Addiction and the Brain (PSGY1005)

Hallucinogens (and Ecstasy)

PSYCHOPHARMACOLOGY 2e, Figure 15.3

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Outline

Part 1

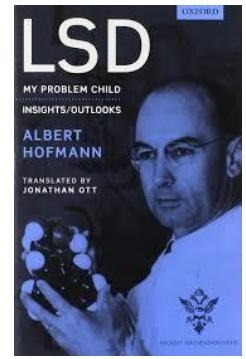
- Hallucinogens (classical hallucinogens and dissociative anaesthetics), their main psychological effects and history of use
- Ecstasy (MDMA)
- Harms and legal regulation of hallucinogens and Ecstasy

Part 2

- Neuropharmacological targets and neural mechanisms underlying hallucinogenic drug action
- Adverse effects of dissociative anaesthetics and Ecstasy
- Hallucinogen/Ecstasy treatment of neuropsychiatric disorders

Hallucinogens

- Induce an altered state of consciousness, characterized by distortions of perception, hallucinations or visions, ecstasy, dissolution of self boundaries and the experience of union with the world.
- Alternatively referred to as ‘psychedelics’ (mind revealing/opening) and – less often – ‘psychotomimetic’ (mimicking psychosis) or ‘entheogen’ (generating the divine/spiritual within).
- **Classical hallucinogens** include plant-derived substances, such as psilocybin (from Psycocybe ‘magic’ mushrooms) and mescaline (from peyote cactus), and synthetic drugs, such as LSD. Agonists at serotonin (5-HT), especially 5-HT2A, receptors. Altered state of consciousness is primary effect.

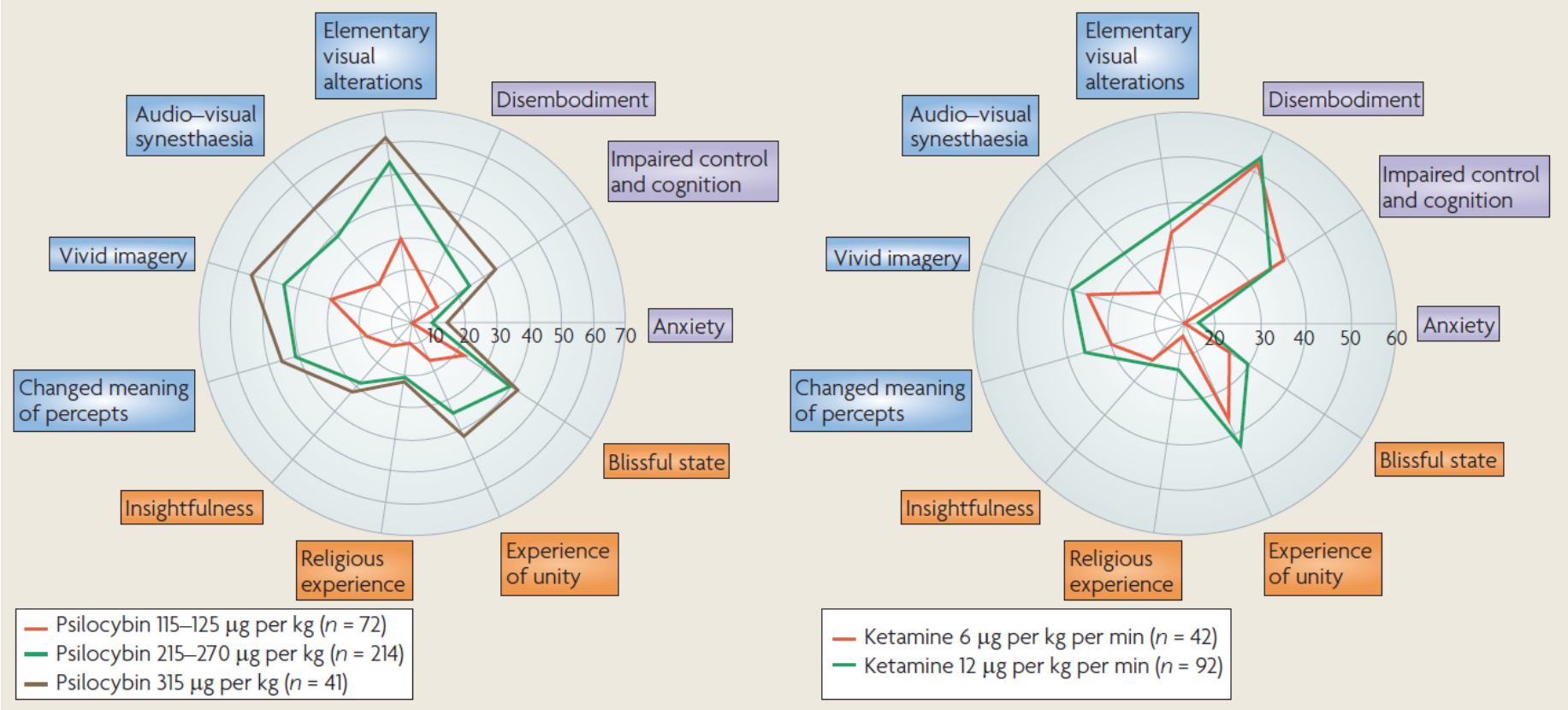


- **Dissociative anaesthetics** are synthetic drugs, such as phencyclidine (PCP) and ketamine; produce anaesthesia (loss of all sensation) at higher doses and altered states of consciousness at lower doses, including ‘disconnection/dissociation’ from environment (loss of time sense, feeling of floating/hovering weightlessly) and body (altered perception of body consistency and out of body experience). Non-competitive NMDA receptor antagonists.

PSYCHOPHARMACOLOGY 2e, Figure 15.13

Comparison of classical hallucinogen (psilocybin) and dissociative anaesthetic (ketamine)

Five-dimensional altered states of consciousness (5DASC) rating scale



5 primary dimensions with subdimensions

-**'oceanic boundlessness'** - referring to positively experienced loss of ego boundaries;

-**'anxious ego-disintegration'** (purple boxes), including thought disorder and loss of self-control;

-**'visionary restructuralization'** (blue boxes), referring to perceptual alterations (such as visual illusions and hallucinations), and altered meaning of percepts;

- **'acoustic alterations'**, including hypersensitivity to sound and auditory hallucinations, and **'altered vigilance'** are not shown.

Box 1, Vollenweider & Kometer (2010) *Nature Rev Neurosci* 11:642

Importance of 'set' (expectations) and 'setting' in determining subjective experience induced by hallucinogenic drugs

- Psychopharmacological actions of hallucinogenic drugs may be less predictable than those of other drugs.

- Hallucinogen effects are heavily dependent on the user's expectations ("set") and the environment ("setting"). For example, expectations and environments that would foster religious or spiritual experiences increase the probability of the drug producing such an effect.

- Stanislov Grof (1975), who supervised many clinical LSD sessions, wrote, "*I consider LSD to be a powerful unspecific amplifier or catalyst of biochemical and physiological processes in the brain*". Barr et al. (1972) stated, *"…the phenomena induced by LSD (and probably by any similar drug) cannot be predicted or understood in purely pharmacological terms; the personality of the drug taker plays an enormous and critical role in determining how much effect there will be and of what particular type*."

- The above also suggests that an individual's response to repeated administration of the same drug and dose may vary.

Nichols, D. E. (2004). Hallucinogens. *Pharmacology & Therapeutics* 101(2):131-181.

Complete the following statement:

Classical hallucinogens include _____ drugs, such as psilocybin and mescaline, and _____ drugs, such as LSD, and they primarily induce _____.

a) **synthetic; plant-derived; altered states of consciousness**

b) **plant-derived; synthetic; altered states of consciousness**

c) **synthetic; plant-derived; delirium, followed by anaesthesia**

d) **plant-derived; synthetic; delirium, followed by anaesthesia**

Complete the following statement:

Dissociative anaesthetics are _____ drugs, such as phencyclidine and ketamine; they produce _____ at lower doses and _____ at higher doses.

a) **synthetic; altered states of consciousness; anaesthesia**

b) **synthetic; anaesthesia; altered states of concisousness**

c) **plant-derived; altered states of consciousness; anaesthesia**

d) **plant-derived; anaesthesia; altered states of consciousness**

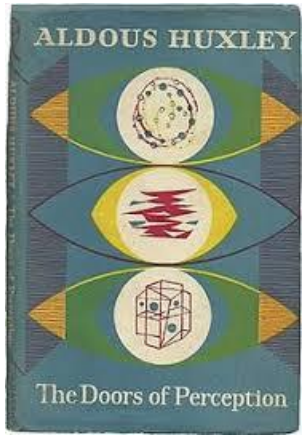
Why is it difficult to predict whether a user of hallucinogens will have a “good trip” or a “bad trip”?

a. **The drug effects depend very much on the user’s expectations.**
b. **The hallucinogens are a heterogeneous drug class with diverse neuropharmacological mechanisms.**
c. **The drug effects very much depend on the environment and the circumstances in which the drug is taken.**
d. **Both a) and c).**

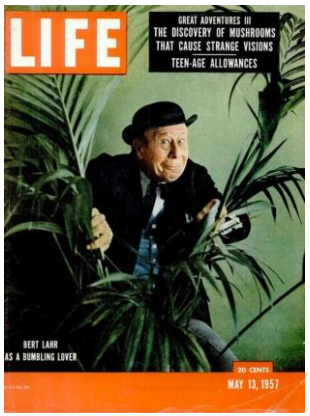
Hallucinogens: historical background 1

- Natural hallucinogens have been used for millennia (possibly longer than any other psychoactive drug because they are in edible mushrooms), often as part of rituals (under control of suitably experienced people).

