utilized to show the levels of problematic cannabis use and illicit drug use for each of the classes, and to give an overview of the relationship between patterns of use of routes of administration and patterns of drug use (purpose 2). Moreover for purpose 2, correlations were drawn between specific routes of administration and drug use patterns (i.e., problematic cannabis use and illicit drug use). Correlations were performed instead of multiple regressions because no specific hypothesis was made about the causal relationship between the variables. Both Pearson and Spearman correlations were conducted in order to determine if there were differences due to the asymmetric distribution of variables. However, as these results were similar, only Pearson correlations are presented. Bivariate correlations and partial correlation controlling for the frequency of cannabis use and other routes of administration were performed in order to observe pure effects associated with

individual administration routes and to take into account the possible covariance and overlap between routes of administration. Finally, further comparative analyses were performed for the distinct cannabis-using subgroups (i.e., "pure cannabis" users *vs.* "cannabis with tobacco" users as well as water pipe users *vs.* non-water pipe users) (purpose 3). Also, t-tests were conducted in order to compare the patterns of drug use between the subgroups.

Results

Prevalence rates and patterns of use of routes of administration of cannabis

Prevalence rates for the different routes of administration are presented on the first two lines of Table 1. We observed that "joint with tobacco" was the most prevalent cannabis administration route, which was used by 97.28% of participants, either solely or together with other routes (mean score: 2.96 on a 5-point scale from 0 to 4). Only 2.72% of the cohort never smoked a joint of cannabis with tobacco. "Joint without tobacco" (38.23%) and "cannabis mixed with food" (37.27%) showed the second highest rates with mean score of use frequencies of 0.55 and 0.47 respectively, whereas the least often used route of administration was water pipes, either with or without tobacco (29.27% and 23.99%, respectively; mean score of use frequencies: 0.41 and 0.34). Less than 10% of cannabis users reported administration of cannabis via other routes (9.3%).

Insert Table 1 about here

Using LCA, we identified that three classes were optimal for the model (LMR-LRT test: p = .030 for 2 *vs*. 3 classes; p > .05 for 3 *vs*. 4 classes). The description for each of these classes is given at

the bottom of Table 1. In this classification, Class 1 was comprised of "moderate cannabis users", who had low levels for all routes of administration, including joints with tobacco ("joint with tobacco" = 1.10; other routes of administration < 0.46), Class 2 referred to users who mostly smoked joints containing tobacco ("joint with tobacco" = 3.67; other routes of administration < 0.45), and Class 3 included "heavy/diversified users", who practiced more diversified delivery methods ("joint with tobacco" = 3.38; other routes of administration > 1.28).

Routes of administration of cannabis and association with pattern of drug use

The descriptive statistics provided in the LCA (Table 1) also showed that the level of problematic cannabis use and number of illicit drugs used increased among the classes (CUDIT: from 3.06 to 12.97; number of illicit drugs used: from 0.34 to 2.16).

Table 2 presents the correlations between each route of administration, CUDIT scores, and the number of illicit drugs used. When the results were unadjusted, intermediate levels of correlation were obtained between all administration routes, CUDIT scores (.27 \leq r \leq .36), and number of illicit drugs used (.09 \leq r \leq .31). However, when the results were adjusted for the frequency of cannabis use, "joint with tobacco" was no longer significantly associated with the CUDIT score or the number of illicit drugs used, whereas the other correlations remained significant and positive, even though they were less significant than in the unadjusted analysis (.12 \leq r \leq .23). When the results were adjusted for both frequency of use and other routes of administration, the correlations were still significant, but again decreased (.06 \leq r \leq .16). Also, "joint with tobacco" was again found to be non-significant. Notably, we observed the strongest correlations for water pipe without tobacco (r = .14 for CUDIT and r = .16 for the number of illicit drugs used).

Insert Table 2 about here

Subgroups of cannabis users and related pattern of drug use

Table 1 also presents results for the different cannabis user subgroups according to routes of administration and LCA. The users of cannabis without tobacco (i.e., "joint and water pipe without tobacco", "cannabis mixed with food") reported lower levels of problematic cannabis use and illicit drug use (CUDIT = 3.19, number of illicit drugs = 0.08) compared to non "pure" cannabis users (joints and water pipes with tobacco, CUDIT = 6.72, number of illicit drugs = 0.71). The difference was significant for both number of illicit drugs used (t[1,761] = -9.32, p < .001) and for problematic cannabis use (t[1,761] = -4.88, p < .001).

