

WEBVTT

NOTE duration:"00:57:27.6900000"

NOTE recognizability:0.932

NOTE language:en-us

NOTE Confidence: 0.9338238

00:00:05.120 --> 00:00:06.464 Thank you everyone for being

NOTE Confidence: 0.9338238

00:00:06.464 --> 00:00:08.120 here on our first meeting for

NOTE Confidence: 0.9338238

00:00:08.175 --> 00:00:10.275 this academic year of our monthly

NOTE Confidence: 0.9338238

00:00:10.275 --> 00:00:11.675 seminar and Psychedelic Science.

NOTE Confidence: 0.9338238

00:00:11.680 --> 00:00:13.186 It's great to see such a

NOTE Confidence: 0.9338238

00:00:13.186 --> 00:00:14.600 a varied and large group.

NOTE Confidence: 0.9338238

00:00:14.600 --> 00:00:16.950 I'm sure we'll have more joining and

NOTE Confidence: 0.9338238

00:00:16.950 --> 00:00:18.560 we'll also as always be recording this,

NOTE Confidence: 0.9338238

00:00:18.560 --> 00:00:20.331 so as as almost always be recording

NOTE Confidence: 0.9338238

00:00:20.331 --> 00:00:22.804 this so we can get to an even broader

NOTE Confidence: 0.9338238

00:00:22.804 --> 00:00:24.520 audience within the old community.

NOTE Confidence: 0.9338238

00:00:24.520 --> 00:00:27.226 We are really privileged today to

NOTE Confidence: 0.9338238

00:00:27.226 --> 00:00:29.831 have Harriet do it speaking with us,

NOTE Confidence: 0.9338238

00:00:29.831 --> 00:00:31.166 someone who who really needs
NOTE Confidence: 0.9338238

00:00:31.166 --> 00:00:32.349 no introduction in this group.
NOTE Confidence: 0.9338238

00:00:32.350 --> 00:00:34.468 And so I'll be very brief.
NOTE Confidence: 0.9338238

00:00:34.470 --> 00:00:36.018 She's Professor of Psychiatry
NOTE Confidence: 0.9338238

00:00:36.018 --> 00:00:37.566 and Behavioral Neuroscience at
NOTE Confidence: 0.9338238

00:00:37.566 --> 00:00:39.207 the University of Chicago and
NOTE Confidence: 0.9338238

00:00:39.207 --> 00:00:40.989 she's been active in this space
NOTE Confidence: 0.9338238

00:00:40.989 --> 00:00:42.870 for longer than than most of us,
NOTE Confidence: 0.9338238

00:00:42.870 --> 00:00:44.230 certainly longer than me.
NOTE Confidence: 0.9338238

00:00:44.230 --> 00:00:47.010 And a lot of lot of interesting and
NOTE Confidence: 0.9338238

00:00:47.010 --> 00:00:48.860 provocative work over the years
NOTE Confidence: 0.9338238

00:00:48.860 --> 00:00:50.735 including work in microdoses recently
NOTE Confidence: 0.9338238

00:00:50.735 --> 00:00:53.206 which is something that where that I
NOTE Confidence: 0.9338238

00:00:53.206 --> 00:00:55.270 think that the ratio of use to data
NOTE Confidence: 0.9338238

00:00:55.270 --> 00:01:00.470 is vastly broader than than in even in
NOTE Confidence: 0.9338238

00:01:00.470 --> 00:01:03.950 the other the the macro dosing field.

NOTE Confidence: 0.9338238

00:01:03.950 --> 00:01:06.260 So really excited to have you here.

NOTE Confidence: 0.9338238

00:01:06.260 --> 00:01:09.176 Harriet thank you for joining us and very,

NOTE Confidence: 0.9338238

00:01:09.176 --> 00:01:12.020 very excited we have to share with us today.

NOTE Confidence: 0.92649025

00:01:12.180 --> 00:01:12.984 All right, great.

NOTE Confidence: 0.92649025

00:01:12.984 --> 00:01:14.860 It's a real pleasure to be here.

NOTE Confidence: 0.92649025

00:01:14.860 --> 00:01:17.058 And let me just make sure that.

NOTE Confidence: 0.9256157

00:01:29.850 --> 00:01:31.728 How's that? Is that all right?

NOTE Confidence: 0.9256157

00:01:31.730 --> 00:01:33.338 Can you see it? Yep. All right.

NOTE Confidence: 0.9256157

00:01:33.338 --> 00:01:34.970 Well, it's a real pleasure to be here.

NOTE Confidence: 0.9256157

00:01:34.970 --> 00:01:37.322 And, you know, I'm a little

NOTE Confidence: 0.9256157

00:01:37.322 --> 00:01:38.890 intimidated by this audience,

NOTE Confidence: 0.9256157

00:01:38.890 --> 00:01:41.284 so I'm happy to turn it into

NOTE Confidence: 0.9256157

00:01:41.284 --> 00:01:43.328 a discussion as we go along.

NOTE Confidence: 0.9256157

00:01:43.330 --> 00:01:45.304 I think there's lots of just

NOTE Confidence: 0.9256157

00:01:45.304 --> 00:01:46.977 interesting issues that come along

NOTE Confidence: 0.9256157

00:01:46.977 --> 00:01:49.049 all along the way that interest us.
NOTE Confidence: 0.9256157

00:01:49.050 --> 00:01:51.875 Also, please feel free to
NOTE Confidence: 0.9256157

00:01:51.875 --> 00:01:53.830 interrupt and contribute your
NOTE Confidence: 0.9256157

00:01:53.830 --> 00:01:55.880 thoughts and knowledge and ideas.
NOTE Confidence: 0.9256157

00:01:55.880 --> 00:01:57.995 So I am gonna talk a little bit about
NOTE Confidence: 0.9256157

00:01:57.995 --> 00:02:00.335 our work with micro dosing and I have
NOTE Confidence: 0.9256157

00:02:00.335 --> 00:02:02.493 a few disclosures here that are not
NOTE Confidence: 0.9256157

00:02:02.493 --> 00:02:04.317 really relevant to the LSD studies.
NOTE Confidence: 0.92597395

00:02:06.400 --> 00:02:08.920 I just gotta get rid of this.
NOTE Confidence: 0.92597395

00:02:08.920 --> 00:02:10.960 There we go. So what is micro dosing?
NOTE Confidence: 0.92597395

00:02:10.960 --> 00:02:13.150 I'm sure you're all familiar with
NOTE Confidence: 0.92597395

00:02:13.150 --> 00:02:15.673 the idea that it's the use of
NOTE Confidence: 0.92597395

00:02:15.673 --> 00:02:17.653 low doses of LSD and sometimes
NOTE Confidence: 0.92597395

00:02:17.653 --> 00:02:19.878 other psychedelic drugs as well.
NOTE Confidence: 0.92597395

00:02:19.880 --> 00:02:22.598 People take it once every three or four days,
NOTE Confidence: 0.92597395

00:02:22.600 --> 00:02:25.320 and they claim that it improves their mood,

NOTE Confidence: 0.92597395

00:02:25.320 --> 00:02:28.240 their cognition, their created creativity,

NOTE Confidence: 0.92597395

00:02:28.240 --> 00:02:32.372 and lots of other response measures as well.

NOTE Confidence: 0.92597395

00:02:32.372 --> 00:02:36.186 The doses that people take are about a

NOTE Confidence: 0.92597395

00:02:36.186 --> 00:02:39.048 tenth of the tripping psychedelic dose,

NOTE Confidence: 0.92597395

00:02:39.050 --> 00:02:41.396 and the practice is extremely widespread

NOTE Confidence: 0.92597395

00:02:41.396 --> 00:02:44.248 and it's had a lot of publicity,

NOTE Confidence: 0.92597395

00:02:44.250 --> 00:02:45.516 positive publicity.

NOTE Confidence: 0.92597395

00:02:45.516 --> 00:02:48.048 On the other hand,

NOTE Confidence: 0.92597395

00:02:48.050 --> 00:02:49.418 as was just mentioned,

NOTE Confidence: 0.92597395

00:02:49.418 --> 00:02:51.470 there have been very few controlled

NOTE Confidence: 0.92597395

00:02:51.530 --> 00:02:53.074 studies to really validate

NOTE Confidence: 0.92597395

00:02:53.074 --> 00:02:55.004 whether these claims have merit.

NOTE Confidence: 0.94744205

00:03:00.370 --> 00:03:03.346 Here are some of the popular So again

NOTE Confidence: 0.94744205

00:03:03.346 --> 00:03:05.714 it's been really popular in the media.

NOTE Confidence: 0.94744205

00:03:05.714 --> 00:03:08.607 And here are a few of the books that

NOTE Confidence: 0.94744205

00:03:08.607 --> 00:03:10.243 have been published specifically
NOTE Confidence: 0.94744205

00:03:10.243 --> 00:03:12.468 about micro dosing and the claims
NOTE Confidence: 0.94744205

00:03:12.468 --> 00:03:14.328 that they make are very broad.
NOTE Confidence: 0.94744205

00:03:14.330 --> 00:03:17.291 So here's one, the first one there is to
NOTE Confidence: 0.94744205

00:03:17.291 --> 00:03:19.888 improve your physical and mental health.
NOTE Confidence: 0.94744205

00:03:19.890 --> 00:03:22.806 Another one is safe, sacred journeys,
NOTE Confidence: 0.94744205

00:03:22.810 --> 00:03:24.808 another to upgrade your life and
NOTE Confidence: 0.94744205

00:03:24.808 --> 00:03:26.810 another one to improve your mood,
NOTE Confidence: 0.94744205

00:03:26.810 --> 00:03:28.290 your marriage and your life.
NOTE Confidence: 0.94744205

00:03:28.290 --> 00:03:30.690 So these are pretty general claims
NOTE Confidence: 0.94744205

00:03:30.690 --> 00:03:33.928 to kind of put to scientific test.
NOTE Confidence: 0.94744205

00:03:33.930 --> 00:03:38.169 So our question when we got into this work,
NOTE Confidence: 0.94744205

00:03:38.170 --> 00:03:39.490 I'm sorry something
NOTE Confidence: 0.9324826

00:03:41.770 --> 00:03:43.440 light touch. So the question
NOTE Confidence: 0.9324826

00:03:43.440 --> 00:03:45.370 that we put to ourselves is,
NOTE Confidence: 0.9324826

00:03:45.370 --> 00:03:47.302 is really does it work and it's

NOTE Confidence: 0.9324826

00:03:47.302 --> 00:03:49.320 something that we can look at

NOTE Confidence: 0.9324826

00:03:49.320 --> 00:03:50.448 under laboratory conditions.

NOTE Confidence: 0.9324826

00:03:50.450 --> 00:03:53.026 And there are reasons both to be

NOTE Confidence: 0.9324826

00:03:53.026 --> 00:03:54.976 optimistic about whether it actually

NOTE Confidence: 0.9324826

00:03:54.976 --> 00:03:57.304 works at a pharmacological levels and

NOTE Confidence: 0.9324826

00:03:57.304 --> 00:03:59.889 also there is reasons to be skeptical.

NOTE Confidence: 0.9324826

00:03:59.890 --> 00:04:02.025 From the point of view of does

NOTE Confidence: 0.9324826

00:04:02.025 --> 00:04:03.890 up to be optimistic.

NOTE Confidence: 0.9324826

00:04:03.890 --> 00:04:06.378 The fact that so many people are using

NOTE Confidence: 0.9324826

00:04:06.378 --> 00:04:08.810 it and claiming benefits from it

NOTE Confidence: 0.9324826

00:04:08.810 --> 00:04:11.010 suggests that there's something there.

NOTE Confidence: 0.9324826

00:04:11.010 --> 00:04:13.290 It seems like if it's completely

NOTE Confidence: 0.9324826

00:04:13.290 --> 00:04:15.264 a snake oil then people would

NOTE Confidence: 0.9324826

00:04:15.264 --> 00:04:17.410 drop off and their enthusiasm.

NOTE Confidence: 0.9324826

00:04:17.410 --> 00:04:19.822 So the the widespread use is one reason to

NOTE Confidence: 0.9324826

00:04:19.822 --> 00:04:22.170 think that there might be something there.

NOTE Confidence: 0.9324826

00:04:22.170 --> 00:04:24.420 There are also plausible neural

NOTE Confidence: 0.9324826

00:04:24.420 --> 00:04:26.670 mechanisms that you are probably

NOTE Confidence: 0.9324826

00:04:26.748 --> 00:04:28.788 more familiar with than I am.

NOTE Confidence: 0.9324826

00:04:28.790 --> 00:04:29.578 Of course,

NOTE Confidence: 0.9324826

00:04:29.578 --> 00:04:31.548 LSD acts on serotonin receptors,

NOTE Confidence: 0.9324826

00:04:31.550 --> 00:04:34.424 which is the same as receptor system

NOTE Confidence: 0.9324826

00:04:34.424 --> 00:04:36.709 that antidepressant drugs work on,

NOTE Confidence: 0.9324826

00:04:36.710 --> 00:04:39.014 and there's evidence that it might

NOTE Confidence: 0.9324826

00:04:39.014 --> 00:04:40.550 have antiinflammatory effects and

NOTE Confidence: 0.9324826

00:04:40.606 --> 00:04:42.466 it might have neurogenic effects.

NOTE Confidence: 0.9324826

00:04:42.470 --> 00:04:44.535 So there's some plausible neural

NOTE Confidence: 0.9324826

00:04:44.535 --> 00:04:47.121 mechanisms by which it might have

NOTE Confidence: 0.9324826

00:04:47.121 --> 00:04:49.376 some sort of antidepressant effect.

NOTE Confidence: 0.9324826

00:04:49.380 --> 00:04:51.580 There are also very promising

NOTE Confidence: 0.9324826

00:04:51.580 --> 00:04:53.780 clinical reports with high doses

NOTE Confidence: 0.9324826

00:04:53.855 --> 00:04:56.235 of LSD that high doses of LSD

NOTE Confidence: 0.9324826

00:04:56.235 --> 00:04:58.585 reduce symptoms of depression in

NOTE Confidence: 0.9324826

00:04:58.585 --> 00:05:00.460 treatment resentment patients,

NOTE Confidence: 0.9324826

00:05:00.460 --> 00:05:01.920 and there's also some

NOTE Confidence: 0.9324826

00:05:01.920 --> 00:05:03.380 evidence from animal models.

NOTE Confidence: 0.9330807

00:05:05.540 --> 00:05:07.700 There are also reasons to be

NOTE Confidence: 0.9330807

00:05:07.700 --> 00:05:09.140 skeptical about the claims.

NOTE Confidence: 0.9330807

00:05:09.140 --> 00:05:11.060 First of all, and most importantly,

NOTE Confidence: 0.9330807

00:05:11.060 --> 00:05:13.600 the users claims are deeply

NOTE Confidence: 0.9330807

00:05:13.600 --> 00:05:15.632 confounded by their expectancies.

NOTE Confidence: 0.9330807

00:05:15.640 --> 00:05:17.952 Nobody uses a drug like this on a

NOTE Confidence: 0.9330807

00:05:17.952 --> 00:05:19.454 regular basis without expecting

NOTE Confidence: 0.9330807

00:05:19.454 --> 00:05:21.604 some sort of beneficial effects

NOTE Confidence: 0.9330807

00:05:21.604 --> 00:05:23.638 and they'll continue to take it.

NOTE Confidence: 0.9330807

00:05:23.640 --> 00:05:26.279 And any effects that they do experience

NOTE Confidence: 0.9330807

00:05:26.279 --> 00:05:28.976 are then interpreted often as as
NOTE Confidence: 0.9330807

00:05:28.976 --> 00:05:31.396 being beneficial or or supportive.
NOTE Confidence: 0.9330807

00:05:31.400 --> 00:05:33.470 And so it's it's really difficult
NOTE Confidence: 0.9330807

00:05:33.470 --> 00:05:35.357 to determine whether it's really
NOTE Confidence: 0.9330807

00:05:35.357 --> 00:05:36.695 the pharmacological effects
NOTE Confidence: 0.9330807

00:05:36.695 --> 00:05:38.479 or the expectancy effects.
NOTE Confidence: 0.9330807

00:05:38.480 --> 00:05:38.846 Secondly,
NOTE Confidence: 0.9330807

00:05:38.846 --> 00:05:40.676 the pharmacology of these very
NOTE Confidence: 0.9330807

00:05:40.676 --> 00:05:42.880 low doses is poorly understood.
NOTE Confidence: 0.9330807

00:05:42.880 --> 00:05:44.596 We don't know what the optimal
NOTE Confidence: 0.9330807

00:05:44.596 --> 00:05:46.200 doses are for micro dosing.
NOTE Confidence: 0.9330807

00:05:46.200 --> 00:05:48.216 We don't know what the receptor
NOTE Confidence: 0.9330807

00:05:48.216 --> 00:05:50.519 actions of these very low doses are.
NOTE Confidence: 0.9330807

00:05:50.520 --> 00:05:53.358 So without knowing the pharmacology well,
NOTE Confidence: 0.9330807

00:05:53.360 --> 00:05:56.440 it's hard to really go into a a
NOTE Confidence: 0.9330807

00:05:56.440 --> 00:05:58.781 clinical investigation of of and

NOTE Confidence: 0.9330807

00:05:58.781 --> 00:06:00.278 possible antidepressant effects.

NOTE Confidence: 0.9330807

00:06:00.280 --> 00:06:02.422 And one of the things that concerns

NOTE Confidence: 0.9330807

00:06:02.422 --> 00:06:05.164 me is the heterogeneity of the of

NOTE Confidence: 0.9330807

00:06:05.164 --> 00:06:07.354 the claimed and apparent benefits.

NOTE Confidence: 0.9330807

00:06:07.360 --> 00:06:09.229 And here's just a brief listing of

NOTE Confidence: 0.9330807

00:06:09.229 --> 00:06:11.348 some of the claims that people have

NOTE Confidence: 0.9330807

00:06:11.348 --> 00:06:13.368 made along the way. They improve.

NOTE Confidence: 0.9330807

00:06:13.368 --> 00:06:15.672 They claim that the drug improves

NOTE Confidence: 0.9330807

00:06:15.672 --> 00:06:16.440 their creativity,

NOTE Confidence: 0.9330807

00:06:16.440 --> 00:06:18.000 which actually turns out to

NOTE Confidence: 0.9330807

00:06:18.000 --> 00:06:19.560 be very difficult to measure.

NOTE Confidence: 0.9330807

00:06:19.560 --> 00:06:22.440 That improves energy, productivity, focus.

NOTE Confidence: 0.9330807

00:06:22.440 --> 00:06:23.240 I won't read them all,

NOTE Confidence: 0.9330807

00:06:23.240 --> 00:06:25.487 but you can see that there's quite

NOTE Confidence: 0.9330807

00:06:25.487 --> 00:06:27.110 a variety spiritual awareness,

NOTE Confidence: 0.9330807

00:06:27.110 --> 00:06:28.292 leadership, develop wisdom,
NOTE Confidence: 0.9330807

00:06:28.292 --> 00:06:29.868 so all these claims,
NOTE Confidence: 0.9330807

00:06:29.870 --> 00:06:32.270 so it's our job as pharmacologist,
NOTE Confidence: 0.9330807

00:06:32.270 --> 00:06:34.326 psychopharmacologist to figure out
NOTE Confidence: 0.9330807

00:06:34.326 --> 00:06:37.502 which of these have an empirical basis
NOTE Confidence: 0.9330807

00:06:37.502 --> 00:06:39.950 and then of course decreased depression,
NOTE Confidence: 0.9330807

00:06:39.950 --> 00:06:42.230 anxiety and even menopausal symptoms.
NOTE Confidence: 0.9330807

00:06:42.230 --> 00:06:44.168 So it seems unlikely that one
NOTE Confidence: 0.9330807

00:06:44.168 --> 00:06:46.628 drug could do all of these things.
NOTE Confidence: 0.9330807

00:06:46.630 --> 00:06:49.326 And so it's our job to try and
NOTE Confidence: 0.9330807

00:06:49.326 --> 00:06:51.407 figure out what does it do.
NOTE Confidence: 0.9330807

00:06:51.410 --> 00:06:53.566 So there's a need for controlled studies.
NOTE Confidence: 0.9330807

00:06:53.570 --> 00:06:56.510 What are its effects on either mood
NOTE Confidence: 0.9330807

00:06:56.510 --> 00:06:58.490 or objective behavioral measures?
NOTE Confidence: 0.9330807

00:06:58.490 --> 00:07:00.450 Who benefits? So does it.
NOTE Confidence: 0.9330807

00:07:00.450 --> 00:07:03.138 The are the effects of the drug

NOTE Confidence: 0.9330807

00:07:03.138 --> 00:07:05.170 dependent on the either psychiatric

NOTE Confidence: 0.9330807

00:07:05.170 --> 00:07:06.930 symptoms or personality or

NOTE Confidence: 0.9330807

00:07:06.930 --> 00:07:09.450 preexisting state of the individual?

NOTE Confidence: 0.9330807

00:07:09.450 --> 00:07:10.545 Who's taking it?

NOTE Confidence: 0.9330807

00:07:10.545 --> 00:07:13.100 At what doses is the drug effective

NOTE Confidence: 0.9330807

00:07:13.175 --> 00:07:14.367 and for how long?

NOTE Confidence: 0.9330807

00:07:14.370 --> 00:07:16.946 And what exactly is the role of

NOTE Confidence: 0.9330807

00:07:16.946 --> 00:07:17.682 the expectancies?

