ResearchGate

See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/343747086

Psychedelic Science in Post-Covid Psychiatry

Article *in* Irish Journal of Psychological Medicine · August 2020

DOI: 10.1017/ipm.2020.94

CITATIONS
7

READS
480

8 authors, including:



John Richard Kelly
Trinity College Dublin
28 PUBLICATIONS **2,075** CITATIONS
SEE PROFILE



Matthew T Crockett
Beaumont Hospital
32 PUBLICATIONS **121** CITATIONS
SEE PROFILE

Some of the authors of this publication are also working on these related projects:

Dural arteriovenous fistulae View project

All content following this page was uploaded by John Richard Kelly on 20 September 2020.

The user has requested enhancement of the downloaded file.

Irish Journal of Psychological Medicine, page 1 of 6.
© The Author(s), 2020. Published by Cambridge University Press on behalf of The College of Psychiatrists of Ireland. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted re-use, distribution, and reproduction in any medium, provided the original work is properly cited.
EDITORIAL
doi:10.1017/ipm.2020.94

Psychedelic science in post-COVID-19 psychiatry

J. R. Kelly[1,2,*], M. T. Crockett[3], L. Alexander[4], M. Haran[5], A. Baker[6], L. Burke[6], C. Brennan[6] and V. O'Keane[1,2]

[1] *Department of Psychiatry, Trinity College Dublin, Dublin, Ireland*
[2] *Tallaght University Hospital, Dublin, Ireland*
[3] *Department of Neurological Intervention and Imaging, Sir Charles Gairdner Hospital, Perth, Western Australia, Australia*
[4] *Health Service Executive, Dublin, Ireland*
[5] *Daughters of Charity Disability Services, Dublin, Ireland*
[6] *Sheaf House, Exchange Hall, Tallaght, Dublin, Ireland*

The medium- to long-term consequences of COVID-19 are not yet known, though an increase in mental health problems are predicted. Multidisciplinary strategies across socio-economic and psychological levels may be needed to mitigate the mental health burden of COVID-19. Preliminary evidence from the rapidly progressing field of psychedelic science shows that psilocybin therapy offers a promising transdiagnostic treatment strategy for a range of disorders with restricted and maladaptive habitual patterns of cognition and behaviour, notably depression, addiction and obsessive compulsive disorder. The COMPASS Pathways (COMPASS) phase 2b double-blind trial of psilocybin therapy in antidepressant-free, treatment-resistant depression (TRD) is underway to determine the safety, efficacy and optimal dose of psilocybin. Results from the Imperial College London Psilodep-RCT comparing the efficacy and mechanisms of action of psilocybin therapy to the selective serotonin reuptake inhibitor (SSRI) escitalopram will soon be published. However, the efficacy and safety of psilocybin therapy in conjunction with SSRIs in TRD is not yet known. An additional COMPASS study, with a centre in Dublin, will begin to address this question, with potential implications for the future delivery of psilocybin therapy. While at a relatively early stage of clinical development, and notwithstanding the immense challenges of COVID-19, psilocybin therapy has the potential to play an important therapeutic role for various psychiatric disorders in post-COVID-19 clinical psychiatry.

Received 09 June 2020; Revised 31 July 2020; Accepted 13 August 2020

Key words: Coronavirus, COVID-19, depression, psilocybin, psychedelics, selective serotonin reuptake inhibitors, treatment-resistant depression.

Crises induce a wide range of psychological reactions, with varying degrees of adaptability. The combination of uncertainty and social distancing induced by the COVID-19 pandemic can lead to excessive fear/anxiety, loneliness and depressive thoughts (Holmes *et al.* 2020, Luykx *et al.* 2020, Vindegaard & Benros, 2020). While the medium- to long-term mental health consequences are not yet known, an increase in psychological and psychiatric problems are predicted (Horesh & Brown, 2020, O'Connor *et al.* 2020, Türközer & Öngür, 2020), with an excess burden on vulnerable groups (Kelly, 2020). The implementation of a range of multidisciplinary strategies across socio-economic and psychological levels may be needed to mitigate the mental health burden of COVID-19.