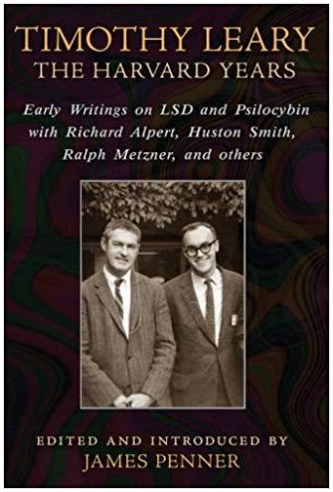
- Plant-derived hallucinogens and LSD entered Northern American and European mainstream culture in first half of 20th century.



Mescaline experience, 1954



Gordon Wasson, 1957

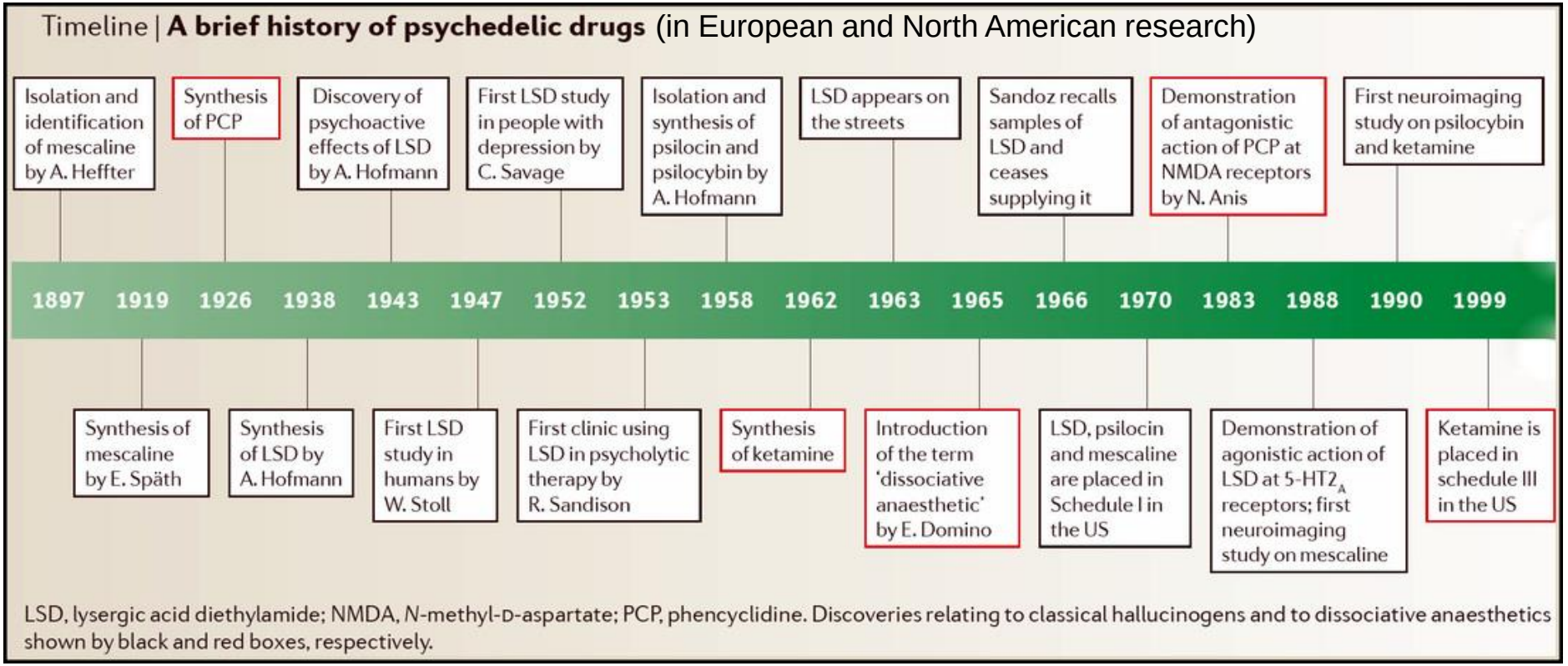


Timothy Leary, Richard Alpert

- PCP developed as anaesthetic in mid1950; ketamine synthesized as safer alternative in 1962 – still used as anaesthetic in humans (when limited anaesthesia infrastructure and support and in children, which show less pronounced psychological effects) and in animals.

Hallucinogens: historical background

- In Europe and North America, there was substantial interest by researchers in understanding hallucinogenic drug actions and to exploit them clinically (either by using them for research to reveal mechanisms of altered states of consciousness in neuropsychiatric disorders or by using them for therapy).
- On the other hand, especially the classical hallucinogens became associated with 1960s counterculture and were made illegal.



Box 1, Vollenweider & Kometer (2010) *Nature Rev Neurosci* 11:642

- Ketamine approved as depression treatment in US in 2019

https://www.fda.gov/news-events/press-announcements/fda-approves-new-nasal-spray-medication-treatment-resistant-depression-available-only-certified

Ecstasy (MDMA)

- MDMA (3,4-methylene-dioxymethamphetamine) is an amphetamine with strong effects on serotonin transmission.

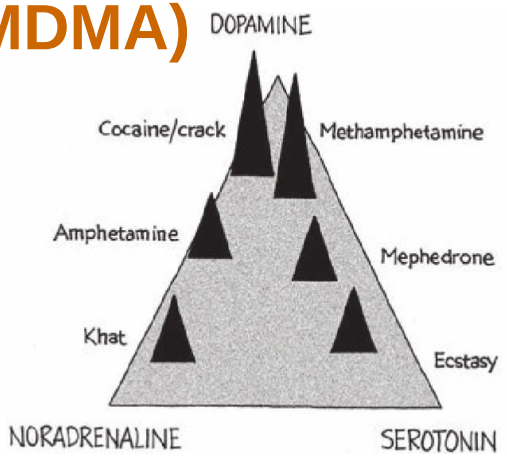


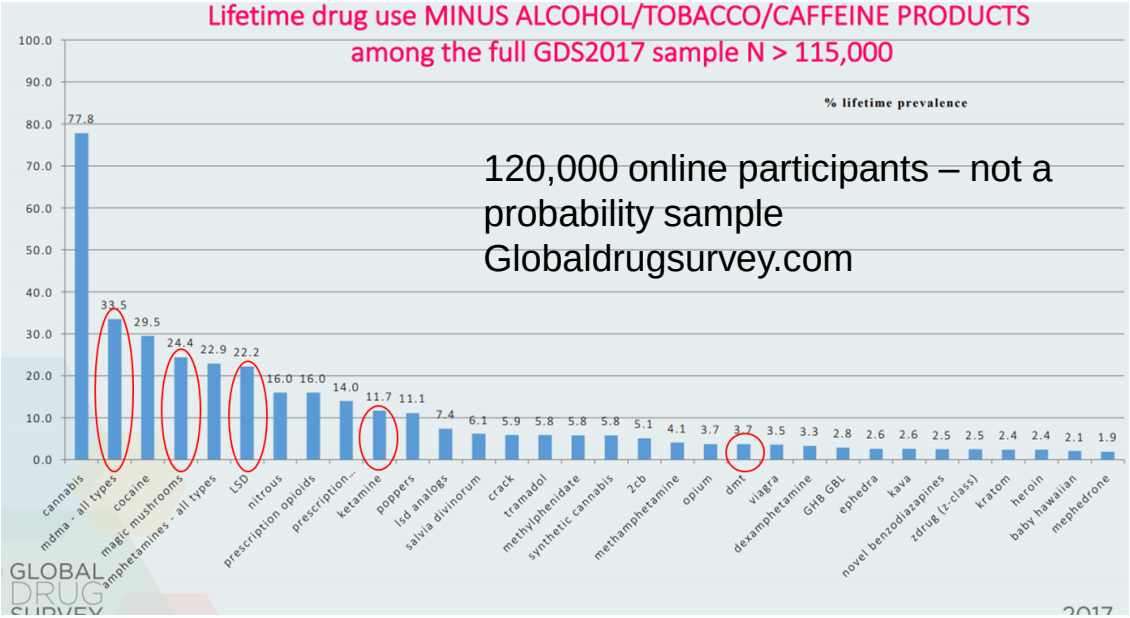
Fig. 4.4., Nutt (2012) Drugs – without the hot air.

