Psychedelic Psychiatry, Psychotherapy, and Spirituality
Speakers: Jon Cole, Val Curran, Andy Parrott, Peter Oehen, & Rick Doblin
Moderated by Ben Sessa

MDMA Debate

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Jon Cole: Essentially I'm going to ask you some questions, this is very interactive. If I were a researcher looking into the safety of MDMA and I applied to the government for some money, how many of you, if you were the government, would give me that money? [Audience raises hands] That's way more than I thought. Okay, if I were to ask you, "would you give me money to look at the danger of MDMA?" how many of you think the government would put their hand in their pockets and give it to me? Such is the nature of research that you reverse what normally happens when I ask that question. Normally when I ask that question everyone thinks the government should put his hand in his pocket and pay to demonstrate that ecstasy or MDMA is dangerous and those people feel that the government should not pay to show that MDMA is safe. However those amongst you who know anything around the science, will know that the experiments to show the safety will be exactly the same. What it shows is that there's a financial imperative for us to discuss danger when discussing drugs like MDMA. This is why I call it the ecstasy paradigm. Therefore I've not got slides or discussions of research studies, simply because I don't think that's relevant. What I think is relevant is our discussion around the *narratives* of MDMA and related compounds and what we really need to discuss is why are we focusing on safety or danger when in reality the experiments are the same? What we're focusing on is our interpretation of them. So, therefore that's what I want to leave you with. The simple question: Is it the narrative? Or is it the danger? Thank you.

Val Curran: I'm going to follow now by trying to summarize the main issues, which I hope will help stimulate the debate. I don't need to tell you a lot, but the benefits of MDMA are very clear. We recently used the Nutt framework to ask 1500 drug users to rate the 20 most common drugs including alcohol and tobacco and other illicit drugs. MDMA came up highest of all 20 drugs in terms of acute benefits and second only to LSD in terms of chronic benefits. And empathy, as a clinical psychologist, is important for me; empathy in the therapy situation is hugely important. The drug has potential benefits. We've heard how it stimulates the release of neuropeptide oxytocin, which is the human bonding hormone. It's what bonds the baby and mother through the breast milk and through the whole process of birth. This debate, as Jon Cole has just talked about, has been based on harms, all sorts of political, economic, and other reasons. The harms are in terms of what happens immediately after you have the drug: a few days later is the short term. The long term has been the main debate. And then something that we've been particularly interested in is what happens after you stop. So I want to challenge what the scientific evidence is on these things. Acutely we've given ecstasy in a horrible old basement room in St. Mary's Hospital people love it even when you make them come in at 9 in the morning. They get a huge kind of empathy and they really enjoy doing the experiment. We have to turn people down we get so many volunteers. Just to be fair the science shows it does have some impairing effects. It impairs memory acutely. In this study we gave either ecstasy alone, ecstasy plus alcohol (2-3 units of alcohol), alcohol alone, or just a double placebo drink and pill. And what you see clearly is that ecstasy, 45 to 120 minutes after you've taken it, does impair memory. It stops you from remembering words, but it also enhances your ability to control your impulses. A Dutch study shows this. And it focuses your attention and speeds up your psychomotor function. But you won't see *that* in the newspapers. You'll only see memory impairment. A few days after use, we showed a long time ago, you get a midweek dip in mood, a midweek low, but seven days later, that's gone. You're back to normal. So again it's only a fluctuating thing, which we think coincides with changes to serotonin in the brain. Long term there's been such rubbish written about this drug, such bad science. This is a paper from a very respected Dutch group

who had done the only prospective study of MDMA. They took people from coffee shops before they'd used ecstasy and followed them through and did brain imaging, cognitive testing, after some of them had started using the drug. I don't know if I've got a pointer, but I've circled: this is a memory test where you're shown related words and then you're asked to recognize 30 words. This got published in a highly prestigious journal, Archives of General Psychiatry. And what it shows is that kids that went on to use ecstasy; before they'd used ecstasy they remembered nearly all of the 30 words. After they'd started using ecstasy you'd still reckon their performance was pretty amazing. What they did was to show impairment. They said that in this group 22% of them had actually shown a slight decline, right, one word. Whereas in the group who'd never used ecstasy didn't show that. Only 6.7% showed the decline. The authors concluded that low doses of ecstasy are associated with a decrease in verbal memory function. Which suggests ecstasy-induced neurotoxicity. You don't have to be a scientist to realize that is absolute rubbish. There have been an awful lot of very poor neuroimaging studies done in the field. The best one to date is one done in Canada by Steven Kish. And they did show a reduction in an index of your brain's serotonin function. Serotonin is an important neurochemical, especially in things like depression. But even though there was a reduction in current users, especially in memory areas, hippocampus, and in perceptual areas like the occipital cortex if you look (it's probably too small to see clearly), but the dark dots are ecstasy users and the grey dots aren't. Nothing was abnormal in the ecstasy users. The overlap between the two groups was huge. No abnormality either in terms of memory or brain function in ecstasy users. The year before, using the same radio-ligands Kish used to look at serotonin in brains, we found that when people have given up using ecstasy there was absolutely no difference in their brains compared to people who had used similar other drugs or no drugs at all. We've also shown no memory impairment a year after people have given up compared to people who use drugs other than ecstasy. And John Halpern has similarly shown in a paper recently out, no memory impairment in people who use ecstasy but were not a load of other drugs like cocaine and amphetamine. No withdrawal syndrome has been identified. Since we've been researching ecstasy I've

never met a single ecstasy addict. The American government, NIDA, are paying someone called Linda Cottler enormous grants to go out and show that ecstasy users fit the psychiatric classification for addiction. The only way she's shown it at all is by finding people, over half of whom also use heroin, so completely atypical of the ecstasy-using population.