Accumulating clinical data shows that psilocybin therapy may be an effective therapeutic strategy across a range of disorders, including depression (Carhart-Harris *et al.* 2016, Davis *et al.* 2019), obsessive compulsive disorder (Moreno *et al.* 2006) and addiction disorders (Garcia-Romeu *et al.* 2019, Johnson *et al.* 2017). In addition, clinical trials are underway to investigate psilocybin therapy in anorexia nervosa (NCT04052568) and there may be a role for psilocybin therapy in the treatment of anxiety disorders (Weston *et al.* 2020).

Recent advances in psychedelic science are gradually unravelling the multimodal mechanisms underlying the therapeutic effect of psilocybin therapy (for example Carhart-Harris & Friston, 2019, Lord *et al.* 2019, Preller *et al.* 2020, Varley *et al.* 2020). Psilocybin reliably alters an individual's state of consciousness, probably through agonist mechanisms at the 5-HT2A receptor, especially in the deep pyramidal cells in the cortex (Nutt *et al.* 2020). The transient, dose-dependent alteration of the complex interconnected neural networks of the brain (Lord *et al.* 2019, Varley *et al.* 2020) encompassing the self-reflecting 'ego', induced by psilocybin, can lead to profound experiences of connectivity to others and the environment (Erritzoe *et al.* 2018, Griffiths *et al.* 2006, 2016, Grob *et al.* 2011, Kettner *et al.* 2019, Smigielski *et al.* 2019) and can be harnessed by psilocybin therapy to re-conceptualise restricted and maladaptive habitual patterns of cognition and behaviour.

*Address for correspondence: Dr J.R. Kelly, PhD, Senior Registrar/Lecturer in Psychiatry, Trinity College Dublin & Tallaght Hospital, Trinity Centre for Health Sciences, Tallaght University Hospital, Dublin 24, Ireland.
(Email: kellyjr@tcd.ie).

As such, psilocybin therapy provides a translatable, transdiagnostic treatment strategy that can be further refined by a precise-personalised approach (Kelly *et al.* 2017, Lewis *et al.* 2020, Preller *et al.* 2016, 2020, Studerus *et al.* 2012). Advancing precise-personalised psilocybin therapy is of particular importance given the individual variation in responses, high rates of relapse in psychiatric disorders and contraindication in psychotic and manic conditions (Carhart-Harris *et al.* 2018). It has been suggested that internalising disorders may be a useful broad construct for the therapeutic application of psilocybin therapy (Nutt & Carhart-Harris, 2020). Moreover, given the transdiagnostic potential, a dimensional framework (Insel, 2014) that aligns with bio-psycho signatures could also be leveraged to enhance the targeted application of psilocybin therapy and further unravel the mechanisms underpinning the acute and persistent therapeutic effects. Indeed, further exploration of psilocybin's impact on neuroimmunoendocrine pathways (Galvão *et al.* 2018, Hasler *et al.* 2004, Nau *et al.* 2013, Strajhar *et al.* 2016, Szabo, 2015), including the microbiome–gut–brain axis, may provide additional insights into the persisting therapeutic effects (Kelly *et al.* 2019c, Kuypers, 2019).

Notwithstanding the limitations of animal models in fully capturing the different aspects of psilocybin therapy (Jefsen *et al.* 2019, Meinhardt *et al.* 2020), preclinical data have shown that serotonergic psychedelics, including psilocybin, can induce hippocampal neurogenesis (Catlow *et al.* 2013, Morales-Garcia *et al.* 2017, Vaidya *et al.* 1997), promote dendritic spine growth and stimulate synapse formation in the prefrontal cortex (González-Maeso *et al.* 2007, Ly *et al.* 2018). Preclinical data also suggest that psychedelics lead to 5-HT2A receptor-mediated glutamate release (Ly *et al.* 2018), and a recent magnetic resonance spectroscopy study in healthy humans found that psilocybin administration was associated with increased glutamate in the medial prefrontal cortex (Mason *et al.* 2020).

