MIND MEDICINE AUSTRALIA

MDMA

By Drug Science and Mind Medicine Australia

Part 1 - History and Law

Drug Science

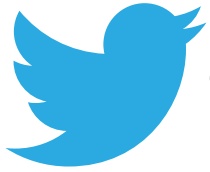
Drug Science

Drug Science was formed by a committee of scientists with a passionate belief that the pursuit of knowledge should remain free of all political and commercial interest.

Founded in 2010 by Professor David Nutt, following his removal from his post as Chair of the Advisory Council on the Misuse of Drugs, Drug Science is the only completely independent, science-led drugs charity, uniquely bringing together leading drugs experts from a wide range of specialisms to carry out ground-breaking research into drug harms and effects.

The Drug Science mission is to provide an evidence base free from political or commercial influence, creating the foundation for sensible and effective drug laws. Equipping the public, media and policy makers with the knowledge and resources to enact positive change.

Drug Science want to see a world where drug control is rational and evidence-based; where drug use is better informed and drug users are understood; where drugs are used to heal not harm



@Drug_Science

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Mind Medicine Australia is seeking to establish safe and effective psychedelic-assisted treatments for mental illness in Australia. As a registered charity (DGR-1 status), Mind Medicine Australia are supporting clinical research and working towards regulatory-approved and evidence-based psychedelic-assisted therapies. Mind medicine Australia operate as a nexus between medical practitioners, academia, government, regulatory bodies, philanthropists, and other partners.

Mind Medicine Australia is focused specifically on the clinical application of medicinal psilocybin and medicinal MDMA for certain mental illnesses. They do not advocate for recreational use of psychedelics, MDMA, or any other prohibited substances, nor do they advocate for any changes to the law with respect to recreational use. Their focus is wholly clinical.

@MindMedicineAU

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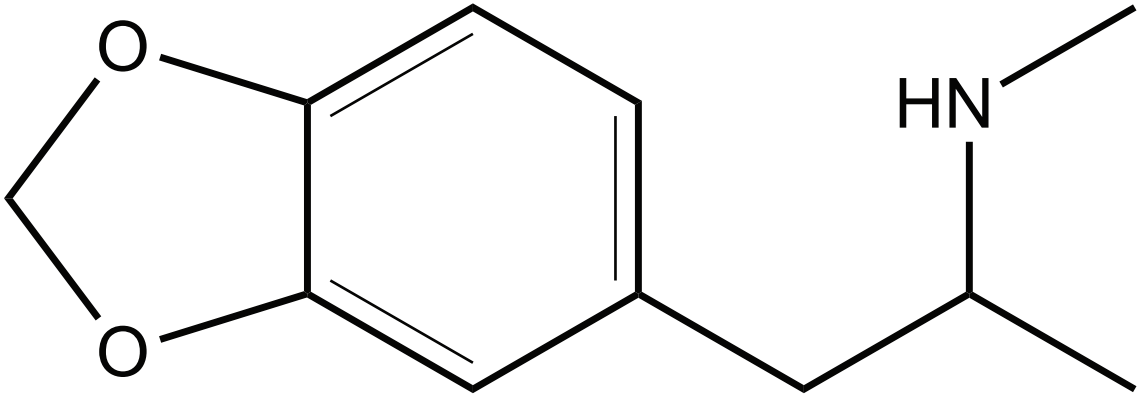
What is MDMA?

3,4-methylenedioxy methamphetamine (**MDMA**) is chemically related to the stimulant drug, amphetamine

MDMA has some stimulant effects in humans, along with distinct additional effects that class it as an "**empathogen**" or "**entactogen**"

The empathogenic effects of MDMA increase feelings of closeness with others, and promote bonding

These effects of MDMA appear to be beneficial in support of certain forms of psychotherapy for mental health conditions such as post-traumatic stress disorder (**PTSD**)



MDMA

History of MDMA

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1912
MDMA was first synthesised in 1912 by chemists at the pharmaceutical company, Merck in Germany, and was patented at that time as an intermediate in the synthesis of a compound, hydrastinine, that had been developed as a regulator of bleeding. MDMA at that time was called “methylsafrylamin” in Merck internal documentation