NOTE Confidence: 0.9330807

00:07:17.690 --> 00:07:21.536 So the expectancies you could get

NOTE Confidence: 0.9330807

00:07:21.540 --> 00:07:23.400 apparently beneficial effects

NOTE Confidence: 0.9330807

00:07:23.400 --> 00:07:25.260 purely from expectancy,

NOTE Confidence: 0.9330807

00:07:25.260 --> 00:07:28.095 or it could be that the expectancy

NOTE Confidence: 0.9330807

00:07:28.095 --> 00:07:30.518 could interact with the pharmacological

NOTE Confidence: 0.9330807

00:07:30.518 --> 00:07:33.896 effects to produce some desired outcome.

NOTE Confidence: 0.9330807

00:07:33.900 --> 00:07:35.365 Some of the preclinical evidence

NOTE Confidence: 0.9330807

00:07:35.365 --> 00:07:37.588 that you as a group are probably
NOTE Confidence: 0.9330807

00:07:37.588 --> 00:07:38.980 very familiar with that.
NOTE Confidence: 0.9330807

00:07:38.980 --> 00:07:40.040 For example,
NOTE Confidence: 0.9330807

00:07:40.040 --> 00:07:42.160 repeated LSD normalized active
NOTE Confidence: 0.9330807

00:07:42.160 --> 00:07:43.220 avoidance learning,
NOTE Confidence: 0.9330807

00:07:43.220 --> 00:07:45.782 which is a model of depression,
NOTE Confidence: 0.9330807

00:07:45.782 --> 00:07:47.146 antidepressant effect,
NOTE Confidence: 0.9330807

00:07:47.146 --> 00:07:49.874 and reverse signaling abnormalities.
NOTE Confidence: 0.9330807

00:07:49.880 --> 00:07:52.620 In the olfactory bulbectomy model
NOTE Confidence: 0.9330807

00:07:52.620 --> 00:07:54.533 of depression neurogenesis,
NOTE Confidence: 0.9330807

00:07:54.533 --> 00:07:58.598 LSD reportedly increases indicators of
NOTE Confidence: 0.9330807

00:07:58.598 --> 00:08:01.948 neural neuronal growth social behavior.
NOTE Confidence: 0.9330807

00:08:01.948 --> 00:08:04.218 Repeated LSD increased social behavior
NOTE Confidence: 0.9330807

00:08:04.218 --> 00:08:07.522 in my since a series of very elegant
NOTE Confidence: 0.9330807

00:08:07.522 --> 00:08:09.976 studies coming from McGill and also
NOTE Confidence: 0.9330807

00:08:09.976 --> 00:08:12.040 similarly stress induced anxiety.

NOTE Confidence: 0.9330807

00:08:12.040 --> 00:08:14.770 Repeated LSD reversed stress into

NOTE Confidence: 0.9330807

00:08:14.770 --> 00:08:17.911 induced anxiety like behavior in mice.

NOTE Confidence: 0.9330807

00:08:17.911 --> 00:08:20.377 So these are all very promising

NOTE Confidence: 0.9330807

00:08:20.377 --> 00:08:22.340 bits of preclinical evidence.

NOTE Confidence: 0.9330807

00:08:22.340 --> 00:08:24.743 And I I I'd like to just say that

NOTE Confidence: 0.9330807

00:08:24.743 --> 00:08:26.960 one of my particular interests is

NOTE Confidence: 0.9330807

00:08:26.960 --> 00:08:29.951 to try and bridge what gets found in

NOTE Confidence: 0.9330807

00:08:29.951 --> 00:08:32.373 the animal studies and what we can

NOTE Confidence: 0.9262907

00:08:32.380 --> 00:08:35.656 study in humans. So I I I see that

NOTE Confidence: 0.9262907

00:08:35.660 --> 00:08:37.736 there's a need for really parallel,

NOTE Confidence: 0.9262907

00:08:37.740 --> 00:08:39.570 closely parallel studies in the

NOTE Confidence: 0.9262907

00:08:39.570 --> 00:08:41.985 animals and in the humans to as

NOTE Confidence: 0.9262907

00:08:41.985 --> 00:08:44.568 sort of a proof of concept to go on

NOTE Confidence: 0.9262907

00:08:44.568 --> 00:08:46.644 to figure out what the mechanisms

NOTE Confidence: 0.9262907

00:08:46.644 --> 00:08:49.330 are underlying these drug effects.

NOTE Confidence: 0.9262907

00:08:49.330 --> 00:08:52.410 So a number of studies have been published

NOTE Confidence: 0.9262907

00:08:52.410 --> 00:08:55.124 with humans and there is one whole

NOTE Confidence: 0.9262907

00:08:55.124 --> 00:08:57.450 category of survey, self report study.

NOTE Confidence: 0.9262907

00:08:57.450 --> 00:08:59.850 So these are usually Internet studies,

NOTE Confidence: 0.9262907

00:08:59.850 --> 00:09:02.218 online studies where they ask you are you

NOTE Confidence: 0.9262907

00:09:02.218 --> 00:09:04.925 a micro doser and do you like the effects,

NOTE Confidence: 0.9262907

00:09:04.930 --> 00:09:06.690 Do you get beneficial effects?

NOTE Confidence: 0.9262907

00:09:06.690 --> 00:09:08.034 And you can see that there

NOTE Confidence: 0.9262907

00:09:08.034 --> 00:09:09.730 might be a real bias in there.

NOTE Confidence: 0.9262907

00:09:09.730 --> 00:09:11.226 Those studies,

NOTE Confidence: 0.9262907

00:09:11.226 --> 00:09:14.520 those survey questionnaires rarely reveal

NOTE Confidence: 0.9262907

00:09:14.520 --> 00:09:17.670 lack of effect or negative effects,

NOTE Confidence: 0.9262907

00:09:17.670 --> 00:09:19.178 are almost always positive.

NOTE Confidence: 0.9262907

00:09:19.178 --> 00:09:20.309 And so again,

NOTE Confidence: 0.9262907

00:09:20.310 --> 00:09:22.360 they're very much influenced by

NOTE Confidence: 0.9262907

00:09:22.360 --> 00:09:24.790 expectancies and then by selection bias.

NOTE Confidence: 0.9262907

00:09:24.790 --> 00:09:25.396 That is,

NOTE Confidence: 0.9262907

00:09:25.396 --> 00:09:27.820 the people who report on them are generally

NOTE Confidence: 0.9262907

00:09:27.887 --> 00:09:29.987 enthusiastic about the drug effects.

NOTE Confidence: 0.9262907

00:09:29.990 --> 00:09:32.918 There was a very interesting citizen

NOTE Confidence: 0.9262907

00:09:32.918 --> 00:09:35.846 science study by Zaggetti in 2021

NOTE Confidence: 0.9262907

00:09:35.846 --> 00:09:39.312 where they allowed micro dosers to

NOTE Confidence: 0.9262907

00:09:39.312 --> 00:09:41.802 blind their own Drug Administration

NOTE Confidence: 0.9262907

00:09:41.802 --> 00:09:44.560 in their own home environment.

NOTE Confidence: 0.9262907

00:09:44.560 --> 00:09:47.612 So they used their own drug and they were

NOTE Confidence: 0.9262907

00:09:47.612 --> 00:09:49.880 at the the researchers allowed them to

NOTE Confidence: 0.9298195

00:09:53.150 --> 00:09:55.026 sort of formulate put their drugs into

NOTE Confidence: 0.9298195

00:09:55.026 --> 00:09:57.028 envelope so that they didn't know what

NOTE Confidence: 0.9298195

00:09:57.028 --> 00:09:58.750 they were getting but the researchers

NOTE Confidence: 0.9298195

00:09:58.804 --> 00:10:00.508 didn't know what they were getting.

NOTE Confidence: 0.9298195

00:10:00.510 --> 00:10:02.902 So that then they over a period of

NOTE Confidence: 0.9298195

00:10:02.902 --> 00:10:04.618 several weeks they got either placebo
NOTE Confidence: 0.9298195

00:10:04.618 --> 00:10:07.353 or a low dose or a higher dose of
NOTE Confidence: 0.9298195

00:10:07.353 --> 00:10:09.183 their preferred micro dose drug.
NOTE Confidence: 0.9298195

00:10:09.190 --> 00:10:11.185 And it was. It's an elegant study.
NOTE Confidence: 0.9298195

00:10:11.190 --> 00:10:13.702 And basically though their
NOTE Confidence: 0.9298195

00:10:13.702 --> 00:10:16.625 conclusion was that they saw some
NOTE Confidence: 0.9298195

00:10:16.625 --> 00:10:18.350 beneficial effects of micro dosing.
NOTE Confidence: 0.9298195

00:10:18.350 --> 00:10:20.672 But when they took into account
NOTE Confidence: 0.9298195

00:10:20.672 --> 00:10:22.657 the people who recognized that
NOTE Confidence: 0.9298195

00:10:22.657 --> 00:10:24.865 they had received an active drug,
NOTE Confidence: 0.9298195

00:10:24.870 --> 00:10:27.948 the if the beneficial effects disappeared.
NOTE Confidence: 0.9298195

00:10:27.950 --> 00:10:31.070 And so they concluded from this
NOTE Confidence: 0.9298195

00:10:31.070 --> 00:10:34.922 that they were unable to exclude the
NOTE Confidence: 0.9298195

00:10:34.922 --> 00:10:37.106 possibility that people's expectancies,
NOTE Confidence: 0.9298195

00:10:37.110 --> 00:10:39.294 that is their idea that they
NOTE Confidence: 0.9298195

00:10:39.294 --> 00:10:40.750 might have beneficial effects,

NOTE Confidence: 0.9298195

00:10:40.750 --> 00:10:42.278 could have accounted for

NOTE Confidence: 0.9298195

00:10:42.278 --> 00:10:43.424 the beneficial effects.

NOTE Confidence: 0.9298195

00:10:43.430 --> 00:10:46.390 Now researchers have come up with this idea

NOTE Confidence: 0.9298195

00:10:46.390 --> 00:10:49.629 that for something to be a true micro dose,

NOTE Confidence: 0.9298195

00:10:49.630 --> 00:10:52.726 it has to be below the

NOTE Confidence: 0.9298195

00:10:52.726 --> 00:10:54.790 detectable threshold of effects.

NOTE Confidence: 0.9298195

00:10:54.790 --> 00:10:57.958 So and so that this is a very

NOTE Confidence: 0.9298195

00:10:57.958 --> 00:10:58.750 stringent criterion.

NOTE Confidence: 0.9298195

00:10:58.750 --> 00:11:00.766 So you're giving a drug and you see no

NOTE Confidence: 0.9298195

00:11:00.766 --> 00:11:02.722 self reported effects and they're hoping

NOTE Confidence: 0.9298195

00:11:02.722 --> 00:11:04.870 that it will have beneficial effects.

NOTE Confidence: 0.9298195

00:11:04.870 --> 00:11:06.970 From my point of view,

NOTE Confidence: 0.9298195

00:11:06.970 --> 00:11:09.364 I think this is too stringent criterion.

NOTE Confidence: 0.9298195

00:11:09.370 --> 00:11:11.785 I think it's possible that people who

NOTE Confidence: 0.9298195

00:11:11.785 --> 00:11:14.393 are micro dosing out in the world

NOTE Confidence: 0.9298195

00:11:14.393 --> 00:11:16.278 are actually experiencing some subtle
NOTE Confidence: 0.9298195

00:11:16.278 --> 00:11:18.910 drug effects and so it might be unfair
NOTE Confidence: 0.9298195

00:11:18.910 --> 00:11:20.738 to exclude them completely and you
NOTE Confidence: 0.9298195

00:11:20.738 --> 00:11:22.514 might be excluding the very people
NOTE Confidence: 0.9298195

00:11:22.514 --> 00:11:24.367 who might get beneficial effects.
NOTE Confidence: 0.9298195

00:11:24.370 --> 00:11:27.314 It's a very difficult,
NOTE Confidence: 0.9298195

00:11:27.314 --> 00:11:30.958 troublesome methodological issue to overcome.
NOTE Confidence: 0.9298195

00:11:30.960 --> 00:11:31.836 In any case,
NOTE Confidence: 0.9298195

00:11:31.836 --> 00:11:33.880 the citizen science study was was good.
NOTE Confidence: 0.9298195

00:11:33.880 --> 00:11:35.600 It showed some beneficial effects,
NOTE Confidence: 0.9298195

00:11:35.600 --> 00:11:38.800 but not if you excluded the people who
NOTE Confidence: 0.9298195

00:11:38.800 --> 00:11:41.237 correctly identified the drug that they got.
NOTE Confidence: 0.9298195

00:11:41.240 --> 00:11:44.705 So then we've done a series of
NOTE Confidence: 0.9298195

00:11:44.705 --> 00:11:46.313 laboratory based studies under
NOTE Confidence: 0.9298195

00:11:46.313 --> 00:11:47.797 double-blind conditions and I'll
NOTE Confidence: 0.9298195

00:11:47.797 --> 00:11:49.439 describe those to you here.

NOTE Confidence: 0.94028884
00:11:51.760 --> 00:11:54.000 These are done with healthy
NOTE Confidence: 0.94028884
00:11:54.000 --> 00:11:56.240 volunteers for the most part.
NOTE Confidence: 0.94028884
00:11:56.240 --> 00:11:58.000 They're also done under
NOTE Confidence: 0.94028884
00:11:58.000 --> 00:11:58.880 double-blind conditions.
NOTE Confidence: 0.94028884
00:11:58.880 --> 00:12:01.028 And in our laboratory we are
NOTE Confidence: 0.94028884
00:12:01.028 --> 00:12:03.136 able to administer drugs under
NOTE Confidence: 0.94028884
00:12:03.136 --> 00:12:04.960 truly double-blind conditions.
NOTE Confidence: 0.94028884
00:12:04.960 --> 00:12:06.658 So we tell the participants that
NOTE Confidence: 0.94028884
00:12:06.658 --> 00:12:08.243 they might receive any of a
NOTE Confidence: 0.94028884
00:12:08.243 --> 00:12:09.643 wide range of drugs so that we
NOTE Confidence: 0.94028884
00:12:09.643 --> 00:12:11.237 say you might get a stimulant,
NOTE Confidence: 0.94028884
00:12:11.240 --> 00:12:12.400 you might get a tranquilizer,
NOTE Confidence: 0.94028884
00:12:12.400 --> 00:12:13.800 you might get a hallucinogen,
NOTE Confidence: 0.94028884
00:12:13.800 --> 00:12:15.840 A placebo and some studies and
NOTE Confidence: 0.94028884
00:12:15.840 --> 00:12:17.920 antihistamine or a or a alcohol.
NOTE Confidence: 0.94028884

00:12:17.920 --> 00:12:20.512 So we give them a whole range of
NOTE Confidence: 0.94028884

00:12:20.512 --> 00:12:22.136 different possible categories of drugs.
NOTE Confidence: 0.94028884

00:12:22.136 --> 00:12:24.647 So they really don't know what kind of
NOTE Confidence: 0.94028884

00:12:24.647 --> 00:12:26.679 drug they're going to get in the study.
NOTE Confidence: 0.94028884

00:12:26.680 --> 00:12:28.738 And we believe and I think there's
NOTE Confidence: 0.94028884

00:12:28.738 --> 00:12:31.180 good reason to think that if you just
NOTE Confidence: 0.94028884

00:12:31.180 --> 00:12:33.340 told them either alcohol or placebo or
NOTE Confidence: 0.94028884

00:12:33.340 --> 00:12:36.630 only MDMA or placebo then or LSD or placebo,
NOTE Confidence: 0.94028884

00:12:36.630 --> 00:12:38.736 then they're going to be very much biased
NOTE Confidence: 0.94028884

00:12:38.736 --> 00:12:40.878 that any drug effect that they experience,
NOTE Confidence: 0.94028884

00:12:40.880 --> 00:12:42.357 they're going to attribute to the drug.
NOTE Confidence: 0.94028884

00:12:42.360 --> 00:12:44.709 So we go to a lot of trouble to
NOTE Confidence: 0.94028884

00:12:44.709 --> 00:12:46.286 really do this extra blinding.
NOTE Confidence: 0.94028884

00:12:46.286 --> 00:12:48.967 Most of our studies have been with
NOTE Confidence: 0.94028884

00:12:48.967 --> 00:12:51.476 single doses of the drugs and
NOTE Confidence: 0.94028884

00:12:51.476 --> 00:12:53.120 we measure behavioral responses,

NOTE Confidence: 0.94028884

00:12:53.120 --> 00:12:56.720 so measure different tasks and

NOTE Confidence: 0.94028884

00:12:56.720 --> 00:12:57.902 different mood measures.

NOTE Confidence: 0.94028884

00:12:57.902 --> 00:13:00.266 We also have done some studies

NOTE Confidence: 0.94028884

00:13:00.266 --> 00:13:02.718 with EE G and FM RI and then we've

NOTE Confidence: 0.94028884

00:13:02.718 --> 00:13:04.599 done one study where we give,

NOTE Confidence: 0.94028884

00:13:04.600 --> 00:13:07.520 we gave repeated doses in the same people.

NOTE Confidence: 0.94028884

00:13:07.520 --> 00:13:09.110 So I'll describe those studies to

NOTE Confidence: 0.94028884

00:13:09.110 --> 00:13:11.037 you and I'll also very briefly at

NOTE Confidence: 0.94028884

00:13:11.037 --> 00:13:12.657 the end describe a recent study

NOTE Confidence: 0.94028884

00:13:12.657 --> 00:13:14.310 that was published by Murphy at

NOTE Confidence: 0.94028884

00:13:14.310 --> 00:13:16.270 all where they used both laboratory

NOTE Confidence: 0.94028884

00:13:16.270 --> 00:13:18.160 and naturalistic settings.

NOTE Confidence: 0.9380628

00:13:22.190 --> 00:13:24.206 So just to kind of go over the what

NOTE Confidence: 0.9380628

00:13:24.206 --> 00:13:26.186 we've done in our laboratory studies,

NOTE Confidence: 0.9380628

00:13:26.190 --> 00:13:29.389 single doses of LSD, their doses are

NOTE Confidence: 0.9380628

00:13:29.390 --> 00:13:33.744 odd doses of 6.513 and 26 micrograms.

NOTE Confidence: 0.9380628

00:13:33.750 --> 00:13:35.988 We measure subjective and behavioral effects.

NOTE Confidence: 0.9380628

00:13:35.990 --> 00:13:38.160 I just said that already healthy volunteers

NOTE Confidence: 0.9380628

00:13:38.160 --> 00:13:40.386 and most recently we've also looked at

NOTE Confidence: 0.9380628

00:13:40.386 --> 00:13:41.936 depressed participants and I'll show

NOTE Confidence: 0.9380628

00:13:41.936 --> 00:13:44.305 you the results of that and then that.

NOTE Confidence: 0.9380628

00:13:44.305 --> 00:13:47.536 So most of them are single doses and then

NOTE Confidence: 0.9380628

00:13:47.536 --> 00:13:50.105 one study was done with repeated doses

NOTE Confidence: 0.9380628

00:13:50.105 --> 00:13:53.347 of either placebo or 13 or 16 micrograms.

NOTE Confidence: 0.93114233

00:13:57.550 --> 00:13:59.230 I've already said they were double.

NOTE Confidence: 0.93114233

00:13:59.230 --> 00:14:00.734 The studies are double-blind

NOTE Confidence: 0.93114233

00:14:00.734 --> 00:14:01.478 and placebo-controlled.

NOTE Confidence: 0.93114233

00:14:01.478 --> 00:14:04.458 So all the in, in with one exception,

NOTE Confidence: 0.93114233

00:14:04.458 --> 00:14:05.589 all the studies,

NOTE Confidence: 0.93114233

00:14:05.590 --> 00:14:07.310 in all the studies it's within the subject.

NOTE Confidence: 0.93114233

00:14:07.310 --> 00:14:10.046 So the same subjects get drug and placebo

NOTE Confidence: 0.93114233

00:14:10.046 --> 00:14:11.830 in or or actually in two of the studies.

NOTE Confidence: 0.93114233

00:14:11.830 --> 00:14:13.430 Now that's between subjects.

NOTE Confidence: 0.93114233

00:14:13.430 --> 00:14:15.238 So, But they're all placebo-controlled.

NOTE Confidence: 0.93114233

00:14:15.238 --> 00:14:17.700 The participants are healthy men and women.

NOTE Confidence: 0.93114233

00:14:17.700 --> 00:14:20.980 We exclude anyone with psychiatric,

NOTE Confidence: 0.93114233

00:14:20.980 --> 00:14:25.100 serious psychiatric background and

NOTE Confidence: 0.93114233

00:14:25.100 --> 00:14:26.820 anyone with substance use history,

NOTE Confidence: 0.93114233

00:14:26.820 --> 00:14:28.934 anyone who's taking any kind of medication.

NOTE Confidence: 0.93114233

00:14:28.940 --> 00:14:30.816 They had to be 18 to 35.

NOTE Confidence: 0.93114233

00:14:30.820 --> 00:14:33.305 They had to report using at least

NOTE Confidence: 0.93114233

00:14:33.305 --> 00:14:35.720 one one lifetime use of psychedelic

NOTE Confidence: 0.93114233

00:14:35.720 --> 00:14:37.898 and that was really to reassure

NOTE Confidence: 0.93114233

00:14:37.898 --> 00:14:40.009 ourselves we didn't want to be

NOTE Confidence: 0.93114233

00:14:40.009 --> 00:14:41.779 the first ones to administer a

NOTE Confidence: 0.93114233

00:14:41.779 --> 00:14:44.320 drug like this to healthy people.