Researchers from the Center for Psychedelic and Consciousness Research at Johns Hopkins University recently focussed on the claustrum, a thin sheet of grey matter, embedded in the white matter of the cerebral hemispheres and situated between the putamen and the insular cortex, with a rich supply of 5-HT2A receptors and glutamatergic connectivity to the cerebral cortex, and thought to be associated with cognitive task switching (Barrett *et al.* 2020b, Krimmel *et al.* 2019). Psilocybin acutely reduced claustrum activity and altered its connectivity with the default mode network and frontoparietal task control network, in a study involving 15 healthy volunteers, thus implicating this region as a key mediator in psilocybin therapy (Barrett *et al.* 2020b).

The same research group, in an open-label pilot study of 12 healthy volunteers, showed that psilocybin reduced both negative affect and amygdala responses to emotional stimuli 1 week after psilocybin, whereas by 1 month after psilocybin the responses returned to baseline (Barrett *et al.* 2020a). At both 1 week and 1 month after psilocybin, there were global increases in brain functional connectivity (Barrett *et al.* 2020a). A previous study in healthy controls also showed reduced amygdala reactivity, particularly on the right side, to negative and neutral stimuli due to psilocybin (Kraehenmann *et al.* 2015). In contrast, an open-label study of 19 subjects with treatment-resistant depression (TRD) showed that psilocybin increased amygdala responses to emotional faces (Roseman *et al.* 2018) and decreased functional connectivity between the ventromedial prefrontal cortex and the right amygdala 1 day after psilocybin (Mertens *et al.* 2020). Larger studies may be needed to resolve the complexities.

In the midst of this evolving 'Psychedelic Revolution in Psychiatry' (Nutt *et al.* 2020) and potential increasing recreational psychedelic use, albeit from 0.55% in 2015 to 0.86% in 2018, in a sample of 168,000 members of the public (Yockey *et al.* 2020), the Royal Australian and New Zealand College of Psychiatrists (RANZCP) recently published a clinical memorandum on the 'Therapeutic use of psychedelic substances' (RANZCP, 2020). This memorandum acknowledges not only the emerging therapeutic potential of psychedelics but also the need for more efficacy and safety data, particularly on potential long-term effects, to inform future potential use in psychiatric practice.

In terms of acceptability and tolerability, results from the Global Drug Survey (2019) of 85,000 people showed only 18% of those surveyed, who have never used psychedelics, said they would accept psilocybin therapy for depression or PTSD, increasing to 59% in those who had previously tried psychedelics (Winstock & Johnson, 2019). The reported fears related to 'brain damage and bad trips' (Winstock & Johnson, 2019). Psilocybin therapy data from John Hopkins University, over a 16-year period, encompassing 250 volunteers and 380 sessions, reported no major psychological issues, with 0.9% of volunteers experiencing minor and transient psychological issues (Carbonaro *et al.* 2016). However, high-quality clinical data on the long-term effects of psychedelics are lacking. For example, there is very limited data on hallucinogen-persisting perception disorder (HPPD), a rare condition that involves the continued presence of sensory disturbances (Halpern *et al.* 2018; Martinotti *et al.* 2018; Orsolini *et al.* 2017). A review by Halpern and colleagues suggests that HPPD is, in most cases, due to a 'subtle over-activation of predominantly neural visual pathways that worsens anxiety after ingestion of

arousal-altering drugs, including non-hallucinogenic substances' (Halpern *et al.* 2018). The authors note that a personal or family history of anxiety and pre-drug use complaints of tinnitus, eye floaters and concentration problems may predict vulnerability for HPPD (Halpern *et al.* 2018). Similarly, the impact of regular psychedelic use on the brain is limited (Bouso *et al.* 2015; Halpern *et al.* 2005). Although, it is important to note that psilocybin therapy studies do not use regular dosing, using between 1 and at most 3 doses of psilocybin.

