

WEBVTT

NOTE duration: "00:59:29.450"

NOTE Confidence: 0.6508448

00:00:00.160 --> 00:00:00.659 Okay.

NOTE Confidence: 0.88786215

00:00:07.040 --> 00:00:08.100 We'll get started

NOTE Confidence: 0.983523

00:00:08.559 --> 00:00:10.260 probably in about two minutes.

NOTE Confidence: 0.983523

00:00:10.320 --> 00:00:11.440 Just wanna give folks a

NOTE Confidence: 0.983523

00:00:11.440 --> 00:00:11.940 couple

NOTE Confidence: 0.99471825

00:00:12.240 --> 00:00:13.780 minutes to join in.

NOTE Confidence: 0.96262634

00:00:15.975 --> 00:00:17.355 Really excited to have

NOTE Confidence: 0.9404758

00:00:17.975 --> 00:00:20.475 doctor Pittenger and doctor De Aquino

NOTE Confidence: 0.99856806

00:00:21.175 --> 00:00:21.675 here.

NOTE Confidence: 0.9900443

00:00:31.020 --> 00:00:32.220 Okay. Why don't we go

NOTE Confidence: 0.9900443

00:00:32.220 --> 00:00:33.600 ahead and get started?

NOTE Confidence: 0.9724483

00:00:35.180 --> 00:00:36.239 Well, welcome to

NOTE Confidence: 0.90167576

00:00:36.780 --> 00:00:38.300 the need for research on

NOTE Confidence: 0.90167576

00:00:38.300 --> 00:00:38.800 psychedelics,

NOTE Confidence: 0.99101466

00:00:39.180 --> 00:00:40.159 chronic pain,
NOTE Confidence: 0.9948518

00:00:40.780 --> 00:00:41.280 and,
NOTE Confidence: 0.9992915

00:00:41.739 --> 00:00:43.120 opioid use disorder.
NOTE Confidence: 0.97107

00:00:43.775 --> 00:00:46.035 This is a teaching seminar
NOTE Confidence: 0.97107

00:00:46.095 --> 00:00:47.935 for early stage investigators and
NOTE Confidence: 0.97107

00:00:47.935 --> 00:00:49.475 individuals who may be
NOTE Confidence: 0.9995437

00:00:49.855 --> 00:00:50.995 transitioning towards
NOTE Confidence: 0.99526024

00:00:51.455 --> 00:00:52.975 the area of opioid use
NOTE Confidence: 0.99526024

00:00:52.975 --> 00:00:54.115 disorder or pain.
NOTE Confidence: 0.9954774

00:00:56.810 --> 00:00:57.930 We're really lucky to have
NOTE Confidence: 0.9954774

00:00:57.930 --> 00:00:59.710 two experts in this area.
NOTE Confidence: 0.9745992

00:01:00.890 --> 00:01:02.670 The first is doctor Christopher
NOTE Confidence: 0.9745992

00:01:02.730 --> 00:01:03.230 Pettinger,
NOTE Confidence: 0.86236405

00:01:03.930 --> 00:01:05.930 who's the Elizabeth Meers and
NOTE Confidence: 0.86236405

00:01:05.930 --> 00:01:08.830 House Jamieson professor of psychiatry
NOTE Confidence: 0.86236405

00:01:08.970 --> 00:01:10.350 at Yale School of Medicine.

NOTE Confidence: 0.9939499
00:01:11.105 --> 00:01:12.625 He's the deputy chair for
NOTE Confidence: 0.9939499
00:01:12.625 --> 00:01:13.125 translational
NOTE Confidence: 0.9984884
00:01:13.425 --> 00:01:13.925 research,
NOTE Confidence: 0.97970283
00:01:14.625 --> 00:01:16.165 director of clinical neuroscience
NOTE Confidence: 0.9838786
00:01:16.465 --> 00:01:16.965 research,
NOTE Confidence: 0.9664011
00:01:17.345 --> 00:01:18.625 and director of the Yale
NOTE Confidence: 0.9664011
00:01:18.625 --> 00:01:19.765 program for psychedelic
NOTE Confidence: 0.89481837
00:01:20.305 --> 00:01:21.745 science, as well as the
NOTE Confidence: 0.89481837
00:01:21.745 --> 00:01:22.785 co director of the Yale
NOTE Confidence: 0.89481837
00:01:22.785 --> 00:01:23.825 setup for brain and mind
NOTE Confidence: 0.89481837
00:01:23.825 --> 00:01:24.865 health at the Yale School
NOTE Confidence: 0.89481837
00:01:24.865 --> 00:01:25.525 of Medicine.
NOTE Confidence: 0.9236268
00:01:26.240 --> 00:01:27.440 We will also be joined
NOTE Confidence: 0.9236268
00:01:27.440 --> 00:01:28.980 by doctor De Aquino
NOTE Confidence: 0.9814322
00:01:29.360 --> 00:01:31.040 who's an assistant professor of
NOTE Confidence: 0.9814322

00:01:31.040 --> 00:01:33.040 psychiatry here at Yale, and
NOTE Confidence: 0.9814322

00:01:33.040 --> 00:01:34.240 he will he is also
NOTE Confidence: 0.9814322

00:01:34.240 --> 00:01:35.360 the assistant chief of the
NOTE Confidence: 0.9814322

00:01:35.360 --> 00:01:36.420 inpatient psychiatry
NOTE Confidence: 0.8023382

00:01:37.040 --> 00:01:39.520 clinical neuroscience research unit, and
NOTE Confidence: 0.8023382

00:01:39.520 --> 00:01:40.880 the assistant director of the
NOTE Confidence: 0.8023382

00:01:40.880 --> 00:01:42.295 research affairs of of the
NOTE Confidence: 0.8023382

00:01:42.295 --> 00:01:44.375 clinical neurosurge unit here at
NOTE Confidence: 0.8023382

00:01:44.375 --> 00:01:44.875 Yale.
NOTE Confidence: 0.924536

00:01:45.255 --> 00:01:46.615 So very excited to have
NOTE Confidence: 0.924536

00:01:46.615 --> 00:01:47.515 our two speakers.
NOTE Confidence: 0.9772204

00:01:48.535 --> 00:01:50.615 And without further ado, we'll
NOTE Confidence: 0.9772204

00:01:50.615 --> 00:01:51.655 we'll let you guys take
NOTE Confidence: 0.9772204

00:01:51.655 --> 00:01:52.935 it away. Thank you, Chris
NOTE Confidence: 0.9772204

00:01:52.935 --> 00:01:53.835 and JP.
NOTE Confidence: 0.9639213

00:01:55.450 --> 00:01:55.950 Great.

NOTE Confidence: 0.98804957
00:01:56.970 --> 00:01:58.090 Thank you, everyone. It's really
NOTE Confidence: 0.98804957
00:01:58.090 --> 00:01:58.890 a pleasure to be here
NOTE Confidence: 0.98804957
00:01:58.890 --> 00:01:59.930 with you today. We'll jump
NOTE Confidence: 0.98804957
00:01:59.930 --> 00:02:00.750 right in.
NOTE Confidence: 0.9834267
00:02:01.850 --> 00:02:03.290 I'm not an expert either
NOTE Confidence: 0.9834267
00:02:03.290 --> 00:02:04.990 in substance use or pain,
NOTE Confidence: 0.98065907
00:02:05.450 --> 00:02:06.330 but I have done some
NOTE Confidence: 0.98065907
00:02:06.330 --> 00:02:07.770 work in psychedelics, and I'm
NOTE Confidence: 0.98065907
00:02:07.770 --> 00:02:08.169 gonna,
NOTE Confidence: 0.9632026
00:02:08.794 --> 00:02:10.235 start with maybe about twenty
NOTE Confidence: 0.9632026
00:02:10.235 --> 00:02:12.635 minutes, a broad overview of,
NOTE Confidence: 0.9632026
00:02:12.794 --> 00:02:14.555 what psychedelics are and an
NOTE Confidence: 0.9632026
00:02:14.555 --> 00:02:15.435 introduction to some of the
NOTE Confidence: 0.9632026
00:02:15.435 --> 00:02:16.555 current research that's been done
NOTE Confidence: 0.9632026
00:02:16.555 --> 00:02:17.675 over the last fifteen years
NOTE Confidence: 0.9632026

00:02:17.675 --> 00:02:18.635 or so and what's been
NOTE Confidence: 0.9632026

00:02:18.635 --> 00:02:19.915 called by some of the
NOTE Confidence: 0.9632026

00:02:19.915 --> 00:02:21.629 psychedelic renaissance. And then I'll
NOTE Confidence: 0.9632026

00:02:21.629 --> 00:02:22.909 pass it off to Joao
NOTE Confidence: 0.9632026

00:02:22.909 --> 00:02:24.349 who's going to talk, in
NOTE Confidence: 0.9632026

00:02:24.349 --> 00:02:25.470 a more focused manner. He
NOTE Confidence: 0.9632026

00:02:25.470 --> 00:02:26.989 he is an expert in
NOTE Confidence: 0.9632026

00:02:26.989 --> 00:02:28.430 both, addictions and pain, and
NOTE Confidence: 0.9632026

00:02:28.430 --> 00:02:29.230 he'll talk a little bit
NOTE Confidence: 0.9632026

00:02:29.230 --> 00:02:29.950 more about what we know,
NOTE Confidence: 0.9632026

00:02:29.950 --> 00:02:31.150 which isn't a lot to
NOTE Confidence: 0.9632026

00:02:31.150 --> 00:02:32.450 date, but what we know
NOTE Confidence: 0.9212095

00:02:32.750 --> 00:02:34.129 about use in these conditions.
NOTE Confidence: 0.9639776

00:02:34.505 --> 00:02:35.864 And then what we're hoping
NOTE Confidence: 0.9639776

00:02:35.864 --> 00:02:36.825 to do twenty minutes each
NOTE Confidence: 0.9639776

00:02:36.825 --> 00:02:37.625 and then have some time

NOTE Confidence: 0.9639776
00:02:37.625 --> 00:02:38.825 for discussion at the end.
NOTE Confidence: 0.9639776
00:02:38.825 --> 00:02:39.724 That's the plan.
NOTE Confidence: 0.9929995
00:02:40.105 --> 00:02:40.825 And I will try to
NOTE Confidence: 0.9929995
00:02:40.825 --> 00:02:42.185 keep an eye on the
NOTE Confidence: 0.9929995
00:02:42.185 --> 00:02:43.565 time to keep to that.
NOTE Confidence: 0.92501116
00:02:45.544 --> 00:02:47.305 Okay. I have disclosures. I
NOTE Confidence: 0.92501116
00:02:47.305 --> 00:02:48.505 do do do some consulting
NOTE Confidence: 0.92501116
00:02:48.505 --> 00:02:49.305 in this space. It's not
NOTE Confidence: 0.92501116
00:02:49.305 --> 00:02:50.400 relevant anything I'll be talking
NOTE Confidence: 0.92501116
00:02:50.400 --> 00:02:51.919 about today. So what is
NOTE Confidence: 0.92501116
00:02:51.919 --> 00:02:53.439 a psychedelic? Psychedelic is a
NOTE Confidence: 0.92501116
00:02:53.439 --> 00:02:54.639 is a fairly complicated word
NOTE Confidence: 0.92501116
00:02:54.639 --> 00:02:55.439 and is used in different
NOTE Confidence: 0.92501116
00:02:55.439 --> 00:02:56.639 ways in different contexts, and
NOTE Confidence: 0.92501116
00:02:56.639 --> 00:02:57.700 that can breed confusion.
NOTE Confidence: 0.9770798

00:02:58.239 --> 00:02:59.120 And so I wanna spend
NOTE Confidence: 0.9770798

00:02:59.120 --> 00:03:00.639 a moment unpacking it. There
NOTE Confidence: 0.9770798

00:03:00.639 --> 00:03:02.400 are really three ways that
NOTE Confidence: 0.9770798

00:03:02.400 --> 00:03:03.760 the word is used. The
NOTE Confidence: 0.9770798

00:03:03.760 --> 00:03:05.504 first is as a class
NOTE Confidence: 0.9770798

00:03:05.504 --> 00:03:07.665 of drug or pharmacological, which
NOTE Confidence: 0.9770798

00:03:07.665 --> 00:03:08.944 is what's illustrated on this
NOTE Confidence: 0.9770798

00:03:08.944 --> 00:03:09.444 slide.
NOTE Confidence: 0.9733276

00:03:09.745 --> 00:03:10.944 The second is it's a
NOTE Confidence: 0.9733276

00:03:10.944 --> 00:03:12.004 type of psychological
NOTE Confidence: 0.94113386

00:03:12.305 --> 00:03:13.985 experience, a psychedelic trip, a
NOTE Confidence: 0.94113386

00:03:13.985 --> 00:03:16.385 psychedelic experience, psychedelic art,
psychedelic
NOTE Confidence: 0.94113386

00:03:16.385 --> 00:03:18.000 music, sort of a a
NOTE Confidence: 0.94113386

00:03:18.000 --> 00:03:18.500 somewhat
NOTE Confidence: 0.9658553

00:03:19.120 --> 00:03:20.959 vague but evocative description of
NOTE Confidence: 0.9658553

00:03:20.959 --> 00:03:22.099 a class of experience,
NOTE Confidence: 0.98407054

00:03:23.040 --> 00:03:23.780 or aesthetic.
NOTE Confidence: 0.9884631

00:03:24.239 --> 00:03:25.200 And the third is as
NOTE Confidence: 0.9884631

00:03:25.200 --> 00:03:27.120 an approach to treatment, the
NOTE Confidence: 0.9884631

00:03:27.120 --> 00:03:28.180 psychedelic medicine
NOTE Confidence: 0.98252475

00:03:28.480 --> 00:03:30.065 paradigm, which is the idea
NOTE Confidence: 0.98252475

00:03:30.065 --> 00:03:31.665 of using a mind or
NOTE Confidence: 0.98252475

00:03:31.665 --> 00:03:34.245 consciousness altering substance in conjunction
NOTE Confidence: 0.98252475

00:03:34.544 --> 00:03:35.445 with a psychotherapeutic
NOTE Confidence: 0.9995888

00:03:35.905 --> 00:03:36.405 manipulation
NOTE Confidence: 0.99496627

00:03:37.105 --> 00:03:37.765 to produce
NOTE Confidence: 0.96210784

00:03:38.145 --> 00:03:39.105 a a net effect that
NOTE Confidence: 0.96210784

00:03:39.105 --> 00:03:40.465 is at least intended to
NOTE Confidence: 0.96210784

00:03:40.465 --> 00:03:41.425 be greater than the sum
NOTE Confidence: 0.96210784

00:03:41.425 --> 00:03:42.720 of its parts. So that
NOTE Confidence: 0.96210784

00:03:43.040 --> 00:03:44.480 necessary synergy as opposed to

NOTE Confidence: 0.96210784

00:03:44.480 --> 00:03:45.920 just the additive effect of

NOTE Confidence: 0.96210784

00:03:45.920 --> 00:03:46.420 pharmacological

NOTE Confidence: 0.98332477

00:03:46.720 --> 00:03:48.480 and psychological effects that we,

NOTE Confidence: 0.98332477

00:03:48.720 --> 00:03:50.020 more commonly deploy

NOTE Confidence: 0.97822386

00:03:50.480 --> 00:03:51.920 in psychiatry. So these are

NOTE Confidence: 0.97822386

00:03:51.920 --> 00:03:53.120 the three senses in which

NOTE Confidence: 0.97822386

00:03:53.120 --> 00:03:54.160 the term is used. And,

NOTE Confidence: 0.97822386

00:03:54.160 --> 00:03:55.120 again, I think it's useful

NOTE Confidence: 0.97822386

00:03:55.120 --> 00:03:56.335 to parse that out just

NOTE Confidence: 0.97822386

00:03:56.335 --> 00:03:58.255 because often disagreements or confusions

NOTE Confidence: 0.97822386

00:03:58.255 --> 00:03:59.375 come from the fact that

NOTE Confidence: 0.97822386

00:03:59.375 --> 00:04:00.735 people are using the same

NOTE Confidence: 0.97822386

00:04:00.735 --> 00:04:01.875 words in different ways,

NOTE Confidence: 0.9960418

00:04:02.495 --> 00:04:03.615 and can be avoided if

NOTE Confidence: 0.9960418

00:04:03.615 --> 00:04:04.435 we're more clear.

NOTE Confidence: 0.95328057

00:04:04.975 --> 00:04:06.175 Focusing on the first sense
NOTE Confidence: 0.95328057

00:04:06.175 --> 00:04:07.255 of the word, which, would
NOTE Confidence: 0.95328057

00:04:07.375 --> 00:04:08.415 what it what is a
NOTE Confidence: 0.95328057

00:04:08.415 --> 00:04:09.375 psychedelic in terms of a
NOTE Confidence: 0.95328057

00:04:09.375 --> 00:04:10.255 kind of drug or a
NOTE Confidence: 0.95328057

00:04:10.255 --> 00:04:11.075 kind of molecule,
NOTE Confidence: 0.97261477

00:04:11.580 --> 00:04:12.700 Many of the common drugs
NOTE Confidence: 0.97261477

00:04:12.700 --> 00:04:13.900 that are called psychedelics are
NOTE Confidence: 0.97261477

00:04:13.900 --> 00:04:15.819 illustrated on this slide. Over
NOTE Confidence: 0.97261477

00:04:15.819 --> 00:04:16.779 on the left side, the
NOTE Confidence: 0.97261477

00:04:16.779 --> 00:04:18.620 tryptamines and the ergolines, these
NOTE Confidence: 0.97261477

00:04:18.620 --> 00:04:20.220 are drugs like psilocybin, five
NOTE Confidence: 0.97261477

00:04:20.220 --> 00:04:22.320 methoxy, DMT, DMT, Ibogaine,
NOTE Confidence: 0.9994586

00:04:23.180 --> 00:04:24.240 as well as LSD
NOTE Confidence: 0.9487243

00:04:24.860 --> 00:04:26.479 that have psychedelic effects
NOTE Confidence: 0.8854153

00:04:27.074 --> 00:04:29.175 through the consciousness altering effects

NOTE Confidence: 0.8854153

00:04:29.395 --> 00:04:30.595 through their activities in the

NOTE Confidence: 0.8854153

00:04:30.595 --> 00:04:31.095 serotonin

NOTE Confidence: 0.9880502

00:04:31.555 --> 00:04:32.995 two a receptor. And these

NOTE Confidence: 0.9880502

00:04:32.995 --> 00:04:34.354 are sometimes called the classic

NOTE Confidence: 0.9880502

00:04:34.354 --> 00:04:36.055 psychedelics, and that's the narrowest,

NOTE Confidence: 0.9880502

00:04:36.354 --> 00:04:37.794 cleanest definition of what a

NOTE Confidence: 0.9880502

00:04:37.794 --> 00:04:38.850 psychedelic is.