Andy Parrott: Thanks Ben for inviting me. I'm going to explain how I came to believe that ecstasy is far more damaging than when I first started doing studies. So my first studies were in 1993 to 1996, largely interview studies. And we got lots of positive subjective reports. And this is when it's called an entactogen. I published two to three papers during this period. And, like many people at the time, I believed it was quite different from many of the other psychoactive substances. It was an entactogen, eats. However we also found initial reports of problems. We had people who said they had taken it and had bad experiences. One of the people in one of our interviews said they wouldn't touch it again because their experience with it was so bad. A few others said they'd had bad experiences, which were quite unlike earlier experiences they'd had on the drug. And also we saw recovery problems as Val pointed out in the previous slide. Many of our users recalled that they had mid-week blues, which has now been well replicated. We've looked about in a number of studies and found more problems mid-week. So, it's certainly a euphoric drug when taken, but it certainly has untold effects in recovery period. So if you asked me, then in 1996, would I recommend it for therapy, I'd be very neutral. I'd say, "Well it seems to have a positive profile but also it seems to have negative effects as well." So the overall profile from 1996 would have been neutral. We then found the first study of memory deficits compared with young matched non-users. This confirmed an earlier American study, which is more of a clinical report of nine users who also had psychiatric problems. This has now been confirmed in published studies. It's probably thirty, forty, fifty studies, which have found deficits. Most of those studies controlled for other drug use including cannabis. Rogers undertook a big government sponsored meta-analysis in 2009. They had seven measures, which they had sufficient data on - they had been done in eight or nine studies or more -

where they could do a meta-analysis. In seven of the measures they concluded that ecstasy was more damaging than poly-drug user controls. The control group was crucially other drug users not using ecstasy. One measure they didn't find a deficit was NART, which is a measure of intelligence. The other six measures were all memory measures. The meta-analysis concluded there were specific memory problems in ecstasy users. We've also looked at higher cognitive problems, particularly pre-frontal problems. The number of groups that find problems in higher executive deficits: problem solving, social intelligence. Again most studies these days need to control for cannabis in their statistical analysis or in the groups. You also find acute type reactions. One of the intriguing things about ecstasy is the wide variation in individual responses. Some people seem to be very robust. Many people have mild problems and some people have quite severe problems. We find this in the serotonin syndrome. Occasionally people develop quite a strong syndrome and a small proportion need hospital emergency treatment. If you talk to medics who work in emergency Saturday nights the past ten to fifteen years, they said they often have stimulant abusers/users (whatever you like to call it) in their hospitals. They're almost invariably treated successfully. People now know how to treat the hyperthermic reactions successfully and most people are released the following day, on Sunday morning, but it is certainly a severe bad reaction. The mid-week problems we've talked about...

In 1997 I found the first case of psychiatric problems. This is a young recreational user who reported phobic anxiety, which they attributed to being an ecstasy user. We then did some studies and we found raised psychiatric problems in lots of ecstasy users. Again, this is compared with other drug users as well. Other users also have problems - cocaine, amphetamine, methamphetamine - they're all associated with psychiatric distress. MDMA is not dissimilar from those. In 2006 I'd have said, "No, it wasn't a safe drug." More recently I've been looking at the effect of environmental co-factors and these seem to exacerbate the problems. If you look at dancing music, psychosocial factors, the theory is it's not just the drug alone. It's the concomitant stimulation which leads to the brain being over stimulated and this

leads to a positive on-drug experience, but it also leads to negative recovery problems in the week afterward. We found people that danced the most report the strongest mid-week recovery when matched for drug use. It's a combination of drug and physical over stimulation, which seems to be the problem. Further along, I'm writing a review on this at the moment and at low doses MDMA has very little effect on temperature. Visual defects: Several groups have now reported subtle deficits in occipital cortex. Social intelligence, which I think is relevant to MDMA as a therapy, seems to be reduced in regular users. Neurotoxicity: In the Kish/Nell paper, Val Curran said, "the effects weren't particularly marked." Let's go over that. I'll talk about one error. In the occipital cortex 51% of the ecstasy user group had SERT levels below the lowest region of the control group. There was a lack of overlap. Many of the ecstasy users had quite strong deficits. In conclusion, I wouldn't recommend it.

Peter Oehen: As a psychiatrist and psychotherapist I'm greatly frustrated by the number of people I encounter in my private practice who I'm not able to treat properly because - there are multiple reasons for this...there are multiple reasons why people are treatment resistant, not only PTSD and as Ben said in his introduction this afternoon we are desperately in need of ways of enhancing psychotherapy. Leuner, grandfather of psychedelic therapy in Europe once made the approximation that only 50% of people can be treated by psychotherapy, so we need something that's an enhancer. From my point of view, from what I've seen, MDMA can be this drug; can be one of the drugs. I strongly advocate to differentiate between the therapeutic use where you would administer one dose of 125 mg in a completely different setting, no physical exercise. It has been shown that, for example, the cortisol levels when exercising go way up and if you are lying down on the couch they are lower, much lower. Maybe that's one explanation for the damage that it could cause. We should investigate. We have the chance now with these studies going on to combine these studies with neurophysiologic studies. That would be really interesting and support evidence of damage or benefits. Thank you.

Rick Doblin: Hello. First off, I'd like to thank Andy Parrott and all the other researchers that have looked at the risks of MDMA and of ecstasy. I think it's essential that we have a clear understanding of what the risks are. However I think it's been the case that the risk data has been exaggerated and the potential benefits have been denied. Whenever you're doing a risk-benefit analysis, if there are any risks and there are no benefits then you would conclude that it's not appropriate to use the drug. But if you look at Medline and you put in ecstasy or MDMA there are over 3,500 papers that have been published at a cost of over $300 million. There's only one paper on a completed study on the therapeutic benefits of MDMA and that's Michael Mithoefer's study. That paper, though, has fundamentally shown that there are benefits. I think Andy's data that he talked to us about, about he's now convinced that MDMA is unsafe for therapeutic use...it all comes from recreational use of MDMA. So, I think it's completely inappropriate...although it's valuable, it's not enough. We need to look at the risks in a therapeutic context and we don't see the kind of risks that he's talking about. But, even if we did - you know Aspirin kills a lot of people. People are allergic to penicillin. We don't have to show or we don't have to claim that MDMA is this rare drug that has no risks and only benefits. The temptation in a way is for advocates to be boxed into that corner because the other side is saying there are all risks and no benefits. But what we're really looking for is an accurate comparison of risks and benefits and then a weighing of them from actual research in therapeutic contexts. I have seen over the years that the risks data has been used to suppress researching benefits. From 1985 when MDMA was criminalized to 1992 when the FDA opened the door to MDMA research, seven years went by with no possibility of permission to do MDMA research into therapeutic uses. That has now changed. Andy spoke about the first study of the neurocognitive consequences in nine subjects. That study was funded by MAPS. What you don't probably realize - that was done by Larry Price and George Ricaurte**.** It was done at Yale. We are trying to be the leaders of the research into the risks of MDMA when used in a therapeutic context and also the benefits. That particular study was done...I paid for the neuropsychologist to do the analysis - Ricaurte was doing other measurements, tryptophan challenge tests and things like that. I got this report from

neuropsychologists and it said there's nothing here remarkable. There are a few changes, but it could easily be attributed to the fact that several of the subjects flew in from California, that they had just received tryptophan and their tryptophan challenge test. They're unusually intelligent. There's nothing here. And to my surprise, years later this turned into a paper with John Crystal and the neuropsychologist as coauthors. I called the neuropsychologist and I said, "How could you do this? I don't understand the difference between the report that you gave and the paper that was published." He said, "If you ever release the report I gave you I'm going to sue you." I was like, "This is my property. I paid for it. How could you possibly do that?" You can see that there is a tendency to exaggerate the risks in order to get publications. So, I think the risk research is absolutely essential, but I think it's been highly biased by motivations coming from funders to justify cruel and counter-productive prohibition. I think that the potential patients who could be benefiting from this is a major social cost that usually is not weighed into any of these discussions.

