RESEARCH REPORT

The respiratory effects of cannabis dependence in young adults

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Abstract
Aim. *To evaluate the relationship between cannabis dependence and respiratory symptoms and lung function in young adults, while controlling for the effects of tobacco smoking.* **Setting and participants.** *Nine hundred and forty-three young adults from a birth cohort of 1037 subjects born in Dunedin, New Zealand in 1972/1973 were studied at age 21.* **Measurements.** *Standardized respiratory symptom questionnaires were administered. Spirometry and methacholine challenge tests were undertaken. Cannabis dependence was determined using DSM-III-R criteria. Descriptive analyses and comparisons between cannabis-dependent, tobacco-smoking and non-smoking groups were undertaken. Adjusted odds ratios for respiratory symptoms, lung function and airway hyper-responsiveness (PC_{20}) were measured.* **Findings.** *Ninety-one subjects (9.7%) were cannabis-dependent and 264 (28.1%) were current tobacco smokers. After controlling for tobacco use, respiratory symptoms associated with cannabis dependence included: wheezing apart from colds, exercise-induced shortness of breath, nocturnal wakening with chest tightness and early morning sputum production. These were increased by 61%, 65%, 72% (all $p < 0.05$) and 144% ($p < 0.01$) respectively, compared to non-tobacco smokers. The frequency of respiratory symptoms in cannabis-dependent subjects was similar to tobacco smokers of 1–10 cigarettes/day. The proportion of cannabis-dependent study members with an FEV_1/FVC ratio of $< 80\%$ was 36% compared to 20% for non-smokers ($p = 0.04$). These outcomes occurred independently of co-existing bronchial asthma.* **Conclusion.** *Significant respiratory symptoms and changes in spirometry occur in cannabis-dependent individuals at age 21 years, even although the cannabis smoking history is of relatively short duration.*

Introduction

The smoking of cannabis has become an important health and social issue. The frequency with which it is being used regularly is increasing, particularly among young adults, although current trends vary between countries and between

different age cohorts.[1-4] In a recent investigation study in New Zealand, 52.4% of 992 New Zealand subjects aged 21 years had used cannabis at least once in the previous year (1992).[5] The prevalence of cannabis *dependence*, as defined by DSM-III-R,[6] was 9.7% at age 21 (males 14.3%, females 4.7%).[5]

Cannabis releases a range of gaseous and particulate material similar to tobacco when it undergoes combustion. Although the frequency of use, even in regular smokers, may be less than for tobacco, the smoking dynamics differ (increased puff volume and inhalation time) and thus the respiratory "burden" of the inhaled material is likely to be substantial.[7]

The effects of tobacco smoking on respiratory health are enormous, with chronic obstructive pulmonary disease (COPD) being among the most important. This chronic progressive condition occurs in approximately 15% of cigarette smokers. Functional impairment usually presents only after 20–30 years of exposure and is usually irreversible.[8] In laboratory animals exposure to cannabis smoke causes acute inflammatory changes in the airways.[9] More recently, it has been demonstrated that pathological changes similar to those associated with tobacco smoking also occur in the airways of humans who smoke cannabis.[10,11] In a study of selected individuals, regular cannabis smoking has also been shown to result in acute changes in lung function after as little as 6 weeks.[12]

These data suggest that in regular users, smoking cannabis has the potential to cause similar forms of respiratory disease as occur in tobacco smokers. Only limited longitudinal data are available to test this hypothesis, and the results are conflicting.[13,14] Similarly, there are few controlled cross-sectional studies describing the effect of cannabis smoking on respiratory health.[15,16] To our knowledge, there are no studies examining these relationships in individuals whose use of cannabis is frequent and problematic, i.e. who are cannabis *dependent*. Indeed, quantifying cannabis consumption has been a recognized methodological problem in earlier investigations.[13]

Given the increasing public debate in many countries about the merits of decriminalizing and/or legalizing cannabis use, more information is urgently required about its health effects. We have therefore examined the relationship between cannabis dependence, respiratory symptoms and lung function in a New Zealand birth cohort of nearly 1000 individuals studied at age 21. Our aim was to establish the extent of respiratory morbidity even after limited exposure, and to make comparisons between cannabis-dependent individuals and cigarette smokers.

