THE ACID TEST

Psychedelic drugs such as LSD, MDMA and ketamine show promise in the treatment of mental health problems. By **David Ader**

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The crossover between illicit drugs and medicines is nothing new. Opiates like heroin and morphine can be our most effective medical painkillers, yet cause immense harm to individuals and society.

Some drugs that are currently illicit were originally invented or discovered for use in medicine. Conversely, some medicines have been developed from drugs that have become illegal – cannabis had been used for thousands of years, and made widely illegal, before the medicine Sativex was recently derived from it to treat multiple sclerosis.

Perhaps surprisingly, this crossover has so far mostly been limited to painkillers, tranquilisers and stimulants. The family of psychedelic and hallucinogenic drugs that include some of our most powerful and popular mind-altering illegal drugs, including MDMA, LSD and magic mushrooms containing psilocybin, have mostly not been mined for medical benefits.

In the UK, these three drugs are all not only Class A, but also Schedule 1, meaning that – unlike heroin, for example – they are not authorised for medical use and cannot legally be prescribed by doctors. The reasoning is they are judged by the Home Office to have no therapeutic value. Even so, ketamine is used widely as an anaesthetic, and there are a few other exceptions too. The over-the-counter cough suppressant dextromethorphan (DXM) is a powerful dissociative hallucinogen when used in quantities way above the stated dose. However, on the whole, this class of drugs are not permitted for use as medicines, and none are used in the treatment of mental illnesses.

Yet a growing number of voices are calling for just that to happen – and they are not only from people who are in favour of a more liberal approach to drugs.

More and more serious scientists, publishing in venerable academic journals, are highlighting the potential effectiveness of LSD, ketamine, MDMA, psilocybin and compounds derived from cannabis for a variety of mental illnesses. People suffering from common, difficult and debilitating illnesses including alcoholism, depression, post-traumatic stress disorder (PTSD), anxiety disorders and schizophrenia might have their condition alleviated by these new psychedelic medicines. But only if some or all of the promising early research findings translate into proven benefits, and the necessary regulatory and legal barriers are crossed. It's a big if. The trialling of new medicines is lengthy even when the drugs appear to be innocuous and have few side effects, and the legal and political barriers are real.

Professor David Nutt, former Chair of the Advisory Council on the Misuse of Drugs, certainly thinks that the legal obstacles are significant, and he speaks with a moralistic fervour on the issue, saying in 2012: "Regulations, which are arbitrary, actually make it virtually impossible to research these drugs. The effect these laws have had on research is greater than the effects that [George] Bush stopping stem cell research has had because it's been going on since the 1960s."

It's hard to support this comparison though. Even Schedule 1 drugs in the UK can be used for research purposes, although a Home Office licence is needed. For its part, the Home Office insists that bona fide institutions are perfectly able to conduct research into illegal drugs, and only necessary safeguards are in place. Given the difficulties and enormous expense involved in researching and bringing any drug to market, one extra level of delay and cost caused by having to obtain a licence should be relatively insignificant. And in any case, the amount of research that is going on in these areas belies Professor Nutt's claims; it only takes a second on Google Scholar to find many recent trials involving Schedule 1 drugs.

On the effectiveness of some of today's recreational drugs in the treatment of mental health problems, there are a few combinations in particular that crop up repeatedly in the literature, and for which the findings are especially positive. The longest-established link must be between LSD and alcoholism.

As long ago as 1958, American scientists were writing reviews of the existing research into LSD for a variety

of psychotherapy treatments – most notably for alcoholism – and individual studies date back to at least 1950.

The mechanism by which it might work is theorised to involve many of the same emotional states described by recreational users – the feeling of greater connection on a closer interpersonal level with the therapist, reduced inhibition, defensiveness, guilt and resistance to repressed memories – which enable the patient to discuss problems and issues that they would not usually be able to or feel comfortable doing.

The experience appears to have been felt by some to have been so powerful that a single dose had a lasting effect. Bill Wilson, the co-founder of Alcoholics Anonymous, was apparently convinced of the benefits, which he thought owed to LSD's ability to provoke the 'spiritual awakening' that he believed was an essential part of the process of recovery.

