“illegal” drugs and the future of psychiatry

David Nutt  FRCP  FRCPsych  FMedSci  DLaws
Imperial College London
The Open University

d.nutt@imperial.ac.uk
profdavidnutt@twitter.com
Starting with psychedelics - an enduring presence in human existence
LSD – the ergot derivative that re-instigated psychedelic in the 1950s

Albert Hofmann – the discoverer of LSD and psilocybin - at 100
Clinical research with LSD in the 1950s and 1960s

- Hundreds of psychiatrists worldwide
- 1000 clinical papers
- 40,000 patients
- 40 books
- 6 International conferences

Results were overwhelmingly positive, describing safe and effective treatments.
(Masters and Houston, 1971)
Then came “The War on Drugs”

Impact of the 1971 UN Psychotropics Convention on psychedelic research

Kyar et al 2017 TIPS
2010 - Fighting back through brain imaging

The Beckley Foundation/Imperial College
Psychedelic Research Programme
Psilocybin attenuates activity in the brain region linked to depression. Carhart-Harris, PNAS 2012

As do treatments for depression:
- SSRIs: Kennedy et al. 01
- CBT: Goldapple et al. 04
- Sleep deprivation: Gillin et al. 01
- ECT: Bonne et al. 96
- Placebo: Mayberg et al. 02
- Deep brain stimulation: Mayberg et al. 05
- Ketamine: Deakin et al. 08
Psilocybin uncouples default mode network (DMN) which mediates our sense of self.

**Placebo**
strong correlations in activity between frontal and posterior parietal regions

**Psilocybin**
correlations lost or even negative

Seed region

---

Carhart-Harris et al. PNAS 2012
DMN is overactive in depression and this predicts extent of rumination

A) PCC functional connectivity – excessive in depression

B) Greater PCC to SCC (subgenual cingulate cortex) connectivity in depression

PCC - SCC functional connectivity predicts rumination

Berman et al 2011
Psilocybin in treatment resistant depression

Depression Severity (BDI) vs time

Baseline | 1 wk | 3 months
---|---|---
Severe (≥30) | 33.7 (7.1) | 15.2 (11) | d = 2.1
No depression (≤9) | 8.7 (8.4) | d = 3.2

Carhart-Harris et al Lancet Psychiatry 2016
What next for other psychiatric disorders?

Recent positive open trials of psilocybin in addiction to
- **Tobacco** (John Hopkins) – double-blind RCT underway
- **Alcohol** (New Mexico)

**Ongoing**
- RCT -v- escitalopram – reporting soon – Imperial College
- Anorexia –John Hopkins and Imperial College
- OCD - Imperial College
- Planned Heroin addiction (Bristol/Imperial College)
- And pain syndromes - + cluster headaches

But illegal status still profoundly limits research and increases costs
1970s - Sasha Shulgin synthesized MDMA & gave it to himself, his wife and friends who were psychotherapists.

Positive reports of MDMA as adjunct to psychotherapy; no controlled trials.

How the world has changed in ten years

Then → ecstasy causes brain damage

Now → MDMA can heal the brain from trauma
MDMA-v- placebo for treatment resistant PTSD
% meeting PTSD diagnosis – pre/post

80% of MDMA treated group go into remission

Mithoefer et al Journal of Psychopharmacology 2010
Imaging gives the clue → MDMA reduces brain blood flow
- in hippocampus and amygdala

Which probably explains its utility if PTSD exposure therapy
Building on MDMA successes in PTSD
BIMA: Bristol Imperial MDMA Alcoholism study

MDMA for trauma-related alcohol dependence
Modelled on the Mithoefer studies

MDMA 125/62.5 mg sessions 2 weeks apart in a 12 week treatment programme

Dr Ben Sessa = clinical lead

14 patients successfully treated – only 2 returned to prior drinking levels over 6 months [paper in preparation]
What we need to do now

Much more research especially after covid19 with predicted increase in depression and PTSD

But very difficult on account of Schedule 1 status

So re-Schedule or provide exemptions

→ ACMD, Drug Science and other organizations asking for exemptions for research

→ Can RCPsych support this please? Ideally leading the other Royal Colleges
Thanks

To the Neuropsychopharmacology team &
Our funders –
• Alexander Mosley Charitable Trust
• Beckley Foundation
• MRC