Methods

The Dunedin Multidisciplinary Health and Development Study is a longitudinal investigation of the health, development and behaviour of a cohort of 1037 children born in Dunedin, New Zealand between 1 April 1972 and 31 March 1973.[17] Study members have been assessed at age 3, 5, 7, 9, 11, 13, 15, 18 and most recently at 21 years. At age 18 and 21, 924 and 946 individuals (90.6 and 92.7% of 1020 still living) were available for follow-up assessment.

Tobacco smoking

A smoking history was obtained using a self-administered confidential questionnaire. Tobacco smokers were defined as those who admitted to smoking tobacco daily for 1 year consuming at least one cigarette daily. The tobacco-smoking group was stratified into three subgroups: light (1–10), moderate (11–20), and heavy (more than 20 cigarettes per day). Those who had smoked only occasionally were classified as non-smokers.

Cannabis use and dependence

Cannabis use during the previous 12 months was assessed using a modified version of the Diagnostic Interview Schedule (DIS).[18] DSM-III-R criteria were then used to characterize cannabis dependence, as described in detail elsewhere.[5,6] Briefly, subjects were asked questions relating to time spent using, obtaining or recovering from the effects of cannabis; impairment of their ability to control cannabis use; continued use despite social, psychological or physical health problems attributed to cannabis use; tolerance; cannabis use in hazardous situations; and whether cannabis use had led to neglect of any of their usual occupational, social or recreational activities. In order to be diagnosed as dependent a subject had to use cannabis daily or almost daily, respond "yes, definitely" to at least three of the above questions and indicate that, for at

least one, the problem had been present for at least 1 month or had recurred over a longer period of time. This stricter definition was chosen rather than just cannabis use *per se* so that casual users would be excluded from the group of interest. Where subjects used cannabis but did not meet criteria for dependence, they were categorized as non-users.

Respiratory symptoms

Subjects completed a self-administered respiratory questionnaire. This included questions from the 1978 ATS/DLD questionnaire[19,20] and the IUATLD questionnaire.[21] Questions relating to respiratory symptoms during the previous 12 months were selected as being most relevant for this analysis (Table 1). Previously acquired longitudinal data were used to classify the study members as having or not having diagnosed asthma during childhood and adolescence.

Pulmonary function testing

Information regarding subjects' tobacco and cannabis use was not available to technical staff. Subjects were not specifically asked to refrain from smoking either tobacco or cannabis prior to pulmonary function tests being carried out. All subjects performed spirometry to ATS standards using a water-sealed Godart spirometer.[22] The best forced expired volume in 1 second (FEV_1) and forced vital capacity (FVC) from three reproducible attempts (within 0.2 l) were recorded. Methacholine challenge tests were carried out using the same modified Chai protocol as in assessments at age 9, 11, 13 and 15, as described previously.[23] The provocative concentration eliciting a 20% fall in FEV_1 (PC_{20} mg/ml) was calculated by interpolation of the logarithmic dose–response curve.