- Has stimulant properties, increasing alertness and 'energy, and hallucinogenic-like properties, increasing sociability and talkativeness and inducing an '*altered state of consciousness with emotional and sensual overtones . . . can be compared in its effects to marijuana, to psilocybin devoid of the hallucinatory component*' (Schulgin & Nichols, as cited in Textbook, 2nd ed, Box 6.1).
  The unique pattern . . . of high . . . oceanic boundlessness, low visionary restructuralization and low dread of ego-dissolution produced by MDMA discriminates it from hallucinogens and stimulants (Vollenweider et al., 1998, Neuropsychopharmacology 19:241-251).
  Overall, the 'alteration of consciousness' may be much weaker, though, than the one produced by LSD (Holze et al., 2020, Neuropsychopharmacology 45:462)

- Has been suggested for use in psychotherapy (with recent focus on PTSD), but has also become notorious for use in the rave scene and ecstasy-related deaths (more on this later).

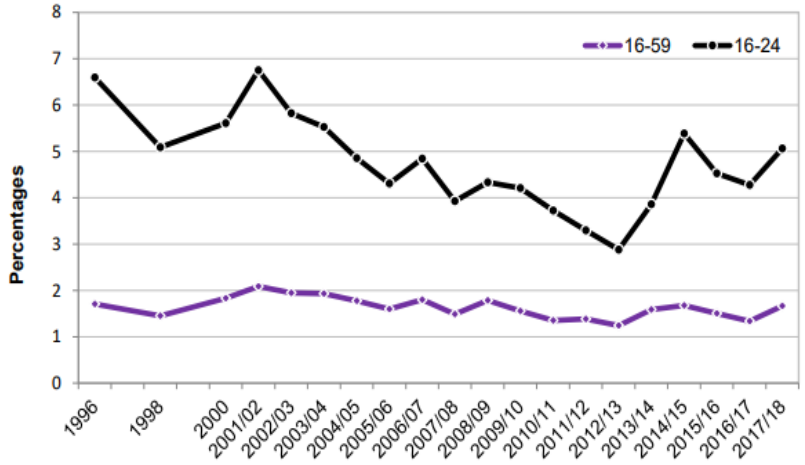
Use of hallucinogens and MDMA – current trends

Global Drug Survey 2017



Crime Survey for England and Wales 2017/18

Figure 1.5: Proportion of adults using ecstasy in the last year, 16 to 59 and 16 to 24 year olds, 1996 to 2017/18 CSEW



Proportion of 16-59 year olds using:

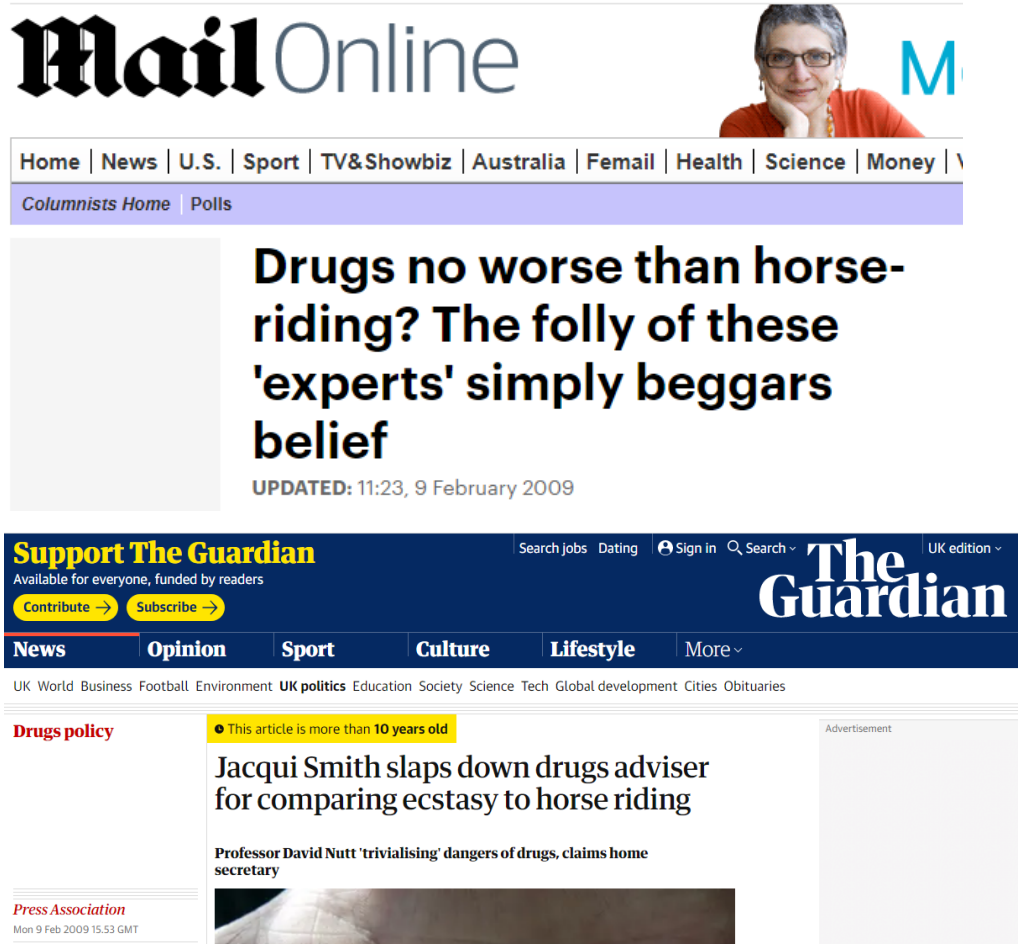
LSD, 0.4%

Magic mushrooms, 0.4%

Ketamine, 0.8%

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/729249/drug-misuse-2018-hosb1418.pdf

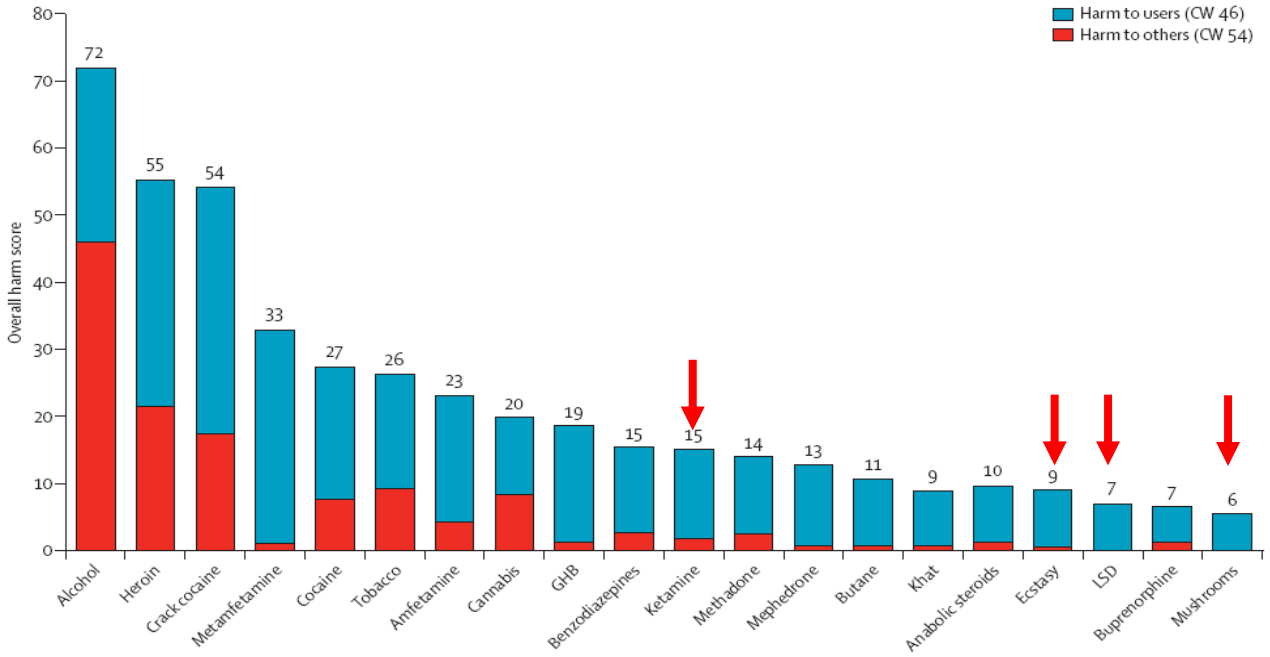
Ecstasy - less dangerous than horse riding?



- David Nutt, then the Chair of the governments Advisory Council for the Misuse of Drugs (ACMD), made the provocative claim that ecstasy use may be less dangerous than horse riding in order to promote debate about drug harms and legality of drugs.
- See chapter 2 in his 2012 book for details.

