CHAPTER 3B

Disentangling cause and effect in the relationship between cannabis and psychosis: Are we there yet?

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The debate over the role of cannabis in promoting psychosis is an important one because it concerns a potential risk factor that could be specifically targeted in early treatment interventions. It is therefore with great interest that we read the recent article by Kraan and co-workers [1] in Psychological Medicine reporting the results of a meta-analysis on the association between cannabis use and transition to psychosis in individuals at ultra-high risk. Aggregating data from seven studies that collectively included > 1000 subjects, the authors report that overall lifetime cannabis use was not related to transition to psychosis. Subsequently, Kraan et al. performed a second meta-analysis on a subset of five of the initial seven studies and concluded that current cannabis abuse or dependence predicted psychosis.

After perusing the five studies used in the second meta-analysis, we are left with several methodical questions. The authors’ main focus is on elucidating the impact of a current diagnosis of cannabis abuse and dependence on the transition to psychosis. However, at least based on the available published material, the time frame of DSM-IV abuse and dependence in relation to transition to psychosis is sufficiently specified in only two of the pertinent five studies [2, 3]. It should also be noted that the two studies by Auther and co-workers [4, 5] contain overlapping samples and that Valmaggia et al. [6] do not provide a DSM-IV diagnosis of dependence in their report.

The authors interpret their results as evidence for a dose-response relationship between cannabis use and transition to psychosis because current cannabis dependence rather than lifetime cannabis use was associated with transition. However, an alternative explanation of this finding could be that higher transition rates reflect the cumulative result of problem behaviors generally associated with drug addiction. Impairments linked with drug addiction may include reduced problem solving, lack of social support and failure to fulfill major role obligations, all of which are all likely to be important risk factors for the transition to psychosis [7]. Importantly, the amount of substance consumption – and thereby the amount of exposure to the toxic agent – is itself not a criterion for a DSM-IV diagnosis of abuse or dependence. We would also like to note that important confounding factors such as use of other drugs [8, 9] were not sufficiently taken into account by the authors. Unfortunately, even the confounder alcohol [4] was not included in the analysis, although five of the studies used in the analysis report having recorded data on alcohol use.
Taken together, the relationship between cannabis use and psychosis remains complex and in need of further research. Moreover, we see the risk of overestimating the effects of cannabis on progression to psychosis if other important risk factors are neglected or not properly controlled for.
References


In reply to the correspondence of Johannes Rentzsch, Kristin Koller and Golo Kronenberg

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Letter to the editor

In the commentary of Johannes Rentzsch, Kristin Koller and Golo Kronenberg concerns are addressed to our article ‘Cannabis use and transition to psychosis in individuals at Ultra High Risk: Review and Meta-Analysis’ in Psychological Medicine (2016). The authors raise questions about our methodology and the interpretation of our findings. We hope that the more detailed information of our study presented below can clarify our methods used and overcome the uncertainties.

The authors’ first concern is that in only two of the five studies used in the second meta-analysis the time frame of DSM-IV [1] abuse and dependence disorder was specified [2, 3]. In the studies of Auther et al. 2012 [4] and Auther et al., 2015 [5], the Kiddie Schedule for Affective Disorders and Schizophrenia – Epidemiologic Version [6] was used. This questionnaire is developed to measure cannabis abuse or dependence according to DSM-IV criteria. Using this questionnaire both lifetime cannabis use and cannabis use six months prior to baseline can be assessed, as has been described in the study of Auther et al., 2012 [4]. The study of Valmaggia et al., 2014 [7] used the Cannabis Experience Questionnaire. In this study data on lifetime use, current use and frequent cannabis use was reported. We agree with the authors that some of these studies did not provide current cannabis use. However, as we have specified in our method section, our criterion for current use was defined as having used cannabis in the previous 12 months.

Their second concern is that the studies of Auther et al., 2012 [4] and Auther et al., 2015 [5] have overlapping samples. Before we conducted our meta-analysis we have contacted dr. Auther for specific details of their study samples. Only 42 of the 370 participants from the Auther et al., 2015 [5] study were used in the Auther et al., 2012 [4] study. After comprehensive consideration we therefore decided to include both studies in our meta-analysis.

The authors correctly commented that in the study of Valmaggia et al., 2014 [7] cannabis use was not defined according to DSM-IV criteria. Although we used the data of the frequent cannabis users, we re-examined our meta-analytical data without this study to determine whether this would significantly alter the results. Excluding the study of Valmaggia et al., 2014 our findings on the effect of current cannabis abuse or dependence remain significant (OR=1.88, 95% CI= 1.17 – 2.59, p=0.009).

We agree that our findings should be interpreted cautiously, because there are several confounding factors that were not controlled for. The authors argue that for instance alcohol use was not controlled for while five studies did report on alcohol use. However, in only two of the five studies that we could include in our second meta-analysis data on alcohol use were specified. The same applies for the
other confounding factors mentioned by the authors; these were not systematically specified in the included studies and were therefore not controlled for in our analysis. To conclude, we fully agree that the relationship between cannabis use and psychosis is in need for further research and we believe that our meta-analysis contributed a small but important part in unraveling this relationship.
References


