Making a medicine out of MDMA
Ben Sessa & David Nutt

Efficacy of cognitive bias modification interventions in anxiety and depression: meta-analysis
Ioana Cristea et al

Positive attributes in children and reduced risk of future psychopathology
Pablo Vidal-Ribas et al

Recovery-focused cognitive-behavioural therapy for recent-onset bipolar disorder: randomised controlled pilot trial
Steven H. Jones et al
Contents

A1 Editorial Board
A3 Highlights of this issue

Editorials
1 Can psychedelic compounds play a part in drug dependence therapy?
  B. Sessa and M. W. Johnson
4 Making a medicine out of MDMA
  B. Sessa and D. Nunn
6 Léon Bonvin – fallen stars
  Raymond Cavanaugh Jr

Review article
7 Efficacy of cognitive bias modification interventions in anxiety and depression: meta-analysis
  I. A. Crites, R. N. Kok and P. Gijgers

Papers
17 Positive attributes in children and reduced risk of future psychopathology
  P. Voh-Radda, R. Goodman and A. Stangaris
25 Watchmen’s Rorschach – psychiatry in the movies
  Joseph Kane
26 Intergenerational transmission of psychopathy and mediation via psychosocial risk factors
  K. M. Aylott, D. P. Farrington and J. W. Cod

31 Biological psychiatry – in 100 words
  Philip Cowen
32 Word use in first-person accounts of schizophrenia
  S. K. Fineberg, S. Deutsch-Link, M. Ichinose, T. McQuinness, A. J. Boisseau, C. K. Chung and P. Corlett

  Scott Henderson

39 Invited commentary on … Word use in first-person accounts of schizophrenia
  E. Jones

41 Differences in voice-hearing experiences of people with psychosis in the USA, India and Ghana: interview-based study
  T. M. Luhrmann, R. Padmavati, H. Thoror and A. Osei

45 Sadness and mild cognitive impairment as predictors for interferon-alpha-induced depression in patients with hepatitis C
  S. Sankar, R. Sankar, T. Berg and M. Schaeffer

52 Insulin resistance and outcome in bipolar disorder
  C. V. Cakin, M. Rizopoulos, R. Uher, T. Jais, C. M. Slavé, J. S. Gershon, M. C. O’Donovan and M. Albrecht

58 Recovery-focused cognitive-behavioural therapy for recent-onset bipolar disorder: randomised controlled pilot trial

67 Speed of remission in elderly patients with depression: electroconvulsive therapy v. medication

72 Last wills and testaments in a large sample of suicide notes: implications for testamentary capacity
  M. Sinyor, A. Schäffer, I. Hull, C. Peisch and K. Shulman

Short report
77 Gross morphological brain changes with chronic, heavy cannabis use
  V. Loruszzi, N. Salkovskis, S. Whittle, A. Forino, D. I. Lubman, C. Pantelis and M. Yücel

Columns
79 Correspondence
80 Correction
81 Book reviews
83 Contents of Advances in Psychiatric Treatment
84 Contents of the American Journal of Psychiatry
85 Kaleidoscope
87 From the Editor’s desk

Cover picture

Dr Alexander ‘Sasha’ Shulgin (1925–2014), chemist, discovered and synthesized over 200 new psychoactive compounds. Recognising the limitations of animal studies, he tested these on himself and his friends; documenting the results in two books written with his wife Ann: Phenethylamines I have Known and Loved and Tryptamines I Have Known and Loved. He famously rediscovered the drug 3,4-methylenedioxyamphetamine (MDMA) and introduced it to the psychotherapeutic community; MDMA’s ‘empathogenic’ therapeutic properties make it ideal for treating post-traumatic stress disorder (PTSD) and the UK’s first clinical study of MDMA for PTSD is now getting underway in the artist’s own words: The painting portrays Sasha holding an MDMA molecule that has a fiery warm glow and angel’s wings. Ann touches the molecule and gazes into the light. Around them radiate molecular symbols of Shulgin’s many psychedelic discoveries.”

Text by Ben Sessa.

We are always looking for interesting and visually appealing images for the cover of the journal and would welcome suggestions or pictures, which should be sent to Dr Allan Beveridge, British Journal of Psychiatry, 21 Prescot Street, London E1 8BB, UK or bjpsych@psych.ac.uk.
Can psychedelics compounds play a part in drug dependence therapy?

Ben Sessa and Matthew W. Johnson

Summary
After a 40-year hiatus there is now a reawakening of psychedelic drug therapy throughout psychiatry, with studies examining the drugs psilocybin, ketamine, ibogaine and ayahuasca in the treatment of drug dependence. Limitations to these therapies are both clinical and legal, but the possibility of improving outcomes for patients with substance dependency imposes an obligation to research this area.