Harmfulness of hallucinogenic drugs and MDMA

- Expert assessment of harms to user and to others



Nutt et al. (2010)
Lancet 376:1558

- Apart from potential distress caused by the subjective experiences induced by **classical hallucinogenic** drugs (depending on 'set'/'setting' and a particular risk in people with mental health problems), these drugs cause otherwise virtually no physical harm and no dependence.
- **Ecstasy** and **dissociative anaesthetics** (PCP, ketamine) can cause dependence and cause neurodegeneration, although it is debated if typical recreational usage and doses cause neurodegeneration (more on this later).
- **Ecstasy-related deaths**: about 130 in England, Wales and Scotland in 2017; may be related to overheating and dehydration

https://www.manchestereveningnews.co.uk/news/greater-manchester-news/young-people-mortal-danger-experts-17372046

Severe legal restrictions on hallucinogens and MDMA

UK drug regulations

- Three Classes (A, B and C) to determine the penalties for offences such as supply, production and possession of a controlled drug.
- Five schedules regulate the clinical use of controlled substances and their storage and labelling requirements.

Table 1 | **The status of certain substances in the international, UK and US legislation**

Substance	United Nations conventions	UK Misuse of Drugs Regulations	UK Misuse of Drugs Act	US Controlled Substances Act
Amphetamine	Schedule II (1971)	Schedule 2	Class B	Schedule II
Cannabis and cannabis resin	Schedules I and IV (1961)	Schedule 1	Class B	Schedule I
Cannabidiol	Not listed	Not listed	Not listed	Not listed
Cocaine	Schedule I (1961)	Schedule 2	Class A	Schedule II
2-bromo-LSD	Not listed	Schedule 1?	Class A? (uncertain)	Not listed
Heroin (also known as diamorphine)	Schedule I (1961)	Schedule 2	Class A	Schedule I
Ketamine	Not listed	Schedule 4	Class C	Schedule III
LSD (also known as lysergide)	Schedule I (1971)	Schedule 1	Class A	Schedule I
MDMA (also known as ecstasy)	Schedule I (1971)	Schedule 1	Class A	Schedule I
Methamphetamine	Schedule II (1971)	Schedule 2	Class A	Schedule II
Methoxetamine	Not listed	Schedule 1	Class B	Not listed
Psilocybin	Schedule I (1971)	Schedule 1	Class A	Schedule I
THC (also known as dronabinol)	Schedule II (1971)	Schedule 2	Class B	Schedule III
THCV	Not listed	Schedule 1	Class B	Not listed

The UK Misuse of Drugs Act (1971) categorizes drugs into three classes according to harms (A>B>C) and these determine the penalties for possession (7 >5>3 years in prison, respectively) or supply (life>14>14 years, respectively). In the United States, the situation is more complex, in that each drug has its own level of penalties applied. The United Nations conventions and the US Controlled Substances Act use roman numerals for the Schedules (that is, I, II, and so on), whereas the UK Misuse of Drugs Regulations use Arabic numerals (that is, 1, 2, and so on). LSD, lysergic acid diethylamide; MDMA, 3,4-methylenedioxy-*N*-methylamphetamine; THC, Δ^9-tetrahydrocannabinol; THCV, tetrahydrocannabivarin.

Nutt et al. (2013) *Nature Rev Neurosci* 14:577

MDMA (Ecstasy): Which of the following statements is false?

a) MDMA is a stimulant with stronger effects on serotonin transmission than other amphetamines.

b) MDMA induces stronger visual hallucinations than LSD.

c) MDMA is a synthetic drug.

d) MDMA has a higher potential to cause dependence than LSD.

Hallucinogens and Ecstasy: Which of the following statements is false?

a) Available evidence supports that classical hallucinogens are more likely to cause dependence than alcohol.

b) Possession of classical hallucinogens may be punished with a prison sentence.

c) Possession of MDMA may be punished with a prison sentence.

d) Ketamine is still used as anaesthetic in humans.

Some questions for revision

- What are hallucinogenic drugs?

- What are the psychological effects of hallucinogenic drugs?

- How are drugs regulated in the UK?

The MCQs related to hallucinogens and ecstasy will all be based on the material dealt with in my two lectures on this topic. If you understand the material, so that you can answer the lecture MCQs and the revision questions well, you should have no difficulties with the exam MCQs.

Selected reading – Hallucinogens and Ecstasy

***Textbook chapter*:**

Chpt. on Hallucinogens, PCP and ketamine and Box (6.1.) on Ecstasy – for general overview

Selected overviews of topics discussed:

Vollenweider, FX & Kometer, M (2010) The neurobiology of psychedelic drugs: implications for the treatment of mood disorders. *Nature Reviews Neuroscience* 11(9):642-651.

Nutt, David. Drugs - without the hot air : Minimising the harms of legal and illegal drugs, UIT Cambridge Ltd., 2012.
https://ebookcentral.proquest.com/lib/nottingham/detail.action?docID=5285796

See chpt. 2, 4 and 14

All references given in lecture are available online via Nottingham University access.

Outline

Part 1

- Hallucinogens (classical hallucinogens and dissociative anaesthetics), their main psychological effects and history of use
- Ecstasy (MDMA)
- Harms and legal regulation of hallucinogens and Ecstasy

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- Neuropharmacological targets and neural mechanisms underlying hallucinogenic drug action
- Adverse effects of dissociative anaesthetics and Ecstasy
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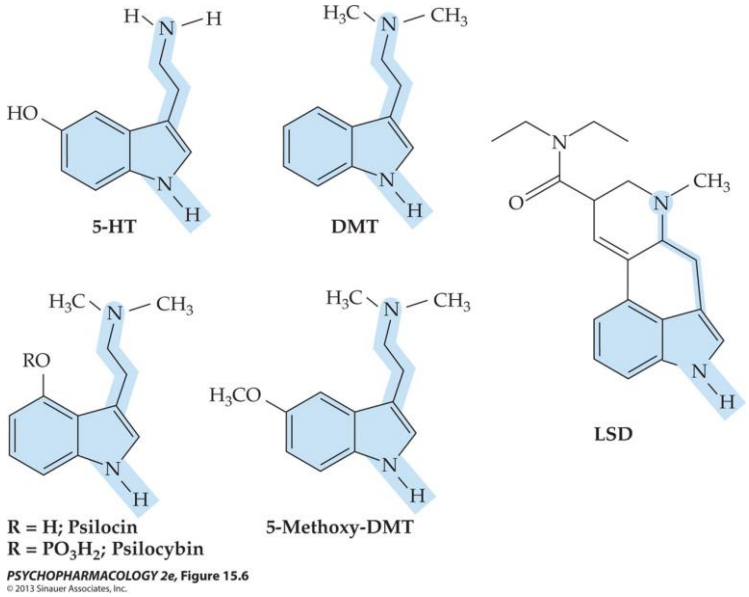
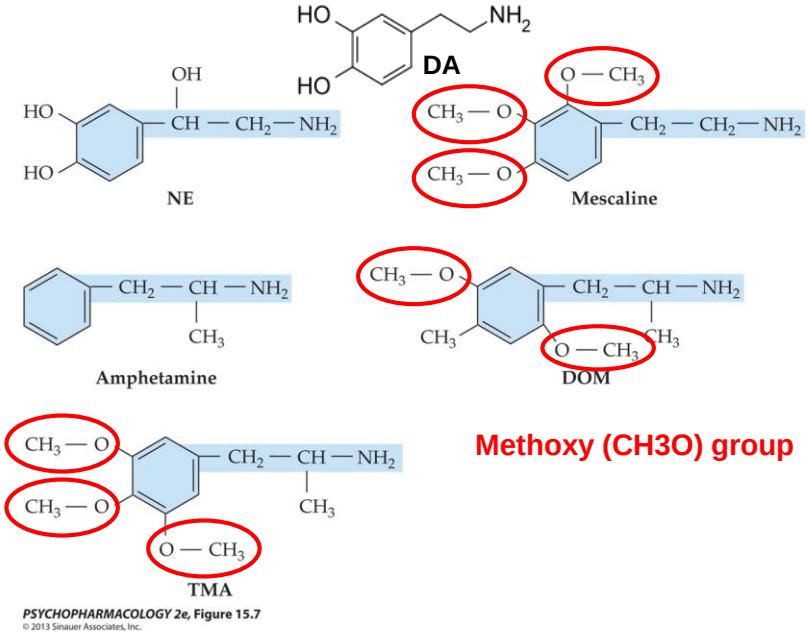
Classical hallucinogens

Indoleamine hallucinogens



Phenethylamine hallucinogens



Indoleamine and phenethylamine hallucinogens activate serotonin (5HT2) receptors, and 5HT2A receptor activation is main contributor to their psychological effects

- High affinity to serotonin (5HT) receptors, especially 5HT2A and C receptor subtypes. (In case of phenethylamines, methoxy[CH3O] groups may contribute to this.)
- Primary neuropharmacological mechanism is agonist activity at 5HT receptors.
- Substantial evidence supports that agonist action at 5HT2A receptors is critical for main psychological effects (for a brief overview, see Halberstadt, 2017, *Curr Biol* 27(4):R156).