I'd now like to switch and say that we have a series of phase II pilot studies all over the world. We're looking at a range of methodological questions that we need to address. What we're going to try to do is find out over the next two to three years: what is our method? How do we refine the method? How do we teach the method? How do we assure ourselves that therapists in different settings are actually adhering to the method? How do we develop a double blind study with a powerful psychoactive drug like MDMA? Are there cultural differences and how do we figure out what they are and how to work around them? Is the cause of PTSD requiring a different treatment or can we enroll people that are victims of sexual assault and also combat related PTSD and also car accidents? Our working assumption is that the cause of the PTSD is irrelevant. Then we go to the FDA and we say, "Here's our data," and we propose a phase III study. If they accept the design and permit us to move forward then we move forward with that. It'll probably take us three years to get to the end of the phase II meeting, another five years and another $8-9 million to get to the end of phase III, then we submit to FDA and I'm anticipating that, in a

decade, if we're fortunate, we will probably have MDMA as a prescription medicine. Thank you.

Ben Sessa: Thank you, all of you first of all for sticking to those rigid time limits that we set of five minutes each. There's a number of things that we need to be cautious about the difference between recreational use and clinical use, we need to appreciate that no drug is 100% safe and we're actually looking at risk versus benefit ratios. Who would like to pick up on some of the points of some of the other speakers first? [Nobody volunteers] Well, I want to just ask, in the audience, do we have any psychiatrists, clinical psychologists or other people who work clinically with patients? I'm interested to know whether or not people have come across morbidity associated with recreational ecstasy use in their clinical practice.

Audience member 1: Not really.

Ben Sessa: I haven't either.

Audience member 3: I've sometimes felt brought down after I've been using it fairly extensively, but nothing that can't be corrected with amino acid supplements.

Ben Sessa: So, you're describing a mild adverse effect. My question was really whether clinicians have found clinically relevant mental disorders associated. Thank you for that, because we are aware that is does have mild subjective negative effects in people. The point I was making: are these effects sub-clinical or are these at a level that are reaching the psychiatric clinics and hospital beds? My broad experience and speaking to other psychiatrists is that they are not of a clinical level. So, I just wanted to make that point.

Rick Doblin: I don't tend to disagree with you Ben, but I am aware of someone who had taken MDMA and under the influence of MDMA had remembered a prior sexual assault, which had led to physical violence where she had almost been killed. Under the influence of MDMA it came up but she wasn't in a context where she felt she could really work it though. And so she ended up checking herself into the emergency room in a hospital to avoid committing suicide. Later she contacted me,

this was in 1984, and I agreed to sit with her in another MDMA experience. It ended up helping her to confront it in a safer context. From that she decided she wanted to become a therapist. She now is a therapist and she's worked on our Spain MDMA/PTSD study. That's something that's now 26 years ago and she's had long-term positive effects. So, I think the context of MDMA is absolutely critical. It's possible to take MDMA in a setting where you end up feeling worse off sometimes for months. My question for Andy is: How can you really, in all good conscience, look at the risk data from non-medical, non-clinical settings and say that justifies a decision that MDMA research in clinical settings is too dangerous to conduct?

Andy Parrott: Well, you've described one straight from 1984? If you look at the Greer and Talbot paper published in 1986, they had twenty-nine clients. Now, these weren't psychiatric clients. They were friends and acquaintances, about nine of who had sort of psychiatric levels of problems. But they weren't psychiatric clients. Now two of those twenty-nine had abreactions to the drug, which lasted more than a week. Many of the participants had abreactions that lasted a day or so, but these two had problems which lasted a few weeks. With one therapeutic administration, you can elicit, you can engender problems.

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Rick Doblin: Would you be influenced if I were to speak to George and say, find out how those two people are doing right now. If we could get that information and give it to you, would that in any way change your attitude about the therapeutic research with MDMA?

Andy Parrott: Well, they actually describe this in the paper. One of the clients got better after a few weeks. The other was given free non-drug assisted psychotherapy for a year. So, the problems of that twenty-ninth person were really quite enduring. And so they needed a fairly prolonged period of therapy after one session. The problem with MDMA is it elicits all sorts of material, both positive and negative. Franz Vollenweider has shown this, lots of other groups have...I've been involved in a study in Australia where we tested people in a laboratory and people had to drive

simulated cars. We didn't get positive moods and it's probably because the environment wasn't positive. In other words, what happens with MDMA is it boosts all material. It's a CNS stimulant. If you're in the wrong environment you may well have negative material boosted. In my final slide I was going to say the crucial factor is the therapy not the drug. In fact, Greer and Talbot said, "The primary thing is the therapy." So, my position is it's far safer just to give therapy.

Ben Sessa: Can Val cut in here?

Val Curran: Sorry, I just can't understand how you get different results from everyone else Andy. If you look across all the studies: Kim Kuypers and Ramaekers**,** the Dutch people - they have lots, we've done stuff, Harriet de Witt's done it, everybody gets these really positive moods. And as I've said we do our studies in the basement of a hospital. It's not at all a nice environment. I think there's something odd about your data. No one else gets it but you. I also think that in your chat with Rick Doblin, if you take any drug there's always going to be one or two or a few people who have a bad reaction, even alcohol.

Andy Parrott: It's the new data we're most surprised at. We expected to get positive effects, so we were very surprised when we didn't.

Val Curran: Are you sure it was ecstasy that you gave?