NOTE Confidence: 0.93114233

00:14:44.320 --> 00:14:44.893 That'd be normal.
NOTE Confidence: 0.93114233

00:14:44.893 --> 00:14:46.230 Weight that to have a high school
NOTE Confidence: 0.93114233

00:14:46.270 --> 00:14:47.318 education fluent in English.
NOTE Confidence: 0.93114233

00:14:47.320 --> 00:14:49.752 So they're they're very,
NOTE Confidence: 0.93114233

00:14:49.752 --> 00:14:52.632 very thoroughly screened to be
NOTE Confidence: 0.93114233

00:14:52.632 --> 00:14:53.824 healthy participants.
NOTE Confidence: 0.93114233

00:14:53.824 --> 00:14:56.944 Our sessions are conducted in
NOTE Confidence: 0.93114233

00:14:56.944 --> 00:14:59.845 the laboratory for between 4:00
NOTE Confidence: 0.93114233

00:14:59.845 --> 00:15:02.680 and at the longest 8 hours in
NOTE Confidence: 0.93114233

00:15:02.680 --> 00:15:04.718 comfortable living room like room,
NOTE Confidence: 0.93114233

00:15:04.720 --> 00:15:07.583 so with couches and and televisions and
NOTE Confidence: 0.93114233

00:15:07.583 --> 00:15:10.598 movies to watch and that kind of thing.
NOTE Confidence: 0.93114233

00:15:10.600 --> 00:15:12.576 So the four studies I'll talk about here
NOTE Confidence: 0.93114233

00:15:12.576 --> 00:15:14.678 are one where we the first study where
NOTE Confidence: 0.93114233

00:15:14.678 --> 00:15:16.638 we looked at single low doses of LSD,
NOTE Confidence: 0.93114233

00:15:16.640 --> 00:15:19.140 we gave the same subjects

NOTE Confidence: 0.93114233

00:15:19.140 --> 00:15:21.208 got 06.513 or 26 micrograms.

NOTE Confidence: 0.93114233

00:15:21.208 --> 00:15:23.560 The second study I'll describe here,

NOTE Confidence: 0.93114233

00:15:23.560 --> 00:15:26.038 we looked at brain measures of

NOTE Confidence: 0.93114233

00:15:26.040 --> 00:15:28.146 reactivity to rewards and in that

NOTE Confidence: 0.93114233

00:15:28.146 --> 00:15:30.838 study we used zero and 26 micrograms.

NOTE Confidence: 0.93114233

00:15:30.840 --> 00:15:32.076 In the third study I'll describe,

NOTE Confidence: 0.93114233

00:15:32.080 --> 00:15:34.360 we gave repeated doses of zero,

NOTE Confidence: 0.93114233

00:15:34.360 --> 00:15:37.965 13 and 36 and that is between

NOTE Confidence: 0.93114233

00:15:37.965 --> 00:15:38.995 subjects design.

NOTE Confidence: 0.93114233

00:15:39.000 --> 00:15:39.831 And then finally,

NOTE Confidence: 0.93114233

00:15:39.831 --> 00:15:41.770 I'll describe the results of our recent

NOTE Confidence: 0.93114233

00:15:41.828 --> 00:15:43.676 study with people with depressed mood.

NOTE Confidence: 0.9319653

00:15:47.030 --> 00:15:49.704 I've already said all this healthy men

NOTE Confidence: 0.9319653

00:15:49.704 --> 00:15:52.310 and women within subject design this,

NOTE Confidence: 0.9319653

00:15:52.310 --> 00:15:53.390 this was our first study.

NOTE Confidence: 0.9319653

00:15:53.390 --> 00:15:55.476 So we actually had eight hour sessions
NOTE Confidence: 0.9319653

00:15:55.476 --> 00:15:57.348 in our laboratory environment because we
NOTE Confidence: 0.9319653

00:15:57.348 --> 00:15:59.830 didn't know how long the drug would last.
NOTE Confidence: 0.9319653

00:15:59.830 --> 00:16:00.870 As I'm sure you know,
NOTE Confidence: 0.9319653

00:16:00.870 --> 00:16:02.802 LSD has a long duration of effect
NOTE Confidence: 0.9319653

00:16:02.802 --> 00:16:05.147 and in the end at these low doses,
NOTE Confidence: 0.9319653

00:16:05.150 --> 00:16:06.910 we don't have to keep them in quite so long.
NOTE Confidence: 0.9319653

00:16:06.910 --> 00:16:07.990 But in this first study,
NOTE Confidence: 0.9319653

00:16:07.990 --> 00:16:10.357 they stayed in for 8 hours at a time.
NOTE Confidence: 0.9319653

00:16:10.360 --> 00:16:11.880 So this kind of gives you an outline
NOTE Confidence: 0.9319653

00:16:11.880 --> 00:16:13.556 of what happens in a typical session.
NOTE Confidence: 0.9319653

00:16:13.560 --> 00:16:15.000 They do all kinds of screening,
NOTE Confidence: 0.9319653

00:16:15.000 --> 00:16:16.254 pregnancy and drug,
NOTE Confidence: 0.9319653

00:16:16.254 --> 00:16:18.344 urine tests before they participate
NOTE Confidence: 0.9319653

00:16:18.344 --> 00:16:21.522 and they get the drug and then we
NOTE Confidence: 0.9319653

00:16:21.522 --> 00:16:23.038 get cardiovascular and subjective

NOTE Confidence: 0.9319653

00:16:23.104 --> 00:16:25.414 subjective ratings every half hour or

NOTE Confidence: 0.9319653

00:16:25.414 --> 00:16:27.608 hour for the duration of the session.

NOTE Confidence: 0.9319653

00:16:27.608 --> 00:16:29.759 And then at the time of peak drug effect,

NOTE Confidence: 0.9319653

00:16:29.760 --> 00:16:32.259 we get behavioral tasks or scan as

NOTE Confidence: 0.9319653

00:16:32.259 --> 00:16:34.903 the case might be or EE G measures

NOTE Confidence: 0.9319653

00:16:34.903 --> 00:16:36.398 as the case might be.

NOTE Confidence: 0.9275157

00:16:39.260 --> 00:16:42.636 So just to give you an idea of

NOTE Confidence: 0.9275157

00:16:42.636 --> 00:16:45.058 the is, do you see this thing?

NOTE Confidence: 0.9275157

00:16:47.100 --> 00:16:47.980 We can see your cursor.

NOTE Confidence: 0.9275157

00:16:47.980 --> 00:16:48.820 Yeah, we can see the Finder,

NOTE Confidence: 0.9275157

00:16:49.420 --> 00:16:50.556 but OK. So anyway,

NOTE Confidence: 0.9275157

00:16:50.556 --> 00:16:51.976 I'll take that into account.

NOTE Confidence: 0.9275157

00:16:51.980 --> 00:16:53.500 There's, it's hiding something there.

NOTE Confidence: 0.9275157

00:16:53.500 --> 00:16:56.420 OK. Just to give you an idea of

NOTE Confidence: 0.9275157

00:16:56.420 --> 00:16:57.767 the doses that we're giving over

NOTE Confidence: 0.9275157

00:16:57.767 --> 00:16:59.984 on the left are ratings of how
NOTE Confidence: 0.9275157

00:16:59.984 --> 00:17:02.700 much people feel a drug effect when
NOTE Confidence: 0.9275157

00:17:02.700 --> 00:17:04.550 they get full psychedelic doses.
NOTE Confidence: 0.9275157

00:17:04.550 --> 00:17:07.350 So 100 and 200 micrograms of LSD,
NOTE Confidence: 0.9275157

00:17:07.350 --> 00:17:09.348 this is the group in Switzerland.
NOTE Confidence: 0.9275157

00:17:09.350 --> 00:17:11.350 These are the ratings of how much drug
NOTE Confidence: 0.9275157

00:17:11.350 --> 00:17:13.188 effect the the scale goes up to 100.
NOTE Confidence: 0.9275157

00:17:13.190 --> 00:17:15.534 And so you can see that it's close
NOTE Confidence: 0.9275157

00:17:15.534 --> 00:17:17.747 to maximal at both 100 and and 200.
NOTE Confidence: 0.9275157

00:17:17.750 --> 00:17:18.971 Actually interestingly there
NOTE Confidence: 0.9275157

00:17:18.971 --> 00:17:21.006 aren't very clear dose dependent
NOTE Confidence: 0.9275157

00:17:21.006 --> 00:17:22.867 effects when you get this high.
NOTE Confidence: 0.9275157

00:17:22.870 --> 00:17:25.030 So both 100 and 200 produce
NOTE Confidence: 0.9275157

00:17:25.030 --> 00:17:26.110 fairly high effects.
NOTE Confidence: 0.92132366

00:17:29.160 --> 00:17:31.095 Then over on the right you can see the
NOTE Confidence: 0.92132366

00:17:31.095 --> 00:17:32.999 ratings on this same sort of questionnaire.

NOTE Confidence: 0.92132366

00:17:33.000 --> 00:17:35.511 How much do you feel a drug effect at

NOTE Confidence: 0.92132366

00:17:35.511 --> 00:17:38.079 the doses that we gave in that single

NOTE Confidence: 0.92132366

00:17:38.079 --> 00:17:39.872 low dose administration and the,

NOTE Confidence: 0.92132366

00:17:39.872 --> 00:17:42.560 the lightest line is the placebo session,

NOTE Confidence: 0.92132366

00:17:42.560 --> 00:17:45.975 this is the ratings of field drug over

NOTE Confidence: 0.92132366

00:17:45.975 --> 00:17:47.830 time during the session you can say

NOTE Confidence: 0.92132366

00:17:47.830 --> 00:17:49.826 that the lightest one at the bottom

NOTE Confidence: 0.92132366

00:17:49.826 --> 00:17:51.824 there is placebo and then you get

NOTE Confidence: 0.92132366

00:17:51.824 --> 00:17:53.679 the lower dose and then the higher

NOTE Confidence: 0.92132366

00:17:53.679 --> 00:17:55.070 middle dose and the highest dose.

NOTE Confidence: 0.92132366

00:17:55.070 --> 00:17:58.409 And so at the highest dose here we're getting

NOTE Confidence: 0.92132366

00:17:58.409 --> 00:18:00.990 ratings that are less than 50% of maximal.

NOTE Confidence: 0.92132366

00:18:00.990 --> 00:18:02.490 So and that's not happening

NOTE Confidence: 0.92132366

00:18:02.490 --> 00:18:03.990 in all the subjects.

NOTE Confidence: 0.92132366

00:18:03.990 --> 00:18:06.915 And so this this sort of formed the basis

NOTE Confidence: 0.92132366

00:18:06.915 --> 00:18:09.626 for trying to find a threshold dose.
NOTE Confidence: 0.92132366

00:18:09.630 --> 00:18:12.885 Again, finding a dose that's either threshold
NOTE Confidence: 0.92132366

00:18:12.885 --> 00:18:16.028 or below threshold is extremely difficult.
NOTE Confidence: 0.92132366

00:18:16.030 --> 00:18:18.422 One of the problems is that people vary
NOTE Confidence: 0.92132366

00:18:18.422 --> 00:18:21.147 a lot in their responses to the drug.
NOTE Confidence: 0.92132366

00:18:21.150 --> 00:18:23.670 So what's a detectable dose to one person
NOTE Confidence: 0.92132366

00:18:23.670 --> 00:18:26.506 might be below threshold to another person.
NOTE Confidence: 0.92132366

00:18:26.510 --> 00:18:28.718 And the other problem as I sort of
NOTE Confidence: 0.92132366

00:18:28.718 --> 00:18:31.076 referred to before is that if you're
NOTE Confidence: 0.92132366

00:18:31.076 --> 00:18:32.816 if you're repeatedly giving doses
NOTE Confidence: 0.92132366

00:18:32.883 --> 00:18:35.007 that are not even detectable then
NOTE Confidence: 0.92132366

00:18:35.007 --> 00:18:36.954 you're you're investing a lot of
NOTE Confidence: 0.92132366

00:18:36.954 --> 00:18:38.264 time and energy into something,
NOTE Confidence: 0.92132366

00:18:38.270 --> 00:18:40.268 into a study where you might
NOTE Confidence: 0.92132366

00:18:40.268 --> 00:18:41.267 not see anything.
NOTE Confidence: 0.92132366

00:18:41.270 --> 00:18:43.467 So it's nice to be able to get

NOTE Confidence: 0.92132366

00:18:43.467 --> 00:18:45.609 at least some kind of reportable

NOTE Confidence: 0.92132366

00:18:45.609 --> 00:18:47.708 subjective effect from the drug anyway.

NOTE Confidence: 0.92132366

00:18:47.710 --> 00:18:50.330 So this is where we are in the in the

NOTE Confidence: 0.92132366

00:18:50.410 --> 00:18:52.830 the range of doses that we're answering.

NOTE Confidence: 0.92132366

00:18:52.830 --> 00:18:53.190 Yeah,

NOTE Confidence: 0.9255704

00:18:53.570 --> 00:18:55.146 can I, can I ask you a question

NOTE Confidence: 0.9255704

00:18:55.146 --> 00:18:56.249 going back to that slide.

NOTE Confidence: 0.9255704

00:18:56.250 --> 00:18:58.370 So just for perspective

NOTE Confidence: 0.9255704

00:19:00.570 --> 00:19:03.010 on the right hand side, the low dose,

NOTE Confidence: 0.9255704

00:19:03.010 --> 00:19:05.937 very low doses of LST, what would you,

NOTE Confidence: 0.9255704

00:19:05.937 --> 00:19:07.791 what kind of drug effects are

NOTE Confidence: 0.9255704

00:19:07.791 --> 00:19:09.808 you are people reporting with,

NOTE Confidence: 0.9255704

00:19:09.810 --> 00:19:11.970 say some of your other studies

NOTE Confidence: 0.9255704

00:19:11.970 --> 00:19:14.826 with drugs like, I don't know,

NOTE Confidence: 0.9255704

00:19:14.826 --> 00:19:17.009 antihistaminics or just for comparison,

NOTE Confidence: 0.9007908

00:19:19.380 --> 00:19:21.396 you mean how much do people report feeling

NOTE Confidence: 0.9007908

00:19:21.396 --> 00:19:23.700 a drug if we gave them, say, amphetamine

NOTE Confidence: 0.9007908

00:19:25.060 --> 00:19:27.380 or an antihistaminic or?

NOTE Confidence: 0.9007908

00:19:27.660 --> 00:19:29.872 Well, we actually haven't

NOTE Confidence: 0.9007908

00:19:29.872 --> 00:19:30.978 given antihistamines.

NOTE Confidence: 0.9007908

00:19:30.980 --> 00:19:32.564 That happens to be one that

NOTE Confidence: 0.9007908

00:19:32.564 --> 00:19:34.420 we used as a distractor.

NOTE Confidence: 0.9007908

00:19:34.420 --> 00:19:36.400 Yeah. OK. So it would depend

NOTE Confidence: 0.9007908

00:19:36.400 --> 00:19:38.620 on the drug and the dose.

NOTE Confidence: 0.9007908

00:19:39.380 --> 00:19:41.020 OK, All right. Thanks.

NOTE Confidence: 0.9355316

00:19:41.400 --> 00:19:43.640 But typically in our studies

NOTE Confidence: 0.9355316

00:19:43.640 --> 00:19:46.280 where we use amphetamine or THC,

NOTE Confidence: 0.9355316

00:19:46.280 --> 00:19:49.066 we would see like ratings of field

NOTE Confidence: 0.9355316

00:19:49.066 --> 00:19:52.441 drug of 70 or 80 something like that

NOTE Confidence: 0.9355316

00:19:52.441 --> 00:19:54.636 or MDMA again it depends on the dose.

NOTE Confidence: 0.9354748

00:19:58.920 --> 00:20:00.576 OK. So then we come up with a

NOTE Confidence: 0.9354748
00:20:00.576 --> 00:20:01.840 challenge of what to measure.
NOTE Confidence: 0.9354748
00:20:01.840 --> 00:20:04.288 So we're we've got these threshold
NOTE Confidence: 0.9354748
00:20:04.288 --> 00:20:06.896 doses and and many of our usual
NOTE Confidence: 0.9354748
00:20:06.896 --> 00:20:08.272 questionnaires for measuring drug
NOTE Confidence: 0.9354748
00:20:08.272 --> 00:20:09.959 effects except for do you feel
NOTE Confidence: 0.9354748
00:20:09.959 --> 00:20:11.369 a drug effect overall are not
NOTE Confidence: 0.9354748
00:20:11.421 --> 00:20:13.037 designed for psychedelic drugs.
NOTE Confidence: 0.9354748
00:20:13.040 --> 00:20:15.105 And so we're struggling with
NOTE Confidence: 0.9354748
00:20:15.105 --> 00:20:16.757 what exactly to measure.
NOTE Confidence: 0.9354748
00:20:16.760 --> 00:20:18.535 And so someone has to
NOTE Confidence: 0.9354748
00:20:18.535 --> 00:20:19.600 design this questionnaire,
NOTE Confidence: 0.9354748
00:20:19.600 --> 00:20:21.875 the five dimensional altered states
NOTE Confidence: 0.9354748
00:20:21.875 --> 00:20:23.240 of consciousness questionnaire,
NOTE Confidence: 0.9354748
00:20:23.240 --> 00:20:25.070 which has these at least.
NOTE Confidence: 0.9354748
00:20:25.070 --> 00:20:27.030 For scales and and there are other
NOTE Confidence: 0.9354748

00:20:27.030 --> 00:20:29.069 versions of it as well which is
NOTE Confidence: 0.9354748

00:20:29.069 --> 00:20:30.779 a series of questions that appear
NOTE Confidence: 0.9354748

00:20:30.845 --> 00:20:33.043 to be sensitive to the effects of
NOTE Confidence: 0.9354748

00:20:33.043 --> 00:20:34.914 psychedelic drugs and so and and
NOTE Confidence: 0.9354748

00:20:34.914 --> 00:20:37.070 more sensitive to any of our other
NOTE Confidence: 0.9354748

00:20:37.138 --> 00:20:39.668 measures of acute subjective effects.
NOTE Confidence: 0.9354748

00:20:39.670 --> 00:20:41.566 So we in our other studies we use
NOTE Confidence: 0.9354748

00:20:41.566 --> 00:20:42.668 something called the addiction
NOTE Confidence: 0.9354748

00:20:42.668 --> 00:20:44.113 Research Center inventory or we
NOTE Confidence: 0.9354748

00:20:44.113 --> 00:20:45.940 use the profile of mood States and
NOTE Confidence: 0.9354748

00:20:45.940 --> 00:20:47.650 some of those things are just don't
NOTE Confidence: 0.9354748

00:20:47.650 --> 00:20:49.350 detect these really unique effects
NOTE Confidence: 0.9354748

00:20:49.350 --> 00:20:51.910 of the of the psychedelic drugs.
NOTE Confidence: 0.9354748

00:20:51.910 --> 00:20:53.870 So this is kind of new territory
NOTE Confidence: 0.9354748

00:20:53.870 --> 00:20:56.180 for us as psychopharmacologist.
NOTE Confidence: 0.9354748

00:20:56.180 --> 00:20:58.340 So measures like reports like I

NOTE Confidence: 0.9354748

00:20:58.340 --> 00:21:01.269 felt one with my surroundings or I

NOTE Confidence: 0.9354748

00:21:01.269 --> 00:21:03.614 experienced a touch of eternity.

NOTE Confidence: 0.9354748

00:21:03.620 --> 00:21:06.722 It's getting into territory that we're

NOTE Confidence: 0.9354748

00:21:06.722 --> 00:21:09.494 not used to measuring or studying.

NOTE Confidence: 0.9354748

00:21:09.500 --> 00:21:12.620 It's it's just such a subtle and and

NOTE Confidence: 0.9354748

00:21:12.620 --> 00:21:15.880 and abstract kind of conceptual experience.

NOTE Confidence: 0.9354748

00:21:15.880 --> 00:21:17.872 But as it turns out this people are

NOTE Confidence: 0.9354748

00:21:17.872 --> 00:21:19.999 able to answer these questions and we

NOTE Confidence: 0.9354748

00:21:19.999 --> 00:21:22.439 are able to quantify the the responses.

NOTE Confidence: 0.9354748

00:21:22.440 --> 00:21:25.144 So I I still struggle with the idea

NOTE Confidence: 0.9354748

00:21:25.144 --> 00:21:28.207 that how do you even for yourself how

NOTE Confidence: 0.9354748

00:21:28.207 --> 00:21:30.673 do you rate something like experience

NOTE Confidence: 0.9354748

00:21:30.673 --> 00:21:33.640 of awe or experience of inner peace.

NOTE Confidence: 0.9354748

00:21:33.640 --> 00:21:35.460 It's just it's just a real challenge

NOTE Confidence: 0.9354748

00:21:35.460 --> 00:21:37.690 to come up with and I and I think we

NOTE Confidence: 0.9354748

00:21:37.690 --> 00:21:39.839 as a field still need to work on that.
NOTE Confidence: 0.9354748

00:21:39.840 --> 00:21:42.752 What are we measuring and what are the
NOTE Confidence: 0.9354748

00:21:42.752 --> 00:21:46.050 the core dimensions of these experiences?
NOTE Confidence: 0.9354748

00:21:46.050 --> 00:21:47.872 But as it turns out, so this scale,
NOTE Confidence: 0.9354748

00:21:47.872 --> 00:21:50.130 this is scale can go up to 100.
NOTE Confidence: 0.9354748

00:21:50.130 --> 00:21:50.530 Oops.
NOTE Confidence: 0.9306214

00:21:53.690 --> 00:21:55.970 These are the ratings in that
NOTE Confidence: 0.9306214

00:21:55.970 --> 00:21:58.426 study of the zero, the low,
NOTE Confidence: 0.9306214

00:21:58.426 --> 00:22:01.868 medium and higher dose of LSD on these
NOTE Confidence: 0.9306214

00:22:01.868 --> 00:22:04.074 on 4 scales, experience of unity,
NOTE Confidence: 0.9306214

00:22:04.074 --> 00:22:04.810 spiritual experience,
NOTE Confidence: 0.9306214

00:22:04.810 --> 00:22:06.342 blissful state and insightfulness.
NOTE Confidence: 0.9306214

00:22:06.342 --> 00:22:09.397 The black bar on the left of each
NOTE Confidence: 0.9306214

00:22:09.397 --> 00:22:11.812 foursome is the placebo and then the
NOTE Confidence: 0.9306214

00:22:11.812 --> 00:22:13.686 rightmost one is the higher dose.
NOTE Confidence: 0.9306214

00:22:13.690 --> 00:22:17.038 And you can see that there is a dose

NOTE Confidence: 0.9306214

00:22:17.038 --> 00:22:19.316 dependent increase on ratings of

NOTE Confidence: 0.9306214

00:22:19.316 --> 00:22:22.194 these questionnaires on these scales.