1927
Basic pharmacological tests were halted for economic reasons

1953 - 54
Toxicological studies were conducted on animals as part of the CIA’s MK-ULTRA program. but MDMA was not tested in humans - by Merck - until 1959

1960
The first published protocol for MDMA synthesis appeared in a Polish scientific journal

1960s
MDA, a close chemical relation to MDMA, was known and used non-clinically throughout the 60s

1970
The first seizure of MDMA tablets was reported in Chicago

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History of MDMA

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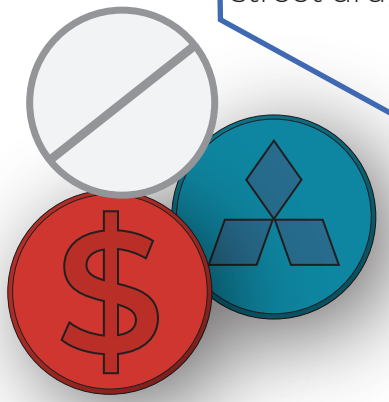
Dr **Alexander "Sasha" Shulgin** became aware of MDMA in the course of his systematic chemical and pharmacological exploration of phenethylamines as psychoactive agents. Around 1976, it is believed that he bioassayed (i.e. self-administered) MDMA in small, incrementally increasing, doses, and discovered its very particular effects on mood - but less so on cognition

In 1977, Shulgin introduced MDMA to his friend **Leo Zeff**, a San Francisco Bay Area psychotherapist, and Zeff delayed his retirement to introduce it in turn to hundreds, possibly thousands, of psychologists and psychotherapists across the USA

MDMA was used extensively as an adjunct to psychotherapy for the treatment of anxiety and post-traumatic stress disorder, and in couples counselling. However, very little formal research was conducted to investigate/establish its therapeutic applications

Awareness of MDMA's prosocial and mood-enhancing effects spread through the 1980s and, probably inevitably, it became popular in the underground electronic music scene. Prior to this, the drug had been known by therapists as "Adam"; at this time, in favour of the arguably more appropriate name "Empathy", MDMA became known in street drug culture as "Ecstasy"



