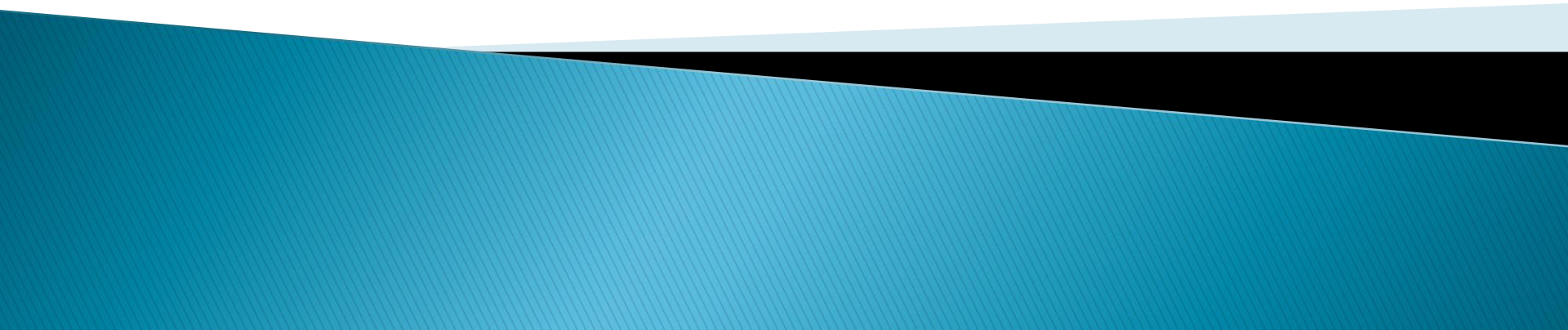


Current Debates in Psychology

Is horse riding really more dangerous than taking ecstasy?

Evaluating the evidence that hallucinogenic drugs should be used for therapeutic purposes.

Dr. Kate Williams



Hallucinogens...

- ▶ What are they?
 - A diverse group of drugs that alter perception, thoughts, emotions, feelings, and consciousness.
- ▶ Where do they come from?
 - Some plants and mushrooms (or their extracts). They can also be human-made.
- ▶ They cause hallucinations or experiences that appear real but are not.
 - They have been used for centuries for religious and sacred rituals.

Common Examples include...

D-lysergic acid diethylamide (LSD):

- powerful mood-changing chemical
- clear or white odourless material
- made from lysergic acid
- found in a fungus that grows on rye
- Also called: Acid, Blotter, Dots, & Yellow Sunshine.



4-methylenedioxy-methamphetamine (MDMA) or (Ecstasy):

- synthetic drug that alters mood & perception
- produces feelings of increased energy, pleasure, emotional warmth, and distorted sensory and time perception.
- popular in the nightclub scene and at all-night dance parties ("raves").



Ayahuasca:

- tea made from one of several Amazonian plants containing *dimethyltryptamine* (DMT), which is the primary mind-altering ingredient.
- Also called Hoasca, Aya, & Yagé



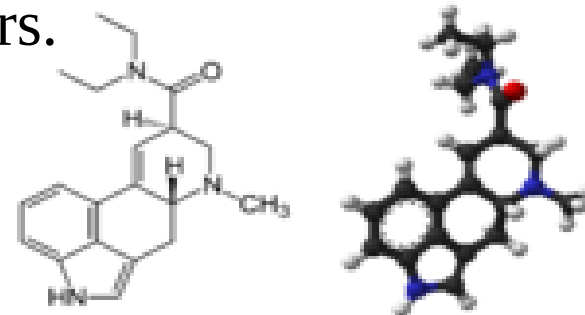
4-phosphoryloxy-N,N-dimethyltryptamine (psilocybin):

- comes from certain types of mushrooms found in tropical & subtropical regions of South America, Mexico, and US.
- Also called Little Smoke, Magic Mushrooms, Purple Passion, & Shrooms.

