12-5-2016

Very Rapid Onset Cannabis Dependence Risk in Relation to Co-Occurring Use of Other Psychoactive Drugs

Olga A. Vsevolozhskaya
University of Kentucky, vsevolozhskaya@uky.edu

Fernando A. Wagner
Morgan State University

James C. Anthony
Michigan State University

Olga A. Vsevolozhskaya,[1] Fernando Wagner,[2] James C. Anthony[3]

[1]University of Kentucky, [2] Morgan State University, [3]Michigan State University

55th Annual Meeting of the American College of Neuropsychopharmacology
Hollywood, Florida - December 4-8

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Abstract

Background: Epidemiological estimates for lifetime cumulative incidence indicate that for every 9-11 who start using cannabis, one becomes a case of the cannabis dependence syndrome (CDS) – i.e., roughly 9%-11%. More recent estimates clarify that CDS risk might be much lower among 'cannabis only' users, due in part to the fact that many 'cannabis only' users try the drug a few times and never again. We turned to Hill functional analysis in order to study CDS probability soon after 1st cannabis use, estimated across strata defined by the number of recent days of cannabis use, with an acknowledgment that a persistence of cannabis use beyond a few trials (may signify a potentially higher risk subgroup).

Methods: United States National Surveys on Drug Use and Health (NSDUH), 2004-2014, sampled and assessed more than 500,000 participants, yielding a nationally representative probability sample of 13,874 newly incident cannabis users, with CDS assessment no more than 12 months since 1st use. For this analysis, we focused on the subgroup of 4,934 subjects with persistence of cannabis use into the 30 days prior to assessment. For this subgroup, we used Hill functions to estimate variations in CDS probability across strata defined by cannabis-using days during the 30 days prior to assessment, and by history of using other psychoactive drug compounds.

Results: Our preliminary results show that among 'cannabis only' users (n=1,811) the probability of CDS starts at about 1% for occasional users (95% bootstrap confidence interval, CI: 0, 2), rising to about 9% for daily users (95% CI: 4.5, 23). However, estimated probability of CDS for daily users is greater when cannabis plus ethanol (but no other drugs) is being used (n=1,753): 63% (95% CI: 47, 84); here, use on same day is not required. Our presentation will show additional Hill function estimates for other cannabis and drug combinations (e.g., cannabis and tobacco, cannabis and alcohol and tobacco).

Conclusions Notwithstanding NSDUH self-report methods and other limitations, the main finding is that probability of observing cannabis dependence is greater when cannabis use co-occurs with other psychoactive drug use. CDS probability is relatively low for 'cannabis only' users even when 'trial' users are excluded. These epidemiological estimates are consistent with a re-appraisal of cannabis dependence risk for 'cannabis only' users.

Methods

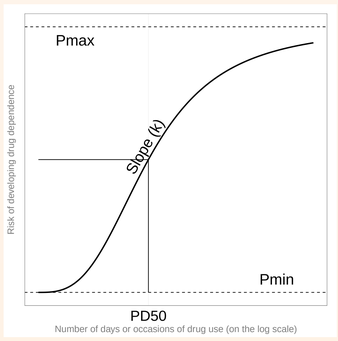

Figure 1: The four parameters – P_{min}, P_{max}, PD_{50} and k, – determine the shape of a Hill curve.

The increasing relationship can be explicitly described by the four parameters of a Hill function:

$$y = f(x) = \frac{P_{max} - P_{min}}{1 + \left(\frac{PD_{50}}{x}\right)^{k}} + P_{min}.$$

- P_{max} = upper limit
- P_{min} = lower limit
- k = slope at the inflection point
- PD_{50} = effective dose 50, i.e., a value of x, for which the value of y is half way between P_{max} and P_{min}

- A non-linear approach via a parametric function provides a straightforward and meaningful four-parameter interpretation.
- More typical epidemiological approaches (e.g., the logistic regression) do not provide the four-parameter estimation quantities used to compare drug combinations.

Results: Variation in Probability of CDS Soon After 1st Cannabis Use

Materials

In aggregate, the National Surveys of Drug Use and Health (NSDUH), 2004-2014, identified 13,874 newly incident cannabis users (<12 months since 1st use). Among them, 4,943 continued use to within 30 days of assessment. Further, concurrent drug combinations with cannabis were: ■tobacco cigarettes only (TCIG; $n = 554$), ■alcohol only (AONLY), $n = 1,753$), ■alcohol & tobacco cigarettes (ALCCIG, $n = 1,391$)

Table 1* Parameters (95% Bootstrap Confidence Intervals)

	P_{min}	P_{max}	PD_{50}	k
CAN ONLY	1.1% (0.0, 2.4%)	9.0% (4.5, 23.9%)	5 days (3, 29)	20 (1, 100)
CAN + CIG	3.0% (0.9, 4.5%)	12.9% (6.3, 18.8%)	13 days (12, 16)	100 (7, 100)
CAN + ALC	1.8% (0.0, 4.1%)	63.3% (47.1, 84.7%)	12 days (11, 13)	100 (13, 100)
CAN + CIG + ALC	4.8% (2.6, 6.4%)	38.1% (24.9, 49.3%)	20 days (19, 23)	100 (16, 100)

*Comparative estimates of Hill function parameters characterizing probability of observing CDS soon after first occurrence of newly incident cannabis use. Data from the United States National Surveys on Drug Use and Health, 2004-2014.