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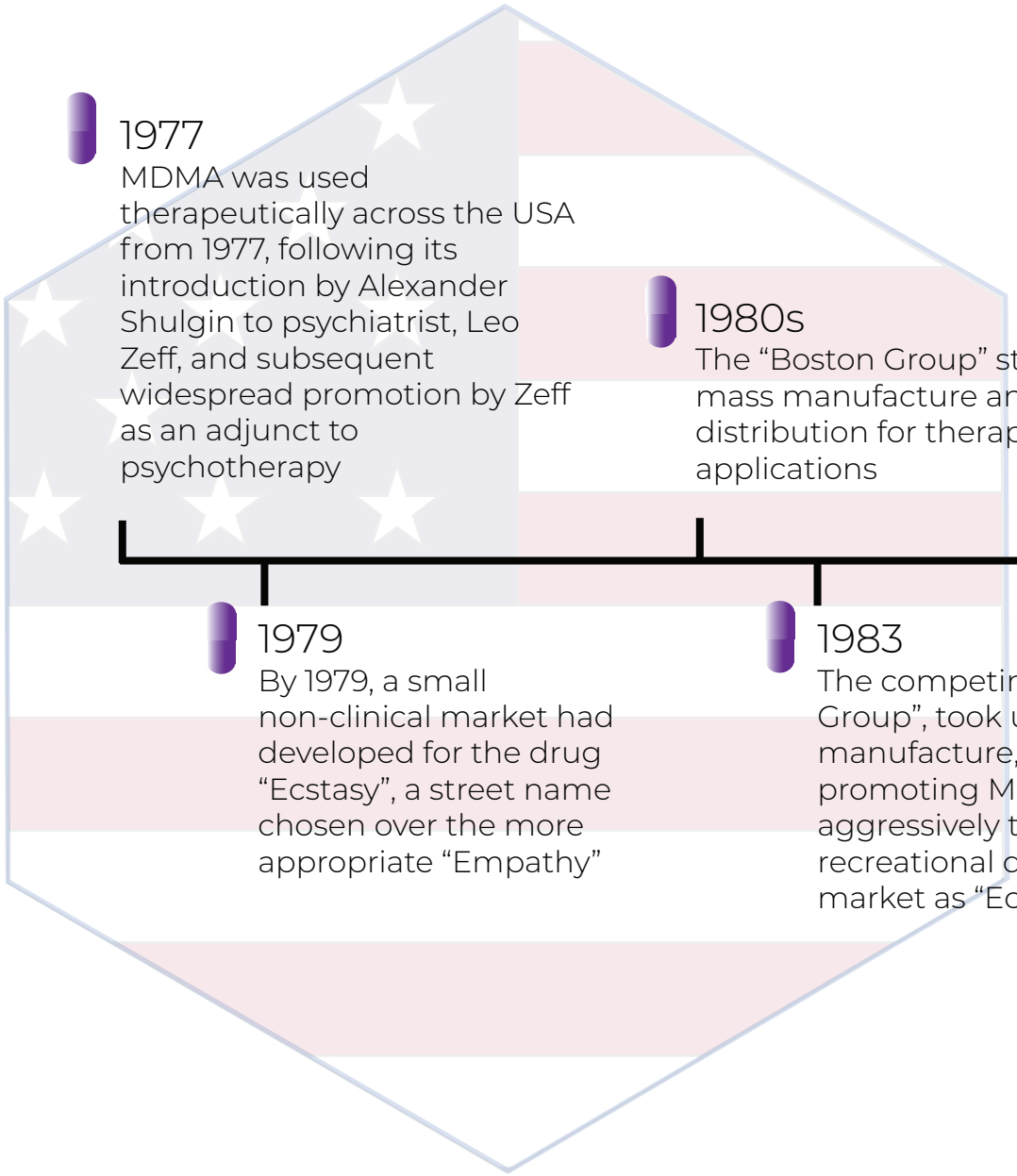
MDMA Use in the USA



1977
MDMA was used therapeutically across the USA from 1977, following its introduction by Alexander Shulgin to psychiatrist, Leo Zeff, and subsequent widespread promotion by Zeff as an adjunct to psychotherapy

1979
By 1979, a small non-clinical market had developed for the drug “Ecstasy”, a street name chosen over the more appropriate “Empathy”

1980s
The “Boston Group” started mass manufacture and distribution for therapeutic applications

1983
The competing, “Texas Group”, took up manufacture, promoting MDMA aggressively to the recreational dance/club market as “Ecstasy”

1985
US state police departments and other authorities, particularly the Drug Enforcement Administration (DEA), responded swiftly to the proliferation of non-clinical MDMA use, and it was placed in Schedule 1, the most restrictive schedule, by emergency ruling in 1985

1988
Its classification as having no medical use, high abuse potential and lacking accepted safety for use under medical supervision, was cemented by the DEA in 1988, after an extensive process of professional and public consultation; in so doing, the DEA overruled the advice of its own court appointee, Administrative Law Judge Francis L. Young

MDMA Use in the UK and Europe

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MDMA reached the UK relatively early, sometime in the 1970s, and **was made illegal in 1977** following the discovery of a clandestine laboratory in the Midlands. The UK government introduced an amendment to the 1971 Misuse of Drugs Act, making MDMA and its analogues Class A drugs.


EVIL OF ECSTASY

Danger drug that is sweeping disco and ruininglives

PILL POTTY 1 PILL POTTY 2 PILL OTTY 3

HORROR OF MY DREAMS

TOUCH WAS TOO MUCH!

It saps all my energy

Broader awareness of MDMA reached the UK from New York in the **early 1980s**, and **quickly became popular** along with the emergence of house and techno electronic dance music from Chicago and Detroit.

While the UK had gone through its own processes of scheduling in 1977, **enforcement began in earnest in 1985**.

MDMA was scheduled in the Netherlands in 1988. Other European countries closely followed suit.