Perhaps unsurprisingly, the number of studies involving LSD seems to increase exponentially in the 1960s but then mostly tail off by about 1970, presumably as the drug became harder to obtain. The statistical power and methodologies of the many studies conducted might not stand up to modern scientific standards – these were often very small studies which dealt with the use of LSD for a very wide variety of mental illnesses. In 2012 Norwegian researchers extracted the data from all these studies, focusing exclusively on alcoholism, and conducted a systematic review and meta-analysis, concluding that a single dose of LSD as part of an alcohol treatment program was indeed associated with a lasting decrease in alcohol use.

A similar mechanism is purported to be behind promising results reported by several studies when seeking to treat PTSD and other similar anxiety disorders using MDMA. The strong sense of empathy with the therapist, feelings of happiness, serenity and warmth, a detachment from unpleasant memories and an increased introspective ability may help the patient to feel safe and in control, while the therapist and patient together address the causes of anxiety. First patented by Merck in 1912, MDMA was originally intended to be a medicine, and if the level of current scientific interest is any indication, it may end up being one again soon.

Perhaps the area with the most striking recent finding is the potential for ketamine to help alleviate the symptoms of severe depression. Widely reported in the press, a trial by researchers at Oxford University and Oxford NHS Foundation Trust found promising results.

The treatment, a much lower dose than is typically used recreationally and hugely lower than when used as an anaesthetic, was given to 28 people whose depression or bipolar disorder was so severe and treatment-resistant that they were in a clinic that usually performs electroconvulsive therapy (ECT, or electric shock therapy). The patients were given one or two small dose injections of ketamine a week, for three weeks. Almost one third of them reported that their depression was reduced by at least 50 per cent within two weeks of starting the treatment. This reduction lasted from just under a month to almost half a year.

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Oxford psychiatrist Dr Rupert MacShane praised the "dramatic effect" of the ketamine treatment on people "whose lives are blighted by chronic severe depression". The side effects – some people experienced nausea, anxiety, confusion and altered perceptions – seem unimportant compared to the serious memory loss that ECT provokes.

The list by no means ends there. Psilocybin is reported to have some similar effects to MDMA for anxiety and PTSD, and cannabidiol (CBD), the second most important psychoactive compound found in cannabis after THC, may be as effective as antipsychotic drugs at treating schizophrenia, but with fewer side effects and an improved effect on the most negative aspects of the condition.

It is important to note again that these studies are coming from highly respected peer-reviewed scientific journals, not from the cannabis legalisation movement. The CBD for schizophrenia result was termed an "exciting finding [that] should stimulate a great deal of research" by Dr. John Krystal, the Chair of Psychiatry at Yale University School of Medicine.

For many of these drugs, though, the potential problems are well known. As the psychiatrist Dr Ben Sessa points out, it is important not to let justified wonder at the sometimes seemingly benign power of these drugs obscure their potential for harm. "The subject of psychedelic psychotherapy in the past collapsed – in part – because it was not only the pop-stars and poets who were preaching about the wonders of LSD, but also some clinicians who allowed themselves to become biased and blinded to the potential dangers of the drug," says Dr Sessa.

As well as worrying about harms, it must also be recognised that the scientific evidence on all the treatments mentioned so far remains promising rather than proven. The science for all these treatments is at a very early stage, and there will need to be many more trials, and many more positive results, before the Department of Health beseech the Home Office to allow therapeutic use of these drugs. It is of course hugely important that the bar is set high and that new medicines (or old medicines repurposed) are comprehensively tested for efficacy and safety. Nonetheless, the mental illnesses in question, for which some psychedelic drugs seem to offer a glimmer of hope, can have lifelong and hugely negative impacts on people's quality of life.

The recent Academy Award-winning film *Dallas Buyers Club*, although perhaps rightly criticised as a poor representation of the development of medicines for HIV/AIDS, did provoke discussion and may still provoke legislation that points in an interesting direction.

Set during the scramble to develop drugs for HIV/AIDS, before any effective medicines existed, the film explores whether people with terminal illnesses should have the 'right to try' anything that might help them, despite the new drugs not having been proven effective or safe.

Depression, anxiety and addiction are of course not terminal illnesses, but then LSD, psilocybin, ketamine and MDMA are not unknown quantities either, and much has been made – notably of course by Professor Nutt again – of the relatively low toxicity of these drugs.

If people with serious mental illnesses demand the 'right to try' these drugs as treatments for their conditions, it is not difficult to imagine a future where the psychedelics join painkillers, tranquilisers and stimulants as both illicit drugs and essential medicines.

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