NOTE Confidence: 0.9800165

00:04:39.330 --> 00:04:40.529 There are other drugs that

NOTE Confidence: 0.9800165

00:04:40.529 --> 00:04:42.790 cause similar or adjacent alterations

NOTE Confidence: 0.9800165

00:04:42.930 --> 00:04:43.670 in consciousness,

NOTE Confidence: 0.9532812

00:04:44.130 --> 00:04:45.830 but through somewhat different mechanisms,

NOTE Confidence: 0.98896027

00:04:46.290 --> 00:04:47.410 often through the flooding of

NOTE Confidence: 0.98896027

00:04:47.410 --> 00:04:48.450 the synapse with lots of

NOTE Confidence: 0.98896027

00:04:48.450 --> 00:04:49.990 serotonin, which is what MDMA

NOTE Confidence: 0.98896027

00:04:50.210 --> 00:04:50.710 does,

NOTE Confidence: 0.9664675

00:04:51.425 --> 00:04:52.705 and other drugs in this
NOTE Confidence: 0.9664675

00:04:52.705 --> 00:04:53.904 in this group, mescaline and
NOTE Confidence: 0.9664675

00:04:53.904 --> 00:04:55.185 these less less well known
NOTE Confidence: 0.9664675

00:04:55.185 --> 00:04:56.944 synthetic drugs. And then there's
NOTE Confidence: 0.9664675

00:04:56.944 --> 00:04:57.824 a large so these are
NOTE Confidence: 0.9664675

00:04:57.824 --> 00:05:00.005 these are called, atypical psychedelics,
NOTE Confidence: 0.9664675

00:05:00.065 --> 00:05:00.865 I think is a useful
NOTE Confidence: 0.9664675

00:05:00.865 --> 00:05:01.745 term for these. There's a
NOTE Confidence: 0.9664675

00:05:01.745 --> 00:05:03.185 little bit less everyone means
NOTE Confidence: 0.9664675

00:05:03.185 --> 00:05:04.145 basically the same thing by
NOTE Confidence: 0.9664675

00:05:04.145 --> 00:05:05.044 classic psychedelics.
NOTE Confidence: 0.95835674

00:05:05.569 --> 00:05:06.690 A little bit more more
NOTE Confidence: 0.95835674

00:05:06.690 --> 00:05:08.210 heterogeneity in how people describe
NOTE Confidence: 0.95835674

00:05:08.210 --> 00:05:09.490 these terms. But I think
NOTE Confidence: 0.95835674

00:05:09.490 --> 00:05:11.250 atypical psychedelics is a pretty
NOTE Confidence: 0.95835674

00:05:11.250 --> 00:05:11.750 good,

NOTE Confidence: 0.9924915

00:05:12.289 --> 00:05:13.190 term for these.

NOTE Confidence: 0.997942

00:05:13.729 --> 00:05:15.110 And then there's a wide

NOTE Confidence: 0.96912926

00:05:15.410 --> 00:05:17.650 selection of heterogeneous, mechanistically and

NOTE Confidence: 0.96912926

00:05:17.650 --> 00:05:20.075 structurally heterogeneous drugs that are

NOTE Confidence: 0.96912926

00:05:20.075 --> 00:05:21.835 sometimes used by psychedelics. I

NOTE Confidence: 0.96912926

00:05:21.835 --> 00:05:23.115 actually don't like using the

NOTE Confidence: 0.96912926

00:05:23.115 --> 00:05:25.115 term psychedelic for these because

NOTE Confidence: 0.96912926

00:05:25.115 --> 00:05:26.235 it just the term becomes

NOTE Confidence: 0.96912926

00:05:26.235 --> 00:05:27.535 so broad that it's useless.

NOTE Confidence: 0.9473431

00:05:27.835 --> 00:05:29.355 But things like salvinorin a,

NOTE Confidence: 0.9473431

00:05:29.355 --> 00:05:30.235 which acts on the kappa

NOTE Confidence: 0.9473431

00:05:30.235 --> 00:05:31.915 opioid receptor, ketamine, which acts

NOTE Confidence: 0.9473431

00:05:31.915 --> 00:05:33.195 on the NMDA receptor as

NOTE Confidence: 0.9473431

00:05:33.195 --> 00:05:35.020 well as others, PCP, also

NOTE Confidence: 0.9473431

00:05:35.020 --> 00:05:37.040 NMDA receptor, Musimol, which is

NOTE Confidence: 0.85138524

00:05:37.420 --> 00:05:38.000 a muscarinic
NOTE Confidence: 0.97328377

00:05:38.300 --> 00:05:39.980 agent. All of these have
NOTE Confidence: 0.97328377

00:05:39.980 --> 00:05:40.480 some,
NOTE Confidence: 0.96735126

00:05:41.020 --> 00:05:42.540 consciousness altering effect. But if
NOTE Confidence: 0.96735126

00:05:42.540 --> 00:05:43.660 we start calling everything with
NOTE Confidence: 0.96735126

00:05:43.660 --> 00:05:45.740 a consciousness altering effect a
NOTE Confidence: 0.96735126

00:05:45.740 --> 00:05:47.260 psychedelic, then why not cocaine?
NOTE Confidence: 0.96735126

00:05:47.260 --> 00:05:48.955 Why not cannabinoids? So I
NOTE Confidence: 0.96735126

00:05:48.955 --> 00:05:50.395 think the term uses loses
NOTE Confidence: 0.96735126

00:05:50.395 --> 00:05:52.075 its specificity to a point
NOTE Confidence: 0.96735126

00:05:52.075 --> 00:05:53.215 that it makes it unhelpful.
NOTE Confidence: 0.96735126

00:05:53.275 --> 00:05:54.475 So I prefer not to
NOTE Confidence: 0.96735126

00:05:54.475 --> 00:05:55.915 call these drugs psychedelics, but
NOTE Confidence: 0.96735126

00:05:55.915 --> 00:05:57.055 sometimes people will.
NOTE Confidence: 0.97437805

00:05:57.995 --> 00:05:58.955 So just just to be
NOTE Confidence: 0.97437805

00:05:58.955 --> 00:06:00.475 aware of this heterogeneity and

NOTE Confidence: 0.97437805

00:06:00.475 --> 00:06:01.960 usage in the literature. We're

NOTE Confidence: 0.97437805

00:06:01.960 --> 00:06:03.720 gonna be talking primarily about

NOTE Confidence: 0.97437805

00:06:03.720 --> 00:06:05.580 the classic psychedelics today.

NOTE Confidence: 0.9362999

00:06:08.200 --> 00:06:10.600 And the research in classic

NOTE Confidence: 0.9362999

00:06:10.600 --> 00:06:12.300 psychedelics is exploding.

NOTE Confidence: 0.9410389

00:06:12.839 --> 00:06:13.960 This is illustrated in a

NOTE Confidence: 0.9410389

00:06:13.960 --> 00:06:15.419 couple slides here.

NOTE Confidence: 0.96565616

00:06:16.055 --> 00:06:17.175 There's a history. I'm I'm

NOTE Confidence: 0.96565616

00:06:17.175 --> 00:06:18.775 not taking time because we

NOTE Confidence: 0.96565616

00:06:18.775 --> 00:06:20.395 wanna keep things focused today

NOTE Confidence: 0.96565616

00:06:20.455 --> 00:06:21.895 to describe the history of

NOTE Confidence: 0.96565616

00:06:21.895 --> 00:06:23.815 psychedelic research, but you probably

NOTE Confidence: 0.96565616

00:06:23.815 --> 00:06:25.574 know that psychedelics would be

NOTE Confidence: 0.96565616

00:06:25.574 --> 00:06:27.255 appreciated by western medicine going

NOTE Confidence: 0.96565616

00:06:27.255 --> 00:06:28.214 back a couple hundred years,

NOTE Confidence: 0.96565616

00:06:28.214 --> 00:06:29.415 but really since the nineteen
NOTE Confidence: 0.96565616

00:06:29.415 --> 00:06:31.230 fifties. They've been appreciated by
NOTE Confidence: 0.96565616

00:06:31.230 --> 00:06:32.589 humanity and used, you know,
NOTE Confidence: 0.96565616

00:06:32.589 --> 00:06:33.630 for thousands of years and
NOTE Confidence: 0.96565616

00:06:33.630 --> 00:06:35.330 used by various indigenous groups.
NOTE Confidence: 0.9852347

00:06:36.029 --> 00:06:36.830 There was a lot of
NOTE Confidence: 0.9852347

00:06:36.830 --> 00:06:37.710 research as well as a
NOTE Confidence: 0.9852347

00:06:37.710 --> 00:06:39.070 lot of recreational use and
NOTE Confidence: 0.9852347

00:06:39.070 --> 00:06:40.130 cultural conversation,
NOTE Confidence: 0.98087084

00:06:40.669 --> 00:06:41.550 from the fifties through the
NOTE Confidence: 0.98087084

00:06:41.550 --> 00:06:42.510 sixties, but then that was
NOTE Confidence: 0.98087084

00:06:42.510 --> 00:06:43.550 largely shut down in the
NOTE Confidence: 0.98087084

00:06:43.550 --> 00:06:44.450 nineteen seventies
NOTE Confidence: 0.969375

00:06:44.955 --> 00:06:46.095 by because of the,
NOTE Confidence: 0.74404967

00:06:46.779 --> 00:06:47.279 the,
NOTE Confidence: 0.91010183

00:06:47.962 --> 00:06:49.615 Controlled Substances Act.

NOTE Confidence: 0.9693704

00:06:50.074 --> 00:06:50.875 And then it's over the

NOTE Confidence: 0.9693704

00:06:50.875 --> 00:06:52.235 last fifteen years or so

NOTE Confidence: 0.9693704

00:06:52.235 --> 00:06:53.354 that there's been this enormous

NOTE Confidence: 0.9693704

00:06:53.354 --> 00:06:54.794 resurgence in interest in research,

NOTE Confidence: 0.9693704

00:06:54.794 --> 00:06:55.995 and that's what's illustrated in

NOTE Confidence: 0.9693704

00:06:55.995 --> 00:06:57.550 these next couple slides. This

NOTE Confidence: 0.9693704

00:06:57.550 --> 00:06:58.990 is an older slide, twenty

NOTE Confidence: 0.9693704

00:06:58.990 --> 00:07:00.190 twenty one, but showing the

NOTE Confidence: 0.9693704

00:07:00.190 --> 00:07:01.970 number of trials in clinicaltrials

NOTE Confidence: 0.9693704

00:07:02.270 --> 00:07:02.930 dot gov

NOTE Confidence: 0.9143868

00:07:03.310 --> 00:07:05.070 investigating the therapeutic use of

NOTE Confidence: 0.9143868

00:07:05.070 --> 00:07:06.910 psychedelics, including the atypical psych

NOTE Confidence: 0.9143868

00:07:07.070 --> 00:07:08.130 psychedelic MDMA.

NOTE Confidence: 0.9593562

00:07:08.509 --> 00:07:09.389 And you can see this

NOTE Confidence: 0.9593562

00:07:09.389 --> 00:07:10.509 dramatic increase. There were a

NOTE Confidence: 0.9593562

00:07:10.509 --> 00:07:11.630 couple of big papers published

NOTE Confidence: 0.9593562

00:07:11.630 --> 00:07:12.995 in twenty sixteen, and that's

NOTE Confidence: 0.9593562

00:07:12.995 --> 00:07:13.794 when it really entered the

NOTE Confidence: 0.9593562

00:07:13.794 --> 00:07:14.914 mainstream of research. So you

NOTE Confidence: 0.9593562

00:07:14.914 --> 00:07:16.354 see this big increase here.

NOTE Confidence: 0.9593562

00:07:16.354 --> 00:07:17.474 On the right, you know,

NOTE Confidence: 0.9593562

00:07:17.474 --> 00:07:18.675 through the same time frame,

NOTE Confidence: 0.9593562

00:07:18.675 --> 00:07:19.794 you see the total number

NOTE Confidence: 0.9593562

00:07:19.794 --> 00:07:20.375 of patients

NOTE Confidence: 0.8876073

00:07:20.754 --> 00:07:22.034 I'm sorry, of individuals and

NOTE Confidence: 0.8876073

00:07:22.034 --> 00:07:22.534 participants

NOTE Confidence: 0.97565156

00:07:22.995 --> 00:07:24.194 who have been engaged in

NOTE Confidence: 0.97565156

00:07:24.194 --> 00:07:26.115 psychedelic research trials. Green is

NOTE Confidence: 0.97565156

00:07:26.115 --> 00:07:27.315 healthy controls and blue is

NOTE Confidence: 0.97565156

00:07:27.315 --> 00:07:28.455 people with a diagnosis

NOTE Confidence: 0.99587834

00:07:28.889 --> 00:07:30.169 in a therapeutic trial. Again,

NOTE Confidence: 0.99587834
00:07:30.169 --> 00:07:31.610 you see this dramatic increase
NOTE Confidence: 0.99587834
00:07:31.610 --> 00:07:32.910 over the same time frame.
NOTE Confidence: 0.9933692
00:07:33.610 --> 00:07:34.570 This is the number of
NOTE Confidence: 0.9933692
00:07:34.570 --> 00:07:36.350 publications going back decades.
NOTE Confidence: 0.96566975
00:07:36.889 --> 00:07:37.930 You see the early era
NOTE Confidence: 0.96566975
00:07:37.930 --> 00:07:39.289 of psychedelic research, but then
NOTE Confidence: 0.96566975
00:07:39.289 --> 00:07:40.650 this explosion in the last
NOTE Confidence: 0.96566975
00:07:40.650 --> 00:07:42.485 fifteen years in publications.
NOTE Confidence: 0.9391703
00:07:43.185 --> 00:07:44.865 And this is an, once
NOTE Confidence: 0.9391703
00:07:44.865 --> 00:07:46.545 a consulting group's estimate of
NOTE Confidence: 0.9391703
00:07:46.545 --> 00:07:48.085 the size of the psychedelic
NOTE Confidence: 0.9391703
00:07:48.225 --> 00:07:49.125 drug market,
NOTE Confidence: 0.96488357
00:07:50.065 --> 00:07:51.105 and the projection that this
NOTE Confidence: 0.96488357
00:07:51.105 --> 00:07:52.145 will be a many billion
NOTE Confidence: 0.96488357
00:07:52.145 --> 00:07:53.425 of dollar billions of dollar
NOTE Confidence: 0.96488357

00:07:53.425 --> 00:07:54.705 market subject to a bunch
NOTE Confidence: 0.96488357

00:07:54.705 --> 00:07:56.225 of assumptions about legalization and
NOTE Confidence: 0.96488357

00:07:56.225 --> 00:07:56.725 access
NOTE Confidence: 0.96828264

00:07:57.070 --> 00:07:57.890 to these drugs.
NOTE Confidence: 0.8969027

00:07:58.350 --> 00:07:59.310 But this is so there's
NOTE Confidence: 0.8969027

00:07:59.310 --> 00:08:00.350 been a lot of industry
NOTE Confidence: 0.8969027

00:08:00.350 --> 00:08:00.850 excitement,
NOTE Confidence: 0.947797

00:08:02.350 --> 00:08:03.870 because of this this projection
NOTE Confidence: 0.947797

00:08:03.870 --> 00:08:05.550 of a burgeoning value in
NOTE Confidence: 0.947797

00:08:05.550 --> 00:08:06.750 this space. And, obviously, that
NOTE Confidence: 0.947797

00:08:06.750 --> 00:08:07.710 is all the usual, the
NOTE Confidence: 0.947797

00:08:07.710 --> 00:08:09.390 benefits, which is new research
NOTE Confidence: 0.947797

00:08:09.390 --> 00:08:10.750 coming into the space, and
NOTE Confidence: 0.947797

00:08:10.750 --> 00:08:11.325 the risks,
NOTE Confidence: 0.94833356

00:08:11.725 --> 00:08:13.105 which is, you know, financial
NOTE Confidence: 0.94833356

00:08:13.165 --> 00:08:13.665 incentives,

NOTE Confidence: 0.97225237
00:08:15.085 --> 00:08:16.765 perverting the the conversation and
NOTE Confidence: 0.97225237
00:08:16.765 --> 00:08:18.285 and influencing how how the
NOTE Confidence: 0.97225237
00:08:18.285 --> 00:08:19.805 research is done. Something for
NOTE Confidence: 0.97225237
00:08:19.805 --> 00:08:20.605 us to be aware of
NOTE Confidence: 0.97225237
00:08:20.605 --> 00:08:21.585 and alert to.
NOTE Confidence: 0.9836205
00:08:21.965 --> 00:08:23.645 Okay. I'm now gonna review
NOTE Confidence: 0.9836205
00:08:23.645 --> 00:08:24.945 some of the classic psychedelics,
NOTE Confidence: 0.85146636
00:08:25.245 --> 00:08:26.250 some of the and and,
NOTE Confidence: 0.8725157
00:08:26.890 --> 00:08:28.090 just to again, with a
NOTE Confidence: 0.8725157
00:08:28.090 --> 00:08:29.290 sort of a thirty thousand
NOTE Confidence: 0.8725157
00:08:29.290 --> 00:08:29.950 foot overview.
NOTE Confidence: 0.99872214
00:08:30.570 --> 00:08:31.950 The the earliest
NOTE Confidence: 0.9788665
00:08:32.330 --> 00:08:33.450 psychedelic in which there was
NOTE Confidence: 0.9788665
00:08:33.450 --> 00:08:35.130 a lot of clinical research
NOTE Confidence: 0.9788665
00:08:35.130 --> 00:08:36.090 back in the fifties and
NOTE Confidence: 0.9788665

00:08:36.090 --> 00:08:38.350 sixties was LSD or lysergic
NOTE Confidence: 0.9788665

00:08:38.410 --> 00:08:39.470 acid diethylamide.
NOTE Confidence: 0.9364686

00:08:40.154 --> 00:08:41.535 This is a semi synthetic,
NOTE Confidence: 0.94494575

00:08:42.154 --> 00:08:43.915 derivative of, molecule that comes
NOTE Confidence: 0.94494575

00:08:43.915 --> 00:08:45.514 from the ergot fungus, and
NOTE Confidence: 0.94494575

00:08:45.514 --> 00:08:46.875 it was produced in nineteen
NOTE Confidence: 0.94494575

00:08:46.875 --> 00:08:48.554 thirty seven. And its psychedelic
NOTE Confidence: 0.94494575

00:08:48.554 --> 00:08:50.654 pro properties were were discovered
NOTE Confidence: 0.94494575

00:08:50.714 --> 00:08:52.475 in nineteen forty three after
NOTE Confidence: 0.94494575

00:08:52.475 --> 00:08:53.214 an accidental,
NOTE Confidence: 0.9640717

00:08:53.940 --> 00:08:55.540 not ingestion, but absorption through
NOTE Confidence: 0.9640717

00:08:55.540 --> 00:08:56.900 the skin by this guy,
NOTE Confidence: 0.9640717

00:08:56.900 --> 00:08:58.660 Albert Hoffman, who's a legend
NOTE Confidence: 0.9640717

00:08:58.660 --> 00:09:00.100 in psychedelic science and is
NOTE Confidence: 0.9640717

00:09:00.100 --> 00:09:01.380 revered by a lot of
NOTE Confidence: 0.9640717

00:09:01.380 --> 00:09:02.520 people in this space.