Water pipe users reported a higher level of problematic cannabis use and more illicit drug use (CUDIT = 9.86, number of illicit drugs = 1.24) than users who did not use water pipes (CUDIT = 4.72, number of illicit drugs = 0.38). Both of these differences were found to be significant (CUDIT: t[1,761] = -14.93, p < .001; number of illicit drugs: t[1,761] = -8.89, p < .001).

Discussion

Our findings are consistent with previous studies [18, 19] showing that the most prevalent administration route for cannabis is "joint with tobacco", which was reported by 97.28% of cannabis users in this study. Nevertheless, cannabis use administered by "joint without tobacco", "water pipe", or "mixed with food" was not negligible (23.99–38.23% of the sample). We identified that different subgroups of cannabis users could be defined based on their preferred routes of administration. In fact, LCA revealed three main groups: "moderate users", who practiced low levels of all routes of administration (i.e. including joint with tobacco); "joint with

tobacco users", who mainly employed "joint with tobacco" and rarely utilized other administration routes; and "heavy/diversified users", who reported using many routes of administration.

The LCA also provided information in regards with pattern of drug use. The "moderate users" displayed low levels of problematic cannabis use and illicit drug use; "joint with tobacco users" had higher scores for problematic cannabis use and illicit drug use; and "heavy/diversified users" showed the highest levels of problematic cannabis use and illicit drug use. Therefore, the use of more routes of administration was associated with greater problems and substance use. Thus, the more diversified an individual's delivery methods, the more they had other drug-related problems, such as problematic cannabis use or increased illicit drug use. For this reason, even though these routes of administration are less used than "joints with tobacco", their harmful effects should not be ignored, especially for establishing preventative measures.

Correlations between specific administration routes and increased drug use also provided insight into the patterns associated with problematic and illicit drug use. However, although the use of joints containing tobacco was linked to problematic cannabis use and illicit drug use, this result may have been confounded by the frequency of cannabis use. Indeed, when findings were adjusted based on the frequency of cannabis use, the correlations were no longer significant. Nevertheless, most of our sample used "joint with tobacco", so it was difficult to compare nonusers to users of this route of administration. Thus, this result does not signify that using joints containing tobacco constitutes a harmless route of administration. Notably, all of the other correlations that we studied were significant for both unadjusted and adjusted models, even if they were lower for the adjusted models, and especially when the overlap between routes of administration was taken into account. This result suggests that diversification in cannabis administration routes could be a pattern that is associated with heavier drug use. In fact, we observed the strongest associations for "water pipe without tobacco" users, which was linked to both problematic cannabis use and illicit drug use, whereas "water pipe with tobacco" showed the second greatest correlation with problematic cannabis use. Again, this result was in accordance with Chabrol et al.'s suggestion [18, 19] that water pipe use (specially without tobacco) may be comparable to "harder" drugs, as it elicits a sharp and strong effect. A previous study specifically underlined the association of bongs (a special kind of water pipe) with cannabis dependence [18, 19]. The association of problematic cannabis use with water pipe use is consistent with this result.

Finally, two subgroups of cannabis users were also investigated: "pure" cannabis users vs. non "pure" cannabis users, and water pipe users vs. non water pipe users. First, the "pure" cannabis users, who solely used routes of administration that did not involve tobacco, showed less illicit drug use and less problematic cannabis use than non "pure" cannabis users. The results were significant despite the small number of "pure" cannabis users (N = 26). This result is consistent with previous studies that investigated cannabis and tobacco co-use [1, 14, 31, 32], which showed "pure" cannabis use to be less harmful than mixed use of cannabis and tobacco. Secondly, the comparison between users and non-users of water pipes showed that water pipe use was associated with higher levels of problematic cannabis use and illicit drug use. Therefore, water pipes seemed especially harmful, as highlighted by previous studies [18, 19]. This study had some limitations. The first one was the sample itself, which was exclusively composed of men. Therefore, further studies will be needed to examine gender differences in relation to this understudied topic in order to know whether these results will be the same among men and women. Another limitation of this study was that it was based on correlations. Thus, we were not able to identify causal links between variation in routes of administration and drug use patterns. For example, do illicit drug users diversify their cannabis administration routes before moving on to other illicit drugs? Further investigations with a longitudinal design will be required to answer this question. Finally, 9.3% of the participants indicated the use of routes of administration that differed from the five main routes analyzed in the current study. Further studies will be needed to identify these "other" routes of administration.

Cannabis use is an important concern worldwide, and recent studies have insisted that cannabis use has detrimental effects on health outcomes [39, 40]. However, these studies have not examined routes of administration of cannabis, which we have shown to be potentially associated with heavy drug use patterns, except in the case of "pure" cannabis.

