EDITORIAL

Cannabis use and mental health: risks and benefits

Wayne Hall[1] · Eva Hoch[2] · Valentina Lorenzetti[3]

In public debates about cannabis policy, two competing claims are often made about how cannabis use may affect mental health. One is that cannabis use by young adults and vulnerable individuals across the lifespan can be a contributory cause of: a cannabis dependence syndrome; schizophreniform psychoses; anxiety and depressive disorders; acute and perhaps chronic cognitive impairment, and structural and functional changes in brain pathways implicated in reward, learning and addiction. The second claim is that cannabis (or some cannabinoids such as cannabidiol) have neuroprotective properties and can be used to treat anxiety, depression, sleep disorders, pain, neurological disorders and dependence on various drugs including cannabis.

The evidence for the first set of associations has often been used to justify a continuation of the prohibition on recreational cannabis use; the evidence for the latter has been used to justify the legalisation of medical cannabis use. This special issue includes a series of papers that map the changing landscape in cannabis potency and cannabis use disorders internationally. These papers evaluate the evidence for the competing claims about the effects of cannabis use on cognition, the brain, mental health and disease.

ElSohly and colleagues document substantial increases in the potency of cannabis in the illicit and licit cannabis markets in USA and EU [1]. It used to be asserted that increased cannabis potency was a by-product of prohibition and that it would be regulated after the legalisation of recreational use.

Contrary to this prediction, the potency of cannabis products has dramatically increased after legalisation in the USA with the advent of cannabis extracts that contain 70% or more THC. The public health effects of these potency increases have yet to be evaluated, but there are reasonable causes for concern that: the number of recreational and regular users will increase; users will experience higher levels of intoxication; there will be more road crashes; and the risks of cannabis dependence, psychoses and cognitive impairment may increase.

Solowij and colleagues report a randomised controlled trial of the acute effects of cannabinoids in persons who do not have a psychiatric diagnosis [2]. They provide the first evidence that high doses of CBD lead to an intoxication characterized by a dissociative state. They also found that the intoxicating effects of THC were potentiated when THC was co-administered with low-dose CBD, but these effects were reduced when THC was administered with high doses of CBD. This early evidence represents a first step to inform guidelines for recommended levels of THC and CBD in medicinal and recreational cannabis products.

Cannabis use acutely impairs cognition and brain function so there is an understandable concern that regular cannabis use by young people may interfere with education and learning. This topic is addressed in two reviews of studies of cognitive function in cannabis users using cognitive tests and neuroimaging. Cousijn and colleagues systematically review human and animal evidence on whether the association between cannabis use and cognitive impairments is moderated by the age at which cannabis users begins [3]. This work generated hypotheses to be tested in future neuroscientific work, namely, whether: in older adults, dependent cannabis use may exacerbate age-related declines, while adolescent users show more deficits in executive functioning but less craving after intoxication, less disinhibition and faster recovery of learning.

Lorenzetti and colleagues meta-analyse the literature on the neuroanatomical correlates of regular cannabis use compared to non-use [4]. Cannabis use was associated with reduced volumes of brain regions integral to learning, reward

✉ Wayne Hall
w.hall@uq.edu.au

1 Centre for Youth Substance Abuse Research, CYSAR K Floor Mental Health Centr, The University of Queensland, Royal Brisbane and Women's Hospital Site, Herston, QL 4029, Australia

2 Cannabinoid Research and Treatment Group, Department of Psychiatry and Psychotherapy, University Hospital, Ludwig-Maximilian-University Munich, Nußbaumstr. 7, 80336 Munich, Germany

3 School of Psychology, Faculty of Health Sciences, Australian Catholic University, Canberra 2601, Australia

and addiction (i.e., hippocampus and orbitofrontal cortex). These pathways have been identified in neuroscientific theories of addiction and their alteration has been documented in substance use disorders other than cannabis. More research is needed to identify individuals who are most vulnerable to these brain changes, the role of vulnerability factors (e.g., age and sex, cannabis dependence and potency, comorbid mental health and drug use) and how brain changes translate to problems related to cannabis use.

Budney and colleagues summarise the considerable body of evidence that cannabis can produce a dependence syndrome much like alcohol and other drugs [5]. Clinical trials evaluating psychological approaches to treating cannabis dependence indicate a substantial scope to improve outcomes. They outline some plausible hypotheses about the effects that cannabis legalisation may have on the prevalence of cannabis dependence, e.g. that increased access to cheaper and more potent legal cannabis products will increase the number of regular cannabis users and hence the number of problem users.

A growing body of work indicates that cannabinoids may alleviate pain, symptoms of common mental disorders and some neurological disorders. The second half of the Special Issue systematically and critically reviews this evidence.

Hoch and colleagues review randomised controlled trials that assess the efficacy and safety of cannabis-based medicine in mental disorders (DSM-III, DSM-IV or DSM-5) [6]. Their systematic review shows some evidence that THC or CBD given as adjuncts to other pharmacotherapies and psychotherapy improved specific symptoms of some disorders (e.g. in dementia, cannabis and opioid dependence, schizophrenia, general social anxiety, post-traumatic stress disorder, anorexia nervosa, attention-deficit/hyperactivity disorder, and Tourette`s disorder). Adverse effects were reported, but these were rarely severe. More definitive treatment recommendations require larger RCTs with longer periods of follow-up, more consistent and valid outcome measures and active comparison treatments.