NOTE Confidence: 0.9209797

00:09:03.140 --> 00:09:04.740 Especially, like and I I

NOTE Confidence: 0.9209797

00:09:04.740 --> 00:09:06.280 I use the word revered

NOTE Confidence: 0.9209797

00:09:06.500 --> 00:09:08.020 knowingly. There's a lot there's

NOTE Confidence: 0.9209797

00:09:08.020 --> 00:09:09.315 a sort of a a

NOTE Confidence: 0.9209797

00:09:09.315 --> 00:09:10.375 great deal of enthusiasm

NOTE Confidence: 0.97274244

00:09:10.835 --> 00:09:12.215 and, and an almost

NOTE Confidence: 0.92117953

00:09:12.595 --> 00:09:13.095 religious,

NOTE Confidence: 0.90581566

00:09:14.035 --> 00:09:15.795 component to to to some

NOTE Confidence: 0.90581566

00:09:15.795 --> 00:09:16.835 some people working in this

NOTE Confidence: 0.90581566

00:09:16.835 --> 00:09:18.035 space. And and Albert Hoffman

NOTE Confidence: 0.90581566

00:09:18.035 --> 00:09:19.075 decided has been called a

NOTE Confidence: 0.90581566

00:09:19.075 --> 00:09:19.975 patron saint.

NOTE Confidence: 0.9845724

00:09:20.755 --> 00:09:21.715 He was a Swiss chemist.

NOTE Confidence: 0.9845724

00:09:21.715 --> 00:09:22.515 He worked for Sandoz, and

NOTE Confidence: 0.9845724

00:09:22.515 --> 00:09:24.195 there's an interesting history behind

NOTE Confidence: 0.9845724

00:09:24.195 --> 00:09:26.059 the production of LSD that
NOTE Confidence: 0.9845724

00:09:26.059 --> 00:09:27.020 I'm not gonna take the
NOTE Confidence: 0.9845724

00:09:27.020 --> 00:09:28.540 time to go into. I'll
NOTE Confidence: 0.9845724

00:09:28.540 --> 00:09:29.500 just say that in the
NOTE Confidence: 0.9845724

00:09:29.500 --> 00:09:30.620 fifties and sixties, there were
NOTE Confidence: 0.9845724

00:09:30.620 --> 00:09:31.679 quite a few trials,
NOTE Confidence: 0.9945401

00:09:32.059 --> 00:09:32.700 and I know that,
NOTE Confidence: 0.94727623

00:09:33.340 --> 00:09:34.380 Joao was gonna come back
NOTE Confidence: 0.94727623

00:09:34.380 --> 00:09:35.580 to some of these. But
NOTE Confidence: 0.94727623

00:09:35.580 --> 00:09:37.100 most research was on alcohol
NOTE Confidence: 0.94727623

00:09:37.100 --> 00:09:38.640 use disorder. This was summarized
NOTE Confidence: 0.94727623

00:09:38.780 --> 00:09:40.184 in a meta analysis by
NOTE Confidence: 0.94727623

00:09:40.265 --> 00:09:41.385 Krebs and Johansson in twenty
NOTE Confidence: 0.94727623

00:09:41.385 --> 00:09:41.545 twenty twelve.
NOTE Confidence: 0.98226464

00:09:43.705 --> 00:09:44.985 This should be LSD. That's
NOTE Confidence: 0.98226464

00:09:44.985 --> 00:09:45.565 a typo.

NOTE Confidence: 0.98101664
00:09:45.945 --> 00:09:46.904 But there were six trials
NOTE Confidence: 0.98101664
00:09:46.904 --> 00:09:48.025 done that were pretty good
NOTE Confidence: 0.98101664
00:09:48.025 --> 00:09:48.985 by the standards of the
NOTE Confidence: 0.98101664
00:09:48.985 --> 00:09:50.425 day, not by modern standards,
NOTE Confidence: 0.98101664
00:09:50.425 --> 00:09:51.785 but pretty good controlled trials
NOTE Confidence: 0.98101664
00:09:51.785 --> 00:09:52.665 by the standards of the
NOTE Confidence: 0.98101664
00:09:52.665 --> 00:09:54.125 day, mostly in male inpatients.
NOTE Confidence: 0.9925726
00:09:54.679 --> 00:09:56.620 And they suggested a significant
NOTE Confidence: 0.9925726
00:09:56.759 --> 00:09:57.259 benefit,
NOTE Confidence: 0.9971989
00:09:57.800 --> 00:09:59.339 in the treatment when LSD
NOTE Confidence: 0.9971989
00:09:59.399 --> 00:10:01.100 was used as an adjunct
NOTE Confidence: 0.9971989
00:10:01.160 --> 00:10:02.699 to other forms of treatment
NOTE Confidence: 0.94158214
00:10:03.000 --> 00:10:04.440 in people with alcohol use
NOTE Confidence: 0.94158214
00:10:04.440 --> 00:10:05.959 disorder. And this is from
NOTE Confidence: 0.94158214
00:10:05.959 --> 00:10:07.985 that meta analysis. So, again,
NOTE Confidence: 0.94158214

00:10:07.985 --> 00:10:09.345 not diving into the details.
NOTE Confidence: 0.94158214

00:10:09.345 --> 00:10:10.304 Joao will will give us
NOTE Confidence: 0.94158214

00:10:10.304 --> 00:10:11.425 a little more. But, but
NOTE Confidence: 0.94158214

00:10:11.425 --> 00:10:12.545 just there there was a
NOTE Confidence: 0.94158214

00:10:12.545 --> 00:10:13.985 pretty decent literature by the
NOTE Confidence: 0.94158214

00:10:13.985 --> 00:10:15.505 standards of the day back
NOTE Confidence: 0.94158214

00:10:15.505 --> 00:10:16.965 in the sixties and the
NOTE Confidence: 0.94158214

00:10:17.265 --> 00:10:18.385 work done in the sixties
NOTE Confidence: 0.94158214

00:10:18.385 --> 00:10:19.925 publication to nineteen seventy,
NOTE Confidence: 0.9703021

00:10:20.630 --> 00:10:21.990 suggesting there's benefit for the
NOTE Confidence: 0.9703021

00:10:21.990 --> 00:10:23.770 treatment of alcohol use disorder.
NOTE Confidence: 0.96089

00:10:25.590 --> 00:10:26.390 And there was a single
NOTE Confidence: 0.96089

00:10:26.390 --> 00:10:27.270 trial that I know of
NOTE Confidence: 0.96089

00:10:27.270 --> 00:10:28.150 in the treatment of opiate
NOTE Confidence: 0.96089

00:10:28.150 --> 00:10:29.350 use disorder, which I, again,
NOTE Confidence: 0.96089

00:10:29.350 --> 00:10:30.230 I know trial is gonna

NOTE Confidence: 0.96089
00:10:30.230 --> 00:10:31.910 come back to. So not
NOTE Confidence: 0.96089
00:10:31.910 --> 00:10:33.510 not gold standard research by
NOTE Confidence: 0.96089
00:10:33.510 --> 00:10:34.545 today's, you know, but it
NOTE Confidence: 0.96089
00:10:34.545 --> 00:10:36.145 wouldn't wouldn't wouldn't, be up
NOTE Confidence: 0.96089
00:10:36.145 --> 00:10:37.425 to snuff by today's standards.
NOTE Confidence: 0.96089
00:10:37.425 --> 00:10:38.865 But there is data from
NOTE Confidence: 0.96089
00:10:38.865 --> 00:10:39.985 what was the mainstream of
NOTE Confidence: 0.96089
00:10:39.985 --> 00:10:40.485 psychiatric
NOTE Confidence: 0.995677
00:10:40.945 --> 00:10:42.165 research at that time.
NOTE Confidence: 0.95282745
00:10:43.665 --> 00:10:44.865 I'll say in in wrapping
NOTE Confidence: 0.95282745
00:10:44.865 --> 00:10:46.304 up about LSD, I don't
NOTE Confidence: 0.95282745
00:10:46.304 --> 00:10:48.260 know of any modern trials
NOTE Confidence: 0.94582987
00:10:48.800 --> 00:10:50.240 looking at LSD and substance
NOTE Confidence: 0.94582987
00:10:50.240 --> 00:10:50.960 use disorder,
NOTE Confidence: 0.8024041
00:10:51.600 --> 00:10:52.420 Joao Mei.
NOTE Confidence: 0.9948179

00:10:53.040 --> 00:10:54.800 But there is an active
NOTE Confidence: 0.9948179

00:10:54.800 --> 00:10:57.060 development program by MindMed Pharmaceuti-
cals
NOTE Confidence: 0.9701848

00:10:57.440 --> 00:10:58.640 trying to develop it for
NOTE Confidence: 0.9701848

00:10:58.640 --> 00:11:00.740 use in generalized anxiety disorder,
NOTE Confidence: 0.9470842

00:11:01.045 --> 00:11:01.925 And they're now they have
NOTE Confidence: 0.9470842

00:11:01.925 --> 00:11:03.445 very promising phase two b
NOTE Confidence: 0.9470842

00:11:03.445 --> 00:11:04.985 data. Phase three is underway,
NOTE Confidence: 0.99633455

00:11:05.285 --> 00:11:06.245 and they're branching out to
NOTE Confidence: 0.99633455

00:11:06.245 --> 00:11:07.765 other indications. So there does
NOTE Confidence: 0.99633455

00:11:07.765 --> 00:11:09.045 continue to be interest in
NOTE Confidence: 0.99633455

00:11:09.045 --> 00:11:10.665 the therapeutic use of LSD.
NOTE Confidence: 0.99837554

00:11:11.765 --> 00:11:12.265 Psilocybin
NOTE Confidence: 0.97251725

00:11:12.804 --> 00:11:14.265 is really where more,
NOTE Confidence: 0.9274376

00:11:15.279 --> 00:11:16.640 research is being done, more
NOTE Confidence: 0.9274376

00:11:16.640 --> 00:11:18.080 in in the broader field
NOTE Confidence: 0.9274376

00:11:18.080 --> 00:11:19.120 as well as in,
NOTE Confidence: 0.9678028

00:11:19.839 --> 00:11:21.040 the treatment of substance use
NOTE Confidence: 0.9678028

00:11:21.040 --> 00:11:22.880 disorder. Psilocybin is a naturally
NOTE Confidence: 0.9678028

00:11:22.880 --> 00:11:24.480 occurring molecule. It was actually
NOTE Confidence: 0.9678028

00:11:24.480 --> 00:11:25.779 synthesized, purified,
NOTE Confidence: 0.935315

00:11:26.160 --> 00:11:27.679 by Arthur Hefter in the
NOTE Confidence: 0.935315

00:11:27.679 --> 00:11:29.745 early twentieth century and then
NOTE Confidence: 0.935315

00:11:29.904 --> 00:11:31.425 synthesized by the same guy,
NOTE Confidence: 0.935315

00:11:31.425 --> 00:11:32.245 Albert Hoffman,
NOTE Confidence: 0.99711955

00:11:32.625 --> 00:11:33.825 in the nineteen fifties.
NOTE Confidence: 0.956615

00:11:34.464 --> 00:11:35.585 This is the chemical structure.
NOTE Confidence: 0.956615

00:11:35.585 --> 00:11:36.625 It looks very similar to
NOTE Confidence: 0.956615

00:11:36.625 --> 00:11:38.304 serotonin. It's a classic psychedelic.
NOTE Confidence: 0.956615

00:11:38.304 --> 00:11:39.925 It binds to serotonin receptors.
NOTE Confidence: 0.956615

00:11:40.225 --> 00:11:41.425 It's been used for centuries
NOTE Confidence: 0.956615

00:11:41.425 --> 00:11:42.385 by people of the Sierra

NOTE Confidence: 0.956615

00:11:42.385 --> 00:11:44.540 Mazteca region in Mexico here

NOTE Confidence: 0.956615

00:11:44.540 --> 00:11:45.500 as well as other regions,

NOTE Confidence: 0.956615

00:11:45.500 --> 00:11:46.220 but this is where it

NOTE Confidence: 0.956615

00:11:46.220 --> 00:11:47.740 was most famously used. And

NOTE Confidence: 0.956615

00:11:47.740 --> 00:11:49.980 it was from, contact with

NOTE Confidence: 0.956615

00:11:49.980 --> 00:11:51.019 the people of this area

NOTE Confidence: 0.956615

00:11:51.100 --> 00:11:52.860 of this region that, the

NOTE Confidence: 0.956615

00:11:52.860 --> 00:11:54.860 western science came into contact

NOTE Confidence: 0.956615

00:11:54.860 --> 00:11:56.480 with, this drug.

NOTE Confidence: 0.97436875

00:11:57.145 --> 00:11:59.225 And there's been more more

NOTE Confidence: 0.97436875

00:11:59.225 --> 00:12:00.765 modern day research in psilocybin

NOTE Confidence: 0.97436875

00:12:00.825 --> 00:12:01.785 than in any of the

NOTE Confidence: 0.97436875

00:12:01.785 --> 00:12:03.245 other classic psychedelics.

NOTE Confidence: 0.9808857

00:12:05.785 --> 00:12:06.985 There were studies in the

NOTE Confidence: 0.9808857

00:12:06.985 --> 00:12:08.745 nineteen seventies nineteen fifties and

NOTE Confidence: 0.9808857

00:12:08.745 --> 00:12:10.905 nineteen sixties suggesting benefit for
NOTE Confidence: 0.9808857

00:12:10.905 --> 00:12:12.480 both addiction and mood. There
NOTE Confidence: 0.9808857

00:12:12.559 --> 00:12:13.920 isn't as much careful work
NOTE Confidence: 0.9808857

00:12:13.920 --> 00:12:14.880 in addiction as there was
NOTE Confidence: 0.9808857

00:12:14.880 --> 00:12:15.540 for LSD,
NOTE Confidence: 0.9769271

00:12:16.720 --> 00:12:18.019 in the fifties and sixties,
NOTE Confidence: 0.9769271

00:12:18.079 --> 00:12:19.279 but definitely enough to suggest
NOTE Confidence: 0.9769271

00:12:19.279 --> 00:12:20.339 that there's a benefit,
NOTE Confidence: 0.9945065

00:12:21.360 --> 00:12:23.139 and to motivate modern research.
NOTE Confidence: 0.9485105

00:12:24.079 --> 00:12:25.839 And recreational use, as I've
NOTE Confidence: 0.9485105

00:12:25.839 --> 00:12:27.279 mentioned, triggered a backlash, which
NOTE Confidence: 0.9485105

00:12:27.279 --> 00:12:28.904 triggered led to the Controlled
NOTE Confidence: 0.9485105

00:12:28.904 --> 00:12:30.445 Substances Act in the nineteen
NOTE Confidence: 0.9485105

00:12:30.665 --> 00:12:32.745 early nineteen seventies, leading to
NOTE Confidence: 0.9485105

00:12:32.745 --> 00:12:34.105 an almost complete shutdown of
NOTE Confidence: 0.9485105

00:12:34.105 --> 00:12:35.644 research for about thirty years.

NOTE Confidence: 0.9650076
00:12:36.904 --> 00:12:38.285 I wanna take this opportunity.
NOTE Confidence: 0.9650076
00:12:38.345 --> 00:12:39.545 I could have shown similar
NOTE Confidence: 0.9650076
00:12:39.545 --> 00:12:41.065 slides for LSD because we
NOTE Confidence: 0.9650076
00:12:41.065 --> 00:12:42.345 think they work in in
NOTE Confidence: 0.9650076
00:12:42.345 --> 00:12:43.649 similar ways in the brain,
NOTE Confidence: 0.9650076
00:12:43.649 --> 00:12:44.610 but I wanna dip just
NOTE Confidence: 0.9650076
00:12:44.610 --> 00:12:45.730 a little bit into the
NOTE Confidence: 0.9650076
00:12:45.809 --> 00:12:46.709 some of the neurobiology
NOTE Confidence: 0.9969317
00:12:47.089 --> 00:12:48.870 about how these substances work.
NOTE Confidence: 0.97280025
00:12:49.889 --> 00:12:51.510 They bind to several serotonin
NOTE Confidence: 0.97280025
00:12:51.570 --> 00:12:53.570 receptors, prominently two a, two
NOTE Confidence: 0.97280025
00:12:53.570 --> 00:12:55.429 c, and one a.
NOTE Confidence: 0.801923
00:12:57.225 --> 00:12:57.725 Nonserotonin
NOTE Confidence: 0.98238456
00:12:58.105 --> 00:12:59.464 serotonergic effects appear to be
NOTE Confidence: 0.98238456
00:12:59.464 --> 00:13:00.745 much lower affinity. So it's
NOTE Confidence: 0.98238456

00:13:00.745 --> 00:13:02.345 probably these receptors that have

NOTE Confidence: 0.98238456

00:13:02.345 --> 00:13:03.785 most of the benefit. This

NOTE Confidence: 0.98238456

00:13:03.785 --> 00:13:05.065 is the crystal structure of

NOTE Confidence: 0.98238456

00:13:05.065 --> 00:13:06.184 the two a receptor. I

NOTE Confidence: 0.98238456

00:13:06.184 --> 00:13:06.825 just like to put it

NOTE Confidence: 0.98238456

00:13:06.825 --> 00:13:07.950 up there because it's pretty.