Andy Parrott: [laughing] We buy from a Swiss pharmaceutical company. I guess Swiss sell pretty high quality, so it was 100 mg of laboratory MDMA. You mentioned Harriet de Witt. She and Gillinder Bedi in New York published two studies where they didn't get positive effects. In both those studies the participants were given other tests in the laboratory. What we wrote about in the paper was the environment. If it's in a negative laboratory environment where you have to do lots of tasks, MDMA probably won't give you a positive experience. If you're experiential...sitting in an armchair, you've got supporting people around you, encouraging, you'll get nice positive experience. It's the environment.

Val Curran: We'll just have to agree to differ, because we do eight-hour studies. They

come at 8:00 in the morning and we keep them all the way through. On the MDMA days they love it.

Ben Sessa: Jon.

Jon Cole: I've got a slightly different take. If we look at all of the neurotoxicity studies, we look at the brain imaging studies, the studies where tryptophan was being administered, if you look in the participants section it clearly says none of these people had a psychiatric problem. In all of the studies that have been quoted around whether they've got neurotoxicity or not, none of them had a psychiatric problem. So, how do we get this notion that all of the psychiatric problems observed in people are due to MDMA and they're due to neurotoxicity? Because people who are clearly demonstrated, according to the papers, to have neurotoxicity, don't have any psychiatric problems. And I've reviewed plenty of these papers as a scientist. One of the things that I didn't want to say because it's potentially libelous and there's a camera pointing at me, is how about the problem that, when challenged, the authors refused to draw the attention of the reader to that fact. I did it in every review and every time when the paper was published it was not there. I think that what we've got to accept is that whilst there's a large amount of research, as Val has pointed out, a lot of it's done very poorly, but there's also a huge publication bias and we have to take that into account when we consider that research.

Ben Sessa: Can we have a question? Robert.

Robert [in audience]: This isn't so much a question as a brief account. From 1981 until 1985 I was a graduate student at the University of Chicago and I had embarked upon a quasi-formal investigation of MDMA where I had handed it out to hundreds of people. Me and my associates...this is actually how Rick got his first MDMA. When I had collected over a hundred written reports of this experience I took it to Daniel X. Freedman, who was the president of the American Psychiatric Association and editor of the *Archives of General Psychiatry*. And I said, "This is a new drug that hardly anyone knows about that is extraordinary and it may be the best thing that psychiatry has ever had." He referred me to Dr. Charles Schuster, who at the time

was the director of the University of Chicago Drug Abuse Research Unit. I gave him and his assistant some. Then in 1985 I was about to give a lecture at the University of Chicago on the curative effect of MDMA. This was the morning that the DEA declared their emergency scheduling of the drug and Dr. Schuster and Dr. Seiden were written up in the Chicago Tribune as the experts on MDMA that said it caused this brain damage, this damage to serotonergic receptors. I was astonished because just two weeks earlier Schuster was supporting my formalizing my research at the University of Chicago. I went to his office and I said, "How could you do this? This is just what happened with LSD. A rumor is introduced and there now there are still people who think that LSD causes brain damage." He took me into his office and he explained to me, and this is exactly what he said, he said, "Look. I have a nice setup here," He had a whole floor at Billings Hospital at the University of Chicago. He said, "The government gives me a lot of money. Sometimes I just have to do what they say." Two years later Dr. Schuster was appointed to head NIDA, the National Institute of Drug Abuse. I think this story indicates that there is a kind of crisis of legitimacy in this whole MDMA debate from the very beginning. That this brain damage stuff is kind of contrived and misleading to justify a political position of the government. In this case it the US.

Audience member: Excuse me. Can I add something?

Ben Sessa: Yes, please.

Audience member: I'd just like add a little bit to the neurotoxicity part of ecstasy story. Both Parrott and Curran referred to the Kish studies showing a decrease in the serotonin transport binding in ecstasy users. I would just like to add a little bit to that story, because it's very difficult to assess toxicity in the living human brain of course. That's part of the reason why we can argue from here to eternity about if it's toxic or not, because actually it's impossible to show. It's not possible to come up with any measurement to really show it. They could attempt to try to show a look at it. It's definitely relevant. In a paper that we will publish in two months we have also mentioned serotonin transporter and it can be...some people view it as a marker of

toxicity. We don't necessarily do that because it could also just be an effect of that state of serotonin depletion, if this serotonin transporter down-regulates. But what I think is important to say is that one thing that we see and also that third study that has not come out yet from the New York group. We see the same thing as the Kish people. We see a quite severe decrease in serotonin transporter binding in the cortex, especially in occipital cortex. It's not necessarily reversible, from the data that we have and also the same is seen in this New York group. The jury is still out to see if there's actually severe...in heavy users, especially, heavy recreational users of ecstasy, if there's changes in the serotonin system or not.

Andy Parrott: Can I respond?

Ben Sessa: Yes, please.

Andy Parrott: In the Kish study they found variation in reduction of the serotonin transporter. What they also found is it correlated with two things. One was cumulative lifetime dosage. So heavier uses had less of the transporter. The second thing that correlated was memory impairment. So the loss of serotonin transporter was correlated with poorer performance on their cognitive tasks.

Audience member: Yes, we actually see the same. We also see an effect, the more lifetime use of ecstasy, the lower the serotonin transporter. We see the same, the New York groups see the same. So, there's some kind of lifetime dose-responses relationship. But, what we also see and what the Kish paper refers to, and actually did mention, because that might be as important, is that they see also a relationship, and we see that, time since last use adds the binding. And that points to a possible reversibility of the findings, so that the serotonin transporter might down-regulate, but it might get back up if you take a break and don't use ecstasy. In our data that will come out it, it looked like after two hundred days of abstinence the serotonin transporter is back in business, especially in sub-cortical regions. We don't see that in the cortex.

Jon Cole: Can we just be very clear. Ecstasy and MDMA are not the same thing.

Audience member: What's the difference, please.

Jon Cole: The difference is ecstasy is the illegal drug in tablet form that very rarely contains MDMA. Most street ecstasy in the UK at the moment contains benzylpiperazines such as tricor butyl-piperazine or meta-coro-phenyl-piperazine. They do not contain 3-4-methylenedioxymethamphetamine. I can point to a sign up there that's embarrassing. We recently did the amnesty bins from Creamfields. There wasn't much MDMA apart from in crystallized form. Let's just be clear ecstasy is a street drug, which may or may not contain MDMA. Therefore we cannot say using it 500 times equates with the exposure to a known dose of MDMA. That's just nonsense.