Declaration of interest
None.

The only radical remedy I know for Dipsomania is Temperance.
William James in The Varieties of Religious Experience

After one hundred years of modern psychiatry the treatments available for enduring remission from drug dependence for alcohol, opiates, stimulants and nicotine remain poor. Although pharmacological treatments exist they are associated with substantial failure rates. A wealth of studies explored psychedelic drug-assisted therapy in the 1950s and 1960s, but this research was curtailed prematurely in the wake of the 1960s recreational drug phenomenon. After a hiatus of several decades this research is being revisited with a number of contemporary studies examining the drugs psilocybin, ketamine, ibogaine and ayahuasca to directly tackle drug dependence.

Why concentrate on drug dependence?
People who are drug-dependent are often stigmatised, maligned by society and blamed. However, the experience of the authors—a child psychiatrist who now works in adult substance misuse (B.S.) and a behavioural psychologist who studies the environmental determinants of drug use (M.W.L.)—is that many of these patients are helpless, needy victims of adverse psychosocial circumstances. Their trajectory into drug dependence has been a journey from childhood trauma. Now they face not only their unresolved trauma but also the plight of drug dependence that ties them to a lifestyle of psychosocial and financial dysfunction. Because of the complexity of their aetiology and the psychological and physiological dependence that results, these disorders are very difficult to treat.

Alcohol addiction
One adult in 20 in the UK is a dependent drinker and one quarter of all adults drink in a hazardous fashion. Alcohol dependency and misuse is a major factor in offending behaviour. It is strongly related to crime, including domestic abuse, antisocial behaviour, public disorder, sexual assault and motoring offences. A meta-analysis of 361 controlled studies of treatments for alcohol dependence in 2002 identified 46 possible interventions. The brief intervention approach ranked highest and motivational enhancement ranked second. Pharmacotherapy with the gamma-aminobutyric acid (GABA) agonist acamprosate and the opiate antagonist naltrexone ranked third and fourth respectively. The lowest ranked approaches were designed to educate, confront, shock or foster insight regarding the nature of alcoholism. There remains a lack of coherence and agreement about the most efficacious alcohol dependence treatment. Meanwhile, taking into account alcohol-related health disorders and disease, crime and antisocial behaviour, accidents, loss of productivity in the workplace and domestic problems, the Department of Health estimates alcohol misuse is now costing around £20 billion a year in England alone.

Opiate dependence
Misuse of heroin and related opioids is a major public health concern, with over 123,000 people injecting heroin in the UK. Those who use heroin have a 12-fold increase in mortality relative to the general population and often present with severe physical, mental, social and criminal legal complications. Methadone and buprenorphine are the most commonly prescribed medications for opioid dependence. They have consistently been found to increase treatment retention and decrease opioid misuse, mortality, HIV risk and crime. However, these substitution treatments have limitations. Methadone is associated with medical risk and is contraindicated for some patients, and both medications are dangerous in combination with sedative drugs.

Stimulant dependence
Cocaine is the second most popularly used illegal drug in the UK. In its powder form it may be snorted or injected, and in its freebase form crack cocaine can be smoked and injected. There is no accepted substitution treatment for cocaine or other stimulants as there are for opiates. Treatments rather involve psychological strategies including contingency management, cognitive-behavioural therapy and motivational interviewing. Drug therapies are largely symptomatic (i.e. addressing comorbid depression, anxiety and insomnia) or treat coexisting opiate dependence.

Nicotine dependence
Although people who smoke are less marginalised than those using other drugs, tobacco is associated with more deaths than any other legal or illegal drug. The numbers are staggering—
tobacco kills over 1.2 million people annually in Europe alone. Although the most effective medications (varenicline, bupropion, nicotine replacement) improve success rates, the large majority of patients relapse even with these medications. There is a desperate need for improvement. An ongoing open-label pilot study in the laboratory of one author (M.W.J.) is showing promising results using psilocybin combined with cognitive-behavioural therapy for smoking cessation. If efficacy and safety are supported by a randomised trial, this approach may hold potential to have a substantial public health impact given the shocking mortality caused by smoking.

Psychedelic therapy and substance misuse

In the 1950s and 1960s psychiatrists Humphry Osmond and Abram Hoffer at the Weyburn Mental Hospital, Saskatchewan, Canada, used lysergic acid diethylamide (LSD) to provide a clinician-induced organic psychosis to encourage sobriety. They found that it was mystical spiritual experiences – not psychotic experiences – with the drugs that were associated with treatment success. With LSD they reported abstinence rates far surpassing other treatments before or since. Osmond, who famously coined the term 'psychedelic', also administered LSD to Bill Wilson, the founder of Alcoholics Anonymous, who recognised LSD therapy as beneficial for alcohol dependence. A large number of studies to treat alcohol dependence with LSD psychotherapy were conducted by other researchers in the 1960s until psychedelic research collapsed for sociopolitical reasons in the wake of large-scale recreational drug use.