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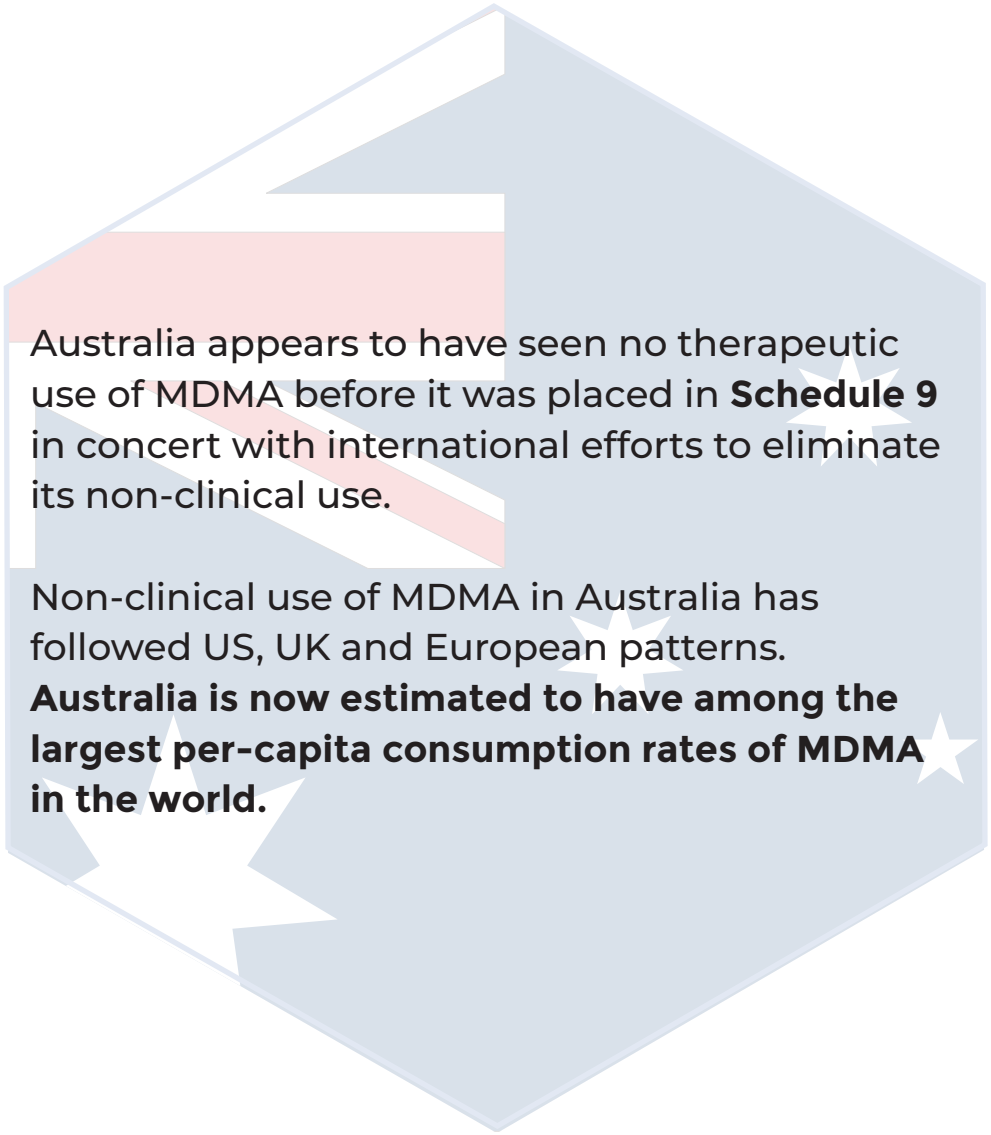
MDMA Use in Australia



Australia appears to have seen no therapeutic use of MDMA before it was placed in **Schedule 9** in concert with international efforts to eliminate its non-clinical use.

