

Correspondence

Psychological Medicine, 46 (2016).

doi:10.1017/S0033291716001434

First published online 25 July 2016

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

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 *et al.* (2016) 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.* (2016) 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 Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) abuse and dependence in relation to transition to psychosis is sufficiently specified in only two of the pertinent five studies (Phillips *et al.* 2002; Buchy *et al.* 2014). It should also be noted that the two studies by Auther *et al.* (2012, 2015) contain overlapping samples and that Valmaggia *et al.* (2014) 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 behaviours 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 (e.g. Collip *et al.* 2013). 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 (e.g. Power *et al.* 2013; Giordano *et al.* 2015) were not sufficiently taken into account by the authors. Unfortunately, even the confounder alcohol (Auther *et al.* 2015) 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.

Acknowledgements

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Declaration of Interest

None.

References

- Auther AM, Cadenhead KS, Carrión RE, Addington J, Bearden CE, Cannon TD, McGlashan TH, Perkins DO, Seidman L, Tsuang M, Walker EF, Woods SW, Cornblatt BA (2015). Alcohol confounds relationship between cannabis misuse and psychosis conversion in a high-risk sample. *Acta Psychiatrica Scandinavica* 132, 60–68.
- Auther AM, McLaughlin D, Carrión RE, Nagachandran P, Correll CU, Cornblatt BA (2012). Prospective study of cannabis use in adolescents at clinical high risk for psychosis: impact on conversion to psychosis and functional outcome. *Psychological Medicine* 42, 2485–2497.
- Buchy L, Perkins D, Woods SW, Liu L, Addington J (2014). Impact of substance use on conversion to psychosis in youth at clinical high risk of psychosis. *Schizophrenia Research* 156, 277–280.
- Collip D, Wigman JT, Myin-Germeys I, Jacobs N, Derom C, Thiery E, Wichers M, van Os J (2013). From epidemiology to daily life: linking daily life stress reactivity to persistence of psychotic experiences in a longitudinal general population study. *PLOS ONE* 8, e62688.
- Giordano GN, Ohlsson H, Sundquist K, Sundquist J, Kendler KS (2015). The association between cannabis abuse

- and subsequent schizophrenia: a Swedish national co-relative control study. *Psychological Medicine* **45**, 407–414.
- Kraan T, Velthorst E, Koenders L, Zwaart K, Ising HK, van den Berg D, de Haan L, van der Gaag M** (2016). Cannabis use and transition to psychosis in individuals at ultra-high risk: review and meta-analysis. *Psychological Medicine* **46**, 673–681.
- Phillips LJ, Curry C, Yung AR, Yuen HP, Adlard S, McGorry PD** (2002). Cannabis use is not associated with the development of psychosis in an ‘ultra’ high-risk group. *Australian and New Zealand Journal of Psychiatry* **36**, 800–806.
- Power BD, Dragovic M, Jablensky A, Stefanis NC** (2013). Does accumulating exposure to illicit drugs bring forward the age at onset in schizophrenia? *Australian and New Zealand Journal of Psychiatry* **47**, 51–58.
- Valmaggia LR, Day FL, Jones C, Bissoli S, Pugh C, Hall D, Bhattacharyya S, Howes O, Stone J, Fusar-Poli P, Byrne M, McGuire PK** (2014). Cannabis use and transition to psychosis in people at ultra-high risk. *Psychological Medicine* **44**, 2503–2512.

J. RENTZSCH, K. KOLLER AND G. KRONENBERG
*Department of Psychiatry and Psychotherapy, Charité –
 Universitätsmedizin Berlin, Campus Mitte, Charitéplatz 1, 10117
 Berlin, Germany*

Address for correspondence: J. Rentzsch, M.D., Department of
 Psychiatry and Psychotherapy, Charité – Universitätsmedizin
 Berlin, Campus Mitte, Charitéplatz 1, 10117 Berlin, Germany.
 (Email: johannes.rentzsch@charite.de)