NOTE Confidence: 0.9306214

00:22:22.194 --> 00:22:24.970 The the I've we've expanded the scale

NOTE Confidence: 0.9306214

00:22:24.970 --> 00:22:27.557 here so this only goes up to 20 and

NOTE Confidence: 0.9306214

00:22:27.557 --> 00:22:29.699 the scale itself goes up to 100 and

NOTE Confidence: 0.9306214

00:22:29.699 --> 00:22:31.925 when you give high doses of psychedelic

NOTE Confidence: 0.9306214

00:22:31.925 --> 00:22:33.970 drugs then they do approach 100.

NOTE Confidence: 0.9306214

00:22:33.970 --> 00:22:35.570 So these are very subtle,

NOTE Confidence: 0.9306214

00:22:35.570 --> 00:22:38.554 but at least we're seeing qualitative

NOTE Confidence: 0.9306214

00:22:38.554 --> 00:22:40.822 effects that are kind of resemble the

NOTE Confidence: 0.9306214

00:22:40.822 --> 00:22:42.845 doses that you see that the effects

NOTE Confidence: 0.9306214

00:22:42.845 --> 00:22:44.550 that you see with higher doses.

NOTE Confidence: 0.9306214

00:22:44.550 --> 00:22:47.508 So we did see detectable effects.

NOTE Confidence: 0.9306214

00:22:47.510 --> 00:22:49.430 You know again this is,

NOTE Confidence: 0.9306214

00:22:49.430 --> 00:22:50.948 I'm sorry this is very sensitive.

NOTE Confidence: 0.9306214

00:22:50.950 --> 00:22:52.889 The very lowest dose I'd have to

NOTE Confidence: 0.9306214

00:22:52.889 --> 00:22:54.559 say didn't maybe on insightfulness

NOTE Confidence: 0.9306214

00:22:54.559 --> 00:22:56.107 it increased in effect,

NOTE Confidence: 0.9306214

00:22:56.110 --> 00:22:59.435 but so it's but we're just a

NOTE Confidence: 0.9306214

00:22:59.435 --> 00:23:02.190 marginal dose effect there.

NOTE Confidence: 0.9306214

00:23:02.190 --> 00:23:02.484 OK.

NOTE Confidence: 0.9306214

00:23:02.484 --> 00:23:04.836 So that was sort of a proof of

NOTE Confidence: 0.9306214

00:23:04.836 --> 00:23:07.920 concept and and it was also a

NOTE Confidence: 0.9306214

00:23:07.920 --> 00:23:10.114 way to determine what doses we

NOTE Confidence: 0.9306214

00:23:10.114 --> 00:23:11.890 should use in our other studies.

NOTE Confidence: 0.9306214

00:23:11.890 --> 00:23:14.202 So we kind of went on from there

NOTE Confidence: 0.9306214

00:23:14.202 --> 00:23:16.444 and the the studies that we've

NOTE Confidence: 0.9306214

00:23:16.444 --> 00:23:18.826 done from there have been either

NOTE Confidence: 0.9306214

00:23:18.906 --> 00:23:20.566 at 13 or 26 micrograms.

NOTE Confidence: 0.9306214

00:23:20.570 --> 00:23:22.999 So the second study that I'll describe

NOTE Confidence: 0.9306214

00:23:22.999 --> 00:23:25.851 to you is 1 on the effects of LS,

NOTE Confidence: 0.9306214

00:23:25.851 --> 00:23:28.017 these low doses of LSD on

NOTE Confidence: 0.9306214

00:23:28.017 --> 00:23:29.720 brain response to reward.

NOTE Confidence: 0.9306214

00:23:29.720 --> 00:23:31.856 So one possibility that in is

NOTE Confidence: 0.9306214

00:23:31.856 --> 00:23:33.709 intriguing is whether low doses

NOTE Confidence: 0.9306214

00:23:33.709 --> 00:23:35.845 of LSD or other psychedelic drugs

NOTE Confidence: 0.9306214

00:23:35.845 --> 00:23:38.249 can alter brain function even at

NOTE Confidence: 0.9306214

00:23:38.249 --> 00:23:40.354 doses that produce minimal effects.

NOTE Confidence: 0.9306214

00:23:40.360 --> 00:23:42.616 So it could be that the reason we're

NOTE Confidence: 0.9306214

00:23:42.616 --> 00:23:44.512 not seeing anything on the subjective

NOTE Confidence: 0.9306214

00:23:44.512 --> 00:23:47.200 effects is or that we that it might be.

NOTE Confidence: 0.9306214

00:23:47.200 --> 00:23:50.080 It's possible that you could see

NOTE Confidence: 0.9306214

00:23:50.080 --> 00:23:52.000 some longterm beneficial effect

NOTE Confidence: 0.9306214

00:23:52.083 --> 00:23:54.418 on psychological function or or

NOTE Confidence: 0.9306214

00:23:54.418 --> 00:23:57.226 or feelings of wellbeing even at

NOTE Confidence: 0.9306214

00:23:57.226 --> 00:23:59.566 doses that that don't produce

NOTE Confidence: 0.9306214

00:23:59.566 --> 00:24:00.970 acute subjective effects.
NOTE Confidence: 0.9306214

00:24:00.970 --> 00:24:03.424 But then you're you're it's it's
NOTE Confidence: 0.9306214

00:24:03.424 --> 00:24:05.610 you're you're really taking a risk.
NOTE Confidence: 0.9306214

00:24:05.610 --> 00:24:07.850 And as a scientist in running that study,
NOTE Confidence: 0.9306214

00:24:07.850 --> 00:24:08.746 if there's no if,
NOTE Confidence: 0.9306214

00:24:08.746 --> 00:24:10.090 you see no effects at all,
NOTE Confidence: 0.9306214

00:24:10.090 --> 00:24:11.050 no physiological effects,
NOTE Confidence: 0.9306214

00:24:11.050 --> 00:24:12.010 no subjective effects.
NOTE Confidence: 0.9306214

00:24:12.010 --> 00:24:13.842 So we want to know whether that we
NOTE Confidence: 0.9306214

00:24:13.842 --> 00:24:15.593 could detect an effect on brain function
NOTE Confidence: 0.9306214

00:24:15.593 --> 00:24:17.330 even at doses that were produced,
NOTE Confidence: 0.9306214

00:24:17.330 --> 00:24:18.986 hardly any subjective effects.
NOTE Confidence: 0.9306214

00:24:18.986 --> 00:24:22.010 So we selected the brain reward signal.
NOTE Confidence: 0.9306214

00:24:22.010 --> 00:24:24.677 That's called r P That's measured with
NOTE Confidence: 0.9306214

00:24:24.677 --> 00:24:27.967 EEG during the monetary incentive delay task.
NOTE Confidence: 0.9306214

00:24:27.970 --> 00:24:28.742 So in the Monitor,

NOTE Confidence: 0.9306214

00:24:28.742 --> 00:24:29.900 I'm sure you're familiar with the

NOTE Confidence: 0.9306214

00:24:29.937 --> 00:24:31.049 monetary incentive delay task.

NOTE Confidence: 0.9306214

00:24:31.050 --> 00:24:32.718 It's a it's a simple behavioral

NOTE Confidence: 0.9306214

00:24:32.718 --> 00:24:34.434 task where people get cues that

NOTE Confidence: 0.9306214

00:24:34.434 --> 00:24:35.799 either signal that they're going

NOTE Confidence: 0.9306214

00:24:35.799 --> 00:24:37.410 to have a win or a loss,

NOTE Confidence: 0.9306214

00:24:37.410 --> 00:24:38.290 and then there's some delay,

NOTE Confidence: 0.9306214

00:24:38.290 --> 00:24:40.290 and then they actually get a win or a loss.

NOTE Confidence: 0.9306214

00:24:40.290 --> 00:24:41.448 And there's a lot of interest,

NOTE Confidence: 0.9306214

00:24:41.450 --> 00:24:42.308 especially anticipatory,

NOTE Confidence: 0.9306214

00:24:42.308 --> 00:24:44.882 in their brain responses to the

NOTE Confidence: 0.9306214

00:24:44.882 --> 00:24:47.018 to the anticipation cue and

NOTE Confidence: 0.9306214

00:24:47.018 --> 00:24:49.424 then also to the feedback queue.

NOTE Confidence: 0.9251433

00:24:49.430 --> 00:24:51.958 It turns out that people who have depression

NOTE Confidence: 0.9251433

00:24:51.958 --> 00:24:54.828 have a smaller rupee by this EE G measure.

NOTE Confidence: 0.9251433

00:24:54.830 --> 00:24:58.478 And so we might predict that if this
NOTE Confidence: 0.9251433

00:24:58.478 --> 00:25:00.740 drug increases, makes people more
NOTE Confidence: 0.9251433

00:25:00.740 --> 00:25:03.890 sensitive to reward that we might see
NOTE Confidence: 0.9251433

00:25:03.978 --> 00:25:07.008 a larger rupee response even acutely.
NOTE Confidence: 0.9251433

00:25:07.010 --> 00:25:08.846 And so that's what we saw.
NOTE Confidence: 0.9251433

00:25:08.850 --> 00:25:11.688 So this is the brains signal.
NOTE Confidence: 0.9251433

00:25:11.690 --> 00:25:15.170 This is time in milliseconds after a a,
NOTE Confidence: 0.9251433

00:25:15.170 --> 00:25:16.570 a queue actually this feed,
NOTE Confidence: 0.9251433

00:25:16.570 --> 00:25:19.370 this queue happens to be the feedback queue.
NOTE Confidence: 0.9251433

00:25:19.370 --> 00:25:21.810 So it's the report that the the signal
NOTE Confidence: 0.9251433

00:25:21.810 --> 00:25:23.548 that people actually won something
NOTE Confidence: 0.9251433

00:25:23.548 --> 00:25:26.026 or lost something or that there was
NOTE Confidence: 0.9251433

00:25:26.091 --> 00:25:29.274 something neutral and the solid line
NOTE Confidence: 0.9251433

00:25:29.274 --> 00:25:33.330 here corresponds to the people's brain,
NOTE Confidence: 0.9251433

00:25:33.330 --> 00:25:35.899 the signal after the under the placebo
NOTE Confidence: 0.9251433

00:25:35.899 --> 00:25:38.168 condition and then the broken lines.

NOTE Confidence: 0.9251433

00:25:38.170 --> 00:25:40.330 First of all that the middle one there

NOTE Confidence: 0.9251433

00:25:40.330 --> 00:25:42.490 is the lower dose of LSD and then

NOTE Confidence: 0.9251433

00:25:42.490 --> 00:25:44.490 this one is the higher dose of LSD.

NOTE Confidence: 0.9251433

00:25:44.490 --> 00:25:46.434 And you can see that both the lower dose

NOTE Confidence: 0.9251433

00:25:46.434 --> 00:25:48.898 and the higher dose increase the brain's

NOTE Confidence: 0.9251433

00:25:48.898 --> 00:25:52.368 response to this receipt of reward signal.

NOTE Confidence: 0.9251433

00:25:52.368 --> 00:25:55.896 So that's consistent at least with this

NOTE Confidence: 0.9251433

00:25:55.896 --> 00:25:58.968 idea that the drug is affecting reactivity

NOTE Confidence: 0.9251433

00:25:58.968 --> 00:26:02.872 to reward basically at at a neural level.

NOTE Confidence: 0.9251433

00:26:02.880 --> 00:26:04.980 And so this is definitely something that

NOTE Confidence: 0.9251433

00:26:04.980 --> 00:26:09.039 needs to be replicated and extended.

NOTE Confidence: 0.9251433

00:26:09.040 --> 00:26:12.881 So we found here that the doses of LSD

NOTE Confidence: 0.9251433

00:26:12.881 --> 00:26:15.129 that are too low to be detected by

NOTE Confidence: 0.9251433

00:26:15.129 --> 00:26:16.895 selfreport measures could produce subtle

NOTE Confidence: 0.9251433

00:26:16.895 --> 00:26:19.720 and alterations as it happens in this study,

NOTE Confidence: 0.9251433

00:26:19.720 --> 00:26:22.996 the 13, both the 13 and the 26 micrograms,

NOTE Confidence: 0.9251433

00:26:23.000 --> 00:26:24.626 they did produce a little bit

NOTE Confidence: 0.9251433

00:26:24.626 --> 00:26:25.439 of subjective effect.

NOTE Confidence: 0.9251433

00:26:25.440 --> 00:26:26.848 So we still haven't,

NOTE Confidence: 0.9251433

00:26:26.848 --> 00:26:29.261 we still haven't shown that that there's

NOTE Confidence: 0.9251433

00:26:29.261 --> 00:26:31.669 a brain response at a dose where there's

NOTE Confidence: 0.9251433

00:26:31.669 --> 00:26:33.198 absolutely no subjective response.

NOTE Confidence: 0.9251433

00:26:33.200 --> 00:26:36.560 So that's still to be to be determined.

NOTE Confidence: 0.9251433

00:26:36.560 --> 00:26:37.160 Harriet,

NOTE Confidence: 0.9251433

00:26:37.160 --> 00:26:37.760 yes,

NOTE Confidence: 0.938183

00:26:38.040 --> 00:26:39.380 you mentioned at the beginning

NOTE Confidence: 0.938183

00:26:39.380 --> 00:26:40.975 that you use active controls in

NOTE Confidence: 0.938183

00:26:40.975 --> 00:26:42.375 some of the studies and that would

NOTE Confidence: 0.938183

00:26:42.375 --> 00:26:43.916 it was that done in this study,

NOTE Confidence: 0.938183

00:26:43.920 --> 00:26:45.677 was there an amphetamine control or anything

NOTE Confidence: 0.9318324

00:26:47.840 --> 00:26:50.038 not in this study. But we have,

NOTE Confidence: 0.9318324

00:26:50.040 --> 00:26:54.880 we have looked at amphetamine on this

NOTE Confidence: 0.9318324

00:26:54.880 --> 00:26:57.512 mid task with EEG in a separate group

NOTE Confidence: 0.9318324

00:26:57.512 --> 00:27:00.406 of subjects and I don't think I have the

NOTE Confidence: 0.9318324

00:27:00.406 --> 00:27:02.600 results fully put together to tell you

NOTE Confidence: 0.9388897

00:27:07.230 --> 00:27:08.070 so. Then the other question,

NOTE Confidence: 0.9388897

00:27:08.070 --> 00:27:10.130 important question is whether these

NOTE Confidence: 0.9388897

00:27:10.130 --> 00:27:11.778 alterations in neural function

NOTE Confidence: 0.9388897

00:27:11.778 --> 00:27:13.910 are change with repeated dosing.

NOTE Confidence: 0.9388897

00:27:13.910 --> 00:27:15.331 So even if we don't see anything

NOTE Confidence: 0.9388897

00:27:15.331 --> 00:27:16.870 at this thing after a single dose,

NOTE Confidence: 0.9388897

00:27:16.870 --> 00:27:19.530 it could be that somehow gradually over

NOTE Confidence: 0.9388897

00:27:19.530 --> 00:27:23.430 time with repeated doses this changes.

NOTE Confidence: 0.9388897

00:27:23.430 --> 00:27:24.858 So the next study that I'll

NOTE Confidence: 0.9388897

00:27:24.858 --> 00:27:26.389 describe is a repeated dose study.

NOTE Confidence: 0.9388897

00:27:26.390 --> 00:27:27.710 This was a between subjects.

NOTE Confidence: 0.9388897

00:27:27.710 --> 00:27:29.270 So most of our studies are within subjects,
NOTE Confidence: 0.9388897

00:27:29.270 --> 00:27:30.658 this one's between subjects.
NOTE Confidence: 0.9388897

00:27:30.658 --> 00:27:32.393 So people were randomly assigned
NOTE Confidence: 0.9388897

00:27:32.393 --> 00:27:34.171 to either be in the placebo group
NOTE Confidence: 0.9388897

00:27:34.171 --> 00:27:36.010 or 13 or 26 microgram group.
NOTE Confidence: 0.9388897

00:27:36.010 --> 00:27:38.628 They got their dose on 4 separate
NOTE Confidence: 0.9388897

00:27:38.628 --> 00:27:41.088 occasions separated by three or four days.
NOTE Confidence: 0.9388897

00:27:41.090 --> 00:27:43.540 So session 123 and four are dosing
NOTE Confidence: 0.9388897

00:27:43.540 --> 00:27:46.235 days where they came into the lab and
NOTE Confidence: 0.9388897

00:27:46.235 --> 00:27:48.783 they sat there for four hours for I
NOTE Confidence: 0.9388897

00:27:48.783 --> 00:27:51.165 think it was four or five hours and
NOTE Confidence: 0.9388897

00:27:51.165 --> 00:27:53.090 got this either placebo or the drug.
NOTE Confidence: 0.9388897

00:27:53.090 --> 00:27:55.490 And then some number of days after that,
NOTE Confidence: 0.9388897

00:27:55.490 --> 00:27:57.234 I think it was a week afterwards or
NOTE Confidence: 0.9388897

00:27:57.234 --> 00:27:59.030 or four days after that they had a
NOTE Confidence: 0.9388897

00:27:59.030 --> 00:28:00.882 post test to see whether anything had

NOTE Confidence: 0.9388897

00:28:00.882 --> 00:28:02.736 changed as a function of receiving

NOTE Confidence: 0.9388897

00:28:02.736 --> 00:28:03.970 these four doses.

NOTE Confidence: 0.92100143

00:28:05.290 --> 00:28:06.610 Yes, I have a question.

NOTE Confidence: 0.92100143

00:28:06.610 --> 00:28:09.028 Yes, why did you choose just three

NOTE Confidence: 0.92100143

00:28:09.028 --> 00:28:10.850 to four days between sessions?

NOTE Confidence: 0.92100143

00:28:11.770 --> 00:28:13.230 Oh, because that's what people

NOTE Confidence: 0.92100143

00:28:13.230 --> 00:28:14.690 do when they micro dose,

NOTE Confidence: 0.92100143

00:28:14.690 --> 00:28:17.030 this is oh I see this is kind of modeling

NOTE Confidence: 0.92100143

00:28:17.030 --> 00:28:18.500 what people do when they're micro

NOTE Confidence: 0.92100143

00:28:18.550 --> 00:28:20.170 dosing that's exactly what they do.

NOTE Confidence: 0.92100143

00:28:20.810 --> 00:28:24.146 OK. But because you might expect that those

NOTE Confidence: 0.92100143

00:28:24.146 --> 00:28:28.410 effects of LST might last much longer on EEG,

NOTE Confidence: 0.92100143

00:28:28.410 --> 00:28:31.010 might last longer than three to four days,

NOTE Confidence: 0.94207275

00:28:32.060 --> 00:28:35.580 that's an interesting question.

NOTE Confidence: 0.94207275

00:28:35.580 --> 00:28:38.772 There's no evidence from our studies or from

NOTE Confidence: 0.94207275

00:28:38.772 --> 00:28:41.539 other people's studies that at these doses,
NOTE Confidence: 0.94207275

00:28:41.540 --> 00:28:44.125 the pharmacological, that there's any
NOTE Confidence: 0.94207275

00:28:44.125 --> 00:28:46.193 measurable effect or pharmacological
NOTE Confidence: 0.94207275

00:28:46.193 --> 00:28:48.498 effect left at three or four days.
NOTE Confidence: 0.94207275

00:28:48.500 --> 00:28:51.167 But you're right, there could be some
NOTE Confidence: 0.94207275

00:28:51.167 --> 00:28:53.334 lasting neural changes and that would
NOTE Confidence: 0.94207275

00:28:53.334 --> 00:28:56.025 be interesting to know that and how that
NOTE Confidence: 0.94207275

00:28:56.025 --> 00:28:58.279 changes across the four sessions, right.
NOTE Confidence: 0.94207275

00:28:58.279 --> 00:29:00.191 So the drug is certainly cleared by the
NOTE Confidence: 0.94207275

00:29:00.191 --> 00:29:02.378 three or four days that we were a little bit
NOTE Confidence: 0.94207275

00:29:02.378 --> 00:29:04.157 worried that there might be accumulation,
NOTE Confidence: 0.94207275

00:29:04.160 --> 00:29:05.910 but there's no evidence at all that
NOTE Confidence: 0.94207275

00:29:05.910 --> 00:29:07.040 there's any accumulation of drug.
NOTE Confidence: 0.9365784

00:29:14.600 --> 00:29:17.370 So we looked at both acute responses to
NOTE Confidence: 0.9365784

00:29:17.370 --> 00:29:20.319 the drug at each of the doses using mood,
NOTE Confidence: 0.9365784

00:29:20.320 --> 00:29:20.992 emotional reactivity.