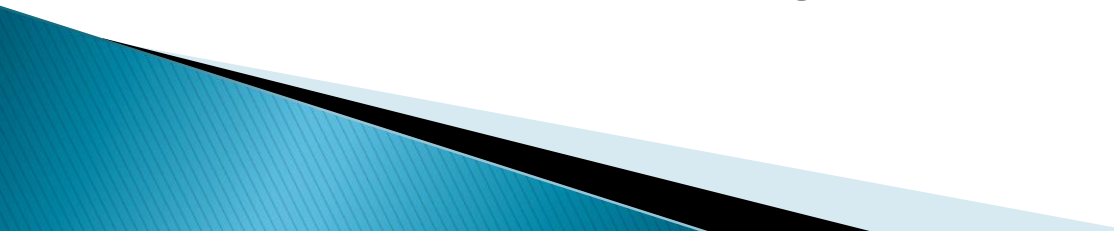


LSD: Brief History...

- ▶ 1938: Synthesised at the Sandoz laboratories in Switzerland by Swiss chemists Albert Hofmann and Arthur Stoll as part of a research programme to find medicinal use of ergot alkaloids.
- ▶ 1943: Hofmann discovered its psychedelic properties after accidentally coming into contact with it during the crystallisation process.
- ▶ 1947: Introduced as a commercial medication for various psychiatric uses.
- ▶ 1940s/1950s: used to examine the connection between behaviour and pharmacology and made available to researchers for experimental studies into the pathogenesis of mental disorders.



LSD: Brief History...

- ▶ 1964: used alongside psychoanalysis as a means for uncovering unconscious material (Strömberg, 1964).
 - ▶ Leading centres of LSD research developed in Scandinavian countries despite international warnings of the dangers/side-effects.
 - ▶ 1950s-1970s, several studies investigated potential therapeutic use in the treatment of neurosis, obsessive–compulsive disorder (OCD), substance dependence, and as an adjunctive therapy in the terminally ill (e.g., Kurland *et al.* 1971; Abraham *et al.* 1996; Grob, 1998; Grof, 2001; Hofmann, 2005; Dyck, 2006; Hintzen and Passie, 2010; Vollenweider and Komater, 2010; Krebs and Johansen, 2012; Bogenschutz, 2013; Burdick and Adinoff, 2013; Baumeister *et al.* 2014; Liester, 2014; Bogenschutz and Johnson, 2016).
- 

LSD: Brief History...

- ▶ 1965: Sandoz request that LSD no longer be registered and by the 1960s it was withdrawn from the market.
- ▶ 1960s: Became central to counter-culture in Western societies.
- ▶ 1968: Possession of LSD became illegal in the US.
- ▶ 1971: Misuse of drugs Act UK lists LSD as a class A drug, which carries a prison sentence of 7 years for possession and a lifetime sentence for supply.
- ▶ Could still be used scientifically in Denmark until 1974.
- ▶ But since the late 1970s clinical research was interrupted.

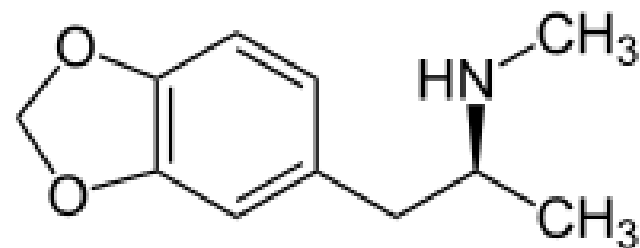
WHY?

LSD: Brief History

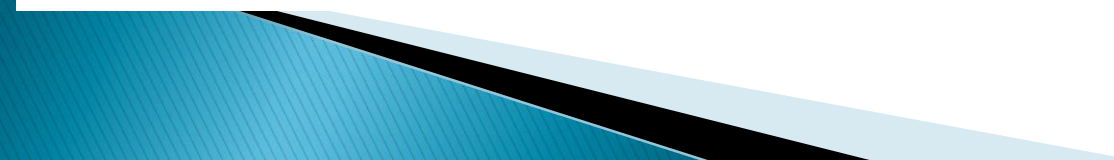
- ▶ Increase in recreational use and links to counter-culture.
- ▶ New rules implemented for investigating novel pharmacological agents.
- ▶ Illegal status in many countries.
- ▶ Methodological limitations:
 - e.g., lack of control groups and follow-up measurements; substantial variation of dose and dosing duration among studies; lack of control for confounding factors such as pre-existing mental health problems (Vollenweider & Kometer, 2010); Baumeister, et al., 2014).