Lowe and colleagues summarise studies of associations between cannabis use and mental health problems [7]. They review evidence from clinical trials on the potential therapeutic effects of cannabis on anxiety, depression and psychosis, and conclude that the evidence is limited by small sample sizes and trial designs that are susceptible to bias. They also summarise evidence from epidemiological studies of recreational users which suggest that daily cannabis use can increase the risks of psychosis and less certainly that of depressive and anxiety disorders.

Crippa and colleagues focus on the therapeutic effects of cannabinoids in Parkinson`s Disease [8]. Patients with this chronic neurodegenerative disorder experience motor symptoms such as bradykinesia, rest tremor, postural disturbances, and rigidity, and other symptoms that include sleep disturbances, cognitive deficits, and psychoses, depression and anxiety. A small number of RCTs failed to show positive results of cannabinoid one receptor agonists/antagonists. Some preclinical studies and a small number of human trials indicate possible neuroprotective and therapeutic effects of cannabidiol in patients with Parkinson`s Disease. Large-scale RCTs are needed to replicate these results and assess the long-term safety of CBD in this disease.

Campbell and colleagues overview the evidence on the effectiveness of cannabinoids in treating chronic non-cancer pain [9]. They discuss the limitations of RCTs in the field, uncertainty about the generalisability of findings and problems with the measurements of the dose and types of cannabinoids used. The authors make recommendations for future research on medicinal cannabinoids in chronic pain.

There are major global changes underway in cannabis regulation. More nation states are legalising medical use, often under liberal guidelines, and an increasing number of US states, Canada and Uruguay have legalised recreational cannabis use. These developments may have an effect on our ability to resolve the considerable uncertainties that remain about the risks and benefits of cannabis use for the brain, cognition and mental health. More liberal policies will probably make it easier to better assess the adverse effects of recreational, dependent and medical use because more people may be using cannabis more often and for longer periods. The absence of criminal penalties will make it easier to include questions on cannabis in epidemiological and other studies of the psychosocial and neural correlates of cannabis use. Paradoxically, while the legalisation of nonmedical use will make it easier in principle to undertake research on medical uses of cannabinoids it will also reduce the incentives that the pharmaceutical industry has to fund clinical trials of medical uses.

References

1. Chandra S, Radwan MM, Majumdar CG, Church JC, Freeman TP, El Sohly MA (2019) New trends in cannabis potency in USA and Europe during the last decade (2008–2017). Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-019-00983-5

2. Solowij N, Broyd S, Greenwood L-M, van Hell H, Martelozzo D, Rueb K, Todd J, Liu Z, Galettis P, Martin J, Murray R, Jones A, Michie PT, Croft R (2019) A randomised controlled trial of vaporised Δ9-tetrahydrocannabinol and cannabidiol alone and in combination in frequent and infrequent cannabis users: acute intoxication effects. Eur Arch Psychiatry Clin Neurosci. 10:15. https://doi.org/10.1007/s00406-019-00978-2

3. Gorey C, Kuhns L, Smaragdi E, Kroon E, Cousijn J (2019) Age-related differences in the impact of cannabis use on the brain and cognition: a systematic review. Eur Arch Psychiatry Clin Neurosci 10:15. https://doi.org/10.1007/s00406-019-00981-7

4. Lorenzetti V, Chye Y, Silva P, Solowij N, Roberts CA (2019) Does regular cannabis use affect neuroanatomy? An updated systematic

review and meta-analysis of structural neuroimaging studies. Eur Arch Psychiatry Clin Neurosci 10:15. https://doi.org/10.1007/s00406-019-00979-1

5. Budney AJ, Sofis MJ, Borodovsky JT (2019) An update on cannabis use disorder with comment on the impact of policy related to therapeutic and recreational cannabis use. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-018-0976-1

6. Hoch E, Niemann D, von Keller R, Schneider M, Friemel CM, Preuss UW, Hasan A, Pogarell O (2019) How effective and safe is medical cannabis as a treatment of mental disorders? A systematic review. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-019-00984-4

7. Lowe DJE, Sasiadek JD, Coles AS et al (2018) Cannabis and mental illness: a review. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-018-0970-7

8. Crippa JAS, Hallak JEC, Zuardi AW, Guimarães FS, Tumas V, dos Santos RG (2019) Is cannabidiol the ideal drug to treat non-motor Parkinson's disease symptoms? Eur Arch Psychiatry Clin Neurosci. 10:15. https://doi.org/10.1007/s00406-019-00982-6

9. Campbell G, Stockings E, Nielsen S (2019) Understanding the evidence for medical cannabis and cannabis-based medicines for the treatment of chronic non-cancer pain. Eur Arch Psychiatry Clin Neurosci. 10:15. https://doi.org/10.1007/s00406-018-0960-9