Continued Cannabis Use and Risk of Incidence and Persistence of Psychotic Symptoms: 10 Year Follow-Up Cohort Study

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Abstract

Objective To determine whether use of cannabis in adolescence increases the risk for psychotic outcomes by affecting the incidence and persistence of subclinical expression of psychosis in the general population (that is, expression of psychosis below the level required for a clinical diagnosis).

Design Analysis of data from a prospective population based cohort study in Germany (early developmental stages of psychopathology study).

Setting Population based cohort study in Germany.

Participants 1923 individuals from the general population, aged 14-24 at baseline.

Main outcome measure Incidence and persistence of subthreshold psychotic symptoms after use of cannabis in adolescence. Cannabis use and psychotic symptoms were assessed at three time points (baseline, T2 (3.5 years), T3 (8.4 years)) over a 10 year follow-up period with the Munich version of the composite international diagnostic interview (M-CIDI).

Results In individuals who had no reported lifetime psychotic symptoms and no reported lifetime cannabis use at baseline, incident cannabis use over the period from baseline to T2 increased the risk of later incident psychotic symptoms over the period from T2 to T3 (adjusted odds ratio 1.9, 95% confidence interval 1.1 to 3.1; P=0.021). Furthermore, continued use of cannabis increased the risk of persistent psychotic symptoms over the period from T2 to T3 (2.2, 1.2 to 4.2; P=0.016). The incidence rate of psychotic symptoms over the period from baseline to T2 was 31% (152) in exposed individuals versus 20% (284) in non-exposed individuals; over the period from T2 to T3 these rates were 14% (108) and 8% (49), respectively.

Conclusion Cannabis use is a risk factor for the development of incident psychotic symptoms. Continued cannabis use might increase the risk for psychotic disorder by impacting on the persistence of symptoms.

Introduction

Cannabis is the most commonly used illicit drug in the world, particularly among adolescents.[1,2] The use of cannabis is consistently associated with mental illness,[3] in particular psychotic disorder.[4-9] It remains a matter of debate, however, whether the association between cannabis and psychosis is causal, or whether early psychotic experiences might in fact prompt cannabis use

as a means of self medication.[10,11] This issue can be resolved only if incident cannabis use is investigated in relation to later incident psychotic symptoms or disorder. Rarely have studies been able to examine the longitudinal relation between cannabis use and psychosis in this fashion.

The issue of self medication was addressed by Henquet and colleagues,[6] using data from the German prospective early developmental stages of psychopathology study.[12,13] The authors investigated the association between cannabis use at baseline and subsequent development of psychotic symptoms at four year follow-up and reported that after adjustment for pre-existing psychotic symptoms, cannabis use at baseline still remained significantly associated with psychotic symptoms at follow-up. There was no evidence of an effect of self medication as pre-existing psychotic symptoms did not significantly predict later cannabis use.[6] Ferdinand and co-workers investigated the role of pre-existing self reported psychotic symptoms and showed a bi-directional association between cannabis and psychotic symptoms over a 14 year follow-up study in the general population.[11] They showed that cannabis use predicted later psychotic symptoms in individuals with no evidence of psychotic symptoms before starting to use cannabis and that the reverse was also true, in that psychotic symptoms predicted cannabis use in those who had not used cannabis before the onset of those symptoms.[11] A prospective population based cohort study also found evidence for a self medication effect.[14] Individuals with self reported hallucinations at the age of 14 had a higher risk of using cannabis on a daily basis at the age of 21. In a sibling pair analysis, however, this study also suggested an independent effect of cannabis use on self reported delusional ideation later in life.[14] Thus, although the cannabis-psychosis link has been investigated in many studies, results on the temporal association between cannabis use and psychotic symptoms remain conflicting. Longitudinal cohort studies with multiple repeated interview based measures of cannabis use and psychotic symptoms are needed to clarify this issue. The EDSP study,[12,13] which completed its recent 10 year follow-up representing the fourth assessment (assessments at baseline, T1, T2, and T3, see also figure 1), is uniquely suitable for the investigation of the temporal association between cannabis and psychosis.

(Enlarge Image) Figure 1.
Study design. Top: testing association between incident cannabis use with onset in period from baseline to T2 and incident psychotic symptoms with onset in period from T2 to T3 in individuals who had not used cannabis at baseline and who had not reported any psychotic experience at T2 (that is, no lifetime psychotic experiences by T2). Bottom: testing association between different cannabis exposure states (combinations of cannabis use at baseline (lifetime), or T2 or both (interval) and persistence of psychotic experiences (that is, presence of psychotic experiences at both T2 (lifetime) and T3 (interval))

[CLOSE WINDOW]Figure 1. Study design. Top: testing association between incident cannabis use with onset in period from baseline to T2 and incident psychotic symptoms with onset in period from T2 to T3 in individuals who had not used cannabis at baseline and who had not reported any psychotic experience at T2 (that is, no lifetime psychotic experiences by T2). Bottom: testing association between different cannabis exposure states (combinations of cannabis use at baseline (lifetime), or T2 or both (interval) and persistence of psychotic experiences (that is, presence of psychotic experiences at both T2 (lifetime) and T3 (interval))