Statistical analysis

Initially odds ratios were calculated for relationships between cannabis dependence, tobacco smoking and respiratory symptoms. Thereafter logistic regression analysis was used to analyse for independent effects of any interactions between cannabis dependence and level of cigarette smoking (none, 1–10, 11–20, 21 + per day). The analysis was controlled for gender because of the known differences between males and females for cannabis use and tobacco smoking.[5] Factorial ANOVA models were constructed to determine the relationship between tobacco smoking and cannabis dependence and FEV_1 % predicted; FEV_1/FVC ratio (as an indicator of airflow obstruction); and PC_{20} methacholine. To further clarify any relationship between tobacco smoking or cannabis dependence and lung function or airway responsiveness, both FEV_1/FVC ratio and PC_{20} were analysed as categorical variables using χ^2 tests. For FEV_1/FVC a conservative cut-point of $< 80\%$ was used to define airflow obstruction. For PC_{20} the standard cut-point of < 8.0 mg/ml was used to define airway hyper-responsiveness. A *p*-value of 0.05 or less was taken to represent statistical significance. The regression procedures and ANOVA models were repeated and controlled for "current asthma", i.e. recurrent wheezing in the 12 months prior to age 21. This was to control for any association between asthma and smoking cigarettes or cannabis dependence on the frequency of respiratory symptoms and pulmonary function changes. No adjustments were made for multiple testing or for environmental tobacco smoke exposure.

Results

Data from 943 study members (92.5% of 1020 living subjects) were available for analysis. There were 588 non-smokers (62.4%), 264 tobacco-only smokers (28.0%), 28 cannabis-dependent non-tobacco smokers (3.0%) and 63 who smoked tobacco and were also cannabis-dependent (6.7%). Thus a total of 91 subjects were cannabis-dependent (69 male). The mean cannabis consumption in cannabis-dependent subjects was 230 times (95% CI; 193.6, 266.4) during the previous 12 months, compared to 40 (95% CI; 31.3, 48.7) among users who did not fulfil criteria for dependence. Cannabis users who were not cannabis-dependent and who did not smoke tobacco ($n = 139$, 14.7%) were included with non-smoking "normal" subjects.

Spirometry and methacholine challenge tests were carried out on 862 (91.4%) and 791 (83.9%) study members, respectively. Of these, 66 (8.3%) showed airway hyper-responsiveness ($PC_{20} < 8$ mg/ml). Of the 125 who reported current asthma (13.3% of full sample), 40 (32.0%) smoked tobacco, four (3.2%) were cannabis-dependent but non-tobacco users, eight (6.4%) smoked tobacco and were cannabis-

Table 1. Adjusted odds ratios and 95% confidence intervals (CI) for self-reported respiratory symptoms in subjects who regularly smoked tobacco (controlled for cannabis dependence), cannabis dependence (controlled for tobacco smoking) and both, compared to non-smokers. Further data are given for cannabis dependence alone