Ecstasy: Brief History

- ▶ 1912: first synthesized by Anton Köllisch, a chemist at the Merck group.
- ▶ 1914: Patented by Merck but never made commercially available.
- ▶ 1953-54: US Army examined toxicity and behavioural effects of animals injected with MDMA (*Hardman, Haavik, & Seevers, 1973*).
- ▶ 1965: synthesized by Alexander Shulgin but psychoactivity not tested. Instructions for synthesis sent to various drug companies (*Benzenhöfer & Passie, 2010*).



Ecstasy: Brief History

- ▶ 1975: first hint of psychoactive effects.
 - ▶ 1976: further reports of effects: positive emotional experiences. Shulgin tried it himself and reported findings in a conference.
 - ▶ 1978: Shulgin and Nichols published report on its psychoactive effect in humans: disinhibiting effects.
 - ▶ Psychotherapists across US & Europe trained by Leo Zeff in the therapeutic use of MDMA.
 - ▶ 1970s: reports of recreational use in US.
 - ▶ 1977: Home Office UK lists MDMA as a Class A drug and placed it under schedule 1 of the Misuse of drugs act 1971.
- 

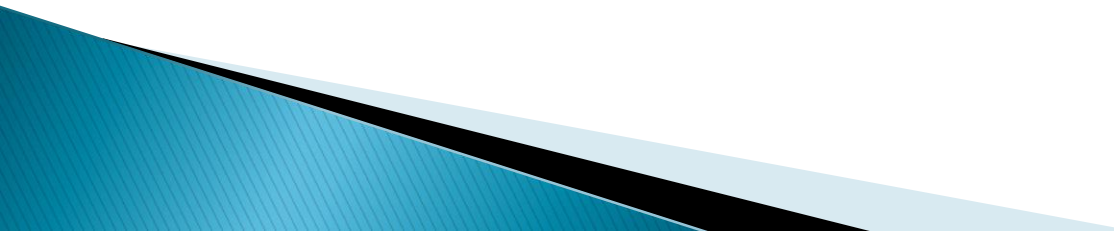
Recent Controversy

► Professor David Nutt:

- British psychiatrist and neuropsychopharmacologist.
- Fiercely campaigns for a change in the current drug laws to allow more research opportunities to examine the effects of hallucinogens.
- Appointed as chairman of the UK governments Advisory Council on the Misuse of Drugs (ACMD) in January 2008.
- But continually clashed with ministers over classifications of drugs.
- 2009: published an editorial in the Journal of Psychopharmacology, which compared the risks associated with horse riding as more dangerous than the risks of taking ecstasy.
- Also, gave a lecture discussing classification of drugs.
 - In it he suggested that alcohol/tobacco were more harmful than LSD, ecstasy, or cannabis.
- By the end of 2009 he was dismissed by the Home secretary.



The Dangers of hallucinogens

- ▶ **LSD**: Very unpredictable – users can experience “bad trips”, including perceptual deficits, loss of understanding, feelings of intense fear and paranoia (Parrott., et al).
 - Experience of psychotic “breakdown”
 - Changes in body temperature, blood pressure & heart rate
 - Loss of appetite, sleeplessness, dry mouth and tremors
 - Impairs distance perception (making things like crossing the road difficult).
 - Negative flashbacks
 - Severe depression
- 

LSD

- ▶ Binds to Serotonin receptors but nature of neurochemical changes is unclear:
Agonistic vs. Antagonistic effect

Agonistic Drug Effects

Drug increases the synthesis of neurotransmitter molecules (e.g., by increasing the amount of precursor).

Drug increases the number of neurotransmitter molecules by destroying degrading enzymes.

Drug increases the release of neurotransmitter molecules from terminal buttons.

Drug binds to autoreceptors and blocks their inhibitory effect on neurotransmitter release.

Drug binds to postsynaptic receptors and either activates them or increases the effect on them of neurotransmitter

Drug blocks the deactivation of neurotransmitter molecules by blocking degradation or reuptake.