Val Curran: That's interesting to know that you've got more data. Kish quotes our study where we've looked at people who've given up ecstasy for at least a year, that was an inclusion criterion. And we found no differences whatsoever. And the other interesting thing about Kish is he found no differences in the striatum, which is where you would expect the differences to be. I think we all agree, it's the time since last use. Reneman's data agrees as well. I think eight out of the nine studies that have looked at people reducing or stopping do show an association between recovery of SERT and times since last use. Our study took two years to do to find the controls. We couldn't find British people who had used stimulants and other things the ecstasy users had used. There weren't anyone. If you'd used ecstasy you'd also used coke and whatever else. So we ended up getting volunteers from South Africa and Australia or New Zealand because the ecstasy movement started later there. I think it's really important how your controls are matched. And you're saying about heavy users showing non-reversibility. I would worry about the effects of lots of other drugs on SERT . Heavy users are going to be using lots of other drugs as well.

Rick Doblin: I'd like to make just one point, too. It's that the real issue I think is functional consequences. The assumption is if there's a change somehow or other that's bad. We're already talking about, and Peter talked about it, how there are changes associated with therapeutic benefits. So first off, this assumption, that any

kind of change is bad. Then there's just this focus in our particular study, we did neurocognitive tests with people who got 3 doses of MDMA, 125 mg plus 62.5 mg after two hours, and there was a slight gain in neurocognitive performance after the MDMA treatment, which is not to be unexpected, because people's emotional issues: their anxiety, depression, PTSD, affect their performance on neurocognitive tests. If we can help people with their PTSD we would assume that their neurocognitive performance would go up. Now the placebo people who also had a 20 point drop in their CAPS, not as much as the MDMA people, they got better as well, slightly in their neurocognitive. I think the key point is: What are the functional consequences? I would like to remind...I don't know how many people have recently heard that - it was about six months ago - George Ricaurte and Una McCann came out with a new paper saying that MDMA causes potentially fatal sleep apnea. That was in the title: potentially fatal sleep apnea. And it just doesn't get the press that it did, anymore, that it used to. You know, there's just this exhaustion in a way with the effort to try to show that MDMA has these fatal consequences. Then how does is back down to a few doses in therapy. That's why I say again to Andy, that we really need to look at risks in a therapeutic context and we are doing our best to study neurocognitive performance. We're going to start doing some sleep measures. We don't really believe there's potentially fatal sleep apnea from MDMA. I think we need to really look at pure MDMA in a therapeutic context and then evaluate it in a comprehensive way.

Andy Parrott: If I could just...one comment needs to be said...serotonin is important for breathing. When you breathe at night, that's controlled by serotonin. If you're an MDMA user you're damaging your serotonin system. That's what Ricaurte and McCann reported. You had young, fit people who weren't overweight. Sleep apnea is usually associated with males who are overweight. It's a disorder where you stop breathing in the night. What was happening was youngsters in their mid-twenties who weren't overweight...was it 25% of their sample? [Nod from another panelist]...had sleep apnea.

Jon Cole: So, how many have died then, Andy? Surely, if we've got millions of ecstasy

users and apnea surely we should have a fatality count in the thousands. Sorry. Does anyone else see the logic of the fact that there are no dead people?

Andy Parrott: I'm not defending the title. I'm just trying to talk about the...

Jon Cole: Where are the dead people? This is nonsense. I'm sorry.

Ben Sessa: I'd like to ask a question about the way in which neurocognitive testing is carried out. Can the panel enlighten me: How many of these studies that demonstrate neurocognitive deficits include urine drug testing on the day of test? Because of course, nobody's disputing that acutely intoxicated with MDMA one can be somewhat disturbed neurocognitively. That is after all why people take it. One man's neurocognitive deficit is another man's party. If you want to bring someone into a laboratory and do neurocognitive testing on them and they are ecstasy users and we've already asked the question: whatever the hell an ecstasy user is, because we don't even know what ecstasy is. Have we got some good studies that really control on the day of testing for any concomitant drug use?

Val Curran: Well yeah. I think both our group and John's group, their latest studies did use, we used hair as well as urine so that we could see what previous drug...the hair is like a tree. Each centimeter of hair grows in a month. You can look at drug use in your hair. In those studies we found no difference between poly drug users and ecstasy users in neurocognitive function. In better-controlled studies I think, Andy will probably disagree, show a lack of difference really.

Ben Sessa: So, when it's well controlled for you, don't see the neurocognitive deficits?

Val Curran: That's my take on it. When they are better studies, they are bigger studies, they are better matched for all the drug use, and then, you know, I think, you don't see it.

Andy Parrott: You're probably not going to be surprised by this. In the Kish study they took hair samples and they proved that they were MDMA users. MDMA was

present in their hair. They also took urine samples to control for recent drug use. The Kish study...if you want to see a good paper...many of the earlier papers were flawed. It's an extremely difficult area to do research in. There are lots of potential confounds. The Kish study - I think many people like Val said it - is now seen as pretty much a gold standard. The…group and Elizabeth Franklin's group in Holland have done lots of very good research. But the Kish was quite remarkable in the number of things they tried to control. They did find memory deficits.

Ben Sessa: Can we take that question from the floor? Is that ok?

Audience member: Given that we are noticing that there's some seeming depletion of serotonergic transporters, how can we consider other means of increasing that? I've recently come across a study of the UDV members that JC Calloway, Dennis McKenna…was part of it as well, where they found that they were psychologically integrated. I believe they also found that they had more serotonergic receptor sites developed in the brain. I believe that's to do with the advanced…the neuro-inhibiting function rather than the psycho... release. So, is there any work being done into how you might address the problem of serotonergic?

Rick Doblin: I have to say that, in our clinical studies, we've explicitly decided not to try to co-administer any other substances with MDMA because we want to try to get a complete picture of what MDMA does by itself. We think it's way premature to conclude that in a therapeutic setting there is some neurotoxic problem at all, anyway. Then to try to do multiple drugs administered at the same time, it's just really too complicated and not necessary. So, we've not seen a need to do that in clinical studies.

Ben Sessa: Torsten

Torsten Passie: I would like to introduce a study that was done ten years ago by Tomasian et al. It was a government-financed study and I only want to give a short introduction. It was five groups...one without any drug use, one with drug use but without ecstasy, and three ecstasy using groups. One was 50-100 doses, one was

100-500 doses, and one 500-2,500 doses, but with other drugs used similar. I mean at the same point of time, which is different from Halpern's new study. This study was showing that the group with the lowest range of accumulative dosage of ecstasy use haven't had any deficit in any parameter and they have done a very thorough study with even PET scans and neuropsychological batteries and everything. The funny thing is that the results of this study were published as a book because it was an end report of a government-financed study. The publications that came out afterward in the international literature, in the English language, they were putting all the ecstasy using groups together so that under the line everybody got the damage. And not so many people are aware of that study but I guess Mr. Parrott, as a specialist should be aware of that. What does he think about the low-range ecstasy-using group and about these results even with other drugs used at the same point in time at rave parties etc?

