The psychobiological dangers of recreational Ecstasy or MDMA.

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Topics to be covered

(20 minute version of a 2 hour talk)

1. Acute or immediate effects of MDMA/Ecstasy
2. Post-MDMA recovery: several days
3. Long term effects in regular users: large variation due multiple drug & non-drug influences, but consistent evidence for damage/problems.
4. Critique of Nutt's (2006) Editorial about MDMA.
5. Critique of Nutt et al (2007) Lancet article.
6. Confirmation that MDMA has a high harm score.
7. Final conclusions: Parrott versus Nutt

Acute or immediate effects of Ecstasy/MDMA

Powerful effects on many neurotransmitters (McDowell'94)

Acute dose - can release 80% of serotonin (Green 2003).

Powerful stimulant - many neurohormones increased

MDMA an energetic stressor (Darvesh & Gudelsky, 2005)

Acute 800% increase in stress hormone cortisol in MDMA dance clubbers (Parrott/Lock et '08)

(cycling to exhaustion 137% cortisol increase.MDMA in lab 100-150% cortisol increase).

Conclusions: MDMA at least as powerful as cocaine & probably stronger – wider psychobiological profile.

Post-MDMA recovery

Lethargy, irritability & sadness (Parrott&Lasky ’98)

Mid-week depression can reach clinical levels (Curran&’97)

Aggression increased mid-week (Curran et al, 2004)

Appetite & food intake reduced (Turner et, 1998)

Sleep impairments mid-week (Jones/Blagrove, 2007)

Time course of these problems several days, with return to baseline by day 7.

Comparison with cocaine: generally a longer duration of recovery problems with MDMA.

Long term effects of recreational Ecstasy/MDMA

‘Recreational Ecstasy/MDMA users… can display a range of functional deficits in neurocognitive test performance, altered cognitive-emotional information processing, raised psychiatric symptom profiles, disordered sleep, sexual dysfunctions, altered EEG patterns, modified event-related potentials, reduced immunocompetence, increased oxidative stress (+81 refs; Parrott 2006 review).

Many factors influence the development of these problems, with some users remaining unimpaired (Parrott, 2006).

Most crucial factor is lifetime ecstasy/MDMA usage

Since above review: impaired social intelligence (Reay’06), sleep apnoea (serotonin & breathing, McCann’08)

Nutt (2006) Editorial.
MDMA is less damaging than alcohol.

Ecstasy/MDMA effects described as follows:

Premature deaths: 10 per year/UK

Brain damage: unsure

Dependency potential: ‘ecstasy is not addictive’

Interpersonal violence: none

Road traffic deaths: none

Safety in Overdose (x15): ‘Ecstasy is less toxic in overdose because it doesn’t cause respiratory depression or block the cough reflex’

Liver cirrhosis: none

Heart damage: none

Parrott (2007) Editorial Reply

Following effects with Ecstasy/MDMA

Deaths. 40/70 year/UK (Schifano'06)

Brain damage. 'Most robust finding was a reduction in serotonin transporter density' (Cowan'07 - review).

Dependency. Two-factor structure: compulsive use & escalating use (Bruno'08, confirming Topp'97)

Aggression. Increased mid-week (Curran'04; Hoshi'06).

Car driving. Can be 'extremely dangerous' (Brookhuis'04)

Overdose. Hyperpyrexia (fever) related deaths (Henry'92)

Liver. 'MDMA has hepatotoxic properties' (Montiel'02).

Liver. Transplants needed in <30 year old Scots (Smith'05)

Cardiac. 'MDMA has profound cardiovascular effects in humans and animals'…'MDMA disrupts metabolic homeostasis in cardiac tissue in rats' (Perinne et al '08).

Overview of Nutt (2006) & introduction to his next paper.

Nearly every statement that Nutt (2006) made about MDMA was incorrect.

He should have realized these problems after reading my detailed reply (sent in 2006). He also attended my ECNP conf talk in Vienna.

Instead he has repeated these errors in his next article.

Nutt and a group of colleagues (2007) proposed a new scale for drug-related harm. Some interesting ideas….but also numerous errors.

Single lone statement about MDMA in Intro/Methods: 'For drugs which have only recently become popular e.g. Ecstasy or MDMA, the longer term health and social consequences can only be estimated from animal toxicology at present'. (Nutt et al, 2007).

Simply ignoring the 1450 published 'human-mdma' research papers !

Nutt et al (2007) Lancet article. Rational scale for drug-related harm.

Physical harm. (maximum possible score =3.0)

	Mean	Acute	Chronic	**Intravenous**
Heroin	2.8	2.8	2.5	**3.0**
Cocaine	2.3	2.0	2.0	**3.0**
Tobacco	1.2	0.9	2.9	0.0
Ecstasy	1.0	1.6	1.6	**0.0**

'The potential for intravenous use is taken into account in the Misuse of Drugs classification and was treated as a separate parameter in our exercise' (Nutt et al, 2007).

