positively experienced drug intoxication in carefully screened, well-controlled and psychologically informed treatment contexts can occur safely[4] and mediate subsequent benefits that persist well beyond the day of administration.

These treatment 'highs' can then be examined through a lens that considers addiction but not exclusively so. We propose that there is value to a broader perspective on the emotional and subjective qualities associated with intoxication – one which acknowledges risk and the prospect of a conceptually novel approach to the varieties of suffering that compel individuals to seek psychiatric care. Psilocybin and MDMA, but not cocaine, seem to support enduring and complex possibilities for self-learning that can be harnessed with psychological interventions.[5] Such data indicate granularity and suggest that positively experienced intoxication is not alone sufficient for therapeutic growth. Similarly, ketamine and its derivatives are not routinely administered in contexts that include psychotherapy, but the combination may facilitate new insights and ways of being for people.[6] Although biological psychiatry has not always concerned itself with these aims, the field is uniquely positioned to help.

The ongoing study of medical hallucinogens may at times overestimate their benefits and underestimate their risks, and, for this, scientific integrity is essential. Moreover, not every 'high' is therapeutic, and models for hallucinogen use that contribute to experiential avoidance, medication dependence and a diminished sense of agency for patients should be scrutinised. However, a nuanced evaluation of risk and appropriate mitigation strategies can support the development of a new kind of psychiatry. Emerging psychiatric interventions, in our view, should not be condemned merely on the basis that some patients report enjoying the associated subjective effects – an intervention is not 'bad' just because it feels 'good'.

Declaration of interest

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David S. Mathai, The Johns Hopkins University School of Medicine, Baltimore, USA; **David B. Yaden**, The Johns Hopkins University School of Medicine, Baltimore, USA; **Kelley C. O'Donnell**, New York University Grossman School of Medicine, New York, USA. Email: pmathai1@jhu.edu

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Author reply

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We agree that a drug is not necessarily bad just because it feels good – drugs that produce generally pleasant effects (e.g. benzodiazepines) are useful in some situations.

The trouble is that when a drug makes you feel euphoric, 'high' or just pleasantly 'merry', it is difficult to distinguish these drug-induced alterations from long-lasting and clinically relevant effects on mood. Depression scores will be lower than they would otherwise be, but this does not indicate that anything has happened to the individual's underlying mood, and evidence for long-term benefits is weak and confounded by the problems we described in our original article. The same effects would occur with alcohol or cocaine. But even unpleasurable or neutral drug-induced experiences may reduce feelings of depression by virtue of distracting people from their underlying feelings.

A further problem is the difficulty – if not impossibility – of doing double-blind studies with drugs that induce psychoactive effects, especially those that produce as unique effects as psychedelics. Many of the people coming forward for research are young men who have used psychedelics before, so know what to expect,[1] and we know that expectations exert a strong influence on outcome across numerous conditions.[2]

Some of the esketamine studies show how profound the placebo effects associated with the administration of psychedelics can be. In the only positive trial of esketamine, people allocated to placebo improved by a huge 17.0 points on the Montgomery–Åsberg Depression Rating Scale over 4 weeks.[3] Having said this, we accept that people may occasionally gain insights through the use of psychoactive substances, though this is not necessarily restricted to psychedelics, and there are safer routes to personal development – such as exercise, art, exposure to nature and psychotherapy.

Furthermore, the opioid crisis has shown just how short-sighted it is to think that the risks of misuse and dependence can be safely contained by 'an adequately supportive treatment setting', with a recent report on esketamine finding evidence of intoxication, tolerance, dependence and abuse from pharmacovigilance data and patient reports,[4] also present in clinical practice.[5] This is only one subset of the harms produced by esketamine, which include bladder damage,[6] cerebrovascular and cardiovascular consequences,[5,7] and concerns over connection to increased suicides.[8] 'Bad trips' are also an issue.[4]

We are particularly concerned by the commercialisation of psychedelic 'treatments'. Ketamine clinics have become an industry in the USA, and venture capitalists are also funding psychedelic research centres, waiting for the go ahead for medical use.[9] Like any business, there is an imperative to expand the market and to keep people coming back; hence, treatment indications are often elastic and include feeling 'blocked', 'lacking purpose' or experiencing stress.[9] Similarly, despite being presented and evaluated as a one-off or short-term intervention, there is a tendency toward long-term use as witnessed in the US ketamine clinic industry.[10] It is likely that these people include many who have become physically or psychologically dependent, as well as those who are desperate for a cure, all of whom make profitable customers.

People have used psychoactive drugs to change and expand their consciousness for centuries, including to block out painful emotions and thoughts; this may have short-term benefits but is rarely an effective strategy in the long run. How these substances are regulated is an important debate and should not be replaced by a process of medicalisation that may end up harming and exploiting vulnerable people.

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Joanna Moncrieff, Professor of Critical and Social Psychiatry, University College London, UK; **Mark Horowitz**, Clinical Research Fellow, University College London, UK. Email: j.moncrieff@ucl.ac.uk

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