Substance and level of use	Attack of shortness of breath	Wheezy/whistling chest with a cold	Wheezy/whistling chest apart from a cold	Attack of exercise-related shortness of breath	Shortness of breath hurrying up a hill	Nocturnal wakening with chest tightness	Attack of shortness of breath at night	Nocturnal wakening due to cough	Cough on wakening first thing in the morning	Sputum production first thing in the morning
1–10 cigarettes/day (n = 159)	1.08 0.63–1.82 13.2	1.62** 1.13–2.32 57.9	2.00** 1.38–2.89 42.8	1.34 0.93–1.94 38.4	1.86** 1.25–2.78 33.3	1.34 0.87–2.08 22.6	1.20 0.63–2.67 8.8	1.84** 1.28–2.66 47.8	2.67** 1.57–4.54 17.0	2.53** 1.53–4.17 19.5
11–20 cigarettes/day (n = 146)	1.41 0.83–2.39 18.0	1.91** 1.31–2.80 60.3	1.97** 1.34–2.90 42.5	1.65* 1.12–2.41 43.2	2.03** 1.33–3.10 32.9	2.00** 1.30–3.07 30.1	1.67 0.90–2.12 11.0	1.44 0.97–2.12 39.7	5.65** 3.47–9.20 30.8	3.81** 2.36–6.15 28.8
21 + cigarettes/day (n = 22)	0.42 0.06–3.23 4.5	4.27** 1.53–11.93 77.3	8.73** 3.12–24.43 72.7	2.00 0.83–4.87 50.0	5.28** 2.11–13.19 54.5	1.88 0.70–5.05 27.3	3.41* 1.08–10.80 22.7	2.63* 1.08–6.44 54.5	11.44** 4.53–28.91 45.5	4.42** 1.66–11.79 36.4
Cannabis dependence† (n = 91)	0.58 0.25–1.32 7.7	1.27 0.79–2.02 57.1	1.61* 1.00–2.58 47.3	1.65* 1.04–2.63 46.2	1.78* 1.06–2.97 34.1	1.72* 1.02–2.88 30.8	0.83 0.35–1.95 7.7	1.39 0.87–2.24 41.8	1.68 0.96–2.95 27.5	2.44** 1.45–4.12 34.1
Cigarettes and cannabis dependence (n = 63)	0.68 0.27–1.72 7.9	2.39** 1.39–4.12 61.9	3.55** 2.05–6.14 50.8	2.54** 1.47–4.38 50.8	3.77** 2.07–6.86 38.1	2.93** 1.59–5.40 36.5	1.33 0.50–3.51 6.3	2.34 0.58–9.40 49.2	7.73** 3.99–15.39 36.5	8.06** 4.18–15.52 44.4
Cannabis dependence without tobacco use (n = 28)	0.61 0.14–2.65 7.1	1.30 0.60–2.80 46.4	2.07 0.94–4.55 39.3	1.45 0.65–3.23 35.7	2.02 0.82–4.98 25.0	1.23 0.45–3.34 17.9	1.79 0.51–6.26 10.7	0.92 0.38–2.23 25.0	1.08 0.25–4.75 7.1	1.30 0.38–4.50 10.7

The first and second lines of each cell are the odds ratios and 95% confidence intervals, respectively. The third line is the number of study members (%) in each category of substance use who reported that symptom. †DSM-III-R defined cannabis dependence. *$p < 0.05$; **$p < 0.01$.

Table 2 *Relationship between cigarette smoking, cannabis dependence and past and current history of asthma in study members*

	Asthma ever[1]		Current asthma[2]		No current asthma[3]		All subjects
	n	(%)	n	(%)	n	(%)	n
Non-smokers[4]	113	(19.2)	73	(12.4)	515	(87.6)	588
Tobacco smokers Only	71	(26.9)	40	(15.2)	224	(84.8)	264
Cannabis-dependent, non-tobacco users	8	(28.6)	4	(14.2)	24	(85.8)	28
Cannabis-dependent and tobacco users	12	(19.0)	8	(12.7)	55	(87.3)	63
Total	204		125		818		943

[1] Reported ever having had asthma during childhood and adolescence up to and including age 21;[2] "current asthma" defined as recurrent wheezing symptoms in the 12 months prior to interview at age 21;[3] all subjects excluding those with "current asthma" defined above;[4] includes cannabis users not demonstrating dependence and not smoking cigarettes.

dependent, while 73 (58.4%) were non-smokers. The proportion of tobacco smokers, cannabis users, and cannabis-dependent subjects was not significantly different between asthmatic and non-asthmatic subjects (Table 2).

Tobacco smokers had an increased frequency of almost all respiratory symptoms compared to non-smokers, most notably morning cough and sputum production (Table 1). For the most part, the probability of symptoms increased with increasing tobacco consumption. For cannabis-dependent subjects, after controlling for tobacco use there was a significant increase in the probability of wheezing apart from colds (61%, $p < 0.05$), exercise-related shortness of breath (65%, $p < 0.05$) including when climbing hills (78%, $p < 0.05$), nocturnal wakening with chest tightness (72%, $p < 0.05$) and morning sputum production (144%, $p < 0.01$). These figures increased to 89%, 76%, 94%, 86% and 348% when casual cannabis users were excluded from the reference group. There was generally an increase in the frequency of other symptoms compared to non-smokers, but these differences did not reach statistical significance. The magnitude of the increase in symptoms among cannabis-dependent subjects (after adjusting for tobacco use) was generally similar to and occasionally greater than that for tobacco smokers of 1–10 cigarettes/day.