Non-clinical use of MDMA in Australia has followed US, UK and European patterns. **Australia is now estimated to have among the largest per-capita consumption rates of MDMA in the world.**

For people aged 14 or older in Australia:

11.2%

of people have used ecstasy in their lifetime

7%

of people in their 20s had recently used ecstasy

2.2%

used ecstasy in the last 12 months

(AIHW National Drug Strategy Household Survey 2016 (results from the 2019 due to be released late 2020))

Scheduling of MDMA

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US authorities, particularly the Drug Enforcement Administration (DEA), responded swiftly to the proliferation of non-clinical MDMA use, and it was placed in Schedule 1 the most restrictive schedule, by emergency ruling in 1985.

Response by the therapeutic community was rapid and vocal, and the DEA convened a process of professional and public hearings to enable assessment of the medical value of MDMA.

The classification of MDMA as having no medical use, high abuse potential and lacking accepted safety for use under medical supervision, was cemented by the DEA in 1988, after an extensive process of professional and public consultation; in so doing, the DEA overruled the advice of its own court appointee, Administrative Law Judge Francis L. Young.

MDMA manufacture and use consequently went underground, but continued to expand in similar manner to other recreational drugs in high demand.

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Why was MDMA Banned?

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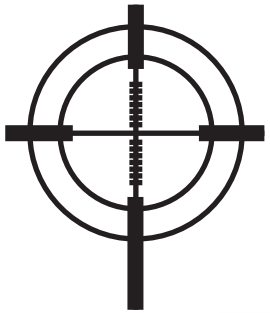

MDMA is classified as a **stimulant** of the amphetamine class, and also as a hallucinogen. Hence, on both counts, MDMA is regarded by government authorities as a drug of abuse.

US President Nixon's "**War on Drugs**" evolved into President Regan's "**Just Say No**" campaign.

CLICK HERE TO WATCH NANCY REAGAN WARNING AMERICANS ABOUT DRUGS AS PART OF THE 'JUST SAY NO' CAMPAIGN'

The US government and medical/research community promulgated concerns, largely unsupported by clinical evidence, about neuronal damage and other long-term health impacts

DEA spokesperson: "*All of the evidence the DEA has received shows that MDMA abuse has become a nationwide problem and that it poses a serious health threat*."

Effective opposition to the official line was hampered by the lack of evidence of therapeutic applications – formal research not conducted partly through fears among psychotherapists that community awareness of MDMA would lead to widespread non-clinical use, with consequent risk of 60s-like response from authorities.

Ironically, widespread non-clinical use did indeed occur, resulting in a small but significant number of deaths and other adverse health outcomes. This "**recreational**" use in unsupervised settings provided evidence and impetus for ever-increasing global law enforcement efforts to eliminate MDMA use in the community

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Potential Harms Caused by MDMA

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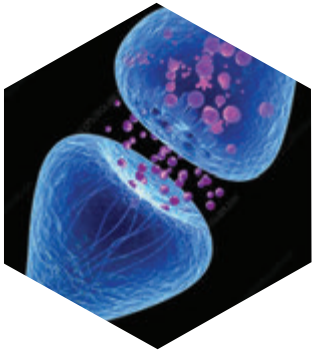
Acute risk of cardiac events (tachycardia and arrhythmias), hyperthermia and hyponatremia, almost exclusively at high (non-therapeutic) doses in non-clinical contexts

Acute risk of serotonin syndrome

- resulting from polydrug use and related to drug interactions

Short-term negative mood 24-48 hours after return to baseline following non-clinical use

- polydrug use and contextual factors likely to contribute



Possible risk of chronic serotonin and dopamine neurotransmitter depletion and/or changes in receptor expression associated with chronic non-clinical use

- unclear if due to polydrug use patterns in non-clinical context

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MDMA Harm Reduction – Pill Testing

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Pill testing is a harm reduction service (also known as drug checking) that analyses the contents of drugs to help avoid unknown and potentially dangerous substances in illicit drugs.

The Loop is a not for profit company which provides drug safety testing, welfare and harm reduction services at nightclubs, festivals and other leisure events.

Appropriate information and counselling is then provided to service users based on their specific test result to encourage choices that reduce overall drug use and the harms associated with taking drugs.

Currently only around 2% of UK festivals provide drug-testing facilities in the UK.