Is the **Intravenous** score of 'zero' for MDMA correct?

Injecting recreational Ecstasy/MDMA.

Topp et (1999) 329 regular Ecstasy users. 54 had injected ecstasy – for the increased *rush/high* (62%) etc...

Three-quarters switched back to oral/intranasal: feelings too intense, come-down too rapid, dependency, health problems.

MDMA injections are *only* reported with heavy ecstasy users (e.g. Janssen, 1999; others).

Need to develop chronic tolerance to be able to handle an MDMA injections.

Injections could be lethal in a novice user.

Conclusions: MDMA is so powerful it is very dangerous to inject. Possibly safer to inject heroin? Score of +3.0.

Nutt et al (2007) Lancet article

Dependence and 'intensity of pleasure' (max=3.0)

	Mean	**Pleasure**	Psychol-Depend	Physical-Depend
Heroin	3.0	**3.0**	3.0	3.0
Cocaine	2.4	**3.0**	2.8	1.3
Tobacco	2.2	**2.3**	2.6	1.8
Ecstasy	1.1	**1.5**	1.2	0.7

- Nutt et al (2007) scored MDMA as **less pleasurable** than tobacco !
- Incomprehensible error - a 'schoolboy howler'… or more deliberate?
- The ridiculously low 'intensity of pleasure' score – does keep the 'total harm' score for MDMA similarly low.

Total harm scores and overall rankings

1st =most harmful. 20th = least harmful. (Nutt et al, 2007)

	Total Harm	Physical Harm	Depend'ce &Pleasure	Social Harm	Overall Rank
Heroin	2.8	2.8	3.0	2.5	1st
Cocaine	2.3	2.3	2.4	2.2	2nd
Tobacco	1.6	1.2	2.2	1.4	9th
Ecstasy (Nutt)	**1.1**	**1.1**	**1.1**	**1.1**	**18th**
Ecstasy (2 corrections)	1.6	2.1	1.6	1.1	9th
Ecstasy (Parrott)	**1.9**	**2.2**	**1.8**	**1.7**	**5th**

Conclusions: MDMA is 5th highest drug on Nutt's harm scale. Similar to other Class A drugs.

Conclusions: my proposal

My area of research expertise – the effects of recreational Ecstasy/MDMA in humans.

Numerous refereed journal articles & conference papers 1994-2008 (+50 journal articles, +120 conf papers).

British Association for Psychopharmacology prize (twice).

Widely-cited reviews covering many aspects of MDMA.

Organised several international Ecstasy conferences.

Editor for several MDMA special journal issues.

Strong empirical base to all my work.

Proposal: MDMA should remain a Class A drug.

Conclusions: David Nutt's proposal

Professor David Nutt has many areas of expertise – but not Ecstasy.

Indeed he has never undertaken any MDMA research.

His two 'opinion' papers about MDMA are full of factual errors.

Furthermore the errors are all biased in one direction.

The Lancet article is truly awful (& should be rescinded).

Both his papers display a staggering disregard for the empirical evidence about MDMA.

Conclusion: David Nutt should withdraw his proposal to downgrade MDMA.

Selected Parrott References (since 2001)

Fox HC et al (2002). Psychopharmacology 162: 203-214 (CANTAB neurocog)

Milani RM et (2005). Hum Psychopharm 20: 1-13 (mdma & cannabis co-use)

Parrott AC (2001). Human Psychopharmacology 16: 557-577 (15 year review)

Parrott AC (2002). Pharmacol Biochem & Behav 71: 837-844 (serotonin syndr)

Parrott AC (2004). Psychopharmacology 173: 234-241 (Is Ecstasy MDMA?)

Parrott AC (2004). Neuropsychobiology 50: 329-335. (temp & raves/dances).

Parrott AC (2005). J Psychopharmacology 19: 71-83 (chronic tolerance)

Parrott AC (2006). J Psychopharmacology 20: 147-63 (energetic stress review)

Parrott AC (2007) J Psychopharmacology 21: 3-9 (mdma versus alcohol)

Parrott AC (2007). Hum Psychopharmacol 22: (MDMA & drug harm scaling)

Note: the above is based on a paper I submitted to the Lancet in reply to Nutt et al (2007). The Lancet rejected it without review.

Parrott/Milani et al (2001). Psychopharmacology 159: 77-82 (UK/Italy)

Parrott/Rodgers et al (2002). Hum Psychopharm 17: 312-19 (self-rated probs)

Parrott/Gouz-May et (2004). J Psychopharm 18: 579-82 (cannabis & MDMA)

Parrott/Rodgers et (2006). Hum Psychopharm 21: 285-298 (dancing hot on E)

Parrott/Lock et (2008). Neuropsychobiology (cortisol in E using clubbers)

Scholey AB, et al (2004). Addictive Behaviors 29: 743-752. (MDMA usage)