Dublin is one of the clinical trial centres participating in a double-blind randomised controlled phase 2b COMPASS trial of psilocybin therapy in TRD (COMP001) (Kelly *et al.* 2019a). Results from this large scale trial, and others, will address concerns regarding psilocybin safety, efficacy and dose optimisation. Moreover, we eagerly await the results from the potentially paradigm shifting, double-blind trial of psilocybin therapy *versus* the selective serotonin reuptake inhibitor (SSRI) escitalopram in depression from the Centre for Psychedelic Research at Imperial College London (Psilodep-RCT, NCT03429075) (Nutt & Carhart-Harris, 2020) and acknowledge that for some people with depression, SSRIs and psilocybin may become 'competitive options' despite postulated mechanistic complementarity, with SSRIs enhancing 5-HT1AR pathway and psilocybin enhancing the 5-HT2AR pathway (Carhart-Harris & Nutt, 2017). However, many people with depression may choose to remain on antidepressants (Kelly *et al.* 2019b) and it is important to determine the safety and efficacy of this approach. 5-HT2AR antagonists, such as ketanserin, block the therapeutic effect of psilocybin (Preller *et al.* 2017), whereas the partial 5-HT1A agonist buspirone may exert inhibitory effects (Pokorny *et al.* 2016). However, apart from anecdotal evidence suggesting a blunted effect (Bonson *et al.* 1996; Bonson & Murphy, 1996), psilocybin therapy in conjunction with SSRI's has never been investigated in TRD.

The gradual emergence from COVID-19 lockdown will see the launch of a new COMPASS clinical study (COMP003) in Dublin and San Diego to determine the antidepressant effect of psilocybin therapy in people with TRD who continue SSRI medication. This exploratory open-label trial will aim to recruit 20 participants with a single or recurrent episode of at least moderate clinical depression between 3 months and 2 years duration that has not responded to an adequate dose and duration of at least two pharmacological treatments. A single dose of oral psilocybin of 25mg will be administered with psychological support to participants who have been taking an SSRI's for at least 6 weeks. The results of this study could have important practical implications for the future of psilocybin therapy and may have implications for future phase 3 trials in TRD, which could pave the way for the integration of psilocybin therapy into clinical psychiatry.

However, both clinical and research psychiatry have been transformed by COVID-19, demanding additional strategies to overcome the considerable challenges (O'Brien & McNicholas, 2020; Türközer & Öngür, 2020). To mitigate the spread of COVID-19 and facilitate the safe reopening and progress of ongoing psilocybin trials, in line with local and national guidelines, a number of measures will be implemented. These include, for example, participant and researcher respiratory symptom checklists, regular temperature checks, access to COVID-19 testing (if indicated), meticulous attention to extra hygiene measures, personal protective equipment (where not expected to negatively impact the participant's experience), and the option of remote study visits (where possible by the protocol). Notwithstanding the challenges and the early stage of clinical development, psilocybin therapy, at the forefront of translational neuroscience and psychiatry, is likely to play an important therapeutic role for certain conditions in post-COVID-19 clinical psychiatry.

Financial support

COMP001 and COMP003 are funded by COMPASS Pathways.

Conflict of interest

Authors have no conflicts of interest to disclose.

Ethical standards

The Cork Clinical Research Ethics Committee approved COMP001 and COMP003. The authors assert that all procedures contributing to this work comply with the ethical standards of the Cork Clinical Research Ethics Committee and with the Helsinki Declaration of 1975, as revised in 2008.

References

Barrett FS, Doss MK, Sepeda ND, Pekar JJ, Griffiths RR (2020a). Emotions and brain function are altered up to one month after a single high dose of psilocybin. *Scientific Reports* **10**, 2214.

Barrett FS, Krimmel SR, Griffiths R, Seminowicz DA, Mathur BN (2020b). Psilocybin acutely alters the functional connectivity of the claustrum with brain networks that support perception, memory, and attention. *Neuroimage*, 116980.

Bonson KR, Buckholtz JW, Murphy DL (1996). Chronic administration of serotonergic antidepressants attenuates the subjective effects of LSD in humans. *Neuropsychopharmacology* **14**, 425–436.

Bonson KR, Murphy DL (1996). Alterations in responses to LSD in humans associated with chronic administration of tricyclic antidepressants, monoamine oxidase inhibitors or lithium. *Behav Brain Res* **73**, 229–233.