NOTE Confidence: 0.9365784

00:29:20.992 --> 00:29:23.344 So having them look at emotional faces

NOTE Confidence: 0.9365784

00:29:23.344 --> 00:29:25.310 and looking at emotional pictures,

NOTE Confidence: 0.9365784

00:29:25.310 --> 00:29:27.725 we had lots of measures of cognition

NOTE Confidence: 0.9365784

00:29:27.725 --> 00:29:29.722 and go no go tasks, all kinds of

NOTE Confidence: 0.9365784

00:29:29.722 --> 00:29:31.509 things that are cognitive measures.

NOTE Confidence: 0.9365784

00:29:31.510 --> 00:29:33.351 And then we also looked at the

NOTE Confidence: 0.9365784

00:29:33.351 --> 00:29:34.950 lasting effects after the four doses.

NOTE Confidence: 0.9365784

00:29:34.950 --> 00:29:37.043 And this was without the drug present

NOTE Confidence: 0.9365784

00:29:37.043 --> 00:29:39.292 to see whether there were any lasting

NOTE Confidence: 0.9365784

00:29:39.292 --> 00:29:41.224 effects on any of these measures.

NOTE Confidence: 0.9365784

00:29:41.230 --> 00:29:43.589 This side summarizes 2 of the measures.

NOTE Confidence: 0.9365784

00:29:43.590 --> 00:29:44.655 This is depression.

NOTE Confidence: 0.9365784

00:29:44.655 --> 00:29:46.785 And then what's this other one?

NOTE Confidence: 0.9365784

00:29:46.790 --> 00:29:48.630 Vigor. This one is vigor.

NOTE Confidence: 0.9365784

00:29:48.630 --> 00:29:50.838 So sense of energy on the

NOTE Confidence: 0.9365784

00:29:50.838 --> 00:29:52.686 profile of mood states this.
NOTE Confidence: 0.9365784

00:29:52.686 --> 00:29:54.566 It shows their responses during
NOTE Confidence: 0.9365784

00:29:54.566 --> 00:29:56.770 each of the four sessions,
NOTE Confidence: 0.9365784

00:29:56.770 --> 00:29:58.880 session 1234 and I'm showing
NOTE Confidence: 0.9365784

00:29:58.880 --> 00:30:01.366 you here the placebo session is
NOTE Confidence: 0.9365784

00:30:01.366 --> 00:30:03.392 the open bar and then I'm sorry,
NOTE Confidence: 0.9365784

00:30:03.392 --> 00:30:05.289 the placebo group is the open bar,
NOTE Confidence: 0.9365784

00:30:05.290 --> 00:30:07.970 the the 13 microgram group is the middle
NOTE Confidence: 0.9365784

00:30:07.970 --> 00:30:10.525 one and then the darker one is the
NOTE Confidence: 0.93268955

00:30:12.730 --> 00:30:15.877 the darker one is the 26 microgram group.
NOTE Confidence: 0.93268955

00:30:15.877 --> 00:30:18.460 And this is across the four sessions.
NOTE Confidence: 0.93268955

00:30:18.460 --> 00:30:21.400 So you can see on session one we see a
NOTE Confidence: 0.93268955

00:30:21.485 --> 00:30:24.260 nice apparent antidepressant effect that
NOTE Confidence: 0.93268955

00:30:24.260 --> 00:30:27.178 is the highest dose compared to placebo.
NOTE Confidence: 0.93268955

00:30:27.180 --> 00:30:29.462 People show a decrease in depression and
NOTE Confidence: 0.93268955

00:30:29.462 --> 00:30:32.534 it's a little bit there on session 2:00 and

NOTE Confidence: 0.93268955

00:30:32.534 --> 00:30:34.740 basically it disappears by session four.

NOTE Confidence: 0.93268955

00:30:34.740 --> 00:30:37.364 And I should say also that their their

NOTE Confidence: 0.93268955

00:30:37.364 --> 00:30:39.460 ratings on these scales before getting

NOTE Confidence: 0.93268955

00:30:39.460 --> 00:30:41.700 the drug on the four days don't change.

NOTE Confidence: 0.93268955

00:30:41.700 --> 00:30:43.975 So there's no shift in the baseline

NOTE Confidence: 0.93268955

00:30:43.975 --> 00:30:44.950 of depression scores.

NOTE Confidence: 0.93268955

00:30:44.950 --> 00:30:46.894 But so we see a quite a pronounced

NOTE Confidence: 0.93268955

00:30:46.894 --> 00:30:49.001 effect on the first day that they get

NOTE Confidence: 0.93268955

00:30:49.001 --> 00:30:50.827 their dose and that that basically

NOTE Confidence: 0.93268955

00:30:50.827 --> 00:30:53.382 there's apparently tolerance to it or it

NOTE Confidence: 0.93268955

00:30:53.382 --> 00:30:55.790 dissipates across the other four sessions.

NOTE Confidence: 0.93268955

00:30:55.790 --> 00:30:57.680 That was also true for these

NOTE Confidence: 0.93268955

00:30:57.680 --> 00:30:58.625 reports of vigor.

NOTE Confidence: 0.93268955

00:30:58.630 --> 00:30:59.180 So people,

NOTE Confidence: 0.93268955

00:30:59.180 --> 00:31:01.380 this is a change score from pre from

NOTE Confidence: 0.93268955

00:31:01.438 --> 00:31:03.310 at the beginning of the session.
NOTE Confidence: 0.93268955

00:31:03.310 --> 00:31:05.585 Pre capsule or it's not a capsule,
NOTE Confidence: 0.93268955

00:31:05.590 --> 00:31:06.890 it's actually a liquid,
NOTE Confidence: 0.93268955

00:31:06.890 --> 00:31:09.909 but so pre drug to the highest point,
NOTE Confidence: 0.93268955

00:31:09.910 --> 00:31:10.790 it's a peak change.
NOTE Confidence: 0.93268955

00:31:10.790 --> 00:31:12.670 So it's the highest point during the session.
NOTE Confidence: 0.93268955

00:31:12.670 --> 00:31:14.678 So you can see there's a significant
NOTE Confidence: 0.93268955

00:31:14.678 --> 00:31:17.066 increase in vigor and that's there
NOTE Confidence: 0.93268955

00:31:17.066 --> 00:31:19.552 on sessions 1-2 and three and
NOTE Confidence: 0.93268955

00:31:19.552 --> 00:31:21.597 basically disappears by session 4:00.
NOTE Confidence: 0.93268955

00:31:21.600 --> 00:31:24.592 So we found that the first dose decreased
NOTE Confidence: 0.93268955

00:31:24.592 --> 00:31:26.480 depression and increased vigor,
NOTE Confidence: 0.93268955

00:31:26.480 --> 00:31:28.305 but that these effects declined
NOTE Confidence: 0.93268955

00:31:28.305 --> 00:31:29.400 with repeated doses.
NOTE Confidence: 0.93268955

00:31:29.400 --> 00:31:31.808 There were no effects on measures of
NOTE Confidence: 0.93268955

00:31:31.808 --> 00:31:33.400 creativity or psychomotor function,

NOTE Confidence: 0.93268955

00:31:33.400 --> 00:31:35.032 and there were no lasting changes

NOTE Confidence: 0.93268955

00:31:35.032 --> 00:31:36.959 on on any of our measures.

NOTE Confidence: 0.93268955

00:31:36.960 --> 00:31:39.476 So mood measures measures,

NOTE Confidence: 0.93268955

00:31:39.476 --> 00:31:41.992 responses to emotional stimuli

NOTE Confidence: 0.93268955

00:31:41.992 --> 00:31:43.482 or psychomotor effects.

NOTE Confidence: 0.93268955

00:31:43.482 --> 00:31:45.570 And we had a I think the measure of

NOTE Confidence: 0.93268955

00:31:45.627 --> 00:31:47.367 creativity was something like the

NOTE Confidence: 0.924145

00:31:49.410 --> 00:31:51.110 some kind of associations task

NOTE Confidence: 0.924145

00:31:51.110 --> 00:31:52.810 where they're supposed to come

NOTE Confidence: 0.924145

00:31:52.874 --> 00:31:54.614 up with words that are related

NOTE Confidence: 0.924145

00:31:54.614 --> 00:31:56.170 or unrelated to other words.

NOTE Confidence: 0.924145

00:31:56.170 --> 00:31:58.246 Anyway, it's a standardized kind of

NOTE Confidence: 0.924145

00:31:58.250 --> 00:32:00.690 word based measure of creativity,

NOTE Confidence: 0.924145

00:32:00.690 --> 00:32:02.450 but we saw no drug effects on that.

NOTE Confidence: 0.9347962

00:32:05.670 --> 00:32:08.988 So this was a little bit discouraging

NOTE Confidence: 0.9347962

00:32:08.990 --> 00:32:10.950 that that we saw these effects at the
NOTE Confidence: 0.9347962

00:32:10.950 --> 00:32:12.677 beginning and the effects that we saw
NOTE Confidence: 0.9347962

00:32:12.677 --> 00:32:14.427 on that first session are similar to
NOTE Confidence: 0.9347962

00:32:14.427 --> 00:32:16.247 effects that we saw in the previous
NOTE Confidence: 0.9347962

00:32:16.247 --> 00:32:17.830 studies across all of our studies.
NOTE Confidence: 0.9347962

00:32:17.830 --> 00:32:19.495 But that it really disappears
NOTE Confidence: 0.9347962

00:32:19.495 --> 00:32:20.827 across the four days.
NOTE Confidence: 0.9347962

00:32:20.830 --> 00:32:23.692 We, I mean we might we could equally as
NOTE Confidence: 0.9347962

00:32:23.692 --> 00:32:26.786 well have seen the opposite that effects
NOTE Confidence: 0.9347962

00:32:26.786 --> 00:32:29.310 might emerge over repeated sessions,
NOTE Confidence: 0.9347962

00:32:29.310 --> 00:32:32.110 but they didn't, they declined.
NOTE Confidence: 0.9347962

00:32:32.110 --> 00:32:32.630 Yes. Sorry,
NOTE Confidence: 0.9347962

00:32:33.030 --> 00:32:35.480 quick question. Did you have
NOTE Confidence: 0.9347962

00:32:35.480 --> 00:32:37.096 any physiological measure like
NOTE Confidence: 0.9347962

00:32:37.096 --> 00:32:39.116 heart rate or blood pressure?
NOTE Confidence: 0.9347962

00:32:39.120 --> 00:32:41.514 And did you see a similar profile?

NOTE Confidence: 0.9347962

00:32:41.520 --> 00:32:43.968 And do you think this is

NOTE Confidence: 0.9347962

00:32:43.968 --> 00:32:45.600 some kind of tachyphylaxis?

NOTE Confidence: 0.9308408

00:32:47.320 --> 00:32:49.120 I should know the answer to that for sure.

NOTE Confidence: 0.9308408

00:32:49.120 --> 00:32:50.984 We had heart rate and blood pressure and

NOTE Confidence: 0.9308408

00:32:50.984 --> 00:32:52.886 I can't remember exactly how whether or

NOTE Confidence: 0.9308408

00:32:52.886 --> 00:32:55.000 how it changed across the four sessions.

NOTE Confidence: 0.9308408

00:32:55.000 --> 00:32:57.954 I'll follow up on it with you.

NOTE Confidence: 0.9308408

00:32:57.960 --> 00:33:02.344 But yes, it does seem to be tolerance,

NOTE Confidence: 0.9308408

00:33:02.350 --> 00:33:04.247 but you know tolerance can develop at

NOTE Confidence: 0.9308408

00:33:04.247 --> 00:33:06.030 different rates to different measures.

NOTE Confidence: 0.9308408

00:33:06.030 --> 00:33:07.110 So it depending on them,

NOTE Confidence: 0.9308408

00:33:07.110 --> 00:33:09.098 I'm sure you know, depending on the

NOTE Confidence: 0.9308408

00:33:09.098 --> 00:33:10.749 mechanism by which the drug acts.

NOTE Confidence: 0.9308408

00:33:10.750 --> 00:33:14.600 So it could be that there's tolerance

NOTE Confidence: 0.9308408

00:33:14.600 --> 00:33:16.675 to this, these CNS effects and not

NOTE Confidence: 0.9308408

00:33:16.675 --> 00:33:18.510 not tolerance to the heart rate,

NOTE Confidence: 0.9308408

00:33:18.510 --> 00:33:19.308 blood pressure effects.

NOTE Confidence: 0.9308408

00:33:19.308 --> 00:33:20.904 Anyway, I'll get back to you

NOTE Confidence: 0.9308408

00:33:20.904 --> 00:33:22.430 on that whether it was true.

NOTE Confidence: 0.9308408

00:33:22.430 --> 00:33:24.214 But there's another thing I want to say

NOTE Confidence: 0.9308408

00:33:24.214 --> 00:33:25.709 about these and and that's the the,

NOTE Confidence: 0.9308408

00:33:25.710 --> 00:33:27.324 the quality of the effects here

NOTE Confidence: 0.9308408

00:33:27.324 --> 00:33:29.179 and that that's that the drug

NOTE Confidence: 0.9308408

00:33:29.179 --> 00:33:30.627 effects are mainly stimulantlike.

NOTE Confidence: 0.9308408

00:33:30.630 --> 00:33:32.742 So the drug is increasing people's

NOTE Confidence: 0.9308408

00:33:32.742 --> 00:33:34.938 feeling of energy and vigor and

NOTE Confidence: 0.9308408

00:33:34.938 --> 00:33:37.104 we're seeing this across the studies

NOTE Confidence: 0.9308408

00:33:37.110 --> 00:33:38.862 and it could very well be that that

NOTE Confidence: 0.9308408

00:33:38.862 --> 00:33:41.002 kind of feeling and and the and the

NOTE Confidence: 0.9308408

00:33:41.002 --> 00:33:42.633 reports are not dissimilar from what

NOTE Confidence: 0.9308408

00:33:42.633 --> 00:33:44.067 we see when we give amphetamine

NOTE Confidence: 0.9308408

00:33:44.067 --> 00:33:45.699 a low dose of amphetamine.

NOTE Confidence: 0.9308408

00:33:45.699 --> 00:33:48.380 So it could be that that experience

NOTE Confidence: 0.9308408

00:33:48.451 --> 00:33:50.915 of kind of energy and vigor and and

NOTE Confidence: 0.9308408

00:33:50.915 --> 00:33:53.360 that that and sort of confidence

NOTE Confidence: 0.9308408

00:33:53.360 --> 00:33:56.526 that amphetamine gives could give

NOTE Confidence: 0.9308408

00:33:56.526 --> 00:33:58.356 the impression that people are

NOTE Confidence: 0.9308408

00:33:58.356 --> 00:34:00.240 performing better in their lives.

NOTE Confidence: 0.9308408

00:34:00.240 --> 00:34:01.590 It's kind of like a mild

NOTE Confidence: 0.9308408

00:34:01.590 --> 00:34:02.800 antidepressant effect in a sense.

NOTE Confidence: 0.9308408

00:34:02.800 --> 00:34:03.290 You know,

NOTE Confidence: 0.9308408

00:34:03.290 --> 00:34:04.760 I mean amphetamines were used as

NOTE Confidence: 0.9308408

00:34:04.760 --> 00:34:06.078 antidepressants for some period of time.

NOTE Confidence: 0.9308408

00:34:06.080 --> 00:34:08.078 So it could be that the,

NOTE Confidence: 0.9308408

00:34:08.080 --> 00:34:08.492 the,

NOTE Confidence: 0.9308408

00:34:08.492 --> 00:34:10.552 the reports of microdosing could

NOTE Confidence: 0.9308408

00:34:10.552 --> 00:34:13.370 be related to this a self report
NOTE Confidence: 0.9308408

00:34:13.370 --> 00:34:15.320 measure of feeling increased bigger.
NOTE Confidence: 0.940767

00:34:16.980 --> 00:34:18.740 Going back to serials
NOTE Confidence: 0.940767

00:34:18.740 --> 00:34:20.060 question about tachyphylaxis,
NOTE Confidence: 0.940767

00:34:20.060 --> 00:34:21.356 there's a preclinical literature
NOTE Confidence: 0.940767

00:34:21.356 --> 00:34:23.946 which I don't know as well as I
NOTE Confidence: 0.940767

00:34:23.946 --> 00:34:25.401 should about the down regulation
NOTE Confidence: 0.940767

00:34:25.401 --> 00:34:27.071 of 2A receptors after exposure
NOTE Confidence: 0.940767

00:34:27.071 --> 00:34:28.539 to a classic psychedelic.
NOTE Confidence: 0.940767

00:34:28.540 --> 00:34:30.238 And I'm wondering if there's any
NOTE Confidence: 0.940767

00:34:30.238 --> 00:34:31.970 literature on the dose dependence of
NOTE Confidence: 0.940767

00:34:31.970 --> 00:34:34.154 that and if there's any like if there's
NOTE Confidence: 0.940767

00:34:34.205 --> 00:34:36.417 a potential mechanism there at these doses.
NOTE Confidence: 0.940767

00:34:36.420 --> 00:34:38.052 I wonder if anyone knows that
NOTE Confidence: 0.940767

00:34:38.052 --> 00:34:39.540 preclinical but like if that's
NOTE Confidence: 0.940767

00:34:39.540 --> 00:34:40.896 been looked at preclinical

NOTE Confidence: 0.9329231

00:34:42.300 --> 00:34:45.792 there's it definitely there's LSD is

NOTE Confidence: 0.9329231

00:34:45.792 --> 00:34:47.684 reportedly there's there's clear components

NOTE Confidence: 0.9329231

00:34:47.684 --> 00:34:50.492 to many of the effects of LSD and I

NOTE Confidence: 0.9329231

00:34:50.492 --> 00:34:52.340 wasn't aware that that was related to

NOTE Confidence: 0.9329231

00:34:52.402 --> 00:34:54.537 down regulation of the two a receptor.

NOTE Confidence: 0.9329231

00:34:54.540 --> 00:34:56.766 You know we don't know for sure

NOTE Confidence: 0.9329231

00:34:56.766 --> 00:34:58.890 that these low doses exactly act

NOTE Confidence: 0.9329231

00:34:58.890 --> 00:35:01.452 on that and not on other receptors.

NOTE Confidence: 0.9329231

00:35:01.460 --> 00:35:03.434 So there's nobody's really had any

NOTE Confidence: 0.9329231

00:35:03.434 --> 00:35:05.620 particular interest in the very low doses.

NOTE Confidence: 0.9329231

00:35:05.620 --> 00:35:09.660 So, but that would that would be a

NOTE Confidence: 0.9329231

00:35:09.660 --> 00:35:13.156 reasonable to explanation and I guess

NOTE Confidence: 0.9329231

00:35:13.156 --> 00:35:14.934 you'd have to do some kind of pet study

NOTE Confidence: 0.9329231

00:35:14.934 --> 00:35:16.506 to really determine that in people.

NOTE Confidence: 0.9250379

00:35:17.070 --> 00:35:19.470 Some somewhat related to that,

NOTE Confidence: 0.9250379

00:35:19.470 --> 00:35:21.670 Rick Strassman did a study
NOTE Confidence: 0.9250379

00:35:21.670 --> 00:35:24.041 where he repeated DMT doses
NOTE Confidence: 0.9250379

00:35:24.041 --> 00:35:27.023 four times within a single day.
NOTE Confidence: 0.9250379

00:35:27.030 --> 00:35:30.118 Oh, and he failed to find any evidence
NOTE Confidence: 0.9250379

00:35:30.118 --> 00:35:32.148 of tolerance and tachyphylaxis
NOTE Confidence: 0.9250379

00:35:32.710 --> 00:35:35.748 really. Yeah, but it's specific to DMT.
NOTE Confidence: 0.9250379

00:35:35.750 --> 00:35:37.224 Sure, there is a,
NOTE Confidence: 0.9250379

00:35:37.224 --> 00:35:38.600 there is no tolerance to DMT.
NOTE Confidence: 0.9250379

00:35:38.600 --> 00:35:39.830 But with other psychedelics,
NOTE Confidence: 0.9250379

00:35:39.830 --> 00:35:41.720 there is some tolerance,
NOTE Confidence: 0.9250379

00:35:41.720 --> 00:35:46.600 Okay clinically reported by users.
NOTE Confidence: 0.9250379

00:35:46.600 --> 00:35:48.460 Okay. That's interesting.
NOTE Confidence: 0.9250379

00:35:48.460 --> 00:35:52.536 Yeah, So suggest different mechanisms.
NOTE Confidence: 0.9250379

00:35:52.536 --> 00:35:54.693 Yeah. But it hasn't been like
NOTE Confidence: 0.9250379

00:35:54.693 --> 00:35:56.158 super studied like it's more
NOTE Confidence: 0.9250379

00:35:56.160 --> 00:35:58.080 like about what people say.

NOTE Confidence: 0.9250379

00:35:58.080 --> 00:36:00.540 Yeah, right, right, right.

NOTE Confidence: 0.9250379

00:36:00.540 --> 00:36:02.015 Honestly, I don't know about

NOTE Confidence: 0.9250379

00:36:02.015 --> 00:36:02.900 the cardiovascular effect,

NOTE Confidence: 0.9250379

00:36:02.900 --> 00:36:03.980 the heart rate and blood pressure,

NOTE Confidence: 0.9250379

00:36:03.980 --> 00:36:05.498 whether that's mediated

NOTE Confidence: 0.9250379

00:36:05.498 --> 00:36:07.980 peripherally or or or through a

NOTE Confidence: 0.9250379

00:36:07.980 --> 00:36:10.220 twoway receptor or you know I just

NOTE Confidence: 0.9250379

00:36:10.294 --> 00:36:12.338 or or where or how that works.