NOTE Confidence: 0.9887981

00:13:08.350 --> 00:13:09.390 But of more relevance, if

NOTE Confidence: 0.9887981

00:13:09.390 --> 00:13:10.030 you look on the right,

NOTE Confidence: 0.9887981

00:13:10.030 --> 00:13:11.150 this is a PET imaging

NOTE Confidence: 0.9887981

00:13:11.150 --> 00:13:12.590 study showing the distribution of

NOTE Confidence: 0.9887981

00:13:12.590 --> 00:13:13.650 the two a receptor

NOTE Confidence: 0.9770088

00:13:14.190 --> 00:13:15.150 over the surface of the

NOTE Confidence: 0.9770088

00:13:15.150 --> 00:13:15.950 brain. And you can see

NOTE Confidence: 0.9770088

00:13:15.950 --> 00:13:17.170 it's found all over,

NOTE Confidence: 0.95072997

00:13:17.470 --> 00:13:19.230 but particularly in regions of

NOTE Confidence: 0.95072997

00:13:19.230 --> 00:13:21.730 the, multimodal or or, association

NOTE Confidence: 0.95072997
00:13:21.870 --> 00:13:23.285 cortex, the default mode network
NOTE Confidence: 0.95072997
00:13:23.285 --> 00:13:24.665 and the posterior cingulate
NOTE Confidence: 0.88229144
00:13:25.045 --> 00:13:27.145 and then, medial prefrontal cortex,
NOTE Confidence: 0.98999053
00:13:27.525 --> 00:13:29.925 lateral temporal cortex shown here
NOTE Confidence: 0.98999053
00:13:29.925 --> 00:13:31.625 and here. So there's,
NOTE Confidence: 0.99787647
00:13:32.085 --> 00:13:33.365 there's a lot of expression
NOTE Confidence: 0.99787647
00:13:33.365 --> 00:13:34.105 in association
NOTE Confidence: 0.994869
00:13:34.565 --> 00:13:35.065 cortex,
NOTE Confidence: 0.9942034
00:13:35.765 --> 00:13:36.630 in the brain.
NOTE Confidence: 0.9904894
00:13:37.350 --> 00:13:38.650 And so it's not terribly
NOTE Confidence: 0.9904894
00:13:38.870 --> 00:13:40.230 surprising that that's where you
NOTE Confidence: 0.9904894
00:13:40.230 --> 00:13:41.610 see a lot of effects
NOTE Confidence: 0.96683955
00:13:42.070 --> 00:13:43.370 when you treat with psilocybin.
NOTE Confidence: 0.96683955
00:13:43.510 --> 00:13:44.790 This is an analysis that
NOTE Confidence: 0.96683955
00:13:44.790 --> 00:13:46.470 was done on data collected
NOTE Confidence: 0.96683955

00:13:46.470 --> 00:13:48.090 in Switzerland where the moratorium
NOTE Confidence: 0.96683955

00:13:48.309 --> 00:13:49.270 on research was never as
NOTE Confidence: 0.96683955

00:13:49.270 --> 00:13:50.415 severe as it was in
NOTE Confidence: 0.96683955

00:13:50.574 --> 00:13:51.875 other western countries,
NOTE Confidence: 0.92591524

00:13:52.255 --> 00:13:54.035 but analyzed by Alan Antisevich
NOTE Confidence: 0.92591524

00:13:54.095 --> 00:13:54.834 and his colleagues,
NOTE Confidence: 0.96300626

00:13:55.214 --> 00:13:56.735 here at Yale. What's shown
NOTE Confidence: 0.96300626

00:13:56.735 --> 00:13:57.774 here, the I'm not gonna
NOTE Confidence: 0.96300626

00:13:57.774 --> 00:13:58.654 dig and dive into all
NOTE Confidence: 0.96300626

00:13:58.654 --> 00:13:59.535 the details, but this is
NOTE Confidence: 0.96300626

00:13:59.535 --> 00:14:01.375 an fMRI study looking at
NOTE Confidence: 0.96300626

00:14:01.375 --> 00:14:02.995 changes in degree connectivity,
NOTE Confidence: 0.99094766

00:14:03.570 --> 00:14:04.770 which is a measure of
NOTE Confidence: 0.99094766

00:14:04.770 --> 00:14:07.110 functional connectivity, sort of how
NOTE Confidence: 0.99094766

00:14:07.250 --> 00:14:08.610 how much is one piece
NOTE Confidence: 0.99094766

00:14:08.610 --> 00:14:10.610 of brain correlated or connected

NOTE Confidence: 0.99094766
00:14:10.610 --> 00:14:12.050 with all the rest on
NOTE Confidence: 0.99094766
00:14:12.050 --> 00:14:12.550 psilocybin
NOTE Confidence: 0.9724637
00:14:12.850 --> 00:14:14.870 compared to within subject control.
NOTE Confidence: 0.9997139
00:14:15.250 --> 00:14:16.450 And what you see here
NOTE Confidence: 0.9997139
00:14:16.450 --> 00:14:17.270 is reduced
NOTE Confidence: 0.92939854
00:14:17.625 --> 00:14:18.445 degree connectivity,
NOTE Confidence: 0.9994979
00:14:18.985 --> 00:14:19.485 decoupling
NOTE Confidence: 0.9706513
00:14:20.025 --> 00:14:20.745 with the rest of the
NOTE Confidence: 0.9706513
00:14:20.745 --> 00:14:21.785 brain in some of these
NOTE Confidence: 0.9706513
00:14:21.785 --> 00:14:23.145 association areas where there are
NOTE Confidence: 0.9706513
00:14:23.145 --> 00:14:24.365 high amounts of receptor,
NOTE Confidence: 0.8545213
00:14:25.145 --> 00:14:26.685 expression. And interestingly,
NOTE Confidence: 0.99320126
00:14:27.225 --> 00:14:28.825 increased coupling with the rest
NOTE Confidence: 0.99320126
00:14:28.825 --> 00:14:30.525 of the brain, increased synchronous
NOTE Confidence: 0.99320126
00:14:30.585 --> 00:14:31.085 activity
NOTE Confidence: 0.95416486

00:14:31.465 --> 00:14:33.300 in primary sensory cortices, the,
NOTE Confidence: 0.95416486

00:14:33.540 --> 00:14:34.740 occipital lobe and the primary
NOTE Confidence: 0.95416486

00:14:34.740 --> 00:14:36.420 visual cortex here, as well
NOTE Confidence: 0.95416486

00:14:36.420 --> 00:14:37.620 as subtle. You see this
NOTE Confidence: 0.95416486

00:14:37.620 --> 00:14:38.580 a little bit less subtly
NOTE Confidence: 0.95416486

00:14:38.580 --> 00:14:40.180 in some other cortices, but
NOTE Confidence: 0.95416486

00:14:40.180 --> 00:14:41.960 this is the, primary somatosensory
NOTE Confidence: 0.95416486

00:14:42.260 --> 00:14:43.860 cortex, and here would be
NOTE Confidence: 0.95416486

00:14:43.860 --> 00:14:45.700 some audit primary auditory cortex.
NOTE Confidence: 0.95416486

00:14:45.700 --> 00:14:46.740 So it looks like an
NOTE Confidence: 0.95416486

00:14:46.740 --> 00:14:48.685 increased synchrony or coupling in
NOTE Confidence: 0.95416486

00:14:48.685 --> 00:14:49.665 primary sensory
NOTE Confidence: 0.97748464

00:14:50.125 --> 00:14:51.985 areas and a decreased synchronicity
NOTE Confidence: 0.97748464

00:14:52.204 --> 00:14:54.225 or coupling in association areas.
NOTE Confidence: 0.97748464

00:14:54.285 --> 00:14:55.324 And this has been used
NOTE Confidence: 0.97748464

00:14:55.324 --> 00:14:56.444 to explain some of the

NOTE Confidence: 0.97748464

00:14:56.444 --> 00:14:57.964 subjective effects that this drug

NOTE Confidence: 0.97748464

00:14:57.964 --> 00:15:00.305 has where there's sensory alterations,

NOTE Confidence: 0.9869003

00:15:00.685 --> 00:15:02.704 not not frank hallucinations usually,

NOTE Confidence: 0.9869003

00:15:02.980 --> 00:15:04.600 but alterations in the sensorium

NOTE Confidence: 0.9532157

00:15:04.980 --> 00:15:06.580 and the dissolving of the

NOTE Confidence: 0.9532157

00:15:06.580 --> 00:15:07.860 coherent sense of self, which

NOTE Confidence: 0.9532157

00:15:07.860 --> 00:15:08.900 is thought to be mediated

NOTE Confidence: 0.9532157

00:15:08.900 --> 00:15:10.180 by the default mode network.

NOTE Confidence: 0.9532157

00:15:10.180 --> 00:15:11.220 So I can make up

NOTE Confidence: 0.9532157

00:15:11.220 --> 00:15:12.180 a story about how the

NOTE Confidence: 0.9532157

00:15:12.180 --> 00:15:13.860 psychological effects map onto these

NOTE Confidence: 0.9532157

00:15:13.860 --> 00:15:15.300 brain effects, although, of course,

NOTE Confidence: 0.9532157

00:15:15.300 --> 00:15:16.280 causal relationships,

NOTE Confidence: 0.9996472

00:15:17.060 --> 00:15:18.280 are difficult to prove.

NOTE Confidence: 0.99567556

00:15:19.154 --> 00:15:20.195 Other things we know about

NOTE Confidence: 0.99567556

00:15:20.195 --> 00:15:21.875 the effects of psilocybin, this
NOTE Confidence: 0.99567556

00:15:21.875 --> 00:15:23.075 is animal work done here
NOTE Confidence: 0.99567556

00:15:23.075 --> 00:15:23.735 at Yale.
NOTE Confidence: 0.95098144

00:15:24.595 --> 00:15:26.195 This was work by, Alex
NOTE Confidence: 0.95098144

00:15:26.195 --> 00:15:27.714 Kwan, who has since left.
NOTE Confidence: 0.95098144

00:15:27.714 --> 00:15:29.075 Similar work has been is
NOTE Confidence: 0.95098144

00:15:29.075 --> 00:15:30.375 being done by Al Kaye,
NOTE Confidence: 0.9635349

00:15:30.755 --> 00:15:32.274 in our department. And what's
NOTE Confidence: 0.9635349

00:15:32.274 --> 00:15:33.235 shown here is how the
NOTE Confidence: 0.9635349

00:15:33.394 --> 00:15:35.670 how psilocybin affects single neurons.
NOTE Confidence: 0.9992798

00:15:36.610 --> 00:15:37.810 This what you're seeing here
NOTE Confidence: 0.9992798

00:15:37.810 --> 00:15:39.410 is a visualization of the
NOTE Confidence: 0.9992798

00:15:39.410 --> 00:15:41.010 apical dendrite of a single
NOTE Confidence: 0.9992798

00:15:41.010 --> 00:15:42.630 neuron in the frontal cortex
NOTE Confidence: 0.9626464

00:15:43.570 --> 00:15:45.090 visualized in vivo in a
NOTE Confidence: 0.9626464

00:15:45.090 --> 00:15:45.890 mouse. So this is a

NOTE Confidence: 0.9626464

00:15:45.890 --> 00:15:47.170 living mouse. We're visualizing a

NOTE Confidence: 0.9626464

00:15:47.170 --> 00:15:48.770 single neuron that's fluorescently labeled.

NOTE Confidence: 0.9626464

00:15:48.770 --> 00:15:50.325 And you zoom in on

NOTE Confidence: 0.9626464

00:15:50.325 --> 00:15:51.525 this dendrite, and you see

NOTE Confidence: 0.9626464

00:15:51.525 --> 00:15:52.965 all these little protuberances. These

NOTE Confidence: 0.9626464

00:15:52.965 --> 00:15:54.325 are dendritic spines, and they're

NOTE Confidence: 0.9626464

00:15:54.325 --> 00:15:55.685 thought to be the site

NOTE Confidence: 0.9626464

00:15:55.685 --> 00:15:56.985 of synaptic contacts.

NOTE Confidence: 0.98801476

00:15:57.445 --> 00:15:58.485 And they can they're able

NOTE Confidence: 0.98801476

00:15:58.485 --> 00:15:59.845 to visualize. The technology here

NOTE Confidence: 0.98801476

00:15:59.845 --> 00:16:01.045 is actually quite remarkable. They're

NOTE Confidence: 0.98801476

00:16:01.045 --> 00:16:02.165 able to visualize the same

NOTE Confidence: 0.98801476

00:16:02.165 --> 00:16:04.165 dendrite over time for over

NOTE Confidence: 0.98801476

00:16:04.165 --> 00:16:04.745 a month

NOTE Confidence: 0.9865268

00:16:05.210 --> 00:16:06.670 and look at these dendritic

NOTE Confidence: 0.9865268

00:16:06.810 --> 00:16:07.850 spines and look at the
NOTE Confidence: 0.9865268

00:16:07.850 --> 00:16:09.530 growth and retraction of synaptic
NOTE Confidence: 0.9865268

00:16:09.530 --> 00:16:10.890 contact. And what you see
NOTE Confidence: 0.9865268

00:16:10.890 --> 00:16:12.590 is that psilocybin increases
NOTE Confidence: 0.92222625

00:16:14.170 --> 00:16:15.550 stable synaptic contacts,
NOTE Confidence: 0.9162287

00:16:16.010 --> 00:16:16.970 not by a huge amount,
NOTE Confidence: 0.9162287

00:16:16.970 --> 00:16:18.010 but but with a clear
NOTE Confidence: 0.9162287

00:16:18.010 --> 00:16:19.150 statistical significance,
NOTE Confidence: 0.99717504

00:16:19.545 --> 00:16:20.925 going out for a month.
NOTE Confidence: 0.9963428

00:16:21.464 --> 00:16:23.245 This is striking because ketamine
NOTE Confidence: 0.9323645

00:16:23.705 --> 00:16:25.305 does something similar, and, actually,
NOTE Confidence: 0.9323645

00:16:25.305 --> 00:16:27.065 so do classical antidepressants like
NOTE Confidence: 0.9323645

00:16:27.065 --> 00:16:27.805 like fluoxetine.
NOTE Confidence: 0.99561614

00:16:29.305 --> 00:16:30.265 But in the case of
NOTE Confidence: 0.99561614

00:16:30.265 --> 00:16:31.865 ketamine, they don't last nearly
NOTE Confidence: 0.99561614

00:16:31.865 --> 00:16:33.640 as long. So psilocybin appears

NOTE Confidence: 0.99561614
00:16:33.640 --> 00:16:34.780 to be having proplasticity,
NOTE Confidence: 0.97716624
00:16:35.480 --> 00:16:37.020 prosynaptic growth effects
NOTE Confidence: 0.9781435
00:16:37.480 --> 00:16:39.000 that last out for over
NOTE Confidence: 0.9781435
00:16:39.000 --> 00:16:39.580 a month.
NOTE Confidence: 0.9961436
00:16:39.960 --> 00:16:40.860 This is hypothesized
NOTE Confidence: 0.9826801
00:16:41.400 --> 00:16:43.000 to be related to its,
NOTE Confidence: 0.9826801
00:16:43.400 --> 00:16:45.160 therapeutic effects, although exactly how
NOTE Confidence: 0.9826801
00:16:45.160 --> 00:16:47.420 that connection works isn't entirely
NOTE Confidence: 0.9826801
00:16:47.560 --> 00:16:48.060 clear.
NOTE Confidence: 0.97916704
00:16:48.775 --> 00:16:50.375 Alright. So psilocybin has been
NOTE Confidence: 0.97916704
00:16:50.375 --> 00:16:51.975 used extensively in clinical studies.
NOTE Confidence: 0.97916704
00:16:51.975 --> 00:16:53.175 It's a slightly cleaner drug
NOTE Confidence: 0.97916704
00:16:53.175 --> 00:16:54.455 than LSD. It has a
NOTE Confidence: 0.97916704
00:16:54.455 --> 00:16:55.975 shorter half life of about
NOTE Confidence: 0.97916704
00:16:55.975 --> 00:16:57.175 four hours, four to six
NOTE Confidence: 0.97916704

00:16:57.175 --> 00:16:58.535 hours, whereas LSD has a
NOTE Confidence: 0.97916704

00:16:58.535 --> 00:16:59.575 half life of, like, fifteen
NOTE Confidence: 0.97916704

00:16:59.575 --> 00:17:00.535 hours, which makes it more
NOTE Confidence: 0.97916704

00:17:00.535 --> 00:17:01.495 difficult to manage in the
NOTE Confidence: 0.97916704

00:17:01.495 --> 00:17:03.300 clinical setting. Also, psilocybin, I
NOTE Confidence: 0.97916704

00:17:03.300 --> 00:17:04.100 think, is a little less
NOTE Confidence: 0.97916704

00:17:04.100 --> 00:17:04.820 scary. I think it was
NOTE Confidence: 0.97916704

00:17:04.820 --> 00:17:05.700 a little easier to get
NOTE Confidence: 0.97916704

00:17:05.700 --> 00:17:06.820 IRBs to sign on to
NOTE Confidence: 0.97916704

00:17:06.820 --> 00:17:07.940 it ten years ago when
NOTE Confidence: 0.97916704

00:17:07.940 --> 00:17:09.300 this was all new, to
NOTE Confidence: 0.97916704

00:17:09.300 --> 00:17:10.980 many people, because it didn't
NOTE Confidence: 0.97916704

00:17:10.980 --> 00:17:11.859 have the the as much
NOTE Confidence: 0.97916704

00:17:11.859 --> 00:17:13.460 cultural baggage as LSD. So
NOTE Confidence: 0.97916704

00:17:13.460 --> 00:17:14.580 for all of these reasons,
NOTE Confidence: 0.97916704

00:17:14.580 --> 00:17:15.540 it's been the focus of

NOTE Confidence: 0.97916704

00:17:15.540 --> 00:17:17.140 most clinical studies in the

NOTE Confidence: 0.97916704

00:17:17.140 --> 00:17:17.960 modern era.