CLICK THE LOGO TO SEE HOW THE LOOP WORKS TO REDUCE DRUG HARM

WE ARE THE LOOP

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The Intervening Years

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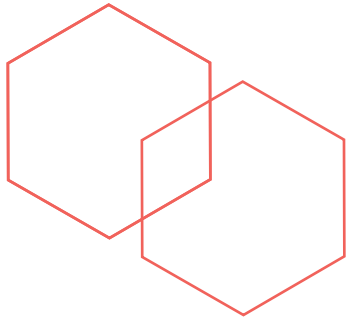
No research was conducted into the potential therapeutic applications of MDMA between 1985 – 2000

However, both the US National Institute of Health and the US National Institute of Drug Abuse conducted some animal-based research to intentionally demonstrate the harms and risks of MDMA

Nonetheless, since MDMA was placed in Schedule 1 in 1985, over **5000 academic articles** on MDMA have been published, and over **1100 human volunteers have been administered MDMA,** including human research into driving impairment conducted at Swinburne University, Australia



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The MDMA Renaissance

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1986
The Multidisciplinary Association for Psychedelic Studies (MAPS) was founded by **Rick**

1986 - 90
MAPS began funding animal toxicity studies & human safety studies at **Stanford University** and **Johns Hopkins University**

1996
The first US **FDA-approved, double-blind, placebo-controlled Phase I** dose-response safety study of MDMA was published by **Charles Grob**, working with MAPS

2004
First MAPS-sponsored **Phase 2 clinical trial of MDMA-assisted therapy for PTSD** was approved by the FDA

MAPS has sponsored **12 completed clinical trials** globally, investigating MDMA-assisted psychotherapy for PTSD, anxiety related to advanced-stage illness, social anxiety in autistic adults, and an ongoing study of healthy subjects via the MDMA therapist training program, with plans for additional studies of MDMA therapy for race-based trauma and transgendered people as well.

All positive outcomes, no SAEs

~60% of participants overall showed long-term remission from PTSD symptoms

MAPS has commenced **Phase 3 trials** in the USA and Canada, with more to come in North America, Europe and Israel, further studying MDMA-assisted therapy **for the treatment of PTSD**. These studies are underwritten by the FDA classification of Breakthrough Therapy status, potentially resulting in FDA and EMA approval of MDMA-assisted therapy for clinical implementation in the USA and the EU.

CLICK HERE TO WATCH HOW MDMA IS BEING USED TO TREAT PTSD

In recent years, a team from Bristol, UK, have further explored potential clinical indications for MDMA-assisted psychotherapy, namely in **treating addictions**. A small open-label pilot study looked at a role for MDMA therapy in treating alcohol use disorder. Publication of full dataset due in late 2020.

For preliminary results from their work, see:

Sessa B, Sakal C, O'Brien S, Nutt D. 2019. First study of safety and tolerability of 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy in patients with alcohol use disorder: preliminary data on the first four participants. BMJ Case Rep 12

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Social Impact of the War on Drugs

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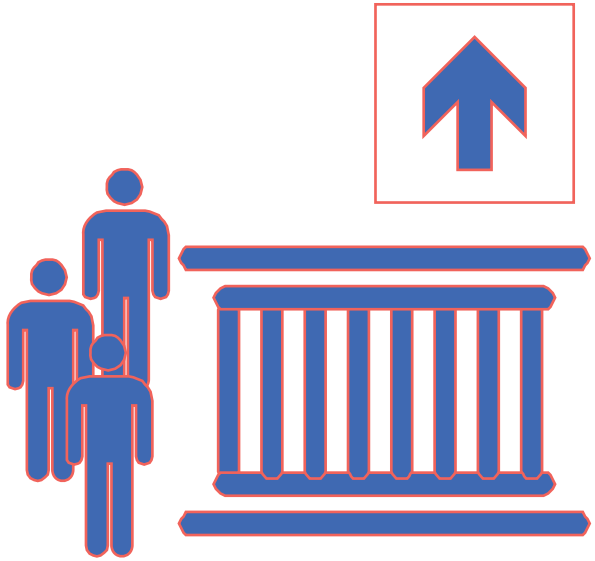
increases in associated **crime**, **social dislocation**, **mental illness** & **comorbidity**