Andy Parrott: Yeah. I'm aware of the publication - those papers I wasn't aware of his chapter in the book.

Torsten Passie: Okay, okay. So, this is the thing, how they fitted it together. At one conference...I may mention that for just a second.... Yeah, I can show you...The funny thing is when Mr. Tomasian was presenting his results at the scientific conference, I was putting my finger up and asking him, "What about that group?" and he told the people, "Yes, you're right. They hadn't had any deficits. But I don't want to mention that because I get funny questions then." [Laughing]

Ben Sessa: The chap in the back there waving. Yes please...

Audience member: Some recreational ecstasy users claim that they use 5-HTP the day after and delay the mid-week blues. Does anyone on the panel know anything about 5-HTP's effects with ecstasy?

Audience member: We've experienced it once.

Audience member: Have you looked at the comedown effects and differentiating between MDMA and ecstasy? We're obviously talking about a drug which we should

claim gives a happy sensation irrespective of context which everybody associates with...you know in my experience, people have associated with very severe downhill feelings afterward, once the effects have worn off. As a prescription for people with psychiatric disorders how would you justify that?

Ben Sessa: Okay, thank you. I wonder whether Peter might be able to come back up on this, because...have you...

Peter Oehen: I didn't understand him. Can you repeat the question?

Ben Sessa: As I understand it the question really is: Can we justify therapeutic use of MDMA when there are these anecdotal experiences of negative comedown effects when used recreationally? Is that right?

Audience member: Yeah

Ben Sessa: Thank you

Peter Oehen: In a therapeutic setting people are instructed about possible comedown effects and, if they are, they take it more easily. They can access help if they need it. People in recreational settings - that's what I see often - do not know about this and they are not very well educated about possible negative effects such as anxiety or depressed mood or when they get into a crisis because subconscious material comes up. So, there is definitely also a need for more education about these things.

Audience member: So, you're saying education is the reason? If people are educated enough about drugs that they realize MDMA isn't dangerous?

Peter Oehen: It's all about mindset, set, and setting. You can compensate...

Audience member: So it's the same with an alcoholic drink, for instance?

Rick Doblin: I'd just like to add that in our therapeutic context - first off that it's not been a substantial issue - but secondly the way in which we conduct the studies is that the people take the MDMA in the morning. They don't take it at night. So they

first off don't lose any sleep. They spend the night in the treatment center and then they have non-drug integrative psychotherapy the next morning. Then we release them to go home and they're called every day for a week on the phone to check-in, to see how they're doing. Then they come back for non-drug psychotherapy on a weekly basis before their next MDMA session three to five weeks afterward. Then we repeat that two to three, times depending on our different studies. There are some times when people have opened up such painful emotional material that they're struggling to deal with it for a period of time. But it's not the idea that that is somehow or other such a problem that the therapy shouldn't be done.

Ben Sessa: Sue.

Susan Blackmore (audience): First a comment and then a question to Andy. My comment is: I'm feeling so horribly naive and upset about this publication bias, publication suppression business. I mean I feel naive because I didn't really believe it but you've told me enough stories here. It bothers me very much, not just in the context of drugs, but in the context that in other ways I'm always defending science against people who say, "Science is just making it up." I mean the potential harm of this is not just to drug legalization to a better world in terms of drugs, but to the whole respect for science in general. And that really bothers me. Anyway, I'm going to go home and digest this and worry about it. My question to Andy concerns - it's a very small one - it concerns this business about the cofactors of dancing and so on. You concluded that the people who dance more or do various other things more, have worse effects. Am I right in assuming this wasn't a real experiment? I mean in a real experiment you take hundred users and you tell these many to dance this much and this many to dance this much. Presumably you're asking them after the fact how much they danced and they could be different people or they could be induced to dance more because of things going on in their brain, that cause and effect could be the other way around.

Andy Parrott: We've done a few studies. I've described one of them. We've got eleven ecstasy users who agreed to go clubbing to their normal club.

Susan Blackmore (audience): Ecstasy users or MDMA users?

Andy Parrott: I'll reply to that as well. They were ecstasy users. They agreed to go dance clubbing in the same venue, in the same group of friends, on two different occasions. On one they take drugs as normal. We weren't allowed to say, "Take ecstasy," but the ethics committee allowed us to say they could take their normal whatever it was. On the other they agreed to abstain from ecstasy or any other stimulant. They didn't take any stimulants. We also took saliva samples and the saliva confirmed MDMA presence in all eleven people when they danced on MDMA. It confirmed their abstinence when they danced the same weekend, the same group of friends, off drug. We have tested this. We've also tested surveys, Internet surveys of people and asked them how much they danced etc. That's where the data comes on the more memory problems. Those that report they dance more report more problems.

Susan Blackmore (audience): Yeah. That's exactly my point. It's they reported they danced more. Now why does dancing more have a greater effect? It could be because it's the dancing, but it could be that they're caused to dance more. You can only make that conclusion if you've actually manipulated this as an experimental variable, can't you?

Andy Parrott: If I can reply again? I'll reply to you [audience member] again next. I'll reply to you [Susan Blackmore]. They also had wrist things, which are called actographs, so we recorded their physical activity. They had the same, similar levels of physical activity dancing - they danced both occasions. We also measured cortisol. The cortisol increase when they're abstinent was very little. When they're on MDMA the cortisol increase was 800%, which is massive. They also got 0 change in testosterone, whereas they got a 75% in testosterone when they danced on ecstasy. It's not dancing per-se it's the combination of the dancing and the MDMA, which is problematic.

Audience member: Is it MDMA now? You said, "ecstasy."

Andy Parrott: They were ecstasy users. We tested their samples, their saliva samples, and all eleven had MDMA in their saliva.

Ben Sessa: Okay. We've got a lot of hands up. Amy.

Amy (audience): What's ecstasy & what's MDMA. If you were to take laboratory MDMA in a club, recreationally sorry, is that safe? If you took normal ecstasy in a recreational environment, what are your views on that?