NOTE Confidence: 0.987876

00:17:18.394 --> 00:17:19.695 I mentioned the psychedelic,

NOTE Confidence: 0.9989146

00:17:20.634 --> 00:17:21.134 medicine

NOTE Confidence: 0.96317214

00:17:21.674 --> 00:17:23.294 paradigm, and that's the idea

NOTE Confidence: 0.96317214

00:17:23.355 --> 00:17:24.234 that you give a drug

NOTE Confidence: 0.96317214

00:17:24.234 --> 00:17:25.835 that has mind operating mind

NOTE Confidence: 0.96317214

00:17:25.835 --> 00:17:28.014 altering or consciousness altering properties,

NOTE Confidence: 0.96317214

00:17:28.234 --> 00:17:29.514 and you couple it with

NOTE Confidence: 0.96317214

00:17:29.514 --> 00:17:30.970 a psychotherapy. And that's how

NOTE Confidence: 0.96317214

00:17:30.970 --> 00:17:32.409 most studies in this space

NOTE Confidence: 0.96317214

00:17:32.409 --> 00:17:33.609 have been done. And what's

NOTE Confidence: 0.96317214

00:17:33.609 --> 00:17:34.570 shown here is the kind

NOTE Confidence: 0.96317214

00:17:34.570 --> 00:17:35.850 of environment in which we

NOTE Confidence: 0.96317214

00:17:35.850 --> 00:17:37.630 do this kind of treatment.

NOTE Confidence: 0.96317214

00:17:37.850 --> 00:17:39.130 This is actually my office.
NOTE Confidence: 0.96317214

00:17:39.130 --> 00:17:40.330 It's where I'm seated right
NOTE Confidence: 0.96317214

00:17:40.330 --> 00:17:41.690 now. And this was from
NOTE Confidence: 0.96317214

00:17:41.690 --> 00:17:42.409 when we were doing a
NOTE Confidence: 0.96317214

00:17:42.409 --> 00:17:43.369 study here on the clinical
NOTE Confidence: 0.96317214

00:17:43.369 --> 00:17:44.809 neuroscience research unit. But the
NOTE Confidence: 0.96317214

00:17:44.809 --> 00:17:46.125 unit a few years ago,
NOTE Confidence: 0.96317214

00:17:46.205 --> 00:17:47.325 the unit was closed because
NOTE Confidence: 0.96317214

00:17:47.325 --> 00:17:48.545 of a pandemic quarantine.
NOTE Confidence: 0.97074944

00:17:49.165 --> 00:17:50.285 And so we had to
NOTE Confidence: 0.97074944

00:17:50.285 --> 00:17:51.965 scramble to, to create a
NOTE Confidence: 0.97074944

00:17:51.965 --> 00:17:53.425 dosing space, and we retrofitted
NOTE Confidence: 0.97074944

00:17:53.565 --> 00:17:54.685 my office. But what you
NOTE Confidence: 0.97074944

00:17:54.685 --> 00:17:55.565 can see, and this is
NOTE Confidence: 0.97074944

00:17:55.565 --> 00:17:57.165 pretty typical of many, though
NOTE Confidence: 0.97074944

00:17:57.165 --> 00:17:58.605 not all studies, is we've

NOTE Confidence: 0.97074944

00:17:58.605 --> 00:17:59.645 tried to make it less

NOTE Confidence: 0.97074944

00:17:59.645 --> 00:18:00.845 clinical appearing. There is a

NOTE Confidence: 0.97074944

00:18:00.845 --> 00:18:02.340 blood pressure machine, but we've

NOTE Confidence: 0.97074944

00:18:02.340 --> 00:18:03.460 tried to sort of mask

NOTE Confidence: 0.97074944

00:18:03.460 --> 00:18:04.440 some of the clinical,

NOTE Confidence: 0.9616764

00:18:04.980 --> 00:18:06.280 clinical office like,

NOTE Confidence: 0.99898857

00:18:07.220 --> 00:18:07.720 characteristics

NOTE Confidence: 0.9751223

00:18:08.020 --> 00:18:09.220 and and make it, make

NOTE Confidence: 0.9751223

00:18:09.220 --> 00:18:10.100 it a little bit more

NOTE Confidence: 0.9751223

00:18:10.100 --> 00:18:10.900 of a of a natural

NOTE Confidence: 0.9751223

00:18:11.059 --> 00:18:12.359 you know, space that evokes

NOTE Confidence: 0.9751223

00:18:12.500 --> 00:18:14.039 nature. This is often done

NOTE Confidence: 0.9880315

00:18:15.225 --> 00:18:17.005 for, these dosing studies.

NOTE Confidence: 0.9463757

00:18:17.545 --> 00:18:18.585 I'm not gonna go through

NOTE Confidence: 0.9463757

00:18:18.585 --> 00:18:19.625 data on the pie. That

NOTE Confidence: 0.9463757

00:18:19.625 --> 00:18:20.825 would be a longer lecture,
NOTE Confidence: 0.9463757

00:18:20.825 --> 00:18:21.705 but I would I'll just
NOTE Confidence: 0.9463757

00:18:21.705 --> 00:18:22.605 say that there's
NOTE Confidence: 0.8801876

00:18:22.905 --> 00:18:24.905 good small single site, but
NOTE Confidence: 0.8801876

00:18:24.905 --> 00:18:26.684 high quality controlled studies
NOTE Confidence: 0.9887858

00:18:27.065 --> 00:18:28.605 in treatments of the anxiety,
NOTE Confidence: 0.9887858

00:18:28.744 --> 00:18:29.885 depression, and existential
NOTE Confidence: 0.97733986

00:18:30.450 --> 00:18:31.809 despair that attends the end
NOTE Confidence: 0.97733986

00:18:31.809 --> 00:18:33.250 of life in patients with
NOTE Confidence: 0.97733986

00:18:33.250 --> 00:18:34.770 advanced cancer. This is where
NOTE Confidence: 0.97733986

00:18:34.770 --> 00:18:36.130 the first clinical trials of
NOTE Confidence: 0.97733986

00:18:36.130 --> 00:18:37.169 the modern era were done
NOTE Confidence: 0.97733986

00:18:37.169 --> 00:18:38.770 published in twenty sixteen. And,
NOTE Confidence: 0.97733986

00:18:38.770 --> 00:18:39.809 again, I think that the
NOTE Confidence: 0.97733986

00:18:39.809 --> 00:18:40.850 invest I was not part
NOTE Confidence: 0.97733986

00:18:40.850 --> 00:18:41.809 of this work, but I

NOTE Confidence: 0.97733986

00:18:41.809 --> 00:18:43.169 think that the investigators who

NOTE Confidence: 0.97733986

00:18:43.169 --> 00:18:44.130 started this work may have

NOTE Confidence: 0.97733986

00:18:44.130 --> 00:18:46.115 started in in, this population

NOTE Confidence: 0.97733986

00:18:46.115 --> 00:18:47.154 because it was easier to

NOTE Confidence: 0.97733986

00:18:47.154 --> 00:18:47.654 get,

NOTE Confidence: 0.9493706

00:18:48.434 --> 00:18:50.195 to get IRB approval in,

NOTE Confidence: 0.9493706

00:18:50.355 --> 00:18:51.794 in an advanced cancer population

NOTE Confidence: 0.9493706

00:18:51.794 --> 00:18:52.595 than it might have been

NOTE Confidence: 0.9493706

00:18:52.595 --> 00:18:54.455 in a young physically healthy

NOTE Confidence: 0.9493706

00:18:54.514 --> 00:18:55.014 population.

NOTE Confidence: 0.8996536

00:18:55.554 --> 00:18:56.434 There've been a lot of

NOTE Confidence: 0.8996536

00:18:56.434 --> 00:18:58.615 studies in major depression, including,

NOTE Confidence: 0.93705875

00:18:59.350 --> 00:19:01.769 two phase three research pair,

NOTE Confidence: 0.9514129

00:19:02.309 --> 00:19:03.990 programs that are being forced

NOTE Confidence: 0.9514129

00:19:03.990 --> 00:19:05.190 and I think are reasonably

NOTE Confidence: 0.9514129

00:19:05.190 --> 00:19:06.950 likely to lead to FDA
NOTE Confidence: 0.9514129

00:19:06.950 --> 00:19:09.029 approval of psilocybin within the
NOTE Confidence: 0.9514129

00:19:09.029 --> 00:19:10.570 next couple years for depression.
NOTE Confidence: 0.99002725

00:19:10.869 --> 00:19:12.169 There's a bunch of complexity
NOTE Confidence: 0.99002725

00:19:12.230 --> 00:19:13.109 there that we don't have
NOTE Confidence: 0.99002725

00:19:13.109 --> 00:19:14.285 time to get into. But
NOTE Confidence: 0.99002725

00:19:14.285 --> 00:19:15.244 my prediction is that we
NOTE Confidence: 0.99002725

00:19:15.244 --> 00:19:16.545 will see approval of psilocybin
NOTE Confidence: 0.99002725

00:19:16.684 --> 00:19:18.065 within two to three years,
NOTE Confidence: 0.98072034

00:19:19.005 --> 00:19:20.145 for major depression.
NOTE Confidence: 0.9679432

00:19:20.845 --> 00:19:22.304 There's some studies in alcoholism.
NOTE Confidence: 0.98801357

00:19:23.005 --> 00:19:24.125 I told you about the
NOTE Confidence: 0.98801357

00:19:24.125 --> 00:19:25.405 work from the fifties, but
NOTE Confidence: 0.98801357

00:19:25.405 --> 00:19:26.145 more recently,
NOTE Confidence: 0.92881227

00:19:26.640 --> 00:19:28.080 Michael Bogenschips and his colleagues
NOTE Confidence: 0.92881227

00:19:28.080 --> 00:19:29.359 at NYU have picked up

NOTE Confidence: 0.92881227

00:19:29.359 --> 00:19:30.100 this baton

NOTE Confidence: 0.95809144

00:19:30.400 --> 00:19:31.600 and, did a a first

NOTE Confidence: 0.95809144

00:19:31.600 --> 00:19:32.880 study in twenty fifteen. This

NOTE Confidence: 0.95809144

00:19:32.880 --> 00:19:33.680 was sort of an open

NOTE Confidence: 0.95809144

00:19:33.680 --> 00:19:34.900 label proof of concept

NOTE Confidence: 0.96492946

00:19:35.280 --> 00:19:36.560 study where you see group

NOTE Confidence: 0.96492946

00:19:36.560 --> 00:19:38.240 of people, treated for alcohol

NOTE Confidence: 0.96492946

00:19:38.240 --> 00:19:39.460 use disorder with psilocybin

NOTE Confidence: 0.97782296

00:19:40.174 --> 00:19:42.195 together with a CBT based,

NOTE Confidence: 0.92834115

00:19:42.815 --> 00:19:44.255 treatment paradigm that in in

NOTE Confidence: 0.92834115

00:19:44.494 --> 00:19:46.275 included both motivational enhancement,

NOTE Confidence: 0.9603814

00:19:46.975 --> 00:19:48.755 and and CBT components.

NOTE Confidence: 0.9567205

00:19:49.615 --> 00:19:51.075 So not a controlled study.

NOTE Confidence: 0.984284

00:19:51.375 --> 00:19:52.755 But they treated with psilocybin

NOTE Confidence: 0.984284

00:19:52.975 --> 00:19:53.855 twice, and they saw a

NOTE Confidence: 0.984284

00:19:53.855 --> 00:19:55.470 dramatic reduction in both percent

NOTE Confidence: 0.984284

00:19:55.549 --> 00:19:56.590 drinking days in blue and

NOTE Confidence: 0.984284

00:19:56.590 --> 00:19:57.950 percent heavy drinking days in

NOTE Confidence: 0.984284

00:19:57.950 --> 00:19:58.450 red.

NOTE Confidence: 0.9498351

00:19:59.309 --> 00:20:00.270 And and it's it's quite

NOTE Confidence: 0.9498351

00:20:00.270 --> 00:20:01.309 a dramatic drop off though,

NOTE Confidence: 0.9498351

00:20:01.309 --> 00:20:02.830 again, without a control group.

NOTE Confidence: 0.9498351

00:20:02.830 --> 00:20:03.869 This was followed up with

NOTE Confidence: 0.9498351

00:20:03.869 --> 00:20:05.230 a large well controlled study.

NOTE Confidence: 0.9498351

00:20:05.230 --> 00:20:05.950 I think this is an

NOTE Confidence: 0.9498351

00:20:05.950 --> 00:20:06.990 n of ninety six. It's

NOTE Confidence: 0.9498351

00:20:06.990 --> 00:20:08.775 a very robust study. Again,

NOTE Confidence: 0.9498351

00:20:08.775 --> 00:20:09.755 coupling psilocybin

NOTE Confidence: 0.9987552

00:20:10.055 --> 00:20:10.555 administration

NOTE Confidence: 0.9963174

00:20:10.935 --> 00:20:12.635 with CBT based treatment.

NOTE Confidence: 0.98297554

00:20:12.935 --> 00:20:13.655 And what you can see

NOTE Confidence: 0.98297554
00:20:13.655 --> 00:20:14.695 is that everyone got better,
NOTE Confidence: 0.98297554
00:20:14.695 --> 00:20:16.135 so their CBT based treatment
NOTE Confidence: 0.98297554
00:20:16.135 --> 00:20:16.635 worked.
NOTE Confidence: 0.9808495
00:20:17.255 --> 00:20:19.015 The people in gray received
NOTE Confidence: 0.9808495
00:20:19.015 --> 00:20:20.455 no psilocybin. They received a
NOTE Confidence: 0.9808495
00:20:20.455 --> 00:20:20.955 placebo.
NOTE Confidence: 0.9468845
00:20:21.369 --> 00:20:22.890 People in blue did receive
NOTE Confidence: 0.9468845
00:20:22.890 --> 00:20:24.669 psilocybin and had a markedly
NOTE Confidence: 0.9468845
00:20:24.809 --> 00:20:26.330 better they everyone got better,
NOTE Confidence: 0.9468845
00:20:26.330 --> 00:20:27.390 but they had a markedly
NOTE Confidence: 0.9468845
00:20:27.690 --> 00:20:28.669 larger effect,
NOTE Confidence: 0.99901277
00:20:29.369 --> 00:20:30.490 and it lasted out for
NOTE Confidence: 0.99901277
00:20:30.490 --> 00:20:31.230 many weeks.
NOTE Confidence: 0.9864689
00:20:32.090 --> 00:20:33.369 So this is very promising.
NOTE Confidence: 0.9864689
00:20:33.369 --> 00:20:34.669 This is the best single
NOTE Confidence: 0.9864689

00:20:34.924 --> 00:20:36.205 study, in the treatment of
NOTE Confidence: 0.9864689

00:20:36.205 --> 00:20:37.885 substance use disorders, this this
NOTE Confidence: 0.9864689

00:20:37.885 --> 00:20:39.804 controlled study for depression. There
NOTE Confidence: 0.9864689

00:20:39.804 --> 00:20:40.924 are some studies in nicotine
NOTE Confidence: 0.9864689

00:20:40.924 --> 00:20:41.424 addiction.
NOTE Confidence: 0.97852397

00:20:41.965 --> 00:20:43.405 They're smaller. Here's a list
NOTE Confidence: 0.97852397

00:20:43.405 --> 00:20:44.924 of some of the, some
NOTE Confidence: 0.97852397

00:20:44.924 --> 00:20:46.284 of the reported studies. There's
NOTE Confidence: 0.97852397

00:20:46.284 --> 00:20:47.905 a couple open label studies.
NOTE Confidence: 0.97852397

00:20:48.125 --> 00:20:49.405 I don't there's a there's
NOTE Confidence: 0.97852397

00:20:49.405 --> 00:20:51.050 a controlled study that's not
NOTE Confidence: 0.97852397

00:20:51.050 --> 00:20:52.170 yet published that I'm aware
NOTE Confidence: 0.97852397

00:20:52.170 --> 00:20:53.369 of that shows promising results,
NOTE Confidence: 0.97852397

00:20:53.369 --> 00:20:54.270 and there are also,
NOTE Confidence: 0.9988008

00:20:54.570 --> 00:20:56.330 some naturalistic survey data that
NOTE Confidence: 0.9988008

00:20:56.330 --> 00:20:57.790 support benefit for nicotine

NOTE Confidence: 0.92134285
00:20:58.490 --> 00:20:59.930 use disorder. This is data
NOTE Confidence: 0.92134285
00:20:59.930 --> 00:21:01.210 from that from a controlled
NOTE Confidence: 0.92134285
00:21:01.210 --> 00:21:02.490 study by Johnson and colleagues
NOTE Confidence: 0.92134285
00:21:02.490 --> 00:21:03.609 twenty fourteen. That was the
NOTE Confidence: 0.92134285
00:21:03.609 --> 00:21:05.025 second controlled study in twenty
NOTE Confidence: 0.92134285
00:21:05.025 --> 00:21:06.244 fifteen showed similar results.
NOTE Confidence: 0.967653
00:21:06.785 --> 00:21:07.285 Impressive,
NOTE Confidence: 0.9251102
00:21:08.145 --> 00:21:10.244 results in a small uncontrolled
NOTE Confidence: 0.9251102
00:21:10.305 --> 00:21:11.345 study. So this work is
NOTE Confidence: 0.9251102
00:21:11.345 --> 00:21:11.845 ongoing.
NOTE Confidence: 0.9698349
00:21:12.625 --> 00:21:13.984 And there's ongoing ongoing work
NOTE Confidence: 0.9698349
00:21:13.984 --> 00:21:15.025 in a bunch of other,
NOTE Confidence: 0.92935413
00:21:15.505 --> 00:21:17.105 conditions. And Joao will will
NOTE Confidence: 0.92935413
00:21:17.105 --> 00:21:17.905 give you give us more
NOTE Confidence: 0.92935413
00:21:17.905 --> 00:21:19.425 details about opiate use disorder
NOTE Confidence: 0.92935413