Indeed, our findings have highlighted that diversification in the routes of administration can be associated with specific patterns of drug use, in particular heavier illicit drug use. This was especially true for water pipe users, whereas "pure" cannabis users, who did not mix their cannabis with tobacco, were an exception. Thereby, these results may be useful for future preventive programs. First, a special focus may be paid to adolescents and young adults who use multiple routes of administration when using cannabis. Second, prevention education should include the notion that multiple routes of administration may be especially harmful, and particularly use of water pipe.

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		Routes of administration						Drug use		
		N	Joint with tobacco	Joint without tobacco	Mixed with food	Water pipe with tobacco	Water pipe without tobacco	CUDIT score ⁴	Nb of illicit drug use ⁴	Frequency of cannabis use ⁴
All users	Prevalence rate ¹	1,763	97.28	38.23	37.27	29.27	23.99	-	-	-
	Mean score ²	1,763	2.96	0.55	0.47	0.41	0.34	6.67 (6.91)	0.70 (1.75)	1.13 (1.49)
"Pure" cannabis use vs. other uses ²	Without tobacco use exclusively Not without tobacco use	26	0.00	1.77	0.81	0.00	0.19	3.19 (3.89) ⁶	$0.08 (0.27)^6$	0.46 (1.21)
	exclusively	1,737	3.00	0.53	0.47	0.41	0.34	6.72 (6.94) ⁶	0.71 (1.76) ⁶	1.84 (1.50)
Water pipe vs. non water pipe uses ²	No water pipe use	1,094	2.82	0.38	0.30	0.00	0.00	4.72 (5.45) ⁷	$0.38(1.14)^7$	0.73 (1.27)
	Water pipe use ³	669	3.19	0.83	0.76	1.07	0.89	9.86 (7.82) ⁷	1.24 (2.34) ⁷	1.79 (1.60)
Latent class analysis ²	Class 1 (moderate users) Class 2 (joints with tobacco	466 ⁵	1.10	0.46	0.27	0.18	0.10	3.06 (3.84)	0.34 (1.49)	0.22 (0.76)
	users) Class 3 (heavy/diversified	1,114 ⁵	3.67	0.45	0.42	0.34	0.18	7.14 (6.88)	0.61 (1.39)	1.31 (1.50)
	users)	183 ⁵	3.38	1.40	1.28	1.36	1.94	12.97 (7.82)	2.16 (3.08)	2.38 (1.49)

Table 1. Subgroups of cannabis users according to the routes of administration they used and associated patterns of drug use.

¹Percentages are given for prevalence rates. Prevalence rate for other routes of administration was 9.30%.

²Means for the frequencies of each route of administration and groups of LCA were given (range 0–4).

³ Water pipe use included water pipe with tobacco and/or water pipe without tobacco: N=246; water pipe without tobacco: N=153; both: N=153.

⁴ Means with standard deviations in brackets are given for drug use.

⁵Classification of individuals based on their most likely latent class membership are given for the LCA results. The corresponding means for the 5 routes of administration

are given for each of the 3 classes.

⁶ Comparison between "pure" cannabis users and users of cannabis with tobacco or using both with and without tobacco routes of administration: t-test for CUDIT score: t(1,761) = -9.32, p < .001; t-test for number of illicit drugs: t(1,761) = -4.88, p < .001.

⁷Comparison between water pipe users and non-water pipe users: t-test for CUDIT score: t(1,761) = -14.93, p < .001; t-test for number of illicit drugs: t(1,761) = -8.89, p < .001.

	Una	djusted	5	usted for by of cannabis use	Adjusted for frequency of cannabis use and other routes of admin.		
	CUDIT	Nb illicit drugs	CUDIT	Nb illicit drugs	CUDIT	Nb illicit drugs	
Joints with tobacco	.30***	.09***	.02	03	.03	02	
Joints without tobacco	.27***	.21***	.12***	$.14^{***}$	$.06^{*}$	$.06^{*}$	
Mixed with food	.31***	.27***	.13***	.19***	$.07^{**}$.12***	
Water pipe with tobacco	.35***	.24***	$.18^{***}$.15***	.11***	.06**	
Water pipe without tobacco	.36***	.31***	.19***	.23***	.14**	.16***	

Table 2. Correlations between routes of administration of cannabis, problematic

cannabis use, and other illicit drug use (N = 1,763)

 $^{*}p < .05; ^{**}p < .01; ^{***}p < .001.$

Partial correlations are presented for correlations adjusted for frequency of cannabis use and for

frequency of cannabis use and other routes of administration.