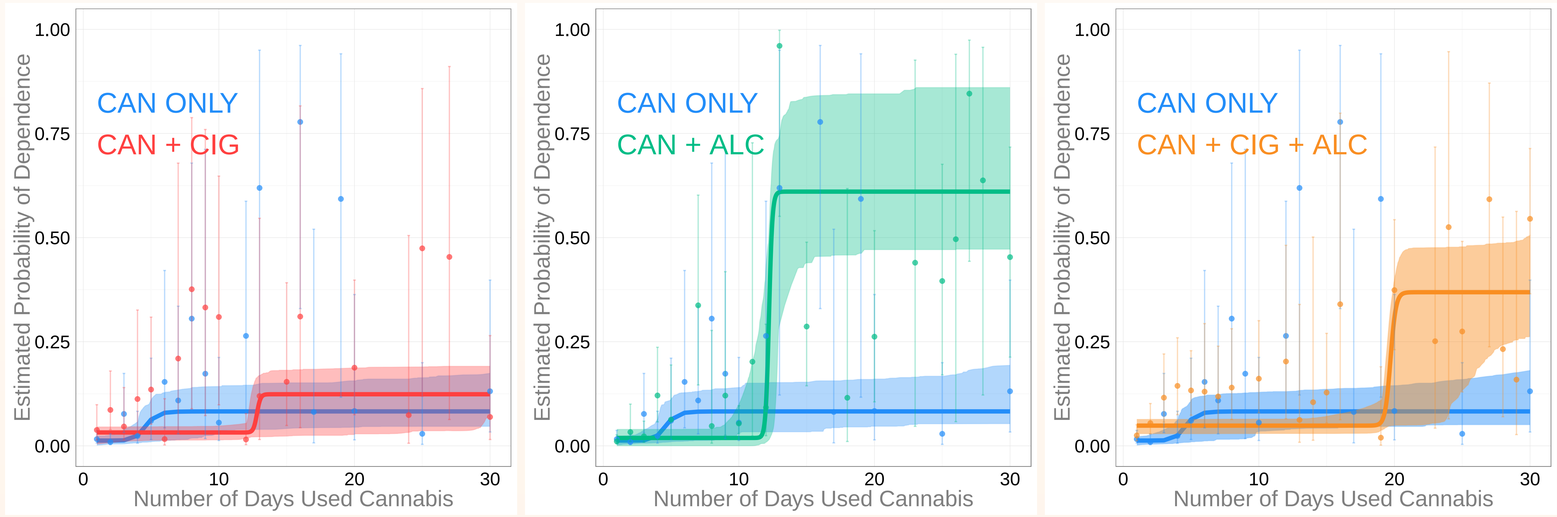

Figure 2: Estimated non-linear Hill functions for the predicted probability of cannabis dependence syndrome observed among newly incident cannabis users within 12 months after 1st use.

Main Findings

Figure 1 presents the estimated Hill function curves with the shaded regions depicting 95% bootstrap confidence intervals (CI). Based on the Hill function parameter estimates, CDS is observed among about 9% of the daily cannabis users with no co-occurring use of alcohol or tobacco cigarettes, with a much lower CDS estimate for infrequent 'cannabis only' users (∼ 2%). Figure 1 also suggests that the co-use of tobacco cigarettes (without alcohol) does not signal increased probability of observing CDS soon after 1st cannabis use, while co-occurring use of alcohol is linked to greater CDS probability among daily cannabis users (∼63%; 95% CI = 47%, 85%). Newly incident cannabis users with recent co-occurring cannabis, tobacco cigarette, and alcohol use are also much more likely to be observed with cannabis dependence versus cannabis only users. Note that in Table 1, estimated PD50 for CAN+CIG+ALC is 20 days (95% CI = 19, 23) versus 12-13 days for other combinations and just 5 days for 'cannabis only' users.

Limitations

Of special concern is the self-report interview survey data from NSDUH. However, in the context of nationally representative sample surveys on this scale, there are few logistically feasible and affordable alternatives to self-report. In addition, cross-sectional data always will be inferior to longitudinal data when fitting Hill functions of this type. Nonetheless, in these cross-sectional estimates, we can forecast what a followup study might show about variation in probability of developing cannabis dependence within 12 months after 1st cannabis use, with relatively smaller estimates for 'cannabis only' users and substantially larger estimates for 'polydrug' newly onset users. Finally, feedback loops might be present (Anthony, 2010) such that cannabis dependence, once it develops, may have prompted infrequent users to become daily users. This possibility is moving our work in the direction of restrictions on the Hill function and other future improvements of our functional analysis approaches to estimation of drug dependence risk.

Funding Source and Disclosure

Disclosure

There are no relevant financial interests to disclose.

Funding Source

Supported via a National Institute on Drug Abuse Senior Scientist Award JCA: K05DA015799.