Increased incarceration rates, particularly in USA, UK, Europe and Australia

CLICK HERE TO WATCH JAY-Z SPEAK ABOUT THE WAR ON DRUGS

Diversion of resources to law enforcement and prison-industrial complex

Establishment & sustenance of global **illicit drug trade**



Effects on **developing economies,** incl. destruction of SE Asian rainforests for harvest of precursors

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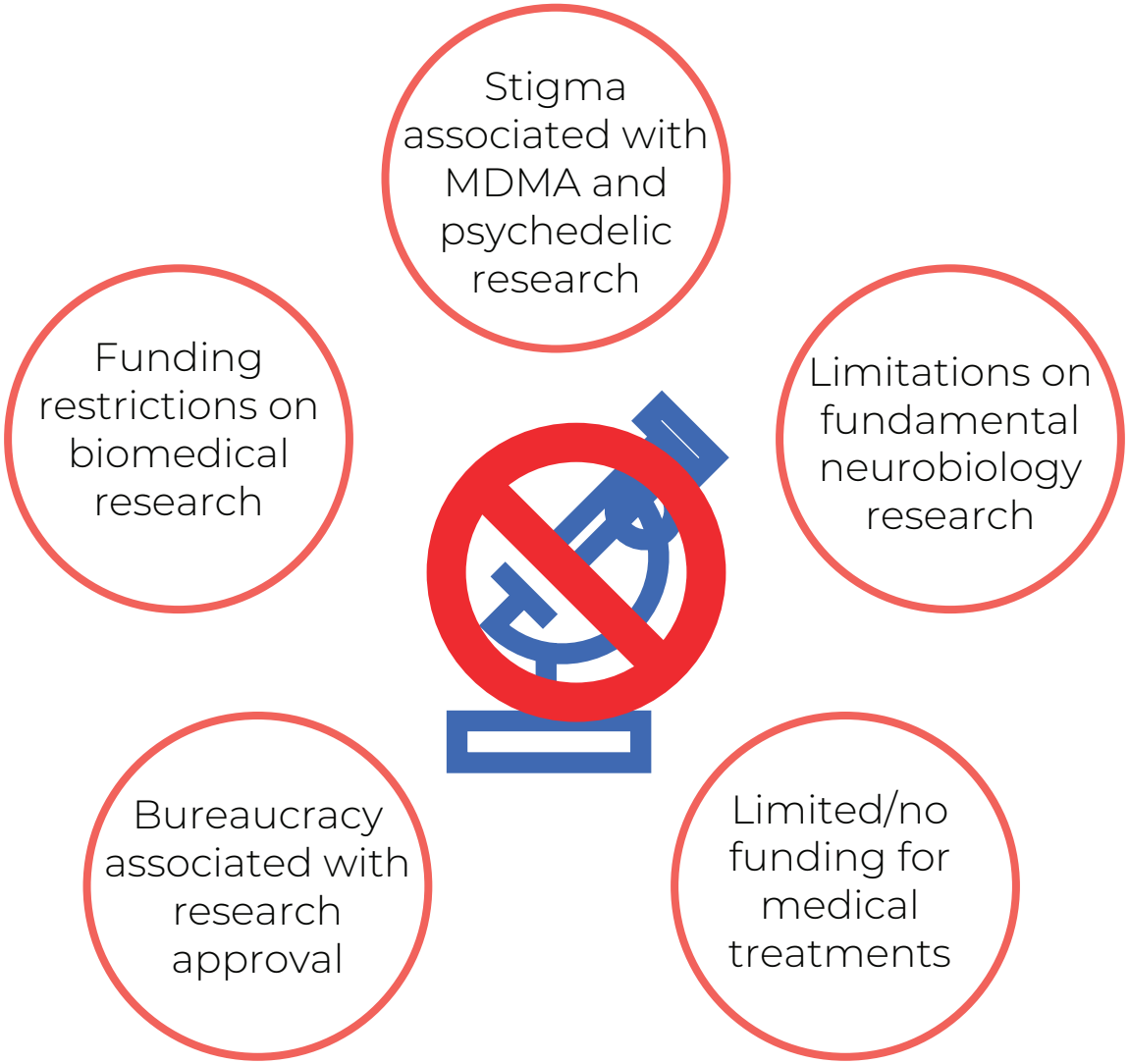
Scientific & Healthcare Impact of the War on Drugs