Cross-cultural use of psychedelics

There are examples of the naturalistic use of psychedelic plants to tackle addictions by indigenous populations: these include the West African use of the iboga root (containing ibogaine), the South American use of ayahuasca (containing dimethyltryptamine) and the North American use of the peyote cactus (containing mescaline); all of which have been reported to reduce rates of alcohol dependence.

Possible therapeutic mechanisms

Personality change is relevant to drug dependence, given that maladaptive personality traits often accompany drug use disorders. Two observational studies from the early 1960s suggested positive personality and other therapeutic changes in criminal offenders. With colleagues, M.W.J. has recently revisited prisoner personality change interventions with positive results. This idea of mystical-spiritual experience resulting in personality change was also explored recently in studies in which volunteers rated the psilocybin experience as having substantial personal meaning and spiritual significance. Subsequently sustained positive changes in attitudes and behaviour were consistent with changes rated by community observers. Another possible mechanism for the anti-addictive properties of hallucinogens may involve an 'afterglow' period of several weeks described in early clinical research. It was suggested that this period gave patients emotional strength to continue abstinence and experience decreased cravings. A recent paper by Bogenschutz & Pommy further explored potential psychological and biological therapeutic mechanisms of psychedelics in the treatment of substance misuse disorders.

Contemporary studies

A team in Russia in the 1990s, driven by the theory behind Osmond's 1950s studies, investigated the potential role for psychedelic drug-assisted psychotherapy with ketamine for both alcohol and opiate addictions. The results of subsequent placebo-controlled studies on more than 1000 patients with alcoholism showed that ketamine produced total abstinence for more than a year in 66% of those in the ketamine group, compared with just 24% of the control group. Despite positive published results the Russian Federation forbids further research with ketamine. In addition to the previously mentioned study of psilocybin and nicotine addiction, an open-label pilot study investigating psilocybin-assisted psychotherapy in alcohol dependence is under way at the University of New Mexico (clinicaltrials.gov registration number NCT01534494). There are also observational studies in Mexico and New Zealand of ibogaine-assisted therapy and a study conducted in Canada looking at the role of ayahuasca in the treatment of drug dependence (see http://maps.org for details of all these studies).

Theoretical objections to psychedelic treatment

There may be objections to treating drug dependence with other potentially misused drugs. However, current treatments for drug dependence already involve maintenance pharmacotherapy with controlled drugs. In seeking enduring remission, psychedelic drug-assisted psychotherapy is not simply maintenance therapy. Moreover, although psychedelic drugs can be misused, many of them (psilocybin, LSD) do not support compulsive drug-seeking.

The psychedelic renaissance

After a 40-year hiatus there is now a reinvigorating of psychedelic drug therapy throughout psychiatry. Research teams at major academic institutions worldwide are investigating psychedelic drug-assisted therapy and several independent research groups have emerged to work collaboratively on the cohesive organisation of research. This research is still in its early stages and the most effective methods have yet to be evaluated. There are several limitations. For example, psychotherapy sessions that last for many hours would be expensive and are unlikely to be a first-line intervention. Moreover, some individuals would be excluded from psychedelic therapy for safety reasons. Another challenge is that many of these drugs are restricted at the Schedule I or Class A level, forbidding all medical use outside of highly regulated medical research. A medical future for these compounds would require a change in regulatory status (e.g. to the level at which compounds with accepted medical use such as morphine and amphetamine are regulated) and a plan for the manufacture of approved compounds.

Patients with drug dependence deserve the opportunity for the best available treatments from their psychiatric services. If there is a chance that psychedelic drug-assisted psychotherapy could improve outcomes for this population of patients, we owe it to them to research this area.

Ben Sessa, MBBS, MScPsych, Addiction, Weston Super-Mare, Cardiff University Medical School, UK; Matthew W. Johnson, PhD, Johns Hopkins School of Medicine, Baltimore, USA

Correspondence: Dr Ben Sessa, Addiction, 35 The Boulevard, Weston Super-Mare BS23 1PE, UK. Email: bensessa@gmail.com

First received 22 Nov 2013, final revision 10 Mar 2014, accepted 7 Oct 2014

References


13 McLellan KA, Johnson MW, Gifford RR. Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness. J Psychopharmacol 2011; 25: 1453-61.


17 Sessa B. Shaping the renaissance of psychedelic research. Lancet 2012; 380: 200-1.