00:21:19.425 --> 00:21:20.085 in particular.
NOTE Confidence: 0.9720944

00:21:20.850 --> 00:21:21.890 We've just completed the first
NOTE Confidence: 0.9720944

00:21:21.890 --> 00:21:23.510 controlled study in obsessive compulsive
NOTE Confidence: 0.9720944

00:21:23.570 --> 00:21:24.930 disorder. So there's evidence of
NOTE Confidence: 0.9720944

00:21:24.930 --> 00:21:26.290 benefit in many of these,
NOTE Confidence: 0.9720944

00:21:26.690 --> 00:21:27.190 contexts.
NOTE Confidence: 0.9858289

00:21:27.490 --> 00:21:29.090 The one interesting exception is
NOTE Confidence: 0.9858289

00:21:29.090 --> 00:21:30.309 anorexia nervosa,
NOTE Confidence: 0.9917914

00:21:30.850 --> 00:21:32.130 where the early studies have
NOTE Confidence: 0.9917914

00:21:32.130 --> 00:21:33.109 not been as promising,
NOTE Confidence: 0.978151

00:21:33.650 --> 00:21:34.950 and work there is ongoing.
NOTE Confidence: 0.97288275

00:21:36.205 --> 00:21:37.404 I'm gonna wrap up. I'll
NOTE Confidence: 0.97288275

00:21:37.404 --> 00:21:38.445 just say there's, you know,
NOTE Confidence: 0.97288275

00:21:38.445 --> 00:21:40.284 another another classic psychedelic is
NOTE Confidence: 0.97288275

00:21:40.284 --> 00:21:40.784 dimethyltryptamine,
NOTE Confidence: 0.89500237

00:21:41.804 --> 00:21:42.764 which is found in the

NOTE Confidence: 0.89500237
00:21:42.764 --> 00:21:43.585 t iahaska,
NOTE Confidence: 0.8889449
00:21:44.284 --> 00:21:46.144 which is, used by indigenous
NOTE Confidence: 0.8889449
00:21:46.205 --> 00:21:47.325 groups in the Amazon and
NOTE Confidence: 0.8889449
00:21:47.325 --> 00:21:48.445 Brazil, but has it used
NOTE Confidence: 0.8889449
00:21:48.445 --> 00:21:49.424 to spread worldwide
NOTE Confidence: 0.9756523
00:21:49.820 --> 00:21:50.720 in a sort of syncretic,
NOTE Confidence: 0.9756523
00:21:50.940 --> 00:21:52.240 quasi religious context.
NOTE Confidence: 0.99009293
00:21:52.619 --> 00:21:54.140 There is some research about
NOTE Confidence: 0.99009293
00:21:54.140 --> 00:21:56.400 Ayahuasca. It's used actively used
NOTE Confidence: 0.99009293
00:21:56.619 --> 00:21:58.320 in, substance abuse treatment
NOTE Confidence: 0.94094527
00:21:58.700 --> 00:22:00.320 centers in South America,
NOTE Confidence: 0.972288
00:22:00.859 --> 00:22:02.059 but the research base at
NOTE Confidence: 0.972288
00:22:02.059 --> 00:22:03.705 this point is quite thin.
NOTE Confidence: 0.972288
00:22:03.705 --> 00:22:05.164 There was a survey study
NOTE Confidence: 0.972288
00:22:05.304 --> 00:22:06.505 shown here a couple years
NOTE Confidence: 0.972288

00:22:06.505 --> 00:22:08.025 ago suggesting that it helped
NOTE Confidence: 0.972288

00:22:08.025 --> 00:22:09.225 with smoking cessation, but this
NOTE Confidence: 0.972288

00:22:09.225 --> 00:22:11.065 is naturalistic survey data. There
NOTE Confidence: 0.972288

00:22:11.065 --> 00:22:12.105 are no controlled studies that
NOTE Confidence: 0.972288

00:22:12.105 --> 00:22:13.325 I'm aware of with Ayahuasca.
NOTE Confidence: 0.938822

00:22:13.705 --> 00:22:15.225 Cyril D'Souza and our VA
NOTE Confidence: 0.938822

00:22:15.225 --> 00:22:16.220 is beginning to and some
NOTE Confidence: 0.938822

00:22:16.220 --> 00:22:17.340 of his colleagues are beginning
NOTE Confidence: 0.938822

00:22:17.340 --> 00:22:18.859 to use synthetic DMT. They're
NOTE Confidence: 0.938822

00:22:18.859 --> 00:22:19.840 starting with depression.
NOTE Confidence: 0.9722809

00:22:20.380 --> 00:22:22.140 But, Anahita Basurnia has a
NOTE Confidence: 0.9722809

00:22:22.140 --> 00:22:23.180 study that's just getting off
NOTE Confidence: 0.9722809

00:22:23.180 --> 00:22:24.700 the ground using DMT for
NOTE Confidence: 0.9722809

00:22:24.700 --> 00:22:25.820 alcohol use disorder. So we're
NOTE Confidence: 0.9722809

00:22:25.820 --> 00:22:27.420 just seeing the beginnings of
NOTE Confidence: 0.9722809

00:22:27.420 --> 00:22:27.920 investigations

NOTE Confidence: 0.98834944

00:22:28.300 --> 00:22:28.960 of DMT,

NOTE Confidence: 0.94401187

00:22:29.260 --> 00:22:30.720 which is the active ingredient,

NOTE Confidence: 0.9754506

00:22:31.894 --> 00:22:33.355 for substance abuse.

NOTE Confidence: 0.97287005

00:22:33.815 --> 00:22:35.095 Ibogaine has gotten a lot

NOTE Confidence: 0.97287005

00:22:35.095 --> 00:22:36.375 of press recently. It's a

NOTE Confidence: 0.97287005

00:22:36.375 --> 00:22:38.475 complicated drug with complicated pharmacology

NOTE Confidence: 0.97287005

00:22:38.615 --> 00:22:39.975 that, honestly, I don't understand

NOTE Confidence: 0.97287005

00:22:39.975 --> 00:22:41.575 particularly well. Does have some

NOTE Confidence: 0.97287005

00:22:41.575 --> 00:22:43.734 effects on, the serotonin two

NOTE Confidence: 0.97287005

00:22:43.734 --> 00:22:44.394 a receptor.

NOTE Confidence: 0.9739976

00:22:45.230 --> 00:22:46.910 It's found naturally in in

NOTE Confidence: 0.9739976

00:22:46.910 --> 00:22:48.109 the bark of trees in

NOTE Confidence: 0.9739976

00:22:48.109 --> 00:22:49.470 West Africa, which is shown

NOTE Confidence: 0.9739976

00:22:49.470 --> 00:22:50.690 here, the aboga tree.

NOTE Confidence: 0.953223

00:22:51.550 --> 00:22:52.990 And there have begun to

NOTE Confidence: 0.953223

00:22:52.990 --> 00:22:54.510 be some some studies of
NOTE Confidence: 0.953223

00:22:54.510 --> 00:22:56.290 Ibogaine. It's again being used
NOTE Confidence: 0.953223

00:22:56.430 --> 00:22:58.030 actively in substance abuse clinics
NOTE Confidence: 0.953223

00:22:58.030 --> 00:22:59.150 in South America and in
NOTE Confidence: 0.953223

00:22:59.150 --> 00:22:59.650 Mexico
NOTE Confidence: 0.97717535

00:23:00.304 --> 00:23:01.424 for substance abuse as well
NOTE Confidence: 0.97717535

00:23:01.424 --> 00:23:02.325 as for trauma.
NOTE Confidence: 0.9953582

00:23:02.945 --> 00:23:03.984 But there isn't a lot
NOTE Confidence: 0.9953582

00:23:03.984 --> 00:23:04.484 of,
NOTE Confidence: 0.9504253

00:23:04.945 --> 00:23:06.885 control really no control data.
NOTE Confidence: 0.8551931

00:23:08.385 --> 00:23:10.225 It it also has, potential
NOTE Confidence: 0.8551931

00:23:10.225 --> 00:23:10.725 cardiotoxic
NOTE Confidence: 0.9314372

00:23:11.025 --> 00:23:12.304 effects. It is a tricky
NOTE Confidence: 0.9314372

00:23:12.304 --> 00:23:13.505 substance to work with. So
NOTE Confidence: 0.9314372

00:23:13.505 --> 00:23:14.225 lots of work to be
NOTE Confidence: 0.9314372

00:23:14.225 --> 00:23:15.025 done here to see if

NOTE Confidence: 0.9314372

00:23:15.025 --> 00:23:16.419 there's any anything.

NOTE Confidence: 0.9724498

00:23:17.279 --> 00:23:18.559 I'm gonna wrap up by

NOTE Confidence: 0.9724498

00:23:18.559 --> 00:23:20.080 by raising this question, are

NOTE Confidence: 0.9724498

00:23:20.080 --> 00:23:21.140 psychedelics addictive?

NOTE Confidence: 0.9969208

00:23:21.600 --> 00:23:22.000 When,

NOTE Confidence: 0.99084246

00:23:22.559 --> 00:23:23.059 psilocybin,

NOTE Confidence: 0.98668283

00:23:23.359 --> 00:23:25.039 LSD, and other psychedelics were

NOTE Confidence: 0.98668283

00:23:25.039 --> 00:23:25.539 classified

NOTE Confidence: 0.9547979

00:23:25.840 --> 00:23:27.760 as schedule one drugs back

NOTE Confidence: 0.9547979

00:23:27.760 --> 00:23:29.625 in the early nineteen seventies.

NOTE Confidence: 0.9547979

00:23:29.625 --> 00:23:30.745 That implies that there is

NOTE Confidence: 0.9547979

00:23:30.745 --> 00:23:32.025 no therapeutic use, and I've

NOTE Confidence: 0.9547979

00:23:32.025 --> 00:23:33.325 shown you there actually was

NOTE Confidence: 0.9547979

00:23:33.465 --> 00:23:34.985 some evidence of therapeutic use,

NOTE Confidence: 0.9547979

00:23:34.985 --> 00:23:35.885 though nothing approved,

NOTE Confidence: 0.9672652

00:23:36.505 --> 00:23:37.705 and that they are highly
NOTE Confidence: 0.9672652

00:23:37.705 --> 00:23:39.465 addictive. And so question, are
NOTE Confidence: 0.9672652

00:23:39.465 --> 00:23:40.205 they addictive?
NOTE Confidence: 0.99697226

00:23:40.760 --> 00:23:41.720 This is data from a
NOTE Confidence: 0.99697226

00:23:41.720 --> 00:23:43.640 survey study done by David
NOTE Confidence: 0.99697226

00:23:43.640 --> 00:23:45.180 Nutt a few years ago.
NOTE Confidence: 0.9666811

00:23:45.640 --> 00:23:47.000 David Nutt is an advocate
NOTE Confidence: 0.9666811

00:23:47.000 --> 00:23:48.280 for psychedelic use, and so
NOTE Confidence: 0.9666811

00:23:48.280 --> 00:23:49.080 I think there's a little
NOTE Confidence: 0.9666811

00:23:49.080 --> 00:23:50.119 bit I think this is
NOTE Confidence: 0.9666811

00:23:50.119 --> 00:23:51.880 a a motivated survey study
NOTE Confidence: 0.9666811

00:23:51.880 --> 00:23:52.760 to to try to make
NOTE Confidence: 0.9666811

00:23:52.760 --> 00:23:54.119 a point. But it did
NOTE Confidence: 0.9666811

00:23:54.119 --> 00:23:55.160 make the point. This is
NOTE Confidence: 0.9666811

00:23:55.160 --> 00:23:56.175 a survey of,
NOTE Confidence: 0.9661833

00:23:56.655 --> 00:23:58.575 of specialists in substance abuse

NOTE Confidence: 0.9661833

00:23:58.575 --> 00:24:00.015 to asking them to rate

NOTE Confidence: 0.9661833

00:24:00.015 --> 00:24:01.295 for a variety of drugs

NOTE Confidence: 0.9661833

00:24:01.295 --> 00:24:02.175 how harmful they are to

NOTE Confidence: 0.9661833

00:24:02.175 --> 00:24:03.375 their users and how harmful

NOTE Confidence: 0.9661833

00:24:03.375 --> 00:24:04.275 they are to others.

NOTE Confidence: 0.97131073

00:24:04.575 --> 00:24:06.015 And you see alcohol, heroin,

NOTE Confidence: 0.97131073

00:24:06.015 --> 00:24:07.535 crack, methamphetamine over here at

NOTE Confidence: 0.97131073

00:24:07.535 --> 00:24:08.815 the left rated as very

NOTE Confidence: 0.97131073

00:24:08.815 --> 00:24:09.315 harmful.

NOTE Confidence: 0.99467987

00:24:09.619 --> 00:24:10.980 And you see mushrooms, the

NOTE Confidence: 0.99467987

00:24:10.980 --> 00:24:12.200 natural occurring psilocybin

NOTE Confidence: 0.90322495

00:24:12.580 --> 00:24:13.300 way over here at the

NOTE Confidence: 0.90322495

00:24:13.300 --> 00:24:14.119 right, LSD,

NOTE Confidence: 0.97325367

00:24:14.580 --> 00:24:16.040 ecstasy, also MDMA.

NOTE Confidence: 0.9727792

00:24:16.500 --> 00:24:17.460 So the point of this

NOTE Confidence: 0.9727792

00:24:17.460 --> 00:24:18.420 is that these were not
NOTE Confidence: 0.9727792

00:24:18.500 --> 00:24:19.859 but not seen as particularly
NOTE Confidence: 0.9727792

00:24:19.859 --> 00:24:21.460 harmful by experts. It's a
NOTE Confidence: 0.9727792

00:24:21.460 --> 00:24:22.660 survey study of experts for
NOTE Confidence: 0.9727792

00:24:22.660 --> 00:24:23.744 what it's worth. But they're
NOTE Confidence: 0.9727792

00:24:23.744 --> 00:24:25.445 clearly in a different category
NOTE Confidence: 0.9727792

00:24:25.505 --> 00:24:27.025 from these very harmful addictive
NOTE Confidence: 0.9727792

00:24:27.025 --> 00:24:27.765 drugs here.
NOTE Confidence: 0.9511544

00:24:28.785 --> 00:24:30.065 Bunch of points to suggest
NOTE Confidence: 0.9511544

00:24:30.065 --> 00:24:32.145 that psychedelics aren't addictive or
NOTE Confidence: 0.9511544

00:24:32.145 --> 00:24:33.125 shouldn't be considered
NOTE Confidence: 0.9574831

00:24:33.425 --> 00:24:34.705 addictive, certainly not to the
NOTE Confidence: 0.9574831

00:24:34.705 --> 00:24:35.205 same
NOTE Confidence: 0.97163147

00:24:35.580 --> 00:24:37.020 point, to the same degree
NOTE Confidence: 0.97163147

00:24:37.020 --> 00:24:38.619 as nicotine or cocaine or
NOTE Confidence: 0.97163147

00:24:38.619 --> 00:24:40.220 methamphetamine or heroin. They have

NOTE Confidence: 0.97163147

00:24:40.220 --> 00:24:41.760 limited reinforcing effects.

NOTE Confidence: 0.9974386

00:24:42.140 --> 00:24:43.760 They often exhibit tachyphylaxis.