NOTE Confidence: 0.9250379

00:36:12.340 --> 00:36:14.391 And so I don't know how I

NOTE Confidence: 0.9250379

00:36:14.391 --> 00:36:15.380 would interpret dissociation

NOTE Confidence: 0.9250379

00:36:15.380 --> 00:36:16.980 between the subjective effect

NOTE Confidence: 0.9250379

00:36:16.980 --> 00:36:18.580 and the cardiovascular effect.

NOTE Confidence: 0.92823356

00:36:21.100 --> 00:36:24.908 Harriet. Just to weigh in on my Harriet,

NOTE Confidence: 0.92823356

00:36:24.908 --> 00:36:26.900 it's Emmanuel Schindler.

NOTE Confidence: 0.92823356

00:36:26.900 --> 00:36:29.412 Back in the grad school I used rabbits

NOTE Confidence: 0.92823356

00:36:29.412 --> 00:36:32.436 as my subjects and with chronic
NOTE Confidence: 0.92823356

00:36:32.436 --> 00:36:34.179 administration of psychedelics,
NOTE Confidence: 0.92823356

00:36:34.180 --> 00:36:36.260 there were decreases of the
NOTE Confidence: 0.92823356

00:36:36.260 --> 00:36:38.340 serotonin 2A receptor but not
NOTE Confidence: 0.92823356

00:36:38.413 --> 00:36:40.309 the serotonin 2C receptor.
NOTE Confidence: 0.92823356

00:36:40.310 --> 00:36:42.070 We looked at some dopamine receptors as well.
NOTE Confidence: 0.92823356

00:36:42.070 --> 00:36:43.558 I can't recall right offhand what
NOTE Confidence: 0.92823356

00:36:43.558 --> 00:36:45.030 happened to the dopamine receptors,
NOTE Confidence: 0.92823356

00:36:45.030 --> 00:36:46.630 but there were differences.
NOTE Confidence: 0.92823356

00:36:46.630 --> 00:36:49.030 And at least those two serotonin
NOTE Confidence: 0.92823356

00:36:49.097 --> 00:36:51.170 receptor subtypes in terms of
NOTE Confidence: 0.92823356

00:36:51.170 --> 00:36:52.710 their other down regulation,
NOTE Confidence: 0.9369082

00:36:53.830 --> 00:36:56.182 well that suggests some ways to kind of
NOTE Confidence: 0.9369082

00:36:56.182 --> 00:36:58.457 look at this tolerance with different
NOTE Confidence: 0.9369082

00:36:58.457 --> 00:37:00.893 you in animal models with different
NOTE Confidence: 0.9369082

00:37:00.962 --> 00:37:03.783 drugs and looking at the at the

NOTE Confidence: 0.9369082

00:37:03.783 --> 00:37:04.976 neurotransmitter receptors regulation.

NOTE Confidence: 0.9369082

00:37:04.976 --> 00:37:06.134 That sounds great.

NOTE Confidence: 0.9369082

00:37:06.134 --> 00:37:08.660 That's interesting. Thank you.

NOTE Confidence: 0.9369082

00:37:08.660 --> 00:37:10.612 Somebody has to look do more with dopamine

NOTE Confidence: 0.9369082

00:37:10.612 --> 00:37:12.418 and the and the psychedelic drugs,

NOTE Confidence: 0.9369082

00:37:12.420 --> 00:37:14.220 I think because this really looks

NOTE Confidence: 0.9369082

00:37:14.220 --> 00:37:15.420 like a dopaminergic effect.

NOTE Confidence: 0.94087976

00:37:18.180 --> 00:37:19.604 All right. Study four,

NOTE Confidence: 0.94087976

00:37:19.604 --> 00:37:21.740 most recently we've looked at people.

NOTE Confidence: 0.94087976

00:37:21.740 --> 00:37:24.890 So we thought, well, after all these

NOTE Confidence: 0.94087976

00:37:24.890 --> 00:37:27.036 relatively negative kind of outcomes,

NOTE Confidence: 0.94087976

00:37:27.036 --> 00:37:29.580 maybe it's because our volunteers are

NOTE Confidence: 0.94087976

00:37:29.653 --> 00:37:32.229 healthy and maybe we would see something

NOTE Confidence: 0.94087976

00:37:32.229 --> 00:37:34.226 in people who report depressed mood.

NOTE Confidence: 0.94087976

00:37:34.226 --> 00:37:36.452 So we compared healthy adults to people

NOTE Confidence: 0.94087976

00:37:36.452 --> 00:37:38.144 who had higher than average scores
NOTE Confidence: 0.94087976

00:37:38.144 --> 00:37:40.170 on the back depression inventory.
NOTE Confidence: 0.94087976

00:37:40.170 --> 00:37:42.690 But they're still not, they're not far,
NOTE Confidence: 0.94087976

00:37:42.690 --> 00:37:44.690 they're far from clinically depressed.
NOTE Confidence: 0.94087976

00:37:44.690 --> 00:37:45.854 We just gave the,
NOTE Confidence: 0.94087976

00:37:45.854 --> 00:37:47.018 we have difficulty finding
NOTE Confidence: 0.94087976

00:37:47.018 --> 00:37:48.770 people who are really depressed.
NOTE Confidence: 0.94087976

00:37:48.770 --> 00:37:50.933 So we gave them the back depression
NOTE Confidence: 0.94087976

00:37:50.933 --> 00:37:52.849 inventory and we included people who
NOTE Confidence: 0.94087976

00:37:52.849 --> 00:37:55.360 scores of greater than 17 in our high
NOTE Confidence: 0.94087976

00:37:55.360 --> 00:37:57.355 depressed group and less than 17 in
NOTE Confidence: 0.94087976

00:37:57.355 --> 00:38:00.145 our low depression group and we gave
NOTE Confidence: 0.94087976

00:38:00.145 --> 00:38:01.870 them 26 micrograms versus placebo.
NOTE Confidence: 0.94087976

00:38:01.870 --> 00:38:03.790 So we wanted to know whether
NOTE Confidence: 0.94087976

00:38:03.846 --> 00:38:05.796 single dose of LSD would produce
NOTE Confidence: 0.94087976

00:38:05.796 --> 00:38:07.516 different effects in these people

NOTE Confidence: 0.94087976

00:38:07.516 --> 00:38:09.306 with and without depressed mood.

NOTE Confidence: 0.93485165

00:38:12.790 --> 00:38:13.870 And this is what we found.

NOTE Confidence: 0.93485165

00:38:13.870 --> 00:38:15.893 Interestingly, we did find that there was

NOTE Confidence: 0.93485165

00:38:15.893 --> 00:38:17.990 a difference in the subjective effects.

NOTE Confidence: 0.93485165

00:38:17.990 --> 00:38:20.582 So this is the low BDI group here on

NOTE Confidence: 0.93485165

00:38:20.582 --> 00:38:23.154 the the green is the low group and

NOTE Confidence: 0.93485165

00:38:23.154 --> 00:38:25.550 the purple is the high BDE group.

NOTE Confidence: 0.93485165

00:38:25.550 --> 00:38:27.542 This is their ratings of positive

NOTE Confidence: 0.93485165

00:38:27.542 --> 00:38:29.874 mood on the profile of mood states

NOTE Confidence: 0.93485165

00:38:29.874 --> 00:38:31.752 before they took the capsule and

NOTE Confidence: 0.93485165

00:38:31.752 --> 00:38:33.945 or the drug and then post so on.

NOTE Confidence: 0.93485165

00:38:33.950 --> 00:38:36.294 When they got placebo of course no change

NOTE Confidence: 0.93485165

00:38:36.294 --> 00:38:38.625 and when the healthy the when the low

NOTE Confidence: 0.93485165

00:38:38.625 --> 00:38:40.950 BDI people got LSD there was no change.

NOTE Confidence: 0.93485165

00:38:40.950 --> 00:38:43.197 But you can see over on the

NOTE Confidence: 0.93485165

00:38:43.197 --> 00:38:45.158 right that the high BDA group,
NOTE Confidence: 0.93485165

00:38:45.158 --> 00:38:47.286 BDI group first of all had lower
NOTE Confidence: 0.93485165

00:38:47.286 --> 00:38:49.139 positive moods towards to begin with
NOTE Confidence: 0.93485165

00:38:49.139 --> 00:38:51.309 which is what you might expect if
NOTE Confidence: 0.93485165

00:38:51.309 --> 00:38:53.163 they have high high depression and
NOTE Confidence: 0.93485165

00:38:53.163 --> 00:38:55.266 that the LSD preferentially increased
NOTE Confidence: 0.93485165

00:38:55.266 --> 00:38:57.726 improve their positive mood scores
NOTE Confidence: 0.93485165

00:38:57.726 --> 00:39:00.309 only in the high BD die group.
NOTE Confidence: 0.93485165

00:39:00.310 --> 00:39:03.446 So this is kind of interesting it
NOTE Confidence: 0.93485165

00:39:03.446 --> 00:39:08.430 suggests that the the mood effects of LSD
NOTE Confidence: 0.93485165

00:39:08.430 --> 00:39:11.510 might depend on the baseline mood states.
NOTE Confidence: 0.93485165

00:39:11.510 --> 00:39:14.600 There's there's no question of here
NOTE Confidence: 0.93485165

00:39:14.600 --> 00:39:16.580 of ceiling effects of course that
NOTE Confidence: 0.93485165

00:39:16.580 --> 00:39:18.351 the positive mood in the healthy
NOTE Confidence: 0.93485165

00:39:18.351 --> 00:39:20.115 people it's it's can go up to.
NOTE Confidence: 0.93485165

00:39:20.120 --> 00:39:21.848 I think I have got the scale from

NOTE Confidence: 0.93485165

00:39:21.848 --> 00:39:24.307 -10 to plus 10 here but it can go

NOTE Confidence: 0.93485165

00:39:24.307 --> 00:39:25.480 substantially higher than that.

NOTE Confidence: 0.93485165

00:39:25.480 --> 00:39:27.532 And in fact we a lot of other are

NOTE Confidence: 0.93485165

00:39:27.532 --> 00:39:29.279 other drugs that we administer

NOTE Confidence: 0.93485165

00:39:29.279 --> 00:39:31.094 amphetamine or alcohol or other

NOTE Confidence: 0.93485165

00:39:31.094 --> 00:39:33.701 drugs that that it clearly the drugs

NOTE Confidence: 0.93485165

00:39:33.701 --> 00:39:35.153 clearly increase positive mood.

NOTE Confidence: 0.93485165

00:39:35.160 --> 00:39:37.235 So here it was preferential

NOTE Confidence: 0.93485165

00:39:37.235 --> 00:39:38.966 to the high BDI people.

NOTE Confidence: 0.93485165

00:39:38.966 --> 00:39:40.424 So it's kind of interesting this

NOTE Confidence: 0.93485165

00:39:40.424 --> 00:39:42.280 to me this is the first evidence,

NOTE Confidence: 0.93485165

00:39:42.280 --> 00:39:45.160 it's kind of a just one small step

NOTE Confidence: 0.93485165

00:39:45.160 --> 00:39:47.080 forward that we are seeing some

NOTE Confidence: 0.93485165

00:39:47.080 --> 00:39:49.102 difference in the in the depressed

NOTE Confidence: 0.93485165

00:39:49.102 --> 00:39:51.484 people and this should be extended

NOTE Confidence: 0.93485165

00:39:51.484 --> 00:39:53.635 by someone to look in really more
NOTE Confidence: 0.93485165

00:39:53.635 --> 00:39:55.612 depressed people and to look at different
NOTE Confidence: 0.93485165

00:39:55.612 --> 00:39:57.593 doses and to look at repeated doses
NOTE Confidence: 0.9352026

00:39:59.720 --> 00:40:02.722 and this is their scores on the five DASC.
NOTE Confidence: 0.9352026

00:40:02.722 --> 00:40:04.414 Again, this is this experience of
NOTE Confidence: 0.9352026

00:40:04.414 --> 00:40:05.840 unity and spiritual experience,
NOTE Confidence: 0.9352026

00:40:05.840 --> 00:40:08.462 and again, we're seeing on this
NOTE Confidence: 0.9352026

00:40:08.462 --> 00:40:10.210 measure of psychedelic effects.
NOTE Confidence: 0.9352026

00:40:10.210 --> 00:40:12.250 That the high BDI group.
NOTE Confidence: 0.9352026

00:40:12.250 --> 00:40:15.130 So here the low BDI group is green
NOTE Confidence: 0.9352026

00:40:15.130 --> 00:40:17.930 and the high BDI group is purple.
NOTE Confidence: 0.9352026

00:40:17.930 --> 00:40:19.512 And you can the solid lines are
NOTE Confidence: 0.9352026

00:40:19.512 --> 00:40:21.040 the drug sessions and the hatched
NOTE Confidence: 0.9352026

00:40:21.040 --> 00:40:22.370 lines of the placebo sessions.
NOTE Confidence: 0.9352026

00:40:22.370 --> 00:40:23.970 And if you go start with the left,
NOTE Confidence: 0.9352026

00:40:23.970 --> 00:40:26.350 you can see that there's a small

NOTE Confidence: 0.9352026

00:40:26.350 --> 00:40:28.229 increase in experience of unity after

NOTE Confidence: 0.9352026

00:40:28.229 --> 00:40:30.937 LSD in the low BDI group and a larger

NOTE Confidence: 0.9352026

00:40:30.937 --> 00:40:33.634 difference in the high BDI group and

NOTE Confidence: 0.9352026

00:40:33.634 --> 00:40:36.539 then similarly in each of the measures,

NOTE Confidence: 0.9352026

00:40:36.540 --> 00:40:37.672 spiritual experience,

NOTE Confidence: 0.9352026

00:40:37.672 --> 00:40:38.804 blissful state,

NOTE Confidence: 0.9352026

00:40:38.804 --> 00:40:42.350 insightfulness and total FIDLSD.

NOTE Confidence: 0.9352026

00:40:42.350 --> 00:40:44.970 Then on on all of these the BDI,

NOTE Confidence: 0.9352026

00:40:44.970 --> 00:40:45.590 I'm sorry,

NOTE Confidence: 0.9352026

00:40:45.590 --> 00:40:48.246 the high BDI group seems to be more

NOTE Confidence: 0.9352026

00:40:48.246 --> 00:40:51.137 sensitive to the psychedelic effects of LSD.

NOTE Confidence: 0.9352026

00:40:51.140 --> 00:40:53.835 Very interesting and it still it's also

NOTE Confidence: 0.9352026

00:40:53.835 --> 00:40:57.008 remains to be seen whether there there's

NOTE Confidence: 0.9352026

00:40:57.008 --> 00:40:59.438 it's something about this population

NOTE Confidence: 0.9352026

00:40:59.438 --> 00:41:02.418 and their tendency to report internal states.

NOTE Confidence: 0.9352026

00:41:02.418 --> 00:41:05.537 So, so it could be that they're more likely
NOTE Confidence: 0.9352026

00:41:05.537 --> 00:41:08.183 to report or more sensitive to reporting.
NOTE Confidence: 0.9352026

00:41:08.190 --> 00:41:09.654 So we've never looked at this
NOTE Confidence: 0.9352026

00:41:09.654 --> 00:41:11.269 group of people with other drugs.
NOTE Confidence: 0.9352026

00:41:11.270 --> 00:41:13.670 So that would be an important
NOTE Confidence: 0.9352026

00:41:13.670 --> 00:41:15.270 comparison condition as well.
NOTE Confidence: 0.9352026

00:41:15.270 --> 00:41:17.489 Anyway was it's encouraging to us to
NOTE Confidence: 0.9352026

00:41:17.489 --> 00:41:19.352 see something like this where there
NOTE Confidence: 0.9352026

00:41:19.352 --> 00:41:21.333 is a different where there is an
NOTE Confidence: 0.9352026

00:41:21.390 --> 00:41:23.308 effect of preexisting mood states.
NOTE Confidence: 0.9411063

00:41:26.160 --> 00:41:27.846 So LSD may have more pronounced
NOTE Confidence: 0.9411063

00:41:27.846 --> 00:41:29.440 pronounced effect on certain measures.
NOTE Confidence: 0.9411063

00:41:29.440 --> 00:41:32.534 I should say interestingly that these this
NOTE Confidence: 0.9411063

00:41:32.534 --> 00:41:34.706 increased higher sensitivity in the high
NOTE Confidence: 0.9411063

00:41:34.706 --> 00:41:37.160 BDI group was not there on all measures.
NOTE Confidence: 0.9411063

00:41:37.160 --> 00:41:38.846 If you looked at their ratings

NOTE Confidence: 0.9411063

00:41:38.846 --> 00:41:40.767 of field drug effect that overall

NOTE Confidence: 0.9411063

00:41:40.767 --> 00:41:42.239 global they were identical.

NOTE Confidence: 0.9411063

00:41:42.240 --> 00:41:44.879 So they're reporting the same magnitude of

NOTE Confidence: 0.9411063

00:41:44.879 --> 00:41:47.443 drug effect but they have qualitatively

NOTE Confidence: 0.9411063

00:41:47.443 --> 00:41:49.718 different responses on the drug.

NOTE Confidence: 0.9411063

00:41:49.720 --> 00:41:51.838 So they they have uncertain measures.

NOTE Confidence: 0.9411063

00:41:51.840 --> 00:41:54.220 They reported greater drug effects

NOTE Confidence: 0.9411063

00:41:54.220 --> 00:41:56.806 needs to be replicated with patients

NOTE Confidence: 0.9411063

00:41:56.806 --> 00:41:59.271 with more severe symptoms and then

NOTE Confidence: 0.9411063

00:41:59.271 --> 00:42:01.609 we need to know whether it's related

NOTE Confidence: 0.9411063

00:42:01.609 --> 00:42:04.057 to other life events like early

NOTE Confidence: 0.9411063

00:42:04.057 --> 00:42:05.693 life trauma for example.

NOTE Confidence: 0.9411063

00:42:05.700 --> 00:42:06.327 And I finally,

NOTE Confidence: 0.9411063

00:42:06.327 --> 00:42:07.790 I just want to just go over

NOTE Confidence: 0.9411063

00:42:07.846 --> 00:42:09.370 this one nice study that Murphy

NOTE Confidence: 0.9411063

00:42:09.370 --> 00:42:10.940 at all has recently published.

NOTE Confidence: 0.9411063

00:42:10.940 --> 00:42:13.550 They actually gave LSD or placebo

NOTE Confidence: 0.9411063

00:42:13.550 --> 00:42:16.012 for six weeks, which is much longer

NOTE Confidence: 0.9411063

00:42:16.012 --> 00:42:17.452 than anyone else has done.

NOTE Confidence: 0.9411063

00:42:17.460 --> 00:42:19.644 They gave the first dose in the laboratory

NOTE Confidence: 0.9411063

00:42:19.644 --> 00:42:21.796 and then the subsequent doses at home.

NOTE Confidence: 0.9411063

00:42:21.800 --> 00:42:23.198 So, and that's useful because then

NOTE Confidence: 0.9411063

00:42:23.198 --> 00:42:24.808 you can look at the concordance

NOTE Confidence: 0.9411063

00:42:24.808 --> 00:42:26.373 between their responses in the

NOTE Confidence: 0.9411063

00:42:26.373 --> 00:42:28.199 laboratory and their responses at home.

NOTE Confidence: 0.9411063

00:42:28.200 --> 00:42:28.473 Interestingly,

NOTE Confidence: 0.9411063

00:42:28.473 --> 00:42:30.111 it turned out that the responses

NOTE Confidence: 0.9411063

00:42:30.111 --> 00:42:31.894 at home were greater than their

NOTE Confidence: 0.9411063

00:42:31.894 --> 00:42:33.114 responses in the laboratory.

NOTE Confidence: 0.9411063

00:42:33.120 --> 00:42:34.968 So it's something about the laboratory

NOTE Confidence: 0.9411063

00:42:34.968 --> 00:42:36.200 environment might have actually

NOTE Confidence: 0.9411063

00:42:36.252 --> 00:42:37.836 dampened the responses a little bit.

NOTE Confidence: 0.9411063

00:42:37.840 --> 00:42:39.404 They looked at safety,

NOTE Confidence: 0.9411063

00:42:39.404 --> 00:42:41.359 effectiveness of blinding and expectancies.

NOTE Confidence: 0.9411063

00:42:41.360 --> 00:42:43.488 They gave questionnaires and

NOTE Confidence: 0.9411063

00:42:43.488 --> 00:42:45.616 psychometrics and cognitive tasks.

NOTE Confidence: 0.9411063

00:42:45.620 --> 00:42:47.972 They found that acutely it increased

NOTE Confidence: 0.9411063

00:42:47.972 --> 00:42:49.540 self ratings of creativity,

NOTE Confidence: 0.9411063

00:42:49.540 --> 00:42:50.554 happiness and energy.

NOTE Confidence: 0.9411063

00:42:50.554 --> 00:42:52.920 Now this is again the the measure

NOTE Confidence: 0.9411063

00:42:52.989 --> 00:42:55.446 of creativity is as is just their

NOTE Confidence: 0.9411063

00:42:55.446 --> 00:42:56.499 own subjective reports.

NOTE Confidence: 0.9411063

00:42:56.500 --> 00:42:58.380 And so we don't know what that is.

NOTE Confidence: 0.9411063

00:42:58.380 --> 00:43:00.200 And it's been difficult to

NOTE Confidence: 0.9411063

00:43:00.200 --> 00:43:01.656 capture in objective measures.