Antagonistic Drug Effects

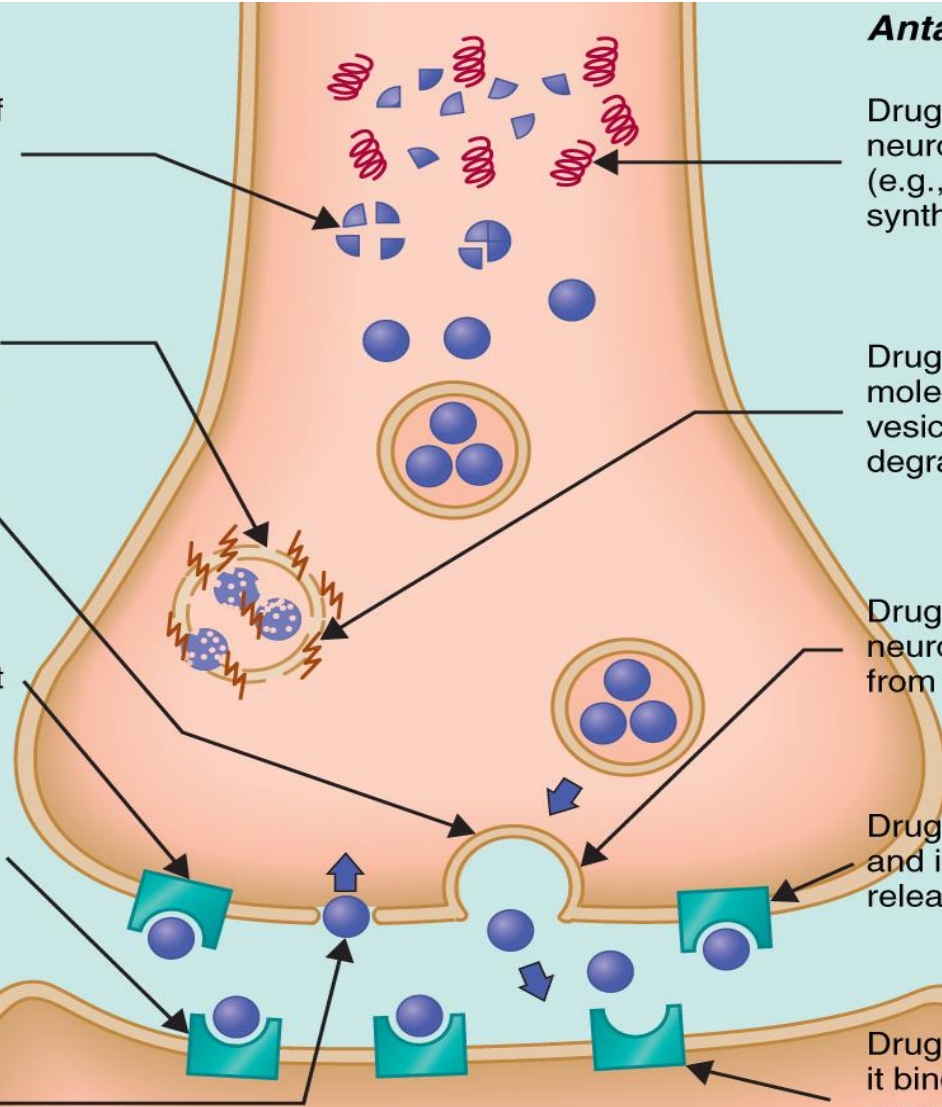
Drug blocks the synthesis of neurotransmitter molecules (e.g., by destroying synthesizing enzymes).

Drug causes the neurotransmitter molecules to leak from the vesicles and be destroyed by degrading enzymes.

Drug blocks the release of the neurotransmitter molecules from terminal buttons.

Drug activates autoreceptors and inhibits neurotransmitter release.

Drug is a receptor blocker; it binds to the postsynaptic receptors and blocks the effect of the neurotransmitter.