Bouso JC, Palhano-Fontes F, Rodríguez-Fornells A, Ribeiro S, Sanches R, Crippa JAS, Hallak JEC, de Araujo DB, Riba J (2015). Long-term use of psychedelic drugs is associated with differences in brain structure and personality in humans. *European Neuropsychopharmacology* **25**, 483–492.

Carbonaro TM, Bradstreet MP, Barrett FS, MacLean KA, Jesse R, Johnson MW, Griffiths RR (2016). Survey study of challenging experiences after ingesting psilocybin mushrooms: acute and enduring positive and negative consequences. *Journal of Psychopharmacology* **30**, 1268–1278.

Carhart-Harris RL, Bolstridge M, Day CMJ, Rucker J, Watts R, Erritzoe DE, Kaelen M, Giribaldi B, Bloomfield M, Pilling S, Rickard JA, Forbes B, Feilding A, Taylor D, Curran HV, Nutt DJ (2018). Psilocybin with psychological support for treatment-resistant depression: six-month follow-up. *Psychopharmacology (Berl)* **235**, 399–408.

Carhart-Harris RL, Bolstridge M, Rucker J, Day CM, Erritzoe D, Kaelen M, Bloomfield M, Rickard JA, Forbes B, Feilding A, Taylor D, Pilling S, Curran VH, Nutt DJ (2016). Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. *Lancet Psychiatry* **3**, 619–627.

Carhart-Harris RL, Friston KJ (2019). REBUS and the anarchic brain: toward a unified model of the brain action of psychedelics. *Pharmacological Review* **71**, 316–344.

Carhart-Harris RL, Nutt DJ (2017). Serotonin and brain function: a tale of two receptors. *Journal of Psychopharmacology* **31**, 1091–1120.

Catlow BJ, Song S, Paredes DA, Kirstein CL, Sanchez-Ramos J (2013). Effects of psilocybin on hippocampal neurogenesis and extinction of trace fear conditioning. *Experimental Brain Research* **228**, 481–491.

Davis AK, May DG, Cosimano M, Johnson MW, Barrett FS, Griffiths RR (2019). Psilocybin-assisted psychotherapy for the treatment of Major Depressive Disorder: Preliminary results from a randomized controlled trial. In *American Psychiatric Associrefconfation Annual Meeting*.

Erritzoe D, Roseman L, Nour MM, MacLean K, Kaelen M, Nutt DJ, Carhart-Harris RL (2018). Effects of psilocybin therapy on personality structure. *Acta Psychiatrica Scandinavica* **138**, 368–378.

Galvão, ACM de Almeida RN, Silva E, Freire FAM, Palhano-Fontes F, Onias H, Arcoverde E, Maia-de-Oliveira JP, de Araújo DB, Lobão-Soares B, Galvão-Coelho NL (2018). Cortisol modulation by ayahuasca in patients with treatment resistant depression and healthy controls. *Front Psychiatry* **9**, 185.

Garcia-Romeu A, Davis AK, Erowid F, Erowid E, Griffiths RR, Johnson MW (2019). Cessation and reduction in alcohol consumption and misuse after psychedelic use. *Journal of Psychopharmacology* **33**, 1088–1101.

González-Maeso J, Weisstaub NV, Zhou M, Chan P, Ivic L, Ang R, Lira A, Bradley-Moore M, Ge, Y, Zhou Q, Sealfon SC, Gingrich JA (2007). Hallucinogens recruit specific cortical 5-HT(2A) receptor-mediated signaling pathways to affect behavior. *Neuron* **53**, 439–452.

Griffiths RR, Johnson MW, Carducci MA, Umbricht A, Richards WA, Richards BD, Cosimano MP, Klinedinst MA (2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: a randomized double-blind trial. *Journal of Psychopharmacology (Oxford, England)* **30**, 1181–1197.

Griffiths RR, Richards WA, McCann U, Jesse R (2006). Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology (Berl)* **187**, 268–283; discussion 284–292.

Grob CS, Danforth AL, Chopra GS, Hagerty M, McKay CR, Halberstadt AL, Greer GR (2011). Pilot study of psilocybin treatment for anxiety in patients with advanced-stage CancerPsilocybin for anxiety in advanced-stage cancer. *JAMA Psychiatry* **68**, 71–78.