Jon Cole: Well, how do you define safe?

Amy (audience): What are the risks you've been talking about and what effects would it have?

Jon Cole: If you look at alcohol, alcohol kills around 4,000 people through direct intoxication per year. And how many of us would consider going down to the pub after this talk to be safe? So, the question is, is the danger always lies - basic principle of toxicology - it's in the dose. So whenever somebody comes to me and says, "Is ecstasy dangerous?" I just go, "What are you talking about?" The thing is, it's the dose of MDMA which may potentially cause an adverse reaction. If we look at the medical statistics on adverse reactions, for drugs like MDMA, the overwhelming majority walk in to A&E and they walk out again. Usually the ones who come in on a gurney and die are the ones who are polydrug users. When we talk about the safety of MDMA in a clinical setting there is data dating back to when Rick started to when Franz Vollenweider did his studies, all the way through to when Andy did his study in Australia. No one's dying. The key thing...the question that you're asking is: In the correct setting, with the correct dose, is MDMA safe? The fact that no one's died...now you could say, "Well okay, that's not an indication of safety." 100,000 people per annum die from doctor administrated drugs. We know that prescribed pharmaceuticals are incredibly dangerous. We also know about issues in the pharmaceutical industry. That's a matter of public record in terms of class action suits, suppression of data, etc. So, I've just upset you [Susan Blackmore] even more. The key thing is: The question that you're asking is very difficult to answer. The

question is whether it's relatively safe compared to the other things that you could do. So for example if we were to use Dave Nutt's example of horse riding or going up into Everest, lot's of people do it. And lot's of people die. But we don't sit around having debates like we're having now.

Amy (audience): My point wasn't just that, as Peter emphasized, about the therapeutic setting. Is it really the context behind it or is it the actual drug itself? I'm confused as to what is most important: the context or the actual substance itself, the street version...

Jon Cole: I've looked into this. Basically, squaties on route marches die of hyperthermia. They fall over, fall into hyperthermia. They die on the spot. The incidence is roughly equivalent to the instance you see in the ecstasy users. What's the link? Extended aerobic exercise, probably with poor hydration, probably reasonable nutrition. Similarly if you look at the serotonin function of marathon runners, it's roughly equivalent to that of ecstasy users. Again, what's the link? Extended aerobic exercise. The thing is, if you sit around having a good time listening to classical music, why would you die? There's enough studies indicating the physiology of MDMA in those environments and I think, for example, at the temperature rise of all of the clinical studies, most of them indicate a temperature rise of 0.5ºC. If you look at animals, almost invariably you're looking at a 2ºC rise in core temperature. The difference is they've got fur. We haven't. We're much more tolerant to the heat stress produced by this compound. It's got to be the setting. If you jump up...if you're going like an idiot for 8 hours what do you expect? [Laughing]

Ben Sessa: I'd like to get to these questions. This lady here and then this chap in the back.

Rick Doblin: What I just wanted to say is - Jon basically raised the question: How many people have died in clinical settings? But there's another measure, which is called the serious adverse event. All of the regulatory agencies in the world require the researchers to report if there's a serious adverse event. That could be going to

the hospital because blood pressure has increased and they needed some special treatment or some psychological problem lasted for over a few days and they had to be hospitalized. There has never been a single serious adverse event in over 475 people who have used MDMA in clinical settings. That isn't to say that it's perfectly safe. I think what we have to constantly get back to is balancing risks and benefits. I think that's what has been suppressed for so long. MAPS is only a tiny non-profit. We have a budget of a little bit over a $1 million a year. We're the only people in the world paying for studies into the therapeutic use of MDMA. That's fundamentally wrong. There should be so much more government money, other major foundation money, so that in this context we've been forced to sort of argue about is there serotonergic neurotoxicity in the absence of any evidence about benefits? And that's finally emerging. I think you cannot look at the risk question without also looking at the benefits. I think if you talk to somebody, like Peter's person, who did those drawings. If you say to her, "If you remember one less word would you pay that price?"

Ben Sessa: Thank you. You've had your hand up. And then there's a gentleman in the back. Yes, please...

Audience member: I want to make two short remarks and one question. First I want to congratulate Andy for coming. I think it's very good that somebody with a different kind of discourse attend a conference, because it's very easy to...

Ben Sessa: I personally invited Andy and indeed all the panel because I have deep respect for all their work. Thank you for pointing that out.

Audience member: The other thing that I want to say is: as an anthropologist I kind of find some resonance with this therapeutic discourse, this kind of exemption for therapeutic use. I find resonance with the religious argument for exemption. There seems to be, sort of in the air, some kind of exclusivity that in this context things are different. And I'd like to go again for Charlie's talk in the morning. That we look into wider perspectives, because as an anthropologist I'm pretty afraid to take drugs with doctors. That's a little provocation, but I respect you a lot for the work of MAPS

and what I'm interested in, what I find kind of this funny circuit system is that the whole proposal to study the efficacy of drugs is to try to see what is their effect, not counting expectations. You kind of make all these techniques double and nobody knows what they're taking and all this kind of "neutral" context. But I find this paradoxical, because we all know that taking drugs depends a lot on expectations. Isn't it important that we try to create these expectations that will heal us. How do you deal with that in scientific terms? Because it's very important that we have a...if you want to create the therapeutic official use you need an accompanying culture of belief in this cosmology and this idea that it will heal us because this is fundamental for healing. I think this kind of conference gives a kind of setting for this. That it's creating this cultural understanding for all of us. That we have some sort of thing we can relate to. That doesn't appear in the discourse. Everybody's trying to detach all these cultural elements to it. But shouldn't we bring it into center stage? Instead of getting rid of it, try to elaborate on it, build on it.

Ben Sessa: There's a guy at the back. He must have a...be very sore with your arm in the air for so long. So please, let's have your question.

Audience member: I was just worrying about the interchangeable use of the words ecstasy and MDMA. If ecstasy can be a combination of many different substances, then how does the term polydrug use come into there?

Ben Sessa: I think we've covered that somewhat. That it is very difficult to make any reasonable comments about recreational ecstasy users and combine that with what we know about MDMA. Do we need to say any more on that?

Audience member: What's ecstasy?

Ben Sessa: Exactly. I think we've already explored that.

Audience member: MDMA's being sold as well and that's adulterated so you get these interchangeable. You just don't know because of the illegality.