The adjusted odds ratios for symptoms in those who smoked tobacco and who were also cannabis-dependent were generally higher than for either tobacco use or cannabis dependence alone. However, analysis of the interactions between tobacco and cannabis did not reveal any statistically significant effects.

There were no significant differences in the adjusted odds ratios for respiratory symptoms between subjects with and without "current asthma" who smoked tobacco and/or cannabis.

The differences in the mean values for FEV_1% predicted or FEV_1/FVC ratio between any of the categories of cannabis-dependent or tobacco-smoking subjects, after controlling for "current asthma", were not significant (Table 3). However, a significantly greater proportion of cannabis-dependent non-tobacco smokers (36%) had a low FEV_1/FVC ratio (less than 80%) compared to non-smokers (20%) ($\chi^2 = 4.06$, df = 1, $p = 0.04$) (Table 3). Similarly 35% of all cannabis-dependent subjects had an FEV_1/FVC ratio of less than 80% ($\chi^2 = 7.35$, df = 1, $p = 0.007$). Neither tobacco use nor cannabis-dependence was a significant factor determining airway hyper-responsiveness except in subjects with "current asthma".

Discussion

The results of this study demonstrate that, in a population of 21-year-old young adults in New Zealand, the likelihood of reporting a broad range of respiratory symptoms was significantly increased in those who were either cannabis-dependent or smoked tobacco or both, com-

Table 3. FEV_1/FVC ratios and PC_{20} methacholine test results by self-reported substance use among members of a longitudinal birth cohort. Only data for study members who underwent the respective lung function tests are reported

	Non-smokers (n = 588)	Tobacco (cigarettes/day)			Cannabis dependence only (n = 28)	Both tobacco use and cannabis dependence (n = 63)
		1–10 (n = 159)	11–20 (n = 146)	21 + (n = 22)		
FEV$_1$/FVC ratio						
Total tested	577	133	110	14	28	60
<80%	115 (20%)	22 (17%)	26 (24%)	4 (29%)	10 (36%)*	21 (35%)**
mean	84.7	85.2	84.7	81.3	83.4	83.9
(95% CI)	(84.2–85.2)	(84.0–86.4)	(83.4–86.5)	(77.7–84.9)	(80.7–86.1)	(82.0–85.8)
PC$_{20}$ methacholine						
Total tested	536	115	101	14	25	52
<8.0 mg/ml	44 (8%)	11 (10%)	5 (5%)	0 (0%)	2 (8%)	4 (8%)

$*p = 0.04$; $**p = 0.007$.

pared to non-smokers. The symptoms most frequently and significantly associated with cannabis dependence were early morning sputum production (144% greater prevalence than non-smokers). Overall, respiratory symptoms in study members who met strict criteria for cannabis dependence were comparable to those of tobacco smokers consuming 1–10 cigarettes daily. In subjects who were both tobacco users and were cannabis-dependent, some effects appeared to be additive, notably sputum production first thing in the morning, which occurred approximately eight times more frequently than in non-smokers. Subjects with previously diagnosed asthma were no more or less likely to take up cigarette smoking or to be cannabis-dependent than those without such a history.

These results add to a growing body of literature in which relationships between tobacco and cannabis use and respiratory health have been explored.[1,5,7,10–16,22] Although a similar pattern of symptoms has been reported in other epidemiological studies,[14,22] interpretation of these earlier study findings has been qualified by difficulties in quantifying cannabis use,[13,22] and the wide age range, and hence the duration of exposure, of the subjects studied (15–49 years).[13,22] In addition a low prevalence rate of "non-tobacco" use in one study sample[22] (14% life-time use, 9% current use) differs from the higher and yet much more rigorously defined 12-month prevalence rates for cannabis use and cannabis dependence obtained in our study population (52% use, 9% dependence).[5] These differences between the two studies may reflect not only differences in methodological approach, but also the major increase in the use of cannabis that has occurred, at least in New Zealand, over the last 10 years, emphasizing the relevance of the current study.