Serotonin system and 5HT2A receptors

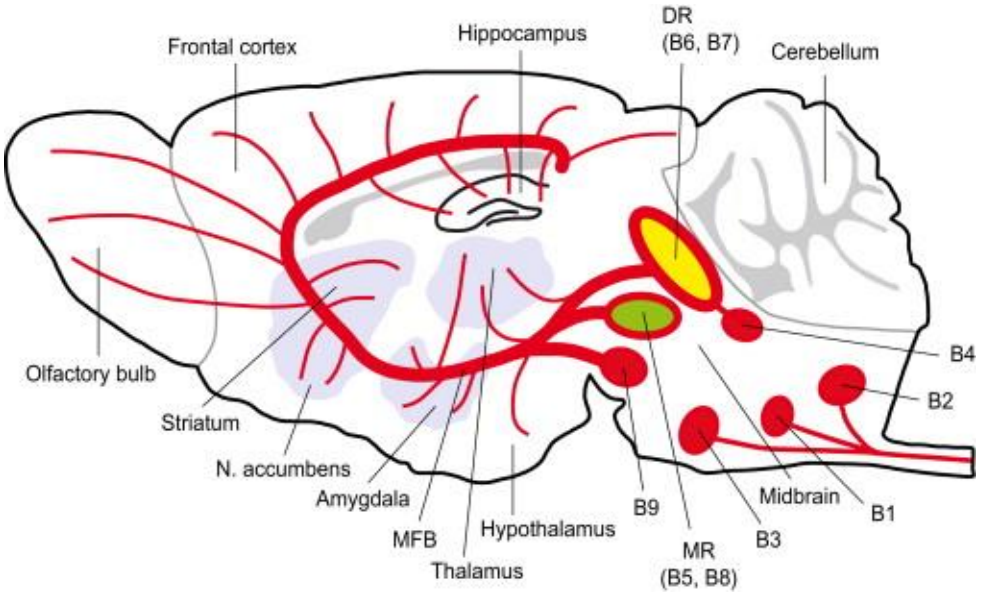
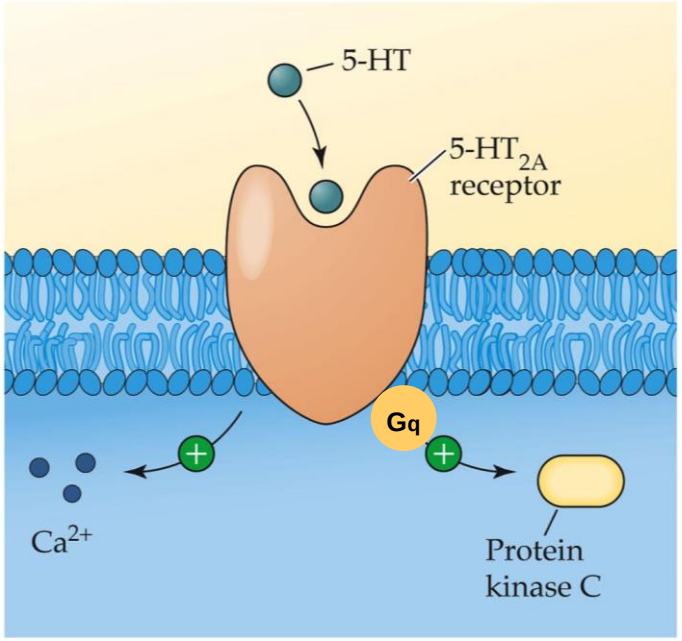


Fig. 1, Lesch & Waider (2012) *Neuron* 76(1):175



PSYCHOPHARMACOLOGY, Figure 6.19 (Part 2) © 2005 Sinauer Associates, Inc.

- Serotonergic raphe nuclei in the midbrain innervate large parts of the brain, including many cortical and subcortical forebrain regions.
- 5HT2A receptors are G protein-coupled receptors; their activation mainly has stimulatory effects on the neuron (increased transmitter release and increased activity).
- 5HT2A receptor activation may stimulate excitatory neurons, including in the prefrontal cortex, which may be critical for the hallucinogenic effects (e.g., Vollenweider & Kometer, 2010; more on this later).

5-HT2A receptors mediate subjective effects of hallucinogens

Psilocybin

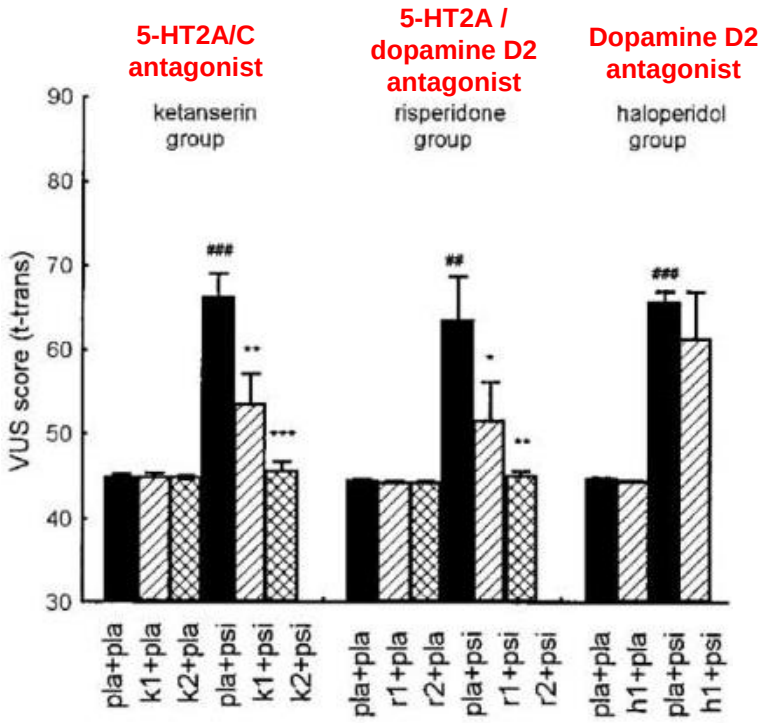
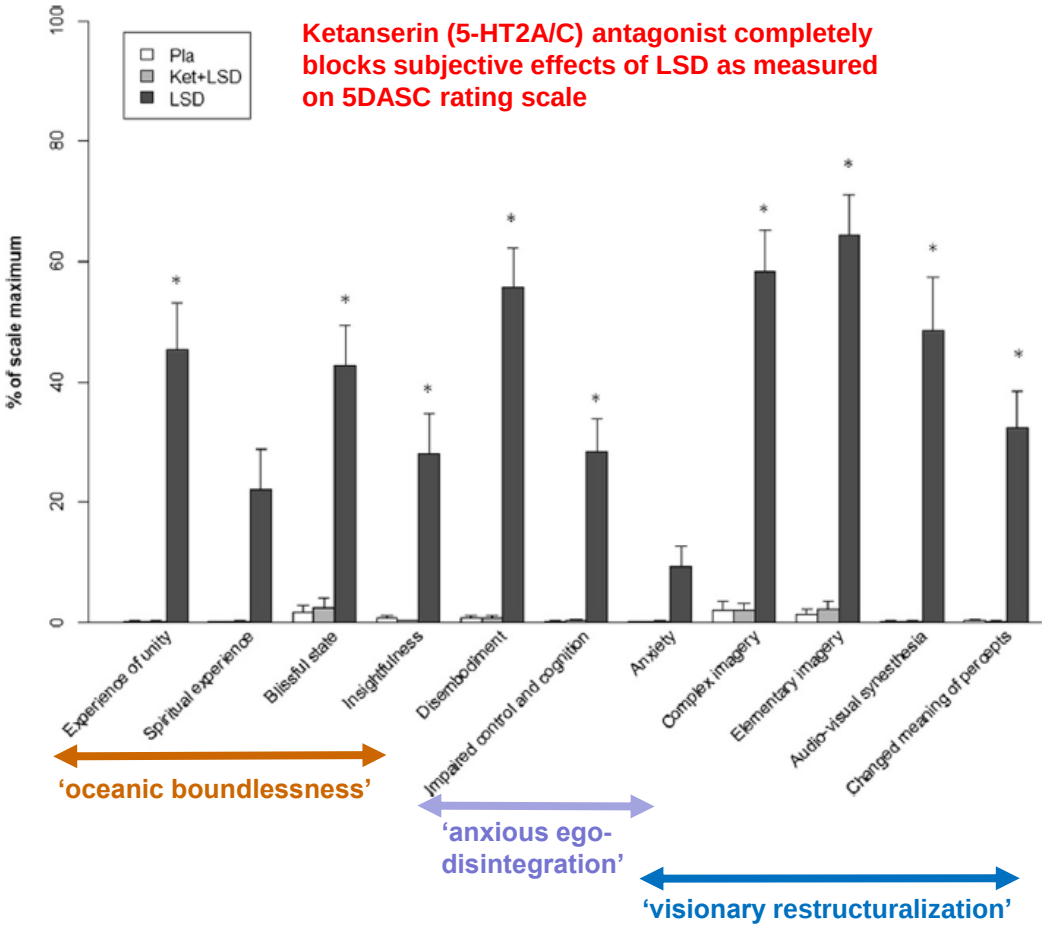


FIG. 1 . The VUS scale rates illusions, hallucinations, and changed meaning. Data are means +/- s.e. (n = 5 for each antagonist): placebo (pla), psilocybin (psi = 0.25 mg/kg), ketanserin (k1 = 20 mg, k2 = 40 mg,p.o.), risperidone (r1 = 0.5 mg, r2 = 1.0 mg, p.o.) and haloperidol (h1 = 0.021 mg/kg, i.v.). Significant increases from placebo to psilocybin: #p p p p p post hoc test).