Halpern JH, Lerner AG, Passie T (2018). A review of hallucinogen persisting perception disorder (HPPD) and an exploratory study of subjects claiming symptoms of HPPD. *Current Topics in Behavioral Neurosciences* **36**, 333–360.

Halpern JH, Sherwood AR, Hudson JI, Yurgelun-Todd D, Pope HG, Jr. (2005). Psychological and cognitive effects of long-term peyote use among Native Americans. *Biological Psychiatry* **58**, 624–631.

Hasler F, Grimberg U, Benz MA, Huber T, Vollenweider FX (2004). Acute psychological and physiological effects of psilocybin in healthy humans: a double-blind, placebo-controlled dose-effect study. *Psychopharmacology (Berl)* **172**, 145–156.

Holmes EA, O'Connor RC, Perry VH, Tracey I, Wessely S, Arseneault L, Ballard C, Christensen H, Cohen Silver R, Everall I, Ford T, John A, Kabir T, King K, Madan I, Michie S, Przybylski AK, Shafran R, Sweeney A, Worthman CM, Yardley L, Cowan K, Cope C, Hotopf M, Bullmore E (2020). Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. *Lancet Psychiatry* **7**, 547–560.

Horesh D, Brown AD (2020). Traumatic stress in the age of COVID-19: a call to close critical gaps and adapt to new realities. *Psychological Trauma* **12**, 331–335.

Insel TR (2014). The NIMH Research Domain Criteria (RDoC) project: precision medicine for psychiatry. *American Journal of Psychiatry* **171**, 395–397.

Jefsen O, Højgaard K, Christiansen SL, Elfving B, Nutt DJ, Wegener G, Müller HK (2019). Psilocybin lacks antidepressant-like effect in the Flinders Sensitive Line rat. *Acta Neuropsychiatrica* **31**, 213–219.

Johnson MW, Garcia-Romeu A, Griffiths RR (2017). Long-term follow-up of psilocybin-facilitated smoking cessation. *The American Journal of Drug and Alcohol Abuse* **43**, 55–60.

Kelly BD (2020). Coronavirus disease: challenges for psychiatry. *British Journal of Psychiatry* **217**, 352–353.

Kelly JR, Baker A, Babiker M, Burke L, Brennan C, O'Keane V (2019a). The psychedelic renaissance: the next trip for psychiatry? *Irish Journal of Psychological Medicine*, 1–5.

Kelly JR, Clarke G, Cryan JF, Dinan TG (2017). Dimensional thinking in psychiatry in the era of the Research Domain Criteria (RDoC). *Irish Journal of Psychological Medicine* **35**, 89–94.

Kelly JR, Cosgrove M, Judd C, Scott K, Loughlin AM, O'Keane V (2019b). Mood matters: a national survey on attitudes to depression. *Irish Journal of Medical Science* **188**, 1317–1327.

Kelly JR, Keane VO, Cryan JF, Clarke G, Dinan TG (2019c). Mood and microbes: gut to brain communication in depression. *Gastroenterology Clinics of North America* **48**, 389–405.

Kettner H, Gandy S, Haijen E, Carhart-Harris RL (2019). From Egoism to Ecoism: psychedelics increase nature relatedness in a state-mediated and context-dependent manner. *International Journal of Environmental Research and Public Health* **16**.

Kraehenmann R, Preller KH, Scheidegger M, Pokorny T, Bosch OG, Seifritz E, Vollenweider FX (2015). Psilocybin-induced decrease in amygdala reactivity correlates with enhanced positive mood in healthy volunteers. *Biological Psychiatry* **78**, 572–581.

Krimmel SR, White MG, Panicker MH, Barrett FS, Mathur BN, Seminowicz DA (2019). Resting state functional connectivity and cognitive task-related activation of the human claustrum. *Neuroimage* **196**, 59–67.

Kuypers KPC (2019). Psychedelic medicine: the biology underlying the persisting psychedelic effects. *Med Hypotheses* **125**, 21–24.