Another issue is the mechanism by which cannabis might increase the risk of psychotic symptoms, particularly whether it might increase the risk by causing persistence of normally transitory developmental expression of psychotic experiences. For most individuals, subclinical expression of psychotic phenomena (that is, expression of psychosis below the level required for a clinical

diagnosis) is transitory and never progresses to psychotic illness.[15] Subthreshold psychotic experiences could, however, become abnormally persistent, depending on the degree of additional exposure to environmental risk factors,[16-18] and progressively greater levels of persistence might be associated with a greater risk for transition to clinical psychotic disorder.[19] Spauwen and colleagues showed that the persistence rate of psychotic experiences was much higher for individuals growing up in an urban rather than a rural environment.[16] Similarly, Cougnard and co-workers provided evidence that childhood trauma, urban environment, and cannabis act additively in increasing the risk of persistence of psychotic experiences.[17] The fact that cannabis use increases risk of psychosis in a dose-response fashion[6,14,20] and that patients with psychosis who continue to use cannabis show more severe and persistent symptoms[21] suggests that cannabis use might increase the risk for psychotic illness by impacting on the persistence rate of psychotic experiences that under normal circumstances (that is, without exposure to cannabis) would have remained transitory phenomena for most people. In a population based 10 year follow-up cohort study of adolescents and young adults, we investigated the association between incident cannabis use and true incidence of psychotic experiences (that is, after exclusion of individuals with lifetime pre-existing psychotic experiences) and risk of persistence of psychotic experiences.

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[CLOSE WINDOW]Table 1. Characteristics of participants by use of cannabis at T2 (3.5 years after baseline) (n=1923). Figures are numbers (percentages)

	Used cannabis (n=393)	Did not use cannabis (n=1530)
Men	119 (30)	807 (53)
Women	274 (70)	723 (47)
Socioeconomic status*:		
Lower	30 (7)	85 (6)
Middle	220 (54)	894 (59)
Upper	137 (34)	524 (35)
Other	22 (5)	6 (0.4)
Urban/rural environmentâ€ :		
Urban	295 (75)	1050 (69)
Rural	98 (25)	480 (31)
Childhood traumaâ€¡:		
Yes	97 (25)	266 (17)
No	296 (75)	1264 (83)
Use of other drugs at baselineÂ§:		
Yes	25 (6)	11 (1)
No	368 (94)	1519 (99)
Use of other drugs at T2Â§:		
Yes	40 (10)	3 (0.2)
No	353 (90)	1527 (99)
Any psychiatric disorder at baseline**Â¶:		
Yes	76 (19)	180 (12)
No	317 (81)	1350 (88)

*Socioeconomic status: lower (lower class, lower middle class), middle (middle middle class), upper (higher middle class, upper class), other (none of the above or missing). Data missing for five participants.

â€ Urban (city of Munich, 10 559/km2), rural (surroundings of Munich, 1432/km2).

â€¡Childhood trauma: any traumatic experience during childhood.

Â§On more than five occasions.

Â¶Other than psychosis, according to M-CIDI diagnoses.

[CLOSE WINDOW]Table 2. Patterns of cannabis use in relation to presence of psychotic symptoms* at T2 (3.5 years after baseline) and T3 (8.4 years after baseline) in risk set (n=1923). Figures are numbers (percentageâ€) of participantsCannabis useâ€¡ Psychotic symptoms at T2 Psychotic symptoms at T3

	Yes	No	Yes	No
Baseline				
Yes	81 (4)	166 (9)	42 (2)	205 (11)
No	355 (18)	1321 (69)	189 (10)	1487 (77)
T2				
Yes	126 (7)	267 (14)	69 (4)	324 (17)
No	310 (16)	1220 (64)	162 (8)	1368 (71)

*Any psychotic symptom lifetime (T2) and interval (T3) as assessed with M-CIDI (G) section.

â€ Some percentages do not total 100 because of rounding.

â€¡On more than five occasions as assessed with M-CIDI (L) section.

[CLOSE WINDOW]Table 3. Association between incident cannabis use at T2 (3.5 years after baseline) and incident psychotic experiences at T3 (8.4 years after baseline) Figures are odds ratios (95% confidence intervals) and P valuesCannabis use at T2 Risk of psychotic experiences at T3

	Unadjusted	Adjusted*
Whole sample	1.8 (1.3 to 2.4), <0.001	1.5 (1.1 to 2.1), 0.018
After exclusionâ€	2.1 (1.3 to 3.4), 0.004	1.9 (1.1 to 3.1), 0.021

*Adjusted for age, sex, socioeconomic status, use of other drugs, childhood trauma, and urban/rural environment.

â€ Excludes individuals with baseline cannabis use and pre-existing psychotic symptoms.

[CLOSE WINDOW]Table 4. Course of psychotic experiences in relation to level of continued cannabis use at T2 (3.5 years after baseline) and T3 (8.4 years after baseline). Figures are numbers (percentages) of participantsCannabis continuation Psychotic experiences at follow-up

	None	At T2 or T3	At T2 and T3
No use	1071 (75)	303 (21)	64 (4)
At baseline but not at T2	59 (64)	25 (27)	8 (9)
At T2 but not at baseline	144 (60)	75 (32)	19 (8)
At baseline and T2	90 (58)	48 (31)	17 (11)

[CLOSE WINDOW]Table 5. Association between continued use of cannabis (over period from baseline to T2) and persistence* of psychotic experiences over period from T2 to T3. Figures are odds ratios (95% confidence intervals) and P valuesCannabis continuation Risk of persistence of psychotic experiences

	Unadjusted	Adjustedâ€
No use	1	1
At baseline but not at T2	2.0 (0.95 to 4.4), 0.068	2.1 (0.9 to 4.7), 0.078
At T2 but not at baseline	1.9 (1.1 to 3.2), 0.022	1.4 (0.8 to 2.5), 0.202
At baseline and T2	2.6 (1.5 to 4.6), 0.001	2.2 (1.2 to 4.2), 0.016

*Persistence of psychotic experiences; present at T2 and T3.

â€ Adjusted for age, sex, socioeconomic status, use of other drugs baseline and T2, childhood trauma, and urban/rural environment.

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