Fig. 1, Vollenweider et al. (1998)
***Neuroreport* 9(17):3897**

LSD



Ketanserin (5-HT2A/C) antagonist completely blocks subjective effects of LSD as measured on 5DASC rating scale

Fig. 1, Preller et al. (2017) *Curr Biol* 27:451-457

In animal studies, behavioural effects of classical hallucinogens are blocked by selective 5HT2A receptor antagonist (Halberstadt, 2015, *Behav Brain Res* 277:99-120).

In terms of their chemical structure, the two main groups of classical hallucinogens are _____ or _____.

a. phenethylamines; indoleamines

b. indoleamines; carbolines

c. carbolines; phenethylamines

d. phenethylamines; acetylcholine

Neuropharmacological mechanisms of classical hallucinogens: Which of the following statements is false?

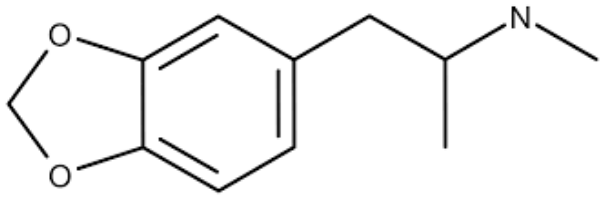
a) **Classical hallucinogens have high affinity to serotonin receptors.**

b) **Stimulation of 5HT2A receptors plays a key role in generating the subjective effects of classical hallucinogens.**

c) **Serotonergic nuclei in the ventral tegmental area of the midbrain innervate large parts of the brain, including many cortical and subcortical forebrain regions, and release serotonin in these brain regions.**

d) **5HT2A receptors are G protein-coupled receptors.**

MDMA ('Ecstasy')



MDMA
3,4-methylene-dioxymethamphetamine

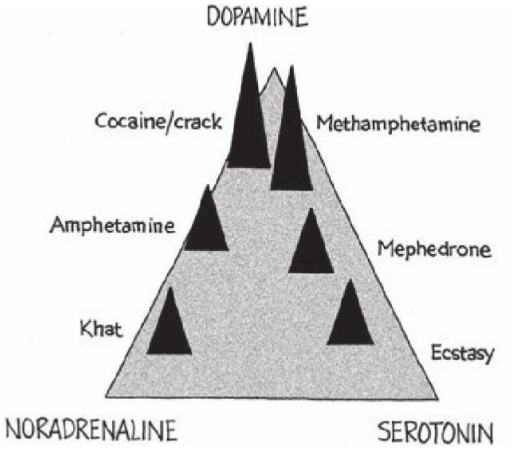
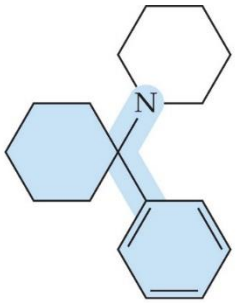


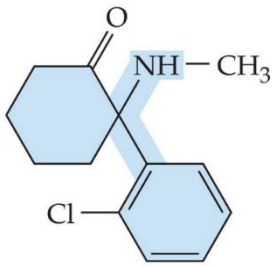
Fig. 4.4., Nutt (2012) Drugs – without the hot air.

- Stimulates serotonin release (probably by interaction with 5HT transporter) and some of MDMA's subjective effects are mediated by 5HT2A receptors (see Liechti et al, 2000, *Neuropsychopharmacology* 22:513; Liechti et al, 2000, *Neurpsychopharmacology* 23:396).
- Also stimulates dopamine release, including in nucleus accumbens, which is thought to contribute to stimulant and rewarding/reinforcing properties (see Bankson & Yamamoto, 2004, *Journal of neurochemistry* 91(4):852).

Dissociative anaesthetics



Phencyclidine (PCP)



Ketamine

PSYCHOPHARMACOLOGY 2e, Figure 15.12
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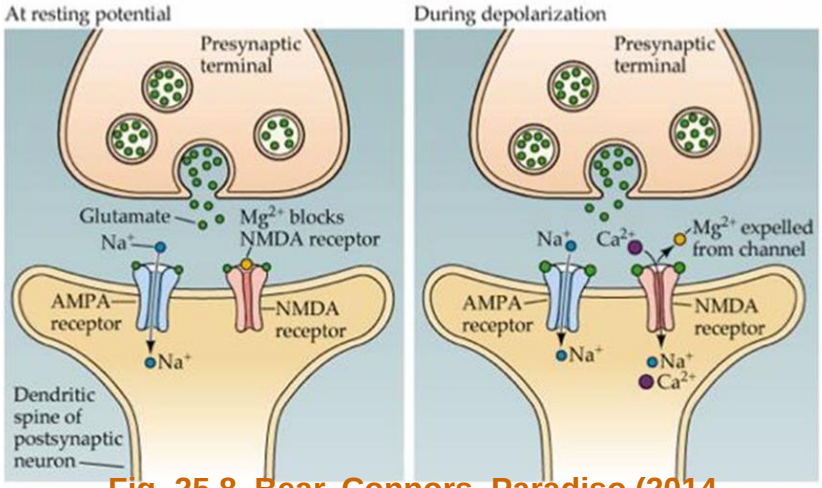
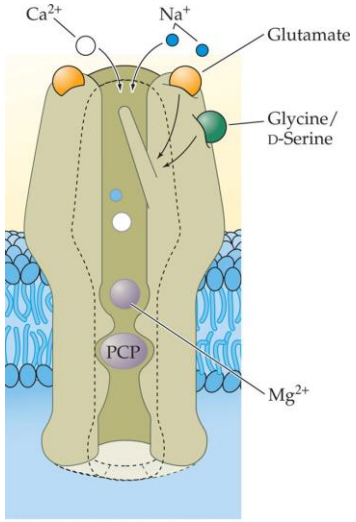
Glutamatergic synapse



NMDA receptor



PSYCHOPHARMACOLOGY 2e, Figure 8.6
© 2013 Sinauer Associates, Inc.

Fig. 25.8, Bear, Connors, Paradiso (2014, 4th Ed) *Neuroscience: exploring the brain*

- Primary neuropharmacological mechanism is blockade of the channel pore of the NMDA-type glutamate receptor (non-competitive NMDA receptor antagonist).
- One prominent idea is that NMDA receptor blockade increases neural excitation in many brain, including cortical, areas (by 'disinhibition', i.e. reducing the activity of inhibitory neurons), which may be a key factor in the psychological effects of dissociative anaesthetics (e.g., Vollenweider & Kometer, 2010; more on this later).
- NMDA receptor antagonists also stimulate prefrontal cortex and nucleus accumbens dopamine release (e.g., Hertel et al, 1995, Behav Brain Res 72(1-2):103-114) and this effect may be mediated by increased neural excitation in cortical regions (Moghaddam et al, 1997, J Neurosci 17(8): 2921-2927).

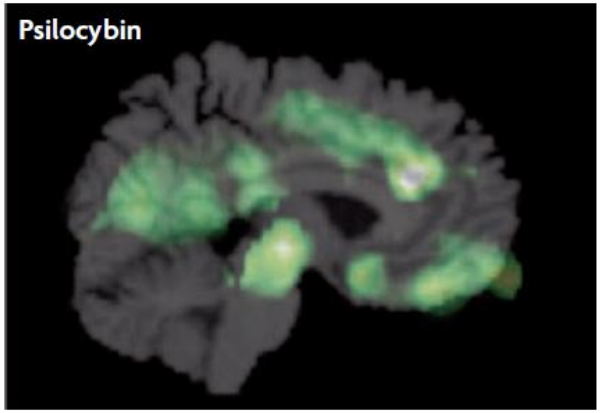
Prefrontal cortical activation – a common neural mechanism for hallucinogenic drug effects?