Val Curran: I think one of the hard things to research over the years since I've been

doing this sort of stuff, is that ecstasy has changed so much. There have been times when ecstasy was MDMA and now it's rubbish. I mean nobody's using it. In history it was good. There was good stuff around. If you're looking at the research over time, you think what if they were doing it ten years ago. Yeah, probably this is MDMA they are talking about. If they're doing it now, we have no idea. So that again creates a very odd literature and evidence base really. That's why we have to go with the studies that have been much more controlled and really checked what's in the pills and all the body fluids that show that.

Andy Parrott: Yeah, I can agree. In my last two years in Swansea we've had difficulty getting ecstasy users. So if you are an ecstasy user and you're taking pure MDMA then please come along to Swansea and we'll test you. [Laughing]

Ben Sessa: This lady down in the front here.

Audience member: You were talking about the recreational use and I think this idea kind of leads me to the whole set and setting. Once we've got to take on board one's mindset, which is what you illustrated. Also I think the environmental factors that you were talking about doubting. In terms of where these people were dancing whether it was the environmental factors taken into consideration i.e. if the club had air-conditioning for example. If there was a garden, if there were safety measures in place for these people should they need it. Were they taking into the consideration the environmental factors?

Andy Parrott: In our Internet survey we simply asked people. In the study I talked about where we had the people go dancing under two drug conditions.

Audience member: But did you ask them if the area where they were dancing was safe for them. Was there air-conditioning? Was there water available? You know...do you know what I mean? So that their setting was optimum. Because it's all well and good to be able to conduct these studies in a laboratory where the temperature's nice and you have all these things available, but what about in a recreational setting where it's unpredictable?

Jon Cole: We did a study in a nightclub and we did the ambient temperature of the dance floor and it was 25.9ºC at about 1:00 in the morning. We also found no temperature rise in any of the participants. I think the thing is, we do need to be careful that that club had air-conditioning and it was turned on. I think that that's a very good point and people need to take that into account when they're assessing these studies, particularly if it's self-report on the Internet.

Audience member: I think we need to do some educating people who are going to take these substances as well.

Rick Doblin: I just wanted to comment that the police have taken notice in the United States that some clubs will provide areas that are lower temperatures than the main dance areas and the police have used that to as a reason to arrest the club owners and to try to take their properties, because it's a sign that they are aware that drug use is taking place in their facilities. There was a case in New Orleans where the DEA explicitly said that if there are rooms that are 15º or more lower than the dance areas that that is a sign that they can be prosecuted for having a club where MDMA is being used. The American Civil Liberties Union finally was able to fight that, but what we have is a perverse situation where the police have a harm maximization strategy. That's what we have with impure drugs, with reducing harm reduction efforts, because they want to scare people from ever trying to do it. And that's the idea I think that worries me a little bit about this concern about suppressing research into therapeutic use. It sort of fits into this overall strategy: We're only looking at risks. We can't have honest drug education for young people because if there's benefits then what are we going to do? How do we explain that to them? And what do they then believe about the other studies? I think we have a perverse situation that we have to some way or another get around. I think to Bia's question about expectancy: For our research we really have one audience and it's not everybody here. It's the regulatory agencies. We have to speak their language. So, we must work within their context. Eventually maybe we can broaden out. That will be a bigger discussion. But for the next ten years or so we must speak directly to the concerns of the regulatory agencies.

Ben Sessa: Okay. This chap here. Black t-shirt.

Audience member: I'd just like to make the point that having worked with survivors of sexual abuse, a very significant portion of those don't respond to therapy. Being a long-term survivor of sexual abuse and as clients which don't recover I think they think that the risk that they run on a day-to-day week-to-week basis is self-harm and suicidal ideation. They'd all think that the types of concerns we're discussing are miniscule. I think that they'd also think that, given the history of working with these substances and the successes that seem to be established, that waiting another ten years is appalling, especially if in fact it's on the level that we've just been talking about, about whether, you know, there's a slight problem with mood on Wednesday. [Laughing] It just seems that the voices of the people that would benefit aren't here today.

Ben Sessa: I think that's a very good comment from someone with a clinical perspective on the risk benefit argument.

Andy Parrott: And if I could...can I just... If you're going to have a drug, which severely depletes serotonin, which is the theory of the mid-week blues, and you've got somebody with suicidal thoughts, then that's a potential danger. They may well have very positive thoughts and good therapy with you on the session. The problem is: What's going to happen in recovery periods two to three days afterward? That's one potential issue which I think needs to be addressed.

Rick Doblin: Let me just say that the FDA has reasonably noticed that with certain kinds of medications there's a low risk - certain antidepressant medications and also Chantix that's used for tobacco cessation - that there is a low risk of a very small minority of people either getting agitated or near potential suicide. So, now they have required all drugs that affect the central nervous system to include measures of suicidality. We have included that now in all of our clinical studies and we will be able to really have clear definite data about that risk.

Ben Sessa: Andy Roberts.

Andy Roberts: In my professional life, the past 22 years I've worked managing hospitals dealing with young vulnerable homeless people usually between the ages of sixteen and twenty-five. I was working in hospitals; I worked during the ecstasy period in between 1985/86 and 1994. I saw hundreds of young people take ecstasy, people from tragic backgrounds who had no one to turn to. It revolutionized their lives to the point where they were transformed people. It's a bit like throwing the baby out with the bath water. Because look, the minuscule harms I've seen to young people working in hospitals have been far far outweighed by the positive experience in young people, many of whom have gone on to bright futures transformed by their ecstasy experience.

Ben Sessa: I think we're kind of...Peter wants to make another point.

Peter Oehen: I'd like to respond to Andy. If you give ecstasy...MDMA, sorry - MDMA to a subject who has a sexual assault history, it's not the same thing if he's in therapy or it's just recreational use. You will have a better therapeutic alliance with them and he will call you up and it'll probably be not just at whims of his serotonergic system, but it will have to do with the material that came up in the session. It's easier to deal with than just Wednesday blues.

Ben Sessa: I think we should wind this up, mainly because otherwise it will not stop. [Laughing] I mean for me...firstly I just want to thank all of our panel and all of you lot for really making my day. It's been a tremendous afternoon looking at all of these issues and this has been the icing on the cake. It's really good to get everyone together, yourselves [the audience] and these guys here [the panel]. Thank you very much. I mean for me we're talking about...Let's all take this forward. Let's bear in mind that we have to look at MDMA versus ecstasy, we have to look at clinical versus recreational, and we have to look at risk versus benefits, because otherwise we're going to get confused. Thank you all so much. Have a lovely evening.