Current Legal Status of MDMA

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UN Convention on Psychotropic Substances (1971)

- MDMA is explicitly listed in Schedule 1

National schedules

US Schedule 1

UK Schedule 1

Australia Schedule 9

All of these Schedules explicitly specify no medical use, high abuse potential and high risk when used in clinical setting

Research permitted with requisite ethics approvals & state and national permits

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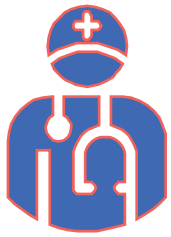
What does this mean for doctors?

What is preventing doctors from considering MDMA-assisted therapies?

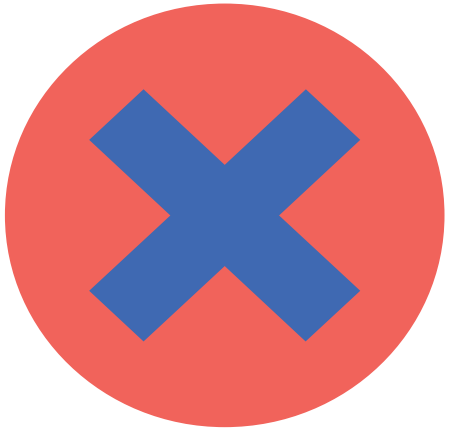


- Lack of evidence base - many doctors do not feel comfortable prescribing something with which they have little or no experience, and which does not have the structured data from randomised controlled trials that is expected today
- Lack of public health system support
- Stigma

Why isn't there a compelling evidence base for MDMA-assisted therapies?

- Research has been curtailed for over 30 years
- Drug schedules
- Lack of research funding
- Stigma
- Ignorance
- Lack of recognition of limitations of existing therapies

What does this mean for patients?



Limited therapies are currently available for mood disorders

E.g. CBT efficacy – 33% full: 33% partial: 33% ineffective

SSRI limitations

Patients are increasingly requesting MDMA-assisted therapy along with other treatments for PTSD, anxiety etc but are unable to receive them

Restrictive prescribing and dispensing practices

Patients dependent on the black market and underground therapy community

The Role of the Medical Student

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As future doctors, it is important that medical students are **aware of the benefits and potential harms of MDMA.** This will enable future doctors to provide patients with valuable information and help support them in their decisions about their treatment plan.

Medical students will also be in a position to help **make real change** to policy by helping to gather patient data and help provide unbiased information about the benefits and potential harms of MDMA.

Where can you find out more?

- drugscience.org.uk
- Drugs, without the hot air, *David Nutt*
- Drug Science Students Society

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References

Drug Policy Alliance. (2020). A Brief History of the Drug War. [online] Available at: http://www.drugpolicy.org/issues/brief-history-drug-war [Accessed 12 Feb. 2020].

Mithoefer MC, Wagner TM, Mithoefer AT, Jerome L, Doblin R. (2010). The safety and efficacy of ±3,4-methylenedioxymethamphetamine-assisted psychotherapy in subjects with chronic, treatment-resistant posttraumatic stress disorder: the first randomized controlled pilot study. J Psychopharmacol. 25:439–52.

Sessa B, Higbed L, Nutt D. (2019). A Review of 3,4-methylenedioxymethamphetamine (MDMA)-Assisted Psychotherapy. Frontiers in Psychiatry 10:138.

Sessa B, Sakal C, O'Brien S, Nutt D. 2019. First study of safety and tolerability of 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy in patients with alcohol use disorder: preliminary data on the first four participants. BMJ Case Rep 12

Vizeli P, Liechti ME. (2017). Safety and pharmacology of acute MDMA administration in healthy subjects. J Psychopharmacol. 31:576–88.