NOTE Confidence: 0.98006904

00:24:44.700 --> 00:24:46.380 There's little evidence for dependence

NOTE Confidence: 0.98006904

00:24:46.380 --> 00:24:48.140 or withdrawal. So these classic

NOTE Confidence: 0.98006904

00:24:48.140 --> 00:24:49.119 markers of adaptivity,

NOTE Confidence: 0.98987496

00:24:49.500 --> 00:24:50.700 they really don't meet the

NOTE Confidence: 0.98987496

00:24:50.700 --> 00:24:52.674 bar. There are, however, potential

NOTE Confidence: 0.98987496

00:24:52.674 --> 00:24:54.274 harms, and it's important to

NOTE Confidence: 0.98987496

00:24:54.274 --> 00:24:56.034 take these into account when,

NOTE Confidence: 0.98987496

00:24:56.595 --> 00:24:58.034 when counseling patients who might

NOTE Confidence: 0.98987496

00:24:58.034 --> 00:24:58.695 be considering

NOTE Confidence: 0.98356104

00:24:59.075 --> 00:25:00.274 using these drugs in the

NOTE Confidence: 0.98356104

00:25:00.274 --> 00:25:00.774 underground,

NOTE Confidence: 0.9726049

00:25:01.075 --> 00:25:02.355 who are actively using them

NOTE Confidence: 0.9726049

00:25:02.355 --> 00:25:03.335 or when considering,

NOTE Confidence: 0.9385123

00:25:03.635 --> 00:25:04.914 research. And I know Joao
NOTE Confidence: 0.9385123

00:25:04.914 --> 00:25:06.250 will come back, to some
NOTE Confidence: 0.9385123

00:25:06.250 --> 00:25:07.210 of that. There are potential
NOTE Confidence: 0.9385123

00:25:07.210 --> 00:25:08.109 harms, dysregulated
NOTE Confidence: 0.96800894

00:25:08.410 --> 00:25:10.809 behavior. They produce psychological distress.
NOTE Confidence: 0.96800894

00:25:10.809 --> 00:25:12.650 They can exacerbate psychotic symptoms,
NOTE Confidence: 0.96800894

00:25:12.650 --> 00:25:13.690 and people with any risk
NOTE Confidence: 0.96800894

00:25:13.690 --> 00:25:14.350 for psychosis
NOTE Confidence: 0.99457645

00:25:14.730 --> 00:25:16.010 are carefully ruled out of
NOTE Confidence: 0.99457645

00:25:16.010 --> 00:25:17.290 most studies in the modern
NOTE Confidence: 0.99457645

00:25:17.290 --> 00:25:17.790 era.
NOTE Confidence: 0.99747425

00:25:18.765 --> 00:25:19.565 You have to worry about
NOTE Confidence: 0.99747425

00:25:19.565 --> 00:25:20.545 interactions, cardiovascular
NOTE Confidence: 0.9758115

00:25:20.845 --> 00:25:21.665 effects, etcetera.
NOTE Confidence: 0.97017634

00:25:21.965 --> 00:25:23.825 The potential for lasting perceptual
NOTE Confidence: 0.97017634

00:25:23.885 --> 00:25:25.244 disturbances, although this is quite

NOTE Confidence: 0.97017634

00:25:25.244 --> 00:25:26.685 rare with therapeutic use as

NOTE Confidence: 0.97017634

00:25:26.685 --> 00:25:28.465 opposed to unregulated high dose

NOTE Confidence: 0.97017634

00:25:28.605 --> 00:25:30.700 recreational use. I'll stop there

NOTE Confidence: 0.97017634

00:25:30.700 --> 00:25:32.059 and hand over to Joao

NOTE Confidence: 0.97017634

00:25:32.059 --> 00:25:33.919 acknowledgments, especially Ben Calmendi,

NOTE Confidence: 0.9491551

00:25:34.220 --> 00:25:35.179 close colleague who sort of

NOTE Confidence: 0.9491551

00:25:35.179 --> 00:25:35.980 pulled me into the work

NOTE Confidence: 0.9491551

00:25:35.980 --> 00:25:36.700 in this space and has

NOTE Confidence: 0.9491551

00:25:36.700 --> 00:25:37.919 led our work in OCD

NOTE Confidence: 0.9491551

00:25:38.139 --> 00:25:39.100 and a variety of other

NOTE Confidence: 0.9491551

00:25:39.100 --> 00:25:40.700 colleagues who've who've supported our

NOTE Confidence: 0.9491551

00:25:40.700 --> 00:25:42.380 work in this space. Funding,

NOTE Confidence: 0.9491551

00:25:42.380 --> 00:25:43.855 thank you all for your

NOTE Confidence: 0.9491551

00:25:43.855 --> 00:25:44.355 attention.

NOTE Confidence: 0.96628207

00:25:44.894 --> 00:25:45.934 I think that was about

NOTE Confidence: 0.96628207

00:25:45.934 --> 00:25:47.215 twenty minutes given our late
NOTE Confidence: 0.96628207

00:25:47.215 --> 00:25:48.674 start. Joel, over to you.
NOTE Confidence: 0.96628207

00:25:48.815 --> 00:25:50.434 Thank you. Thank you, Chris.
NOTE Confidence: 0.9912031

00:25:50.894 --> 00:25:52.095 Just a quick thank you,
NOTE Confidence: 0.9912031

00:25:52.095 --> 00:25:53.215 Chris. That was a wonderful
NOTE Confidence: 0.9912031

00:25:53.215 --> 00:25:53.715 overview.
NOTE Confidence: 0.95540464

00:25:54.975 --> 00:25:55.475 Yep.
NOTE Confidence: 0.9808222

00:25:55.855 --> 00:25:56.595 My pleasure.
NOTE Confidence: 0.98718375

00:25:58.770 --> 00:25:59.750 Let me share.
NOTE Confidence: 0.9036784

00:26:02.130 --> 00:26:03.350 You guys see my slides?
NOTE Confidence: 0.9941819

00:26:05.330 --> 00:26:05.830 Yes.
NOTE Confidence: 0.93122375

00:26:06.770 --> 00:26:08.130 Okay. On the on the
NOTE Confidence: 0.93122375

00:26:08.130 --> 00:26:10.070 theme of, David Nutso,
NOTE Confidence: 0.9778767

00:26:11.250 --> 00:26:12.290 they had a campaign in
NOTE Confidence: 0.9778767

00:26:12.290 --> 00:26:12.950 the UK,
NOTE Confidence: 0.8678753

00:26:13.615 --> 00:26:14.355 quite provocative campaign,

NOTE Confidence: 0.9196422

00:26:15.695 --> 00:26:17.375 that said horse riding kills

NOTE Confidence: 0.9196422

00:26:17.375 --> 00:26:18.674 more than in MDMA.

NOTE Confidence: 0.99820733

00:26:19.695 --> 00:26:20.914 And the reason why,

NOTE Confidence: 0.95852375

00:26:21.934 --> 00:26:22.434 MDMA

NOTE Confidence: 0.7051134

00:26:22.894 --> 00:26:23.394 killed,

NOTE Confidence: 0.94609404

00:26:23.695 --> 00:26:24.894 if you ask him, is

NOTE Confidence: 0.94609404

00:26:24.894 --> 00:26:26.255 because of the hyperthermia. People

NOTE Confidence: 0.94609404

00:26:26.255 --> 00:26:27.294 end up drinking a lot

NOTE Confidence: 0.94609404

00:26:27.294 --> 00:26:28.494 of water and have electrolyte

NOTE Confidence: 0.94609404

00:26:28.494 --> 00:26:28.994 imbalances.

NOTE Confidence: 0.9960642

00:26:29.670 --> 00:26:30.170 So,

NOTE Confidence: 0.84019053

00:26:30.630 --> 00:26:33.130 yeah, quite quite provocative, interesting,

NOTE Confidence: 0.99764246

00:26:34.150 --> 00:26:35.130 interesting guy.

NOTE Confidence: 0.98815584

00:26:36.070 --> 00:26:36.570 So,

NOTE Confidence: 0.8620905

00:26:37.110 --> 00:26:38.390 again, thank you, David, for

NOTE Confidence: 0.8620905

00:26:38.390 --> 00:26:39.130 your invitation.
NOTE Confidence: 0.8458096

00:26:39.590 --> 00:26:40.550 Joel De Aquinos is the
NOTE Confidence: 0.8458096

00:26:40.550 --> 00:26:41.990 professor of psychiatry, and my
NOTE Confidence: 0.8458096

00:26:41.990 --> 00:26:43.035 research sits at the inter
NOTE Confidence: 0.8458096

00:26:43.115 --> 00:26:44.475 intersection of chronic pain and
NOTE Confidence: 0.8458096

00:26:44.475 --> 00:26:45.535 substance use disorders.
NOTE Confidence: 0.96208906

00:26:46.475 --> 00:26:47.455 Here are my disclosures.
NOTE Confidence: 0.9927306

00:26:48.475 --> 00:26:49.515 Chris has just set the
NOTE Confidence: 0.9927306

00:26:49.515 --> 00:26:50.015 stage,
NOTE Confidence: 0.97548014

00:26:50.395 --> 00:26:51.295 with the broader,
NOTE Confidence: 0.92083657

00:26:51.755 --> 00:26:52.815 psychedelic landscape,
NOTE Confidence: 0.99596626

00:26:53.275 --> 00:26:54.795 what these drugs are, why
NOTE Confidence: 0.99596626

00:26:54.795 --> 00:26:56.640 there's renewed interest, and what
NOTE Confidence: 0.99596626

00:26:56.640 --> 00:26:58.160 the conversation looks like right
NOTE Confidence: 0.99596626

00:26:58.160 --> 00:26:59.440 now. My role for the
NOTE Confidence: 0.99596626

00:26:59.440 --> 00:27:00.900 next twenty minutes or so

NOTE Confidence: 0.92926204
00:27:01.280 --> 00:27:02.800 is more pragmatic. So is
NOTE Confidence: 0.92926204
00:27:02.800 --> 00:27:04.320 it I'm gonna describe what
NOTE Confidence: 0.92926204
00:27:04.320 --> 00:27:05.520 we actually know so far
NOTE Confidence: 0.92926204
00:27:05.520 --> 00:27:06.740 in pain and OUD,
NOTE Confidence: 0.9945629
00:27:07.440 --> 00:27:08.640 what we should be measuring
NOTE Confidence: 0.9945629
00:27:08.640 --> 00:27:10.080 if we want this area
NOTE Confidence: 0.9945629
00:27:10.080 --> 00:27:11.859 to mature into responsible
NOTE Confidence: 0.99079466
00:27:12.295 --> 00:27:13.815 clinical science. And I hope
NOTE Confidence: 0.99079466
00:27:13.815 --> 00:27:14.655 that by the end of
NOTE Confidence: 0.99079466
00:27:14.655 --> 00:27:15.575 the talk, I'll I'll have
NOTE Confidence: 0.99079466
00:27:15.575 --> 00:27:16.935 made the case for why
NOTE Confidence: 0.99079466
00:27:16.935 --> 00:27:18.315 we need more rigorous research
NOTE Confidence: 0.9437534
00:27:18.775 --> 00:27:20.775 because access is expanding in
NOTE Confidence: 0.9437534
00:27:20.775 --> 00:27:22.135 ways that may out may
NOTE Confidence: 0.9437534
00:27:22.135 --> 00:27:23.195 outpace evidence.
NOTE Confidence: 0.9634329

00:27:29.109 --> 00:27:30.230 So this is what computers
NOTE Confidence: 0.9634329

00:27:30.230 --> 00:27:31.510 look like when methadone and
NOTE Confidence: 0.9634329

00:27:31.510 --> 00:27:32.970 buprenorphine were synthesized.
NOTE Confidence: 0.976686

00:27:33.669 --> 00:27:34.150 About,
NOTE Confidence: 0.97677654

00:27:34.470 --> 00:27:35.429 a third of people with
NOTE Confidence: 0.97677654

00:27:35.429 --> 00:27:36.789 OUD continue to live with
NOTE Confidence: 0.97677654

00:27:36.789 --> 00:27:39.190 chronic pain despite, being treated
NOTE Confidence: 0.97677654

00:27:39.190 --> 00:27:40.090 with these medications.
NOTE Confidence: 0.95823306

00:27:40.705 --> 00:27:41.585 And I'm sure this is
NOTE Confidence: 0.95823306

00:27:41.585 --> 00:27:42.945 a patient you all recognize,
NOTE Confidence: 0.95823306

00:27:42.945 --> 00:27:45.125 someone on buprenorphine or methadone
NOTE Confidence: 0.95823306

00:27:45.185 --> 00:27:47.025 who's back pain or neuropathic
NOTE Confidence: 0.95823306

00:27:47.025 --> 00:27:47.845 pain or fibromyalgia
NOTE Confidence: 0.97690487

00:27:48.545 --> 00:27:50.725 really dominates their daily experience.
NOTE Confidence: 0.96921945

00:27:51.105 --> 00:27:52.705 They're not just uncomfortable. They're
NOTE Confidence: 0.96921945

00:27:52.705 --> 00:27:54.325 not sleeping. They're not functioning.

NOTE Confidence: 0.96921945
00:27:54.625 --> 00:27:55.365 They're isolated.
NOTE Confidence: 0.996195
00:27:55.859 --> 00:27:56.840 And over time,
NOTE Confidence: 0.99977195
00:27:57.380 --> 00:27:58.200 pain becomes
NOTE Confidence: 0.9894164
00:27:58.500 --> 00:28:00.340 a persistent stressor that wears
NOTE Confidence: 0.9894164
00:28:00.340 --> 00:28:01.240 down coping
NOTE Confidence: 0.9678756
00:28:01.619 --> 00:28:03.400 and and eventually leads to
NOTE Confidence: 0.9678756
00:28:03.460 --> 00:28:05.000 return to using opioids,
NOTE Confidence: 0.7543174
00:28:05.460 --> 00:28:06.200 non medically.
NOTE Confidence: 0.90966403
00:28:06.660 --> 00:28:07.780 And the reality is that
NOTE Confidence: 0.90966403
00:28:07.780 --> 00:28:08.500 we have not had new
NOTE Confidence: 0.90966403
00:28:08.500 --> 00:28:09.540 approaches to treat o u
NOTE Confidence: 0.90966403
00:28:09.540 --> 00:28:10.679 d in half a century
NOTE Confidence: 0.9717757
00:28:11.215 --> 00:28:12.575 other than new formulations of
NOTE Confidence: 0.9717757
00:28:12.575 --> 00:28:14.494 existing drugs and alpha two
NOTE Confidence: 0.9717757
00:28:14.494 --> 00:28:15.935 agonist to to treat opioid
NOTE Confidence: 0.9717757

00:28:15.935 --> 00:28:16.435 withdrawal.
NOTE Confidence: 0.9839995

00:28:17.215 --> 00:28:18.275 And the hypothesis
NOTE Confidence: 0.93749976

00:28:18.655 --> 00:28:20.015 isn't that psychedelics are a
NOTE Confidence: 0.93749976

00:28:20.015 --> 00:28:20.915 new pain killer.
NOTE Confidence: 0.9767209

00:28:21.295 --> 00:28:23.155 The hypothesis is more specific,
NOTE Confidence: 0.9918479

00:28:23.970 --> 00:28:25.650 is that these drugs might
NOTE Confidence: 0.9918479

00:28:25.650 --> 00:28:26.950 engage shared mechanisms,
NOTE Confidence: 0.97262794

00:28:27.490 --> 00:28:28.710 biological and psychological
NOTE Confidence: 0.92640734

00:28:29.090 --> 00:28:30.690 that reduce suffering and improve
NOTE Confidence: 0.92640734

00:28:30.690 --> 00:28:32.290 function. And in some cases
NOTE Confidence: 0.92640734

00:28:32.290 --> 00:28:33.109 may reduce,
NOTE Confidence: 0.99040747

00:28:33.730 --> 00:28:34.630 opioid burden.
NOTE Confidence: 0.9676546

00:28:35.730 --> 00:28:36.929 I like this slide because
NOTE Confidence: 0.9676546

00:28:36.929 --> 00:28:38.370 it forces a reset in
NOTE Confidence: 0.9676546

00:28:38.370 --> 00:28:39.705 how we talk about pain.
NOTE Confidence: 0.89636284

00:28:40.345 --> 00:28:41.945 Pain is a sensory experience,

NOTE Confidence: 0.89636284
00:28:41.945 --> 00:28:43.725 yes, but it's also effective
NOTE Confidence: 0.89636284
00:28:43.945 --> 00:28:45.565 and cognitive. It's threat,
NOTE Confidence: 0.97369057
00:28:45.865 --> 00:28:47.404 it's attention, mood.
NOTE Confidence: 0.98738295
00:28:47.705 --> 00:28:48.904 It it's really a story
NOTE Confidence: 0.98738295
00:28:48.904 --> 00:28:50.585 that someone tells themselves about
NOTE Confidence: 0.98738295
00:28:50.585 --> 00:28:52.125 their body and their future.
NOTE Confidence: 0.9510405
00:28:52.960 --> 00:28:54.180 And now look at opioid
NOTE Confidence: 0.9510405
00:28:54.240 --> 00:28:56.000 phenomena through the same lens,
NOTE Confidence: 0.9510405
00:28:56.000 --> 00:28:56.980 craving, withdrawal,
NOTE Confidence: 0.9617225
00:28:57.360 --> 00:28:58.340 negative affect.
NOTE Confidence: 0.95595455
00:28:58.720 --> 00:29:00.320 These aren't separate from pain.
NOTE Confidence: 0.95595455
00:29:00.320 --> 00:29:00.980 They overlap.
NOTE Confidence: 0.9874989
00:29:01.440 --> 00:29:03.200 And over time, both pain
NOTE Confidence: 0.9874989
00:29:03.200 --> 00:29:04.480 and opioid exposure can be
NOTE Confidence: 0.9874989
00:29:04.480 --> 00:29:05.920 associated with changes in a
NOTE Confidence: 0.9874989

00:29:05.920 --> 00:29:06.900 nervous system
NOTE Confidence: 0.9671485

00:29:07.495 --> 00:29:09.515 that amplify the pain experience,
NOTE Confidence: 0.9671485

00:29:09.654 --> 00:29:11.335 what we often summarize as
NOTE Confidence: 0.9671485

00:29:11.335 --> 00:29:12.154 central sensitization,
NOTE Confidence: 0.9786237

00:29:13.495 --> 00:29:14.715 or in some context,
NOTE Confidence: 0.9897731

00:29:15.015 --> 00:29:16.395 opioid induced hyperalgesia.
NOTE Confidence: 0.9981106

00:29:17.335 --> 00:29:18.715 This is really the somatosensory
NOTE Confidence: 0.8127257

00:29:19.095 --> 00:29:21.255 systems volume knob getting turned
NOTE Confidence: 0.8127257

00:29:21.255 --> 00:29:21.755 up.
NOTE Confidence: 0.9894643

00:29:22.150 --> 00:29:23.929 So so the question becomes,
NOTE Confidence: 0.9989074

00:29:24.550 --> 00:29:25.450 can one intervention
NOTE Confidence: 0.90455204

00:29:25.830 --> 00:29:26.970 interrupt this loop,
NOTE Confidence: 0.9871052

00:29:27.429 --> 00:29:28.710 not just lower a pain
NOTE Confidence: 0.9871052

00:29:28.710 --> 00:29:29.830 score for the day, but
NOTE Confidence: 0.9871052

00:29:29.830 --> 00:29:30.809 improve sleep,
NOTE Confidence: 0.93676317

00:29:31.350 --> 00:29:32.170 reduce avoidance,

NOTE Confidence: 0.9539464
00:29:32.550 --> 00:29:33.770 reduce negative affect,
NOTE Confidence: 0.992275
00:29:34.790 --> 00:29:37.290 and reduce pain, related craving
NOTE Confidence: 0.992275
00:29:37.365 --> 00:29:38.325 in a way that helps
NOTE Confidence: 0.992275
00:29:38.325 --> 00:29:40.585 people stay engaged with medications
NOTE Confidence: 0.992275
00:29:40.725 --> 00:29:41.465 for OUD
NOTE Confidence: 0.7814643
00:29:41.925 --> 00:29:43.445 and and and and with
NOTE Confidence: 0.7814643
00:29:43.445 --> 00:29:43.945 life.
NOTE Confidence: 0.9591532
00:29:46.085 --> 00:29:47.605 And and Chris already described
NOTE Confidence: 0.9591532
00:29:47.605 --> 00:29:48.645 some of this, but, the
NOTE Confidence: 0.9591532
00:29:48.645 --> 00:29:49.525 goal here is really to
NOTE Confidence: 0.9591532
00:29:49.525 --> 00:29:51.385 highlight the systems level neurobiology
NOTE Confidence: 0.9322319
00:29:51.765 --> 00:29:53.450 that makes these drugs interesting
NOTE Confidence: 0.9322319
00:29:53.450 --> 00:29:55.290 for pain and OI. So
NOTE Confidence: 0.9322319
00:29:55.290 --> 00:29:56.510 these circular graphs,
NOTE Confidence: 0.9643518
00:29:57.450 --> 00:29:59.470 visualize whole brain functional connectivity.
NOTE Confidence: 0.9643518