Brain activation pattern

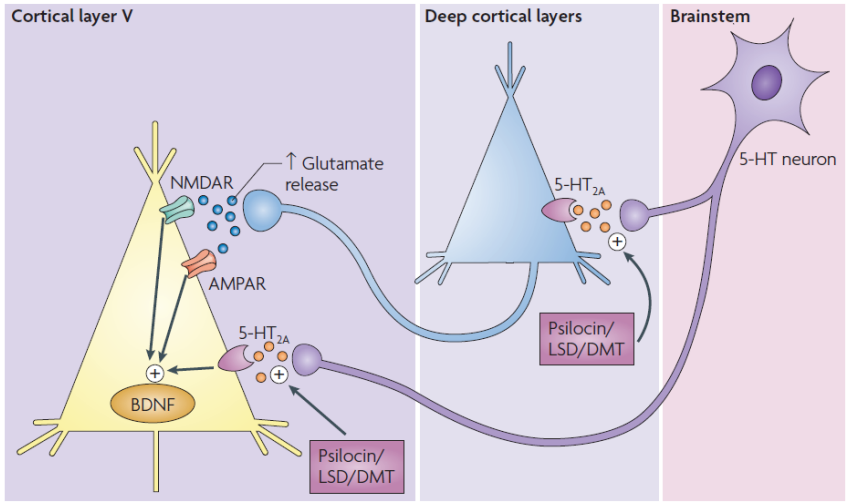
(PET measurements)

Synaptic model of neural effects

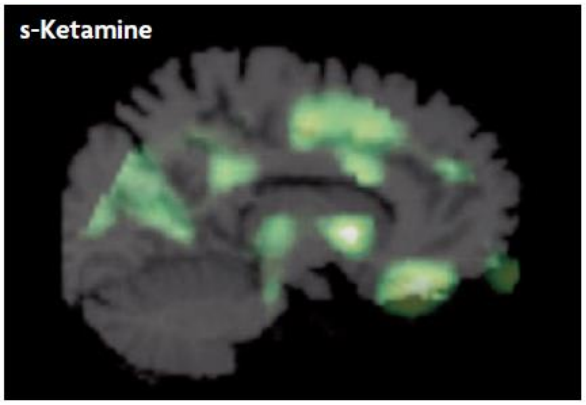
Classical hallucinogens – 5HT2A agonists

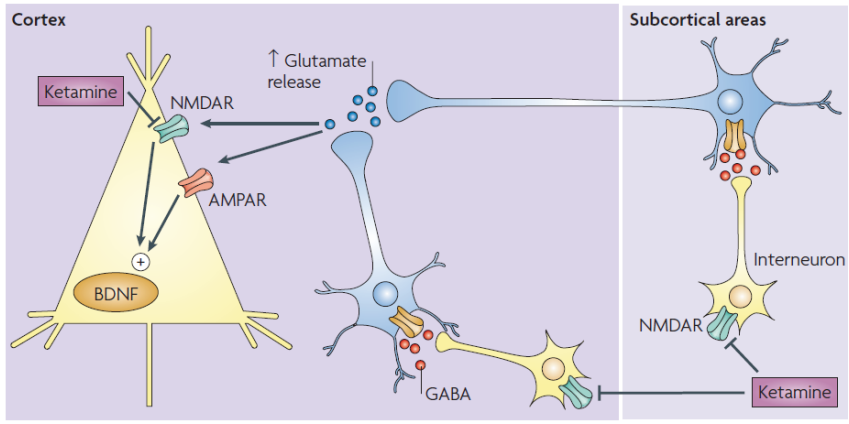


Also compare Carhart-Harris et al (2012, Proc Nat Acad Sci 109(6):2138) who reported **reduced** rather than increased cortical activation following psilocybin, using fMRI.



Dissociative anaesthetics – NMDA receptor antagonists





Adapted from Fig. 1 and 2a, Vollenweider & Kometer (2010) *Nature Rev Neurosci* 11:642

Which of the following statements is false?

a) **MDMA stimulates serotonin release.**

b) **Dissociative anaesthetics, including PCP and ketamine, are competitive NMDA receptor antagonists.**

c) **Dissociative anaesthetics, including PCP and ketamine, block the channel pore of the NMDA receptor.**

d) **There is evidence to support that both classical hallucinogens and dissociative anaesthetics may cause increased neural activation in cortical regions, including the prefrontal cortex.**

Adverse effects of dissociative anaesthetics and MDMA ('Ecstasy')

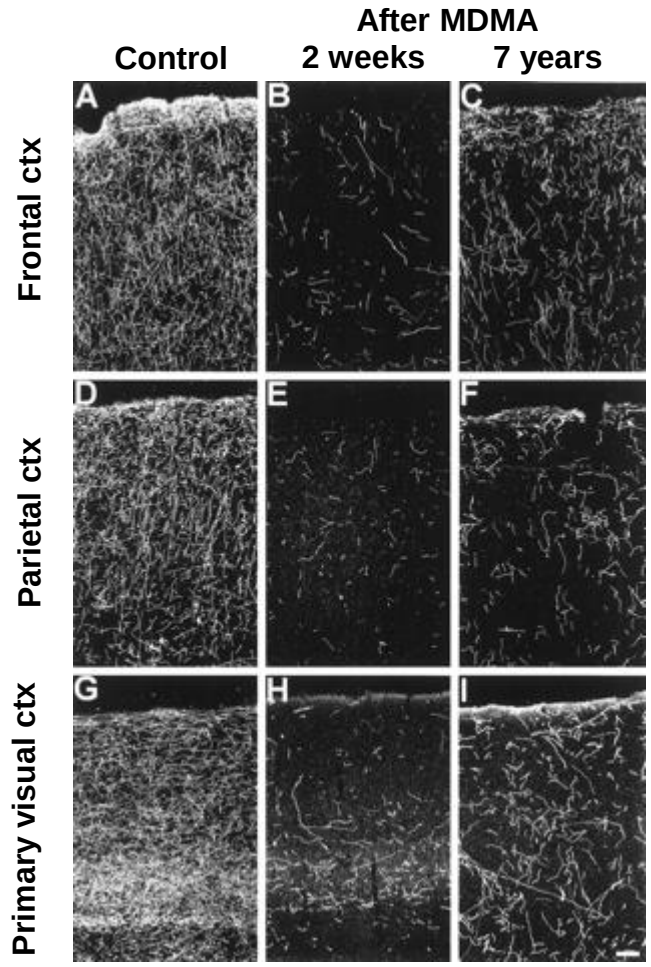
- **Dependence:** Evidence from animal models and humans supports that both dissociative anaesthetics (ketamine, PCP) and MDMA can cause dependence, although the potential for dependence may be weaker than with other drugs of abuse (amphetamines, opioids, alcohol, nicotine) (Degenhardt et al, 2010, *Drug and Alcohol Dependence* 107:1–10; Morgan&Curran, 2012, *Addiction* 107:27–38).
  This may partly be mediated by the increased meso-corticolimbic dopamine release caused by these drugs.

- **Neurodegeneration:** Studies in animal models have long shown that non-competitive NMDA receptor antagonists, including PCP and ketamine (Olney, et al,1989, *Science* 244(4910):1360-1362; Cadinu et al, 2018, *Neuropharmacology* 142:41-62), and MDMA (Parrott,2013, *Neuroscience & Biobehavioral Reviews* 37(8):1466-1484) cause neurodegeneration; MDMA-induced neurodegeneration is selective to serotonergic neurons.
  For MDMA, there is compelling evidence that recreational usage of the drug also damages serotonergic neurons in humans (more on next slide).

- **'Ketamine bladder'/ ketamine-induced ulcerative cystitis** (thickening of bladder wall and low bladder capacity), **kidney dysfunction** and **'k-cramps'** (intense abdominal pain) have also been reported in chronic ketamine users (Morgan&Curran,2012, *Addiction* 107:27–38).

MDMA ('Ecstasy')-induced damage of serotonergic neurons

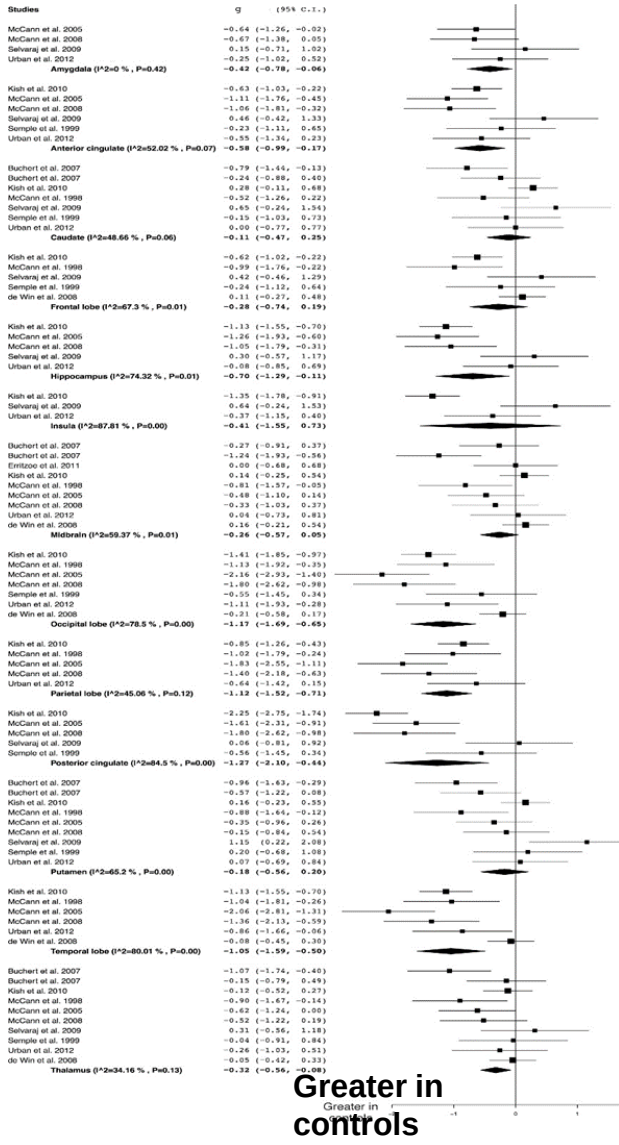
Squirrel monkeys



MDMA: 5 mg/kg 2Xdaily, 4 consecutive days

Fig. 1, Hatzidimitriou et al (1999) J Neurosci 19(12):5096-107

Human recreational users



- Meta–Analysis of neuroimaging studies investigating serotonin transporter (SERT) expression in different brain regions.
- Forest plot showing effect sizes for SERT changes in different brain regions.
- SERT expression was decreased in MDMA users in multiple brain regions, including parietal, temporal,occipital, cingulate cortices, thalamus and hippocampus
- Participants were heavy MDMA users, so impact of moderate MDMA use remains to be examined!