NOTE Confidence: 0.9411063

00:43:01.660 --> 00:43:03.480 The effects were most evident

NOTE Confidence: 0.9411063

00:43:03.480 --> 00:43:05.678 on the first five sessions and
NOTE Confidence: 0.9411063

00:43:05.678 --> 00:43:07.514 they saw no adverse effects and
NOTE Confidence: 0.9411063

00:43:07.514 --> 00:43:09.540 they saw no lasting effects.
NOTE Confidence: 0.9411063

00:43:09.540 --> 00:43:13.122 And this is just one of their figures that
NOTE Confidence: 0.9411063

00:43:13.122 --> 00:43:15.392 the if you just look up at the top one,
NOTE Confidence: 0.9411063

00:43:15.400 --> 00:43:17.004 the top left one,
NOTE Confidence: 0.9411063

00:43:17.004 --> 00:43:19.410 this is daily visual analog scale
NOTE Confidence: 0.9411063

00:43:19.491 --> 00:43:22.394 measures and you can see how how
NOTE Confidence: 0.9411063

00:43:22.394 --> 00:43:24.765 much they felt connected or creative
NOTE Confidence: 0.9411063

00:43:24.765 --> 00:43:27.474 or energetic and that the red line
NOTE Confidence: 0.9411063

00:43:27.474 --> 00:43:30.360 is the control and then you can see
NOTE Confidence: 0.9411063

00:43:30.360 --> 00:43:33.520 and then the the the X axis is days
NOTE Confidence: 0.9411063

00:43:33.520 --> 00:43:35.560 and doses across days basically.
NOTE Confidence: 0.9411063

00:43:35.560 --> 00:43:37.636 So you can see that whatever
NOTE Confidence: 0.9411063

00:43:37.636 --> 00:43:38.674 effects there are,
NOTE Confidence: 0.9411063

00:43:38.680 --> 00:43:40.450 they are really primarily in

NOTE Confidence: 0.9411063

00:43:40.450 --> 00:43:43.200 the first say 3 or so sessions.

NOTE Confidence: 0.9411063

00:43:43.200 --> 00:43:44.544 So there's if you look over

NOTE Confidence: 0.9411063

00:43:44.544 --> 00:43:45.999 at energy in the top right,

NOTE Confidence: 0.9411063

00:43:46.000 --> 00:43:47.770 you can see there's an apparent

NOTE Confidence: 0.9411063

00:43:47.770 --> 00:43:49.828 increase in ratings of how energetic

NOTE Confidence: 0.9411063

00:43:49.828 --> 00:43:52.030 they felt and then that dissipated

NOTE Confidence: 0.9411063

00:43:52.100 --> 00:43:53.720 across sessions over time,

NOTE Confidence: 0.9411063

00:43:53.720 --> 00:43:55.760 how happy they felt in the bottom left,

NOTE Confidence: 0.9411063

00:43:55.760 --> 00:43:56.464 how irritable.

NOTE Confidence: 0.9411063

00:43:56.464 --> 00:43:58.576 That was a decrease in irritable.

NOTE Confidence: 0.9411063

00:43:58.580 --> 00:43:59.665 So you can see first of all

NOTE Confidence: 0.9411063

00:43:59.665 --> 00:44:00.740 there's a lot of variability.

NOTE Confidence: 0.9411063

00:44:00.740 --> 00:44:02.180 You can see that.

NOTE Confidence: 0.9411063

00:44:02.180 --> 00:44:04.340 And then also that the effects,

NOTE Confidence: 0.9411063

00:44:04.340 --> 00:44:06.212 they were subtle and they were

NOTE Confidence: 0.9411063

00:44:06.212 --> 00:44:08.020 not really very long lasting.
NOTE Confidence: 0.93844485

00:44:11.060 --> 00:44:12.140 And this is what they concluded.
NOTE Confidence: 0.93844485

00:44:12.140 --> 00:44:13.511 While microdosing elicited
NOTE Confidence: 0.93844485

00:44:13.511 --> 00:44:15.339 transient mood elevating effects,
NOTE Confidence: 0.93844485

00:44:15.340 --> 00:44:17.818 it was not sufficient to produce
NOTE Confidence: 0.93844485

00:44:17.818 --> 00:44:19.979 produce adhering changes to overall
NOTE Confidence: 0.93844485

00:44:19.979 --> 00:44:22.577 mood or cognition in healthy adults.
NOTE Confidence: 0.93844485

00:44:22.580 --> 00:44:23.800 So what can we conclude
NOTE Confidence: 0.93844485

00:44:23.800 --> 00:44:25.020 from all of these things?
NOTE Confidence: 0.93844485

00:44:25.020 --> 00:44:28.112 That LSD appears to produce mild
NOTE Confidence: 0.93844485

00:44:28.112 --> 00:44:29.618 stimulantlike subjective effects
NOTE Confidence: 0.93844485

00:44:29.618 --> 00:44:32.128 that decline with repeated dosing?
NOTE Confidence: 0.93844485

00:44:32.130 --> 00:44:34.426 There are no effects on objective measures
NOTE Confidence: 0.93844485

00:44:34.426 --> 00:44:36.809 of creativity or psychomotor performance.
NOTE Confidence: 0.93844485

00:44:36.810 --> 00:44:38.875 There is appears to be an increased
NOTE Confidence: 0.93844485

00:44:38.875 --> 00:44:40.210 brain response to reward,

NOTE Confidence: 0.93844485

00:44:40.210 --> 00:44:42.898 and there are more pronounced effects on

NOTE Confidence: 0.93844485

00:44:42.898 --> 00:44:45.530 certain measures in depressed individuals.

NOTE Confidence: 0.93844485

00:44:45.530 --> 00:44:47.360 Lots of questions remain to be

NOTE Confidence: 0.93844485

00:44:47.360 --> 00:44:49.189 answered to keep us all busy.

NOTE Confidence: 0.93844485

00:44:49.190 --> 00:44:50.666 Have we measured the right things?

NOTE Confidence: 0.93844485

00:44:50.670 --> 00:44:51.630 We don't know.

NOTE Confidence: 0.93844485

00:44:51.630 --> 00:44:52.270 We don't.

NOTE Confidence: 0.93844485

00:44:52.270 --> 00:44:54.664 One of the challenges is people are

NOTE Confidence: 0.93844485

00:44:54.664 --> 00:44:57.163 making all these claims and and we

NOTE Confidence: 0.93844485

00:44:57.163 --> 00:44:59.790 could easily be missing exactly the

NOTE Confidence: 0.93844485

00:44:59.790 --> 00:45:02.070 dimension that that the drug acts on.

NOTE Confidence: 0.93844485

00:45:02.070 --> 00:45:04.118 So we could be missing whatever it is

NOTE Confidence: 0.93844485

00:45:04.118 --> 00:45:06.627 that it does that improves people's lives.

NOTE Confidence: 0.93844485

00:45:06.630 --> 00:45:08.310 And are there other ways to

NOTE Confidence: 0.93844485

00:45:08.310 --> 00:45:09.430 measure the beneficial effect.

NOTE Confidence: 0.93844485

00:45:09.430 --> 00:45:11.689 So I think here we have to be creative
NOTE Confidence: 0.93844485

00:45:11.689 --> 00:45:13.505 ourselves to come up with new measures.
NOTE Confidence: 0.93844485

00:45:13.510 --> 00:45:15.428 Who benefits most from the micro dosing?
NOTE Confidence: 0.93844485

00:45:15.430 --> 00:45:17.596 So is it more people with
NOTE Confidence: 0.93844485

00:45:17.596 --> 00:45:19.340 psychiatric conditions or older
NOTE Confidence: 0.93844485

00:45:19.340 --> 00:45:21.640 people or men versus women?
NOTE Confidence: 0.93844485

00:45:21.640 --> 00:45:23.280 And we don't know the answers to those.
NOTE Confidence: 0.93844485

00:45:23.280 --> 00:45:24.498 How long do you have to use
NOTE Confidence: 0.93844485

00:45:24.498 --> 00:45:25.959 it to get beneficial effects?
NOTE Confidence: 0.93844485

00:45:25.960 --> 00:45:28.008 And it from the the limited data that
NOTE Confidence: 0.93844485

00:45:28.008 --> 00:45:30.115 I've shown you here and that we've seen,
NOTE Confidence: 0.93844485

00:45:30.120 --> 00:45:32.334 it isn't necessarily that more longer
NOTE Confidence: 0.93844485

00:45:32.334 --> 00:45:34.998 period of time has a better outcome.
NOTE Confidence: 0.93844485

00:45:35.000 --> 00:45:37.060 If if anything shorter period
NOTE Confidence: 0.93844485

00:45:37.060 --> 00:45:38.296 has better outcome.
NOTE Confidence: 0.93844485

00:45:38.300 --> 00:45:40.100 And then what is the role of expectations?

NOTE Confidence: 0.93844485

00:45:40.100 --> 00:45:41.976 We kind of bend over backwards trying

NOTE Confidence: 0.93844485

00:45:41.976 --> 00:45:43.924 to rule out expectancies to that

NOTE Confidence: 0.93844485

00:45:43.924 --> 00:45:45.734 are contributing to the effects.

NOTE Confidence: 0.93844485

00:45:45.740 --> 00:45:47.774 But of course they could interact

NOTE Confidence: 0.93844485

00:45:47.774 --> 00:45:49.430 with the pharmacological effects in

NOTE Confidence: 0.93844485

00:45:49.430 --> 00:45:51.138 the real world in a beneficial way.

NOTE Confidence: 0.93844485

00:45:51.140 --> 00:45:54.040 Really other questions what are

NOTE Confidence: 0.93844485

00:45:54.040 --> 00:45:55.520 the neural mechanisms underlying

NOTE Confidence: 0.93844485

00:45:55.520 --> 00:45:57.849 the effects and are there what are

NOTE Confidence: 0.93844485

00:45:57.849 --> 00:45:59.379 the relationships to the responses

NOTE Confidence: 0.93844485

00:45:59.434 --> 00:46:01.330 that people see with high doses

NOTE Confidence: 0.93844485

00:46:01.330 --> 00:46:02.278 of psychedelic drugs?

NOTE Confidence: 0.93844485

00:46:02.280 --> 00:46:04.224 So the high doses you just get a

NOTE Confidence: 0.93844485

00:46:04.224 --> 00:46:06.349 single big dose and then some over

NOTE Confidence: 0.93844485

00:46:06.349 --> 00:46:07.929 some weeks and months afterwards

NOTE Confidence: 0.93844485

00:46:07.994 --> 00:46:09.434 you have improved symptomatology
NOTE Confidence: 0.93844485

00:46:09.434 --> 00:46:11.912 and this does that work by the
NOTE Confidence: 0.93844485

00:46:11.912 --> 00:46:13.632 same or different mechanisms than
NOTE Confidence: 0.93844485

00:46:13.632 --> 00:46:15.200 these low dose effects?
NOTE Confidence: 0.93844485

00:46:15.200 --> 00:46:17.276 And is there any promise for
NOTE Confidence: 0.93844485

00:46:17.280 --> 00:46:19.200 low dose LSD as a medication?
NOTE Confidence: 0.92108834

00:46:21.250 --> 00:46:23.133 These are some of the people that
NOTE Confidence: 0.92108834

00:46:23.133 --> 00:46:25.063 contributed and most of them are
NOTE Confidence: 0.92108834

00:46:25.063 --> 00:46:26.487 postdoctoral fellows or collaborators.
NOTE Confidence: 0.92108834

00:46:26.490 --> 00:46:28.898 And the work was funded by the
NOTE Confidence: 0.92108834

00:46:28.898 --> 00:46:31.224 University of Chicago Institute for
NOTE Confidence: 0.92108834

00:46:31.224 --> 00:46:33.050 Translational Medicine. And that's all
NOTE Confidence: 0.92108834

00:46:37.330 --> 00:46:38.248 wonderful. Thank you.
NOTE Confidence: 0.92108834

00:46:41.130 --> 00:46:41.770 Any questions?
NOTE Confidence: 0.92108834

00:46:42.890 --> 00:46:45.282 Yeah, I do. I have many, Harriet.
NOTE Confidence: 0.92108834

00:46:45.282 --> 00:46:46.850 I'll keep it brief.

NOTE Confidence: 0.92108834

00:46:46.850 --> 00:46:49.482 The first one is did you attempt

NOTE Confidence: 0.92108834

00:46:49.482 --> 00:46:51.562 to measure expectancy in any of

NOTE Confidence: 0.92108834

00:46:51.562 --> 00:46:53.606 your studies and do you have any

NOTE Confidence: 0.92108834

00:46:53.684 --> 00:46:56.046 suggestions about how we might

NOTE Confidence: 0.92108834

00:46:56.046 --> 00:46:57.950 do that you know moving forward?

NOTE Confidence: 0.93989545

00:46:58.510 --> 00:47:01.390 I we didn't measure expectancies before.

NOTE Confidence: 0.93989545

00:47:01.390 --> 00:47:02.548 I'm glad you asked the question.

NOTE Confidence: 0.93989545

00:47:02.550 --> 00:47:04.665 We did ask them at the end of the

NOTE Confidence: 0.93989545

00:47:04.665 --> 00:47:06.468 sessions what they thought they got.

NOTE Confidence: 0.93989545

00:47:06.470 --> 00:47:08.227 This is from the repeated dosing study.

NOTE Confidence: 0.93989545

00:47:08.230 --> 00:47:09.430 This is the placebo group,

NOTE Confidence: 0.93989545

00:47:09.430 --> 00:47:11.467 the 13 and the 26 microgram group.

NOTE Confidence: 0.93989545

00:47:11.470 --> 00:47:14.910 This is sessions 1234 and

NOTE Confidence: 0.92753625

00:47:16.400 --> 00:47:17.630 we're not seeing your slides

NOTE Confidence: 0.92753625

00:47:17.630 --> 00:47:18.438 anymore. If you're trying

NOTE Confidence: 0.92753625

00:47:20.560 --> 00:47:22.064 doing lolly's talking for
NOTE Confidence: 0.92753625

00:47:22.064 --> 00:47:23.238 nothing, just a second.
NOTE Confidence: 0.92753625

00:47:26.400 --> 00:47:28.200 This is at least 1000 words in the slide.
NOTE Confidence: 0.92753625

00:47:28.200 --> 00:47:32.200 Just a second. Sorry about that.
NOTE Confidence: 0.92753625

00:47:32.200 --> 00:47:35.680 OK, now share. OK, now back up one,
NOTE Confidence: 0.92753625

00:47:35.680 --> 00:47:37.115 back, back up one. There we go.
NOTE Confidence: 0.92753625

00:47:37.120 --> 00:47:39.199 OK, what do you think you got
NOTE Confidence: 0.92753625

00:47:39.200 --> 00:47:40.608 placebo group 13 microgram.
NOTE Confidence: 0.92753625

00:47:40.608 --> 00:47:43.003 This is the repeated dosing sessions 1234.
NOTE Confidence: 0.92753625

00:47:43.003 --> 00:47:44.984 The red is people who said they
NOTE Confidence: 0.92753625

00:47:44.984 --> 00:47:46.689 thought they got a hallucinogen.
NOTE Confidence: 0.92753625

00:47:46.690 --> 00:47:48.330 So on the placebo group,
NOTE Confidence: 0.92753625

00:47:48.330 --> 00:47:50.192 these this number of people said they
NOTE Confidence: 0.92753625

00:47:50.192 --> 00:47:51.360 thought they got a hallucinogen.
NOTE Confidence: 0.92753625

00:47:51.360 --> 00:47:52.710 And then the Gray here
NOTE Confidence: 0.92753625

00:47:52.710 --> 00:47:54.250 at the bottom is placebo,

NOTE Confidence: 0.92753625

00:47:54.250 --> 00:47:54.961 the 13 micrograms,

NOTE Confidence: 0.92753625

00:47:54.961 --> 00:47:57.263 you can see that a few more people said

NOTE Confidence: 0.92753625

00:47:57.263 --> 00:47:59.321 they thought they got a hallucinogen and

NOTE Confidence: 0.92753625

00:47:59.321 --> 00:48:01.368 then the rest were all over the place.

NOTE Confidence: 0.92753625

00:48:01.370 --> 00:48:02.810 And then the 26 microgram,

NOTE Confidence: 0.92753625

00:48:02.810 --> 00:48:04.924 a few more said they got hallucinogen.

NOTE Confidence: 0.92753625

00:48:04.930 --> 00:48:05.210 So

NOTE Confidence: 0.9307646

00:48:07.780 --> 00:48:09.004 what they thought they were going

NOTE Confidence: 0.9307646

00:48:09.004 --> 00:48:10.630 to get before, they had no idea that

NOTE Confidence: 0.9307646

00:48:10.630 --> 00:48:12.706 we told them any one of these all

NOTE Confidence: 0.9307646

00:48:12.706 --> 00:48:14.054 these different possible categories.

NOTE Confidence: 0.9307646

00:48:14.060 --> 00:48:15.120 And after the sessions,

NOTE Confidence: 0.9307646

00:48:15.120 --> 00:48:16.980 this is what they said they got.

NOTE Confidence: 0.9307646

00:48:16.980 --> 00:48:19.460 And then the depression group,

NOTE Confidence: 0.9307646

00:48:19.460 --> 00:48:20.548 we did something similar.

NOTE Confidence: 0.9307646

00:48:20.548 --> 00:48:22.180 This is the high depression group.
NOTE Confidence: 0.9307646

00:48:22.180 --> 00:48:23.860 This is the low depression group.
NOTE Confidence: 0.9307646

00:48:23.860 --> 00:48:26.020 This is their. Oh, we've cut off the.
NOTE Confidence: 0.9307646

00:48:26.020 --> 00:48:27.280 Oh, here they are. Yeah. OK.
NOTE Confidence: 0.9307646

00:48:27.280 --> 00:48:28.780 This is their LSD session,
NOTE Confidence: 0.9307646

00:48:28.780 --> 00:48:30.160 their placebo session,
NOTE Confidence: 0.9307646

00:48:30.160 --> 00:48:31.965 and the black corresponds to
NOTE Confidence: 0.9307646

00:48:31.965 --> 00:48:33.440 they thought they got placebo.
NOTE Confidence: 0.9307646

00:48:33.440 --> 00:48:35.638 So not surprisingly on the placebo sessions,
NOTE Confidence: 0.9307646

00:48:35.640 --> 00:48:37.758 most people thought they got placebo.
NOTE Confidence: 0.9307646

00:48:37.760 --> 00:48:40.875 And here the hallucinogen is this blue.
NOTE Confidence: 0.9307646

00:48:40.880 --> 00:48:43.553 And so you can see this is a high
NOTE Confidence: 0.9307646

00:48:43.560 --> 00:48:45.758 BDI group and the low BDI group.
NOTE Confidence: 0.9307646

00:48:45.760 --> 00:48:47.237 So that's the number of people who
NOTE Confidence: 0.9307646

00:48:47.237 --> 00:48:48.651 thought they got a hallucinogen rather
NOTE Confidence: 0.9307646

00:48:48.651 --> 00:48:50.115 than a stimulant or a sedative,

NOTE Confidence: 0.9307646

00:48:50.120 --> 00:48:50.910 for example.

NOTE Confidence: 0.9307646

00:48:50.910 --> 00:48:53.675 So that doesn't exactly answer your question,

NOTE Confidence: 0.9307646

00:48:53.680 --> 00:48:54.598 but they didn't,

NOTE Confidence: 0.9307646

00:48:54.598 --> 00:48:56.128 they really didn't have expectancies

NOTE Confidence: 0.9307646

00:48:56.128 --> 00:48:56.434 beforehand.

NOTE Confidence: 0.9307646

00:48:56.440 --> 00:48:57.800 They had no clue what they were going to get.

NOTE Confidence: 0.9291967

00:48:58.910 --> 00:49:01.220 But did you look at the relationship

NOTE Confidence: 0.9291967

00:49:01.220 --> 00:49:02.964 between what they thought they

NOTE Confidence: 0.9291967

00:49:02.964 --> 00:49:05.028 got and what their response was?

NOTE Confidence: 0.9291967

00:49:05.030 --> 00:49:07.144 So in people who thought they got

NOTE Confidence: 0.9291967

00:49:07.144 --> 00:49:09.109 a hallucinogen, did they have

NOTE Confidence: 0.9291967

00:49:09.109 --> 00:49:10.750 a bigger response? And yeah,

NOTE Confidence: 0.9291967

00:49:11.390 --> 00:49:12.990 good question. And we haven't looked at that.

NOTE Confidence: 0.9291967

00:49:15.110 --> 00:49:16.050 We didn't. We haven't looked

NOTE Confidence: 0.9291967

00:49:16.050 --> 00:49:18.110 at that. We could. It's yeah,

NOTE Confidence: 0.9291967

00:49:20.830 --> 00:49:23.089 a related question. I you said that all of

NOTE Confidence: 0.9291967

00:49:23.089 --> 00:49:25.425 your participants had at least one previous

NOTE Confidence: 0.9366989

00:49:27.480 --> 00:49:30.879 experience, but do you have any

NOTE Confidence: 0.9366989

00:49:30.879 --> 00:49:32.637 data on what their attitudes were,

NOTE Confidence: 0.9366989

00:49:32.640 --> 00:49:35.920 whether that previous experience was

NOTE Confidence: 0.9366989

00:49:35.920 --> 00:49:38.645 life changing versus pleasant versus

NOTE Confidence: 0.9366989

00:49:38.645 --> 00:49:41.020 neutral versus lousy, whether that,

NOTE Confidence: 0.9366989

00:49:41.020 --> 00:49:42.700 whether that influenced their

NOTE Confidence: 0.9366989

00:49:42.700 --> 00:49:44.280 expected their expectancies? Here

NOTE Confidence: 0.9366989

00:49:45.720 --> 00:49:47.040 we don't have that information.