Lewis CR, Preller KH, Braden BB, Riecken C, Vollenweider FX (2020). Rostral anterior cingulate thickness predicts the emotional psilocybin experience. *Biomedicines* **8**, 34.

Lord LD, Expert P, Atasoy S, Roseman L, Rapuano K, Lambiotte R, Nutt DJ, Deco G, Carhart-Harris RL, Kringelbach ML, Cabral J (2019). Dynamical exploration of the repertoire of brain networks at rest is modulated by psilocybin. *Neuroimage* **199**, 127–142.

Luykx JJ, Vinkers CH, Tijdink JK (2020). Psychiatry in times of the coronavirus disease 2019 (COVID-19) pandemic: an imperative for psychiatrists to act now. *JAMA Psychiatry*.

Ly, C, Greb AC, Cameron LP, Wong JM, Barragan EV, Wilson PC, Burbach KF, Soltanzadeh Zarandi S, Sood A, Paddy MR, Duim WC, Dennis MY, McAllister AK, Ori-McKenney KM, Gray JA, Olson DE (2018). Psychedelics promote structural and functional neural plasticity. *Cell Reports* **23**, 3170–3182.

Martinotti G, Santacroce R, Pettorruso M, Montemitro C, Spano MC, Lorusso M, di Giannantonio M, Lerner AG (2018). Hallucinogen persisting perception disorder: etiology, clinical features, and therapeutic perspectives. *Search Results* **8**.

Mason NL, Kuypers KPC, Müller F, Reckweg J, Tse DHY Toennes SW, Hutten N, Jansen JFA, Stiers P, Feilding A, Ramaekers JG (2020). Me, myself, bye: regional alterations in glutamate and the experience of ego dissolution with psilocybin. *Neuropsychopharmacology*.

Meinhardt MW, Güngör, C, Skorodumov I, Mertens LJ, Spanagel R (2020). Psilocybin and LSD have no long-lasting effects in an animal model of alcohol relapse. *Neuropsychopharmacology* **45**, 1316–1322.

Mertens LJ, Wall MB, Roseman L, Demetriou L, Nutt DJ, Carhart-Harris RL (2020). Therapeutic mechanisms of psilocybin: changes in amygdala and prefrontal functional connectivity during emotional processing after psilocybin for treatment-resistant depression. *Journal of Psychopharmacology* **34**, 167–180.

Morales-Garcia JA, de la Fuente Revenga M, Alonso-Gil S, Rodriguez-Franco MI, Feilding A, Perez-Castillo A, Riba J (2017). The alkaloids of *Banisteriopsis caapi*, the plant source of the Amazonian hallucinogen Ayahuasca, stimulate adult neurogenesis in vitro. *Scientific Reports* **7**, 5309.

Moreno FA, Wiegand CB, Taitano EK, Delgado PL (2006). Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder. *Journal of Clinical Psychiatry* **67**, 1735–1740.

Nau F, Jr., Yu, B, Martin D, Nichols CD (2013). Serotonin 5-HT2A receptor activation blocks TNF-α mediated inflammation in vivo. *PLOS ONE* **8**, e75426.

Nutt D, Carhart-Harris R (2020). The current status of psychedelics in psychiatry. *JAMA Psychiatry*.

Nutt D, Erritzoe D, Carhart-Harris R (2020). Psychedelic psychiatry's brave new world. *Cell* **181**, 24–28.

O'Brien M, McNicholas F (2020). The use of telepsychiatry during COVID-19 and beyond. *Irish Journal of Psychological Medicine*, 1–17.

O'Connor K, Wrigley M, Jennings R, Hill M, Niazi A (2020). Mental Health Impacts of COVID-19 in Ireland and the Need for a Secondary Care, Mental Health Service Response. *Irish Journal of Psychological Medicine*, 1–18.

Orsolini L, Papanti GD, De Berardis D, Guirguis A, Corkery JM, Schifano F (2017). The "Endless Trip" among the NPS users: psychopathology and psychopharmacology in the hallucinogen-persisting perception disorder. A systematic review. *Front Psychiatry* **8**, 240.