Muller et al (2019) *Neuroscience and Biobehavioural Reviews* 96:10-20.

Ethical challenges associated with research involving MDMA administration to volunteers

- Are the risks due to adverse effects, including dependence and neurodegeneration, acceptable and do they outweigh the potential gains?

- See:

McCann, U. D., & Ricaurte, G. A. (2001). Caveat emptor: editors beware. Neuropsychopharmacology 24(3):333

Lieberman, JA, & Aghajanian, GK, 1999. Caveat emptor: Researcher beware. Neuropsychopharmacology 21(4):471-473

Hallucinogen/MDMA treatment of neuropsychiatric disorders 1

Long-standing interest in use of hallucinogens and MDMA for psychotherapy, but properly controlled clinical trials have only started recently (2000-2010), partly because of the strict legal regulations of hallucinogens.

Classical hallucinogen/MDMA-assisted psychotherapy

- Drug is used on one or a few occasions during psychotherapy sessions to overcome obstacles to successful psychotherapy and to facilitate a therapeutic experience.
- Ongoing research on psilocybin/LSD-assisted psychotherapy for substance-abuse, severe depression and cancer anxiety and on MDMA-assisted psychotherapy for PTSD and alcohol-dependence.
- Encouraging preliminary findings, but several limitations (including small samples, often open-label or no placebo)
- Careful clinical supervision required because of potential for ‘bad trips’
- MDMA toxicity for serotonergic neurons is of concern, although therapeutic effects of MDMA reported at substantially lower doses than those that have been shown to cause neurotoxicity.

Mithoefer (2016) Lancet Psychiatry 3:481–88; Nutt (2019) Dialogues Clin Neurosci 21(2):139-147

Hallucinogen/MDMA treatment of neuropsychiatric disorders 2

Ketamine for severe treatment-resistant depression

- First clinical study in 2000 reported rapid anti-depressant effect of ketamine.
- Well-controlled clinical trials support antidepressant effect of ketamine, although not all patients respond, the duration of antidepressant effect is variable, and not all patient groups may be suitable (e.g., patients with psychosis).
- Potential adverse effects of ketamine are of concern.
- In 2019, nasal spray containing Esketamine (S(+)-ketamine) was approved for treatment-resistant depression in US and Europe, including UK, but NICE has not approved it for NHS funding

https://www.pmlive.com/pharma_news/nice_knocks_back_j_and_js_depression_nasal_spray_spravato_1323578

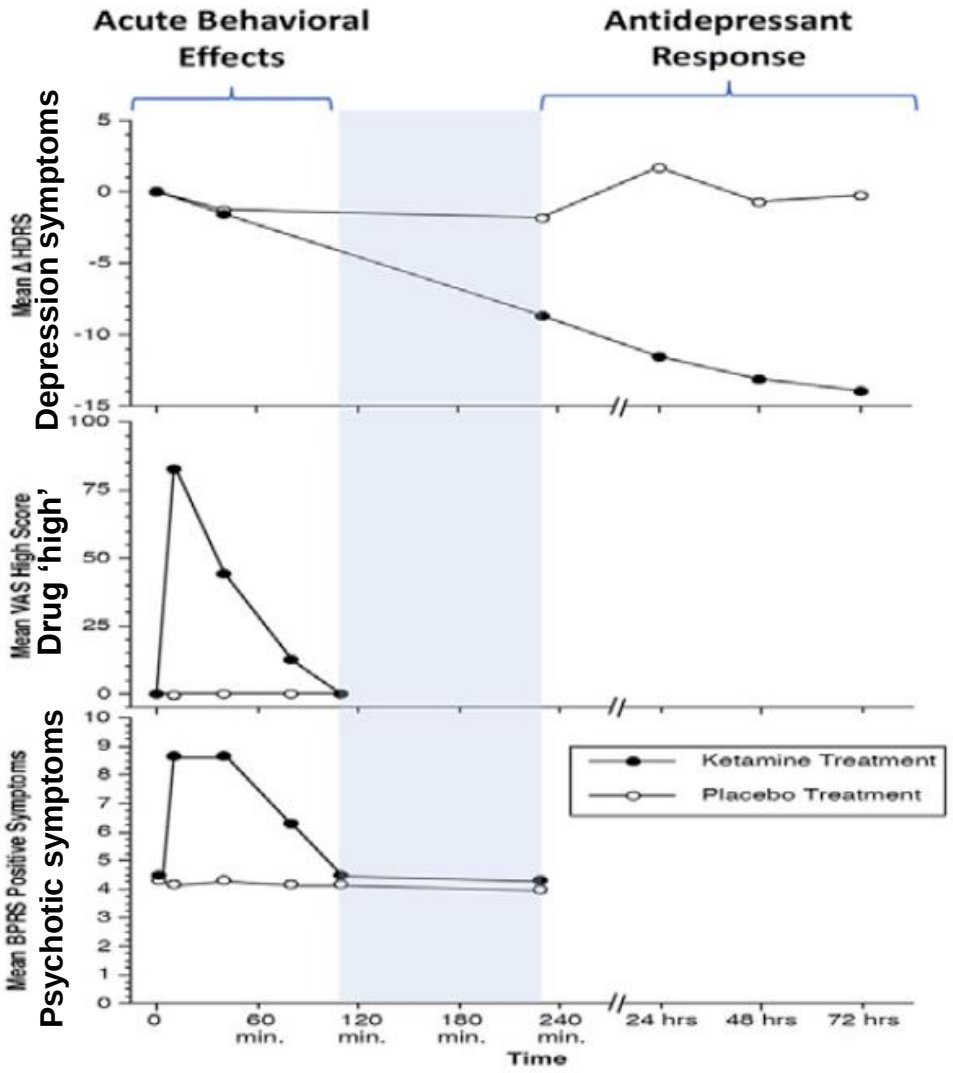


Fig. 1B, Krystal et al (2019)

Singh et al, 2017, Lancet Psychiatry 4:419–26; Krystal et al, 2019, Neuron 101:774

Which of the following statements about adverse effects of hallucinogenic drugs and MDMA is correct?

a) Evidence supports that MDMA, but neither classical hallucinogens, including LSD and psilocybin, nor dissociative anaesthetics, including PCP and ketamine, cause neurodegeneration.

b) MDMA can cause bladder problems.

c) Evidence supports that both dissociative anaesthetics (ketamine, PCP) and MDMA can cause dependence, although the potential for dependence may be weaker than with other drugs of abuse.

d) all of the above.

In 2019, a nasal spray containing Esketamine (S(+)-ketamine) was approved in US and Europe, including UK, to treat which conditions?

a) Alcohol dependence

b) PTSD

c) Treatment-resistant depression

d) All of the above

Some questions for revision

- What are the neuropharmacological mechanisms of hallucinogens and MDMA?

- Which adverse effects are associated with these drugs?

- What is the potential for the use of hallucinogens and MDMA in the treatment of neuropsychiatric disorders?

The MCQs related to hallucinogens and MDMA will all be based on the material dealt with in my lectures. If you understand the material, so that you can answer the lecture MCQs and revision questions well, you should have no difficulties with the exam MCQs.

Selected reading – Hallucinogens and Ecstasy

***Textbook chapter*:**

Chpt. on Hallucinogens, PCP and ketamine and Box (6.1.) on Ecstasy – for general overview

Selected overviews of topics discussed:

Vollenweider, FX & Kometer, M (2010) The neurobiology of psychedelic drugs: implications for the treatment of mood disorders. *Nature Reviews Neuroscience* 11(9):642-651.

Nutt, David. Drugs - without the hot air : Minimising the harms of legal and illegal drugs, UIT Cambridge Ltd., 2012.
https://ebookcentral.proquest.com/lib/nottingham/detail.action?docID=5285796

See chpt. 2, 4 and 14

All references given in lecture are available online via Nottingham University access.