The Dangers of hallucinogens

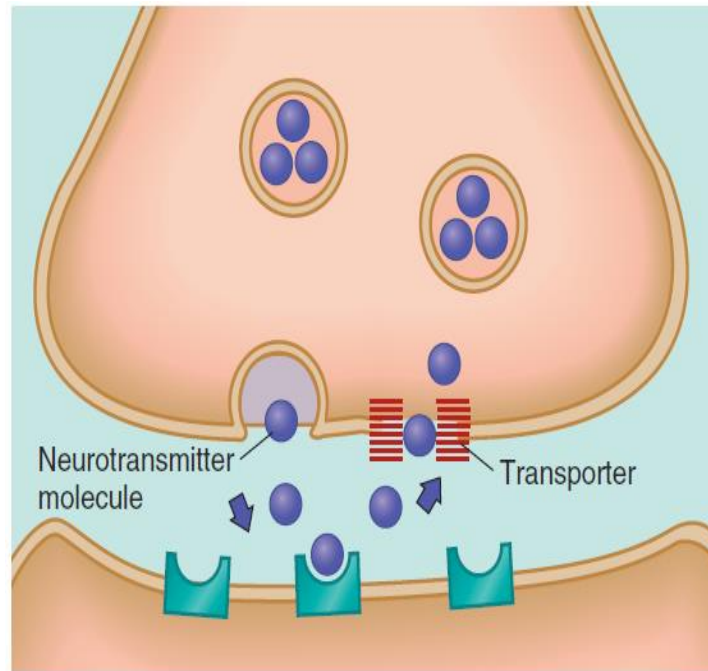
- ▶ **Ecstasy**: associated with various memory and higher-order cognitive deficits (e.g., Fox et al. 2001; 2002; Parrott et al. 2001; Parrott et al. 2004; Rodgers et al. 2003; 2006; Wareing et al. 2000).

Other related problems:

- changes in sleep (McCann et al. 2007; Jones et al. 2008),
- reduced immunocompetence (Connor 2004),
- altered pain thresholds (O'Regan & Clow 2004),
- depression & forms of psychiatric distress (Schifano 2000; Soar et al. 2001),
- occupational problems (Topp et al. 1999),
- neurohormonal changes (Parrott 2009;),
- reduced happiness and greater everyday stress (Scholey et al. 2011).
- Inexperienced therapists unable to deal with drug-induced reaction (Greer & Tolbert, 1986).
- Appetite problems and food cravings – link to serotonin (Schifano, 2000)
- Lack of energy, irritability, brooding, and bad dreams (Liechti et al., 2001).

Ecstasy

- ▶ Induces neurotransmitter activation across neural pathways, e.g., serotonin, dopamine, noradrenaline, and others (Green et al. 2003).
- ▶ Impairs serotonergic function by blocking re-uptake.
- ▶ Impairs executive function, inhibitory control, and decision making (as shown by cortex and limbic functional brain scan abnormalities)



Reuptake

Assessing the effects of hallucinogens

- ▶ Some critics say that one of the main issues with the conclusions drawn from assessing the effects of hallucinogens is that quite a vast amount of research has been conducted with recreational drug users.
 - What confounding factors should be taken into account here?



Hallucinogens: Current State of Affairs

- ▶ Following the interruption of research for roughly 20-30 years, controlled lab studies on hallucinogens re-emerged in the 1990s with healthy volunteers (Hermle *et al.* 1992; Strassman *et al.* 1994).
- ▶ More recent preclinical research (e.g., Baumeister *et al.* 2014; Buchborn *et al.* 2014; Bogenschutz & Johnson, 2016), case reports (e.g., Perrine, 1999; Wilcox, 2014) and observational (e.g., Hendricks *et al.* 2014, 2015) and preliminary experimental studies in healthy volunteers (Griffiths *et al.* 2006, 2011; Studerus *et al.* 2011; Kometer *et al.* 2012; Kraehenmann *et al.* 2016; Schmid *et al.* 2016) suggest that classical hallucinogens such as psilocybin and LSD have anxiolytic, anti-depressive, and anti-addictive properties.
- ▶ And there are currently a number of organisations that fund/conduct medical & scientific research (e.g., Beckley foundation, MAPS).

The brain on LSD

- ▶ <http://edition.cnn.com/videos/world/2016/04/13/effects-of-ldd-on-human-brain-curnow-intv.cnn>
- ▶ The first images of the brain on LSD released by researchers (2016)
- ▶ HOWEVER – What is the main issue with brain imaging studies?

Debate Questions:

1. Should hallucinogenic drugs be made readily available for research purposes? If so, why and who should control this?
 2. Should we be testing the effects of drugs like LSD and Ecstasy on willing and healthy volunteers?
 3. Should we be testing the effects of hallucinogenic drugs on those currently suffering with mental health concerns – what might be the implications of doing this?
 4. Are there any conflicts of interest that may arise from such research/findings?
 5. Are researchers being reckless when making statements of the comparable dangers of drugs to that of horse riding?
- 