Pokorny T, Preller KH, Kraehenmann R, Vollenweider FX (2016). Modulatory effect of the 5-HT1A agonist buspirone and the mixed non-hallucinogenic 5-HT1A/2A agonist ergotamine on psilocybin-induced psychedelic experience. *European Neuropsychopharmacology* **26**, 756–766.

Preller KH, Duerler P, Burt JB, Ji, JL, Adkinson B, Stämpfli P, Seifritz E, Repovš, G, Krystal JH, Murray JD, Anticevic A, Vollenweider FX (2020). Psilocybin induces time-dependent changes in global functional connectivity. *Biological Psychiatry* **88**, 197–207.

Preller KH, Herdener M, Pokorny T, Planzer A, Kraehenmann R, Stämpfli P, Liechti ME, Seifritz E, Vollenweider FX (2017). The fabric of meaning and subjective effects in LSD-induced states depend on Serotonin 2A receptor activation. *Current Biology* **27**, 451–457.

Preller KH, Pokorny T, Hock A, Kraehenmann R, Stämpfli P, Seifritz E, Scheidegger M, Vollenweider FX (2016). Effects of serotonin 2A/1A receptor stimulation on social exclusion processing. *Proceedings of the National Academy of Sciences of the United States of America* **113**, 5119–5124.

RANZCP (2020). The Royal Australian and New Zealand College of Psychiatrists (RANZCP). Therapeutic use of psychedelic substances.

Roseman L, Demetriou L, Wall MB, Nutt DJ, Carhart-Harris RL (2018). Increased amygdala responses to emotional faces after psilocybin for treatment-resistant depression. *Neuropharmacology* **142**, 263–269.

Smigielski L, Scheidegger M, Kometer M, Vollenweider FX (2019). Psilocybin-assisted mindfulness training modulates self-consciousness and brain default mode network connectivity with lasting effects. *Neuroimage* **196**, 207–215.

Strajhar P, Schmid Y, Liakoni E, Dolder PC, Rentsch KM, Kratschmar DV, Odermatt A, Liechti ME (2016). Acute effects of lysergic acid diethylamide on circulating steroid levels in healthy subjects. *J Neuroendocrinol* **28**, 12374.

Studerus E, Gamma A, Kometer M, Vollenweider FX (2012). Prediction of psilocybin response in healthy volunteers. *PLoS One* **7**, e30800.

Szabo A (2015). Psychedelics and Immunomodulation: Novel Approaches and Therapeutic Opportunities. *Frontiers in Immunology* **6**, 358.

Türközer HB, Öngür, D (2020). A projection for psychiatry in the post-COVID-19 era: potential trends, challenges, and directions. *Mol Psychiatry*, 1–6.

Vaidya VA, Marek GJ, Aghajanian GK, Duman RS (1997). 5-HT2A receptor-mediated regulation of brain-derived neurotrophic factor mRNA in the hippocampus and the neocortex. *J Neurosci* **17**, 2785–2795.

Varley TF, Carhart-Harris R, Roseman L, Menon DK, Stamatakis EA (2020). Serotonergic psychedelics LSD & psilocybin increase the fractal dimension of cortical brain activity in spatial and temporal domains. *Neuroimage* **220**, 117049.

Vindegaard N, Benros ME (2020). COVID-19 pandemic and mental health consequences: Systematic review of the current evidence. *Brain, Behavior, and Immunity*, S0889-1591(20)30954-5.

Weston NM, Gibbs D, Bird CIV Daniel A, Jelen LA, Knight G, Goldsmith D, Young AH, Rucker JJ (2020). Historic psychedelic drug trials and the treatment of anxiety disorders. *Depress Anxiety*.

Winstock AR, Johnson MW (2019). Global Drugs Survey: The psychedelic revolution in psychiatry and why patient opinion matters so much. https://www.globaldrugsurvey.com/gds-2019/gds2019-the-psychedelic-revolution-in-psychiatry-and-why-patient-opinion-matters-so-much/

Yockey RA, Vidourek RA, King KA (2020). Trends in LSD use among US adults: 2015–2018. *Drug and Alcohol Dependence* **212**, 108071.

View publication stats