NOTE Confidence: 0.9366989

00:49:47.040 --> 00:49:48.440 I think if it was lousy, they would

NOTE Confidence: 0.9366989

00:49:48.440 --> 00:49:49.640 not have volunteered for our study.

NOTE Confidence: 0.9366989

00:49:49.640 --> 00:49:51.098 So there's obviously the big selection

NOTE Confidence: 0.9366989

00:49:51.098 --> 00:49:52.774 kind of BIOS here of who participates

NOTE Confidence: 0.9366989

00:49:52.774 --> 00:49:54.581 in this kind of study where we say

NOTE Confidence: 0.9366989

00:49:54.581 --> 00:49:55.997 we're going to give you something,

NOTE Confidence: 0.9366989

00:49:56.000 --> 00:49:57.548 we're not going to tell you what it is.

NOTE Confidence: 0.9366989

00:49:57.550 --> 00:50:00.190 So but it during the screening,

NOTE Confidence: 0.9366989

00:50:00.190 --> 00:50:01.190 the psychiatric screening interview,

NOTE Confidence: 0.9366989

00:50:01.190 --> 00:50:03.107 if they had said they had a bad

NOTE Confidence: 0.9366989

00:50:03.107 --> 00:50:04.223 reaction to any of these drugs,

NOTE Confidence: 0.9366989

00:50:04.230 --> 00:50:05.150 we wouldn't accept them.

NOTE Confidence: 0.9323046

00:50:08.670 --> 00:50:11.109 Hi, Harriet, I also have a lot of questions,

NOTE Confidence: 0.9323046

00:50:11.110 --> 00:50:13.830 but I will pick just one or two.

NOTE Confidence: 0.9323046

00:50:13.830 --> 00:50:15.912 I can't recall in the beginning

NOTE Confidence: 0.9323046

00:50:15.912 --> 00:50:19.336 when you had talked about the some

NOTE Confidence: 0.9323046

00:50:19.336 --> 00:50:20.932 of the evidence that people are

NOTE Confidence: 0.9323046

00:50:20.932 --> 00:50:22.550 out there micro dosing already.

NOTE Confidence: 0.9323046

00:50:22.550 --> 00:50:26.620 And I I I wonder, I can't recall are

NOTE Confidence: 0.9323046

00:50:26.620 --> 00:50:29.345 are these studies from from like

NOTE Confidence: 0.9323046

00:50:29.345 --> 00:50:31.355 recent times or have people been

NOTE Confidence: 0.9323046

00:50:31.355 --> 00:50:33.779 doing this since like the 50s and 60s?
NOTE Confidence: 0.9323046

00:50:33.780 --> 00:50:36.180 Have people been doing it for
NOTE Confidence: 0.9323046

00:50:36.180 --> 00:50:38.101 ceremonial purposes but for millennia?
NOTE Confidence: 0.9323046

00:50:38.101 --> 00:50:40.990 I just have a concern that that is a
NOTE Confidence: 0.9323046

00:50:41.062 --> 00:50:43.519 sort of a a novel new new thing that
NOTE Confidence: 0.9323046

00:50:43.519 --> 00:50:45.881 I'm afraid that the Netflix documentaries
NOTE Confidence: 0.9323046

00:50:45.881 --> 00:50:48.265 and such have sort of prompted.
NOTE Confidence: 0.9323046

00:50:48.265 --> 00:50:50.455 What are your thoughts on that?
NOTE Confidence: 0.928331

00:50:51.020 --> 00:50:51.964 I think it's new,
NOTE Confidence: 0.928331

00:50:51.964 --> 00:50:53.380 although as the years go by,
NOTE Confidence: 0.928331

00:50:53.380 --> 00:50:54.780 it's not so new anymore.
NOTE Confidence: 0.928331

00:50:54.780 --> 00:50:56.820 The Fadiman article was one.
NOTE Confidence: 0.928331

00:50:56.820 --> 00:50:58.212 James Fadiman was one of the
NOTE Confidence: 0.928331

00:50:58.212 --> 00:50:59.140 first people promoting it.
NOTE Confidence: 0.928331

00:50:59.140 --> 00:51:01.390 And it must be now 20 years or something
NOTE Confidence: 0.928331

00:51:01.390 --> 00:51:03.007 since he's been promoting that and

NOTE Confidence: 0.928331

00:51:03.007 --> 00:51:05.300 and that it sort of caught on online.

NOTE Confidence: 0.928331

00:51:05.300 --> 00:51:06.780 But it hasn't in the scale of things.

NOTE Confidence: 0.928331

00:51:06.780 --> 00:51:09.620 It hasn't been very long.

NOTE Confidence: 0.928331

00:51:09.620 --> 00:51:11.480 It sort of came from people

NOTE Confidence: 0.928331

00:51:11.480 --> 00:51:12.724 in California, you know,

NOTE Confidence: 0.928331

00:51:12.724 --> 00:51:15.220 and and and they talk to each other.

NOTE Confidence: 0.928331

00:51:15.220 --> 00:51:18.540 I think that there's a real risk of,

NOTE Confidence: 0.928331

00:51:18.540 --> 00:51:21.060 you know, placebo drug use from

NOTE Confidence: 0.928331

00:51:21.060 --> 00:51:22.740 this kind of communication.

NOTE Confidence: 0.928331

00:51:22.740 --> 00:51:23.180 But anyway,

NOTE Confidence: 0.9370067

00:51:24.450 --> 00:51:26.460 and is there any suggestion or

NOTE Confidence: 0.9370067

00:51:26.460 --> 00:51:28.484 any talk either online or in

NOTE Confidence: 0.9370067

00:51:28.484 --> 00:51:30.029 the literature that you're aware

NOTE Confidence: 0.9370067

00:51:30.029 --> 00:51:32.978 of of with with chronic use?

NOTE Confidence: 0.9370067

00:51:32.978 --> 00:51:35.990 In addition to to potential tolerance,

NOTE Confidence: 0.9370067

00:51:35.990 --> 00:51:38.090 are people having withdrawal symptoms

NOTE Confidence: 0.9370067

00:51:38.090 --> 00:51:40.784 if they stop or if they don't have

NOTE Confidence: 0.9370067

00:51:40.784 --> 00:51:42.530 access to their source anymore?

NOTE Confidence: 0.9370067

00:51:42.530 --> 00:51:44.910 Because this is very different

NOTE Confidence: 0.9370067

00:51:44.910 --> 00:51:47.290 from the typical infrequent use,

NOTE Confidence: 0.9370067

00:51:47.290 --> 00:51:49.245 I wonder whether tolerance and

NOTE Confidence: 0.9370067

00:51:49.245 --> 00:51:51.200 you know perhaps dependence and

NOTE Confidence: 0.9370067

00:51:51.265 --> 00:51:53.407 addiction and come about over the.

NOTE Confidence: 0.9218115

00:51:54.500 --> 00:51:55.752 That's a good question.

NOTE Confidence: 0.9218115

00:51:55.752 --> 00:51:57.630 I have not seen any reports

NOTE Confidence: 0.9218115

00:51:57.695 --> 00:51:59.420 of any adverse effects when

NOTE Confidence: 0.9218115

00:51:59.420 --> 00:52:00.815 people stop using again,

NOTE Confidence: 0.9218115

00:52:00.815 --> 00:52:02.235 they're used they're stopping

NOTE Confidence: 0.9218115

00:52:02.235 --> 00:52:03.655 of their own volition.

NOTE Confidence: 0.9218115

00:52:03.660 --> 00:52:05.529 So it's it's hard to know then

NOTE Confidence: 0.9218115

00:52:05.529 --> 00:52:07.194 how much their expectancies of

NOTE Confidence: 0.9218115

00:52:07.194 --> 00:52:08.786 experiencing something bad when

NOTE Confidence: 0.9218115

00:52:08.786 --> 00:52:11.100 they stop using the influences.

NOTE Confidence: 0.9218115

00:52:15.540 --> 00:52:17.740 Any question. Yeah, go ahead. Yeah.

NOTE Confidence: 0.9218115

00:52:20.420 --> 00:52:22.220 Thank you for this talk.

NOTE Confidence: 0.9218115

00:52:22.220 --> 00:52:24.852 My question is about why finally do

NOTE Confidence: 0.9218115

00:52:24.852 --> 00:52:27.419 we really want people to be blind

NOTE Confidence: 0.9218115

00:52:27.420 --> 00:52:30.660 about micro dosing why for the

NOTE Confidence: 0.9218115

00:52:30.660 --> 00:52:33.820 macro dose we never like criticize

NOTE Confidence: 0.9218115

00:52:33.820 --> 00:52:35.620 so hard that people will have

NOTE Confidence: 0.92393154

00:52:35.620 --> 00:52:37.860 a strong alicenogenic effect and

NOTE Confidence: 0.92393154

00:52:37.860 --> 00:52:41.508 that can also that it can drive part

NOTE Confidence: 0.92393154

00:52:41.508 --> 00:52:44.110 of the of the beneficial effects.

NOTE Confidence: 0.92393154

00:52:44.110 --> 00:52:46.382 Yeah what are your thoughts about it.

NOTE Confidence: 0.92393154

00:52:46.382 --> 00:52:48.847 Well it was part of the attraction of

NOTE Confidence: 0.92393154

00:52:48.847 --> 00:52:50.901 studying micro dosing that you could

NOTE Confidence: 0.92393154

00:52:50.901 --> 00:52:53.013 you could test its the pharmacological

NOTE Confidence: 0.92393154

00:52:53.013 --> 00:52:54.936 effects without having to worry

NOTE Confidence: 0.92393154

00:52:54.936 --> 00:52:56.826 about the confound of expectancies.

NOTE Confidence: 0.92393154

00:52:56.830 --> 00:52:58.979 So in in some ways that's the

NOTE Confidence: 0.92393154

00:52:58.979 --> 00:53:01.109 appeal as a as a researcher

NOTE Confidence: 0.9315515

00:53:04.270 --> 00:53:07.094 but why why did people come up with

NOTE Confidence: 0.9315515

00:53:07.094 --> 00:53:09.821 that idea that I I think it it

NOTE Confidence: 0.9315515

00:53:09.821 --> 00:53:11.702 really came from sort of experimental

NOTE Confidence: 0.9315515

00:53:11.702 --> 00:53:13.830 rigor that they really want to see

NOTE Confidence: 0.9315515

00:53:13.886 --> 00:53:15.290 if there's a a pharmacological

NOTE Confidence: 0.9315515

00:53:15.290 --> 00:53:17.510 effect independently of the of the

NOTE Confidence: 0.9315515

00:53:17.510 --> 00:53:19.658 identification of the drug and the

NOTE Confidence: 0.9315515

00:53:19.658 --> 00:53:21.348 possibility that people that their

NOTE Confidence: 0.9315515

00:53:21.348 --> 00:53:23.070 expectancies are influencing it. So

NOTE Confidence: 0.9400144

00:53:25.630 --> 00:53:28.366 somebody just introduced it as a as a

NOTE Confidence: 0.9400144

00:53:28.366 --> 00:53:30.587 necessary criterion and and I agree with

NOTE Confidence: 0.9400144

00:53:30.587 --> 00:53:32.441 you that that the beneficial effects

NOTE Confidence: 0.9400144

00:53:32.441 --> 00:53:34.667 might be there in this exactly the

NOTE Confidence: 0.9400144

00:53:34.667 --> 00:53:36.510 people who do experience something.

NOTE Confidence: 0.92667234

00:53:39.690 --> 00:53:41.355 That's right. There's this sort

NOTE Confidence: 0.92667234

00:53:41.355 --> 00:53:43.730 of vexing problem in the field.

NOTE Confidence: 0.92667234

00:53:43.730 --> 00:53:46.450 One is the technical one of how do we blind?

NOTE Confidence: 0.92667234

00:53:46.450 --> 00:53:48.448 But then there's the conceptual one

NOTE Confidence: 0.92667234

00:53:48.448 --> 00:53:50.446 of whether the concept of blinding

NOTE Confidence: 0.92667234

00:53:50.446 --> 00:53:53.888 is simply impossible to apply.

NOTE Confidence: 0.92667234

00:53:53.890 --> 00:53:57.649 If the dissociating dissociation of the the

NOTE Confidence: 0.92667234

00:53:57.649 --> 00:54:01.290 subjective effects from the effects is fun,

NOTE Confidence: 0.92667234

00:54:01.290 --> 00:54:03.684 is impossible and therefore that's just a

NOTE Confidence: 0.92667234

00:54:03.684 --> 00:54:05.848 miss a misapplication of an older concept.

NOTE Confidence: 0.92667234

00:54:05.850 --> 00:54:07.116 But I don't. I don't. I don't know.

NOTE Confidence: 0.92667234

00:54:07.116 --> 00:54:09.430 I think it's a big big. So I'm

NOTE Confidence: 0.9342517

00:54:12.350 --> 00:54:15.086 I'm kind of drawn to the model of
NOTE Confidence: 0.9342517

00:54:15.086 --> 00:54:17.560 Ssri's where the Ssri's, they don't
NOTE Confidence: 0.9342517

00:54:17.560 --> 00:54:19.785 produce any immediate acute effects.
NOTE Confidence: 0.9342517

00:54:19.790 --> 00:54:21.950 But somehow magically over time,
NOTE Confidence: 0.9342517

00:54:21.950 --> 00:54:23.336 you take them for several weeks
NOTE Confidence: 0.9342517

00:54:23.336 --> 00:54:24.565 and somehow the world looks
NOTE Confidence: 0.9342517

00:54:24.565 --> 00:54:25.990 better and people, you know,
NOTE Confidence: 0.9342517

00:54:25.990 --> 00:54:27.910 the social anxiety disappears And so,
NOTE Confidence: 0.9342517

00:54:27.910 --> 00:54:29.779 you know, ideally the low dose LSD
NOTE Confidence: 0.9342517

00:54:29.779 --> 00:54:31.670 would have worked something like that.
NOTE Confidence: 0.93212765

00:54:34.890 --> 00:54:36.150 Are you type of question
NOTE Confidence: 0.93212765

00:54:36.150 --> 00:54:37.410 at these very low doses?
NOTE Confidence: 0.93212765

00:54:37.410 --> 00:54:40.350 Can you speculate on whether
NOTE Confidence: 0.93212765

00:54:40.350 --> 00:54:43.290 the receptor binding profile and
NOTE Confidence: 0.93212765

00:54:43.290 --> 00:54:45.570 all the effects rather on these
NOTE Confidence: 0.93212765

00:54:45.570 --> 00:54:47.090 different serotonin receptors is

NOTE Confidence: 0.93212765

00:54:47.151 --> 00:54:48.981 different from what you might get

NOTE Confidence: 0.93212765

00:54:48.981 --> 00:54:51.170 at the typically higher doses?

NOTE Confidence: 0.93212765

00:54:51.810 --> 00:54:53.686 No idea. And I would love somebody

NOTE Confidence: 0.93212765

00:54:53.686 --> 00:54:56.360 to look at that. OK. So any of you

NOTE Confidence: 0.93212765

00:54:56.360 --> 00:54:59.730 who are binding experts do it.

NOTE Confidence: 0.9349472

00:55:02.300 --> 00:55:04.876 And one last comment you in your summary

NOTE Confidence: 0.9349472

00:55:04.876 --> 00:55:07.523 slide you had you know you raised a

NOTE Confidence: 0.9349472

00:55:07.523 --> 00:55:09.978 number of questions that we should pursue.

NOTE Confidence: 0.9349472

00:55:09.980 --> 00:55:12.956 And one of them that I, I,

NOTE Confidence: 0.9349472

00:55:12.956 --> 00:55:15.900 I thought you would have on your in your

NOTE Confidence: 0.9349472

00:55:15.900 --> 00:55:19.568 summary slide is that we don't know much

NOTE Confidence: 0.9349472

00:55:19.568 --> 00:55:22.230 about the safety of chronic administration,

NOTE Confidence: 0.9349472

00:55:22.230 --> 00:55:24.380 chronic use of you know

NOTE Confidence: 0.9349472

00:55:24.380 --> 00:55:26.220 these drugs at low doses.

NOTE Confidence: 0.9349472

00:55:26.220 --> 00:55:28.596 We know about very sporadic use

NOTE Confidence: 0.9349472

00:55:28.596 --> 00:55:30.180 and they're generally safe.

NOTE Confidence: 0.9349472

00:55:30.180 --> 00:55:33.060 But as Emmanuel keeps reminding me, we,

NOTE Confidence: 0.9349472

00:55:33.060 --> 00:55:35.700 you know methysagide was withdrawn from

NOTE Confidence: 0.9349472

00:55:35.700 --> 00:55:38.294 the market because with with repeated

NOTE Confidence: 0.9349472

00:55:38.294 --> 00:55:40.122 administration it was associated

NOTE Confidence: 0.9349472

00:55:40.122 --> 00:55:42.540 with fairly serious side effects.

NOTE Confidence: 0.9338277

00:55:46.340 --> 00:55:50.725 Good question. We haven't seen any sort

NOTE Confidence: 0.9338277

00:55:50.725 --> 00:55:53.300 of anecdotal reports of adverse effects,

NOTE Confidence: 0.9338277

00:55:53.300 --> 00:55:54.660 but then we might not,

NOTE Confidence: 0.9338277

00:55:54.660 --> 00:55:56.298 they might not come to the

NOTE Confidence: 0.9338277

00:55:56.298 --> 00:55:57.980 attention of the medical community.

NOTE Confidence: 0.9338277

00:55:57.980 --> 00:56:02.342 So I don't know whether anybody's looked

NOTE Confidence: 0.9338277

00:56:02.342 --> 00:56:04.779 at something like that in animal models,

NOTE Confidence: 0.9338277

00:56:04.780 --> 00:56:06.865 different systems where there would

NOTE Confidence: 0.9338277

00:56:06.865 --> 00:56:09.035 be adverse, you know, toxicity.

NOTE Confidence: 0.9338277

00:56:09.035 --> 00:56:10.815 So I it's possible.

NOTE Confidence: 0.9338277

00:56:10.820 --> 00:56:11.740 I don't know the answer.

NOTE Confidence: 0.933804299999999

00:56:14.220 --> 00:56:17.100 I know that there are groups who are

NOTE Confidence: 0.933804299999999

00:56:17.100 --> 00:56:19.526 trying to find congeners that have

NOTE Confidence: 0.933804299999999

00:56:19.526 --> 00:56:22.788 the least to be activity or trying to

NOTE Confidence: 0.933804299999999

00:56:22.788 --> 00:56:25.891 take out the serotonin to be affinity

NOTE Confidence: 0.933804299999999

00:56:25.891 --> 00:56:30.246 to make them theoretically safer.

NOTE Confidence: 0.933804299999999

00:56:30.250 --> 00:56:31.780 Even with methysurgide not everybody

NOTE Confidence: 0.933804299999999

00:56:31.780 --> 00:56:34.365 who was on it develop the cardiac valve

NOTE Confidence: 0.933804299999999

00:56:34.365 --> 00:56:36.369 fibrosis and and other tissue fibrosis.

NOTE Confidence: 0.933804299999999

00:56:36.370 --> 00:56:38.603 But there were enough that when it

NOTE Confidence: 0.933804299999999

00:56:38.603 --> 00:56:40.676 was widely used and and this was

NOTE Confidence: 0.933804299999999

00:56:40.676 --> 00:56:42.554 not found in the you know in this

NOTE Confidence: 0.933804299999999

00:56:42.554 --> 00:56:44.062 in the initial studies this was not

NOTE Confidence: 0.933804299999999

00:56:44.062 --> 00:56:45.400 something that was found was found

NOTE Confidence: 0.933804299999999

00:56:45.400 --> 00:56:46.808 later once it was used widely.

NOTE Confidence: 0.933804299999999

00:56:46.810 --> 00:56:49.718 So it may come it might come about

NOTE Confidence: 0.933804299999999

00:56:49.718 --> 00:56:51.973 later if and especially if more and

NOTE Confidence: 0.933804299999999

00:56:51.973 --> 00:56:53.809 more people start start doing it.

NOTE Confidence: 0.9334588

00:56:54.250 --> 00:56:55.850 Yeah right. Yeah good point.

NOTE Confidence: 0.9334588

00:56:55.850 --> 00:56:56.930 Something to watch out for.

NOTE Confidence: 0.91763234

00:57:05.090 --> 00:57:07.730 All right. Anything else? Well,

NOTE Confidence: 0.91763234

00:57:07.730 --> 00:57:09.170 thank you so much, Harriet.

NOTE Confidence: 0.91763234

00:57:09.170 --> 00:57:10.470 This has been really,

NOTE Confidence: 0.91763234

00:57:10.470 --> 00:57:12.049 really wonderful to get this,

NOTE Confidence: 0.91763234

00:57:12.049 --> 00:57:13.723 this overview of your of your

NOTE Confidence: 0.91763234

00:57:13.723 --> 00:57:15.089 groundbreaking work in this area.

NOTE Confidence: 0.91763234

00:57:15.090 --> 00:57:16.410 And well, it was a pleasure

NOTE Confidence: 0.91763234

00:57:17.290 --> 00:57:18.832 you all had. You had good

NOTE Confidence: 0.91763234

00:57:18.832 --> 00:57:20.410 questions and keep me thinking.

NOTE Confidence: 0.91763234

00:57:20.410 --> 00:57:22.825 And I look forward to hearing the

NOTE Confidence: 0.91763234

00:57:22.825 --> 00:57:25.129 results of what you're all doing.

NOTE Confidence: 0.91763234

00:57:25.130 --> 00:57:27.102 Great. Thanks. Bye. All right.

NOTE Confidence: 0.91763234

00:57:27.102 --> 00:57:27.686 Thank you very much.