Although self-reported cannabis use without chemical verification could result in underreporting of usage, especially in a health-related study, and particularly where an illicit drug is involved, we think that this is unlikely given the trust of study members in the confidentiality of individual data which has been established over many years, and the high prevalence of occasional cannabis use reported (52% of study members). Nevertheless, because cannabis use could not be quantified accurately, we chose to restrict analysis to subjects whose cannabis use fulfilled the criteria for dependence. The consequent inclusion in the "normal" group of those

non-cigarette smokers who used cannabis occasionally or even regularly but did not meet criteria for dependence would (if exposure were deleterious) have biased our results away from showing an adverse effect in dependent subjects. Only 28 study members were cannabis-dependent but did not smoke tobacco: the small number in this group may explain why between-group comparisons did not reveal any significant interactions between cannabis use and tobacco smoking.

Our results provide new information regarding the age at which the respiratory effects of cannabis use may become apparent. All our sample were 21 years of age when studied. Only one-third of cannabis-dependent subjects at age 21 were also cannabis-dependent at age 18.[5] This suggests a relatively short duration of heavy use in the cannabis-dependent groups. In recent complementary studies, using bronchial biopsy material obtained from smaller groups of young adults using cannabis for limited periods, significant airway inflammation has been observed,[10,11] even in subjects who were asymptomatic and who had no demonstrable changes in lung function. The pathological changes were indistinguishable from the inflammation associated with consuming 20–30 tobacco cigarettes daily.[11] The increased frequency of respiratory symptoms among our study members who smoked tobacco or were cannabis-dependent suggests that similar pathological changes may be occurring in larger populations soon after starting smoking these substances. More importantly, although differences in mean spirometric values for tobacco or cannabis smokers compared to non-smokers were not significant, the number of cannabis-dependent subjects whose lung function showed early airflow obstruction, as determined by an FEV_1/FVC ratio of less than 80%, was significantly greater than for any other group, including tobacco users. This threshold for defining early airflow obstruction is conservative, being well below the lower 95% confidence limit for this parameter in normal subjects in this cohort (84.2%).

Currently, there is a widening debate about decriminalizing and/or legalizing cannabis use. It has been pointed out that the respiratory effects of cannabis smoking are being ignored because, in public health terms, the magnitude of the problem is insignificant when compared to that of tobacco smoking.[23] In contrast, it has been

claimed that the effects of cannabis smoking are *less* than for tobacco,[24] or even that it is "not harmful to health".[25] On the other hand, a recent review of the adverse effects of cannabis suggests that chronic heavy cannabis smoking is associated with increased symptoms of chronic bronchitis[26], as suggested by our own study. Chen *et al.*[27] have reported that cannabis use declines significantly after the age of 30. It is argued that this pattern of use reduces the potential long-term health risks.[23] However, it is not known whether this occurs because cannabis use is illegal, expensive, or gives rise to unwanted side effects. Nor is it clear whether a decline in use applies to individuals who are cannabis-*dependent*.[28]

At present, data regarding the longitudinal effects of cannabis use on pulmonary function offer conflicting results.[13,14] Although it is possible that, similar to tobacco use, discontinuing cannabis smoking prior to age 35 may be accompanied by reversal of adverse effects on lung function, further longitudinal studies are required to confirm this. We plan to reassess our own study members prospectively. In the meantime, the results of this and other studies suggest that if legalizing cannabis use were to promote more longterm use and/or dependence, the risk of developing COPD is potentially as great as among tobacco users, and that the adverse effects are likely to be additive to those of tobacco smoking.

Acknowledgements

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