00:29:59.530 --> 00:30:00.730 So each dot is a
NOTE Confidence: 0.9643518
00:30:00.730 --> 00:30:02.170 node and each line is
NOTE Confidence: 0.9643518
00:30:02.170 --> 00:30:02.750 a connection.
NOTE Confidence: 0.9458283
00:30:03.370 --> 00:30:04.750 On the left, under placebo,
NOTE Confidence: 0.9782215
00:30:05.265 --> 00:30:06.865 connectivity is more segregated. It's
NOTE Confidence: 0.9782215
00:30:06.865 --> 00:30:09.025 more modular. The networks talk
NOTE Confidence: 0.9782215
00:30:09.025 --> 00:30:10.245 mostly within themselves.
NOTE Confidence: 0.9894172
00:30:10.785 --> 00:30:12.085 On the right, under psilocybin,
NOTE Confidence: 0.9889601
00:30:12.465 --> 00:30:13.585 you see a much denser
NOTE Confidence: 0.9889601
00:30:13.585 --> 00:30:15.205 web of cross network links,
NOTE Confidence: 0.9831338
00:30:15.825 --> 00:30:16.965 more global integration.
NOTE Confidence: 0.9710651
00:30:17.425 --> 00:30:18.705 And the takeaway is that,
NOTE Confidence: 0.9710651
00:30:18.705 --> 00:30:19.765 in this case, psilocybin
NOTE Confidence: 0.88024366
00:30:20.570 --> 00:30:21.310 may transiently
NOTE Confidence: 0.9948502
00:30:22.090 --> 00:30:22.590 induce
NOTE Confidence: 0.9994438
00:30:23.050 --> 00:30:24.030 network flexibility

NOTE Confidence: 0.80566573

00:30:24.570 --> 00:30:25.870 or it it may

NOTE Confidence: 0.8741234

00:30:26.170 --> 00:30:27.610 increase the brain the brain's

NOTE Confidence: 0.8741234

00:30:27.610 --> 00:30:29.390 communication bandwidth, if you will,

NOTE Confidence: 0.8741234

00:30:29.690 --> 00:30:31.790 expanding the dynamic or repertoire

NOTE Confidence: 0.8741234

00:30:31.930 --> 00:30:33.310 of these, brain networks.

NOTE Confidence: 0.98806494

00:30:34.054 --> 00:30:34.934 And and why does it

NOTE Confidence: 0.98806494

00:30:34.934 --> 00:30:36.695 matter for pain and and

NOTE Confidence: 0.98806494

00:30:36.695 --> 00:30:37.355 and OUD?

NOTE Confidence: 0.95480263

00:30:38.135 --> 00:30:39.995 Well, both of these conditions

NOTE Confidence: 0.95480263

00:30:40.054 --> 00:30:41.914 involve very rigid, overlearned,

NOTE Confidence: 0.9672127

00:30:42.455 --> 00:30:43.755 threat reward predictions.

NOTE Confidence: 0.9746582

00:30:44.615 --> 00:30:46.535 Pain is a danger. Craving

NOTE Confidence: 0.9746582

00:30:46.535 --> 00:30:47.800 is a need. So So

NOTE Confidence: 0.9746582

00:30:47.800 --> 00:30:49.900 a temporary shift toward flexibility

NOTE Confidence: 0.9741151

00:30:50.520 --> 00:30:51.720 may create a window for

NOTE Confidence: 0.9741151

00:30:51.720 --> 00:30:52.380 new learning,
NOTE Confidence: 0.97384596

00:30:52.680 --> 00:30:54.460 especially if paired with psychotherapy
NOTE Confidence: 0.97384596

00:30:54.680 --> 00:30:55.740 or behavior change.
NOTE Confidence: 0.9901918

00:30:56.120 --> 00:30:56.920 And this is not a
NOTE Confidence: 0.9901918

00:30:56.920 --> 00:30:57.820 proof of efficacy,
NOTE Confidence: 0.93475014

00:30:58.840 --> 00:31:00.220 but it is a mechanistic
NOTE Confidence: 0.93475014

00:31:00.360 --> 00:31:02.620 rationale for plasticity enabled,
NOTE Confidence: 0.994486

00:31:03.184 --> 00:31:03.684 intervention.
NOTE Confidence: 0.9607766

00:31:05.105 --> 00:31:05.845 And again,
NOTE Confidence: 0.8188726

00:31:06.385 --> 00:31:07.345 it turn if it turns
NOTE Confidence: 0.8188726

00:31:07.345 --> 00:31:08.885 out the psychedelics help,
NOTE Confidence: 0.9720771

00:31:09.505 --> 00:31:10.245 with pain,
NOTE Confidence: 0.9844696

00:31:10.545 --> 00:31:11.665 their benefit may not look
NOTE Confidence: 0.9844696

00:31:11.665 --> 00:31:12.625 like a classic kind of
NOTE Confidence: 0.9844696

00:31:12.625 --> 00:31:14.485 music. It may look like
NOTE Confidence: 0.98433423

00:31:15.040 --> 00:31:16.800 changes in how pain is

NOTE Confidence: 0.98433423

00:31:16.800 --> 00:31:18.240 processed and how a person

NOTE Confidence: 0.98433423

00:31:18.240 --> 00:31:19.380 relates to pain.

NOTE Confidence: 0.9597234

00:31:20.000 --> 00:31:21.520 I described this hypothesis in

NOTE Confidence: 0.9597234

00:31:21.520 --> 00:31:22.560 in three lanes, and this

NOTE Confidence: 0.9597234

00:31:22.560 --> 00:31:23.360 is a figure from a

NOTE Confidence: 0.9597234

00:31:23.360 --> 00:31:24.320 paper we wrote about a

NOTE Confidence: 0.9597234

00:31:24.320 --> 00:31:25.060 year ago.

NOTE Confidence: 0.6330027

00:31:25.440 --> 00:31:26.500 First, from ecological,

NOTE Confidence: 0.9403588

00:31:26.800 --> 00:31:29.065 biological lane, there are receptor

NOTE Confidence: 0.9403588

00:31:29.065 --> 00:31:30.745 level effects. So five h

NOTE Confidence: 0.9403588

00:31:30.745 --> 00:31:32.345 two a receptors are very

NOTE Confidence: 0.9403588

00:31:32.345 --> 00:31:33.965 present in somatosensory

NOTE Confidence: 0.8768742

00:31:34.745 --> 00:31:36.424 cortical areas in the dorsal

NOTE Confidence: 0.8768742

00:31:36.424 --> 00:31:36.924 horn.

NOTE Confidence: 0.95532763

00:31:37.544 --> 00:31:39.325 There are potential anti inflammatory,

NOTE Confidence: 0.9971384

00:31:39.945 --> 00:31:40.445 effects
NOTE Confidence: 0.9698291

00:31:40.904 --> 00:31:42.745 and neuroplastic effects, which Chris
NOTE Confidence: 0.9698291

00:31:42.745 --> 00:31:44.909 highlighted. All these mechanisms could
NOTE Confidence: 0.9698291

00:31:44.909 --> 00:31:46.770 plausibly change pain processing.
NOTE Confidence: 0.900748

00:31:47.710 --> 00:31:49.090 Second, there is a psychological
NOTE Confidence: 0.900748

00:31:49.230 --> 00:31:49.730 lane,
NOTE Confidence: 0.9803362

00:31:50.510 --> 00:31:51.809 decreases in pain catastrophizing
NOTE Confidence: 0.9249695

00:31:52.110 --> 00:31:54.110 and avoidance and increases in
NOTE Confidence: 0.9249695

00:31:54.110 --> 00:31:55.090 cognitive flexibility,
NOTE Confidence: 0.96788436

00:31:55.789 --> 00:31:56.270 less,
NOTE Confidence: 0.9280107

00:31:56.590 --> 00:31:58.370 attentional capture by pain.
NOTE Confidence: 0.98540807

00:31:58.885 --> 00:31:59.625 And catastrophizing
NOTE Confidence: 0.92659867

00:32:00.325 --> 00:32:01.605 is basically the mind or
NOTE Confidence: 0.92659867

00:32:01.605 --> 00:32:03.845 the habit of pain means
NOTE Confidence: 0.92659867

00:32:03.845 --> 00:32:04.965 damage and it will never
NOTE Confidence: 0.92659867

00:32:04.965 --> 00:32:07.304 end, and it predicts disability

NOTE Confidence: 0.996417
00:32:07.605 --> 00:32:09.145 as strongly as many biomedical
NOTE Confidence: 0.996417
00:32:09.285 --> 00:32:09.785 variables.
NOTE Confidence: 0.9413968
00:32:10.325 --> 00:32:11.865 And third, a social blame,
NOTE Confidence: 0.9413968
00:32:12.164 --> 00:32:13.625 isolation versus connection,
NOTE Confidence: 0.9288494
00:32:14.400 --> 00:32:16.400 meaning, support. And in chronic
NOTE Confidence: 0.9288494
00:32:16.400 --> 00:32:18.020 pain, as people get disabled,
NOTE Confidence: 0.9956081
00:32:18.400 --> 00:32:20.720 social disconnection becomes often part
NOTE Confidence: 0.9956081
00:32:20.720 --> 00:32:21.620 of the disorder.
NOTE Confidence: 0.9674687
00:32:22.720 --> 00:32:23.920 And we know that addiction
NOTE Confidence: 0.9674687
00:32:23.920 --> 00:32:25.860 circuitry intersects with pain circuitry,
NOTE Confidence: 0.9674687
00:32:25.920 --> 00:32:27.680 particularly in domains like threat
NOTE Confidence: 0.9674687
00:32:27.680 --> 00:32:28.180 processing,
NOTE Confidence: 0.9997831
00:32:28.875 --> 00:32:29.375 negative
NOTE Confidence: 0.92653394
00:32:29.915 --> 00:32:30.235 affect,
NOTE Confidence: 0.93142086
00:32:30.875 --> 00:32:32.635 learning, and and reactivity to
NOTE Confidence: 0.93142086

00:32:32.635 --> 00:32:33.455 drug cues.
NOTE Confidence: 0.96923697

00:32:34.155 --> 00:32:35.855 So so the plausible pathways
NOTE Confidence: 0.96923697

00:32:35.995 --> 00:32:37.595 for benefit aren't just less
NOTE Confidence: 0.96923697

00:32:37.595 --> 00:32:38.895 pain or craving isolation.
NOTE Confidence: 0.84056765

00:32:39.915 --> 00:32:41.115 These drugs may act to
NOTE Confidence: 0.84056765

00:32:41.115 --> 00:32:42.415 be overlapping mechanisms,
NOTE Confidence: 0.9386717

00:32:43.140 --> 00:32:44.020 And the hope is that
NOTE Confidence: 0.9386717

00:32:44.020 --> 00:32:45.780 they can help change the
NOTE Confidence: 0.9386717

00:32:45.780 --> 00:32:47.140 relationship to both pain and
NOTE Confidence: 0.9386717

00:32:47.140 --> 00:32:48.760 opioids so people can reengage
NOTE Confidence: 0.9386717

00:32:48.980 --> 00:32:50.120 with valued activities.
NOTE Confidence: 0.97958755

00:32:50.900 --> 00:32:52.020 But the gap and and
NOTE Confidence: 0.97958755

00:32:52.020 --> 00:32:53.940 the opportunity is studies that
NOTE Confidence: 0.97958755

00:32:53.940 --> 00:32:55.700 intentionally target both pain and
NOTE Confidence: 0.97958755

00:32:55.700 --> 00:32:57.320 OUD are scarce
NOTE Confidence: 0.8731685

00:32:57.780 --> 00:32:59.115 in general, let alone,

NOTE Confidence: 0.9842564
00:32:59.515 --> 00:33:00.895 if they're administering psychedelics,
NOTE Confidence: 0.97232884
00:33:02.155 --> 00:33:04.255 despite this comorbidity being everywhere.
NOTE Confidence: 0.9372851
00:33:05.835 --> 00:33:07.035 This figures from the same
NOTE Confidence: 0.9372851
00:33:07.035 --> 00:33:08.895 review paper, and it organizes
NOTE Confidence: 0.9372851
00:33:09.035 --> 00:33:10.895 mechanisms across the three phases
NOTE Confidence: 0.9372851
00:33:10.955 --> 00:33:12.815 of the addiction cycle. Intoxication,
NOTE Confidence: 0.86769193
00:33:13.850 --> 00:33:15.230 craving and negative affect,
NOTE Confidence: 0.99450624
00:33:16.490 --> 00:33:18.590 and anticipation of opioid use.
NOTE Confidence: 0.9839118
00:33:19.290 --> 00:33:20.810 And the take home here
NOTE Confidence: 0.9839118
00:33:20.810 --> 00:33:21.310 is,
NOTE Confidence: 0.9336419
00:33:21.930 --> 00:33:23.550 the effects could range from,
NOTE Confidence: 0.9336419
00:33:23.770 --> 00:33:24.830 like I said, the regulation
NOTE Confidence: 0.9336419
00:33:24.890 --> 00:33:26.410 of receptors in the dorsal
NOTE Confidence: 0.9336419
00:33:26.410 --> 00:33:27.230 horn to,
NOTE Confidence: 0.8024193
00:33:27.850 --> 00:33:29.070 reduce fear and avoidance
NOTE Confidence: 0.95740724

00:33:29.615 --> 00:33:32.335 to enhanced social connection serving
NOTE Confidence: 0.95740724

00:33:32.335 --> 00:33:33.855 as a buffer or an
NOTE Confidence: 0.95740724

00:33:33.855 --> 00:33:34.835 external inhibitor
NOTE Confidence: 0.9798666

00:33:35.215 --> 00:33:36.995 against relapse later. So,
NOTE Confidence: 0.74183995

00:33:37.695 --> 00:33:39.715 defects are fundamentally by psychosocial.
NOTE Confidence: 0.74183995

00:33:39.935 --> 00:33:40.755 So the outcomes
NOTE Confidence: 0.945951

00:33:41.135 --> 00:33:42.575 in the safety monitoring should
NOTE Confidence: 0.945951

00:33:42.575 --> 00:33:43.955 match, that complexity.
NOTE Confidence: 0.970749

00:33:45.850 --> 00:33:46.809 Okay. But what do we
NOTE Confidence: 0.970749

00:33:46.809 --> 00:33:47.950 know, clinically?
NOTE Confidence: 0.9995993

00:33:48.649 --> 00:33:49.149 For
NOTE Confidence: 0.9880288

00:33:49.769 --> 00:33:51.289 pain, we mostly have early
NOTE Confidence: 0.9880288

00:33:51.289 --> 00:33:53.710 signals, so not conclusive data.
NOTE Confidence: 0.9930993

00:33:54.490 --> 00:33:55.769 There are older studies,
NOTE Confidence: 0.9321432

00:33:56.169 --> 00:33:58.269 administering LSD in cancer pain,
NOTE Confidence: 0.93103665

00:33:58.815 --> 00:34:00.495 that Chris already highlighted in

NOTE Confidence: 0.93103665

00:34:00.495 --> 00:34:02.095 case series like phantom limb

NOTE Confidence: 0.93103665

00:34:02.095 --> 00:34:04.355 pain. These are interesting historically,

NOTE Confidence: 0.9961555

00:34:04.735 --> 00:34:05.695 but most of them are

NOTE Confidence: 0.9961555

00:34:05.695 --> 00:34:07.235 not modern trial design.

NOTE Confidence: 0.9723732

00:34:08.494 --> 00:34:09.234 More recently,

NOTE Confidence: 0.9879589

00:34:09.614 --> 00:34:11.055 there's there have been low

NOTE Confidence: 0.9879589

00:34:11.055 --> 00:34:11.875 dose LSD

NOTE Confidence: 0.9427179

00:34:12.810 --> 00:34:14.330 studies testing pain in lab

NOTE Confidence: 0.9427179

00:34:14.410 --> 00:34:15.150 in the laboratory.

NOTE Confidence: 0.93388075

00:34:16.730 --> 00:34:18.330 For psilocybin, there's there are

NOTE Confidence: 0.93388075

00:34:18.410 --> 00:34:19.370 there is data from a

NOTE Confidence: 0.93388075

00:34:19.370 --> 00:34:19.870 crossover

NOTE Confidence: 0.9289785

00:34:20.170 --> 00:34:22.090 randomized control trial that provided

NOTE Confidence: 0.9289785

00:34:22.090 --> 00:34:23.230 a signal in migraine,

NOTE Confidence: 0.8752664

00:34:23.850 --> 00:34:25.770 and also some, headache cluster

NOTE Confidence: 0.8752664

00:34:25.770 --> 00:34:27.050 reports done at Yale by,
NOTE Confidence: 0.8752664

00:34:27.370 --> 00:34:28.425 Emanuel Schindler.
NOTE Confidence: 0.7561426

00:34:28.905 --> 00:34:29.565 And microneursing,
NOTE Confidence: 0.97961164

00:34:30.265 --> 00:34:31.864 patients ask about this all
NOTE Confidence: 0.97961164

00:34:31.864 --> 00:34:32.905 the time. This is one
NOTE Confidence: 0.97961164

00:34:32.905 --> 00:34:34.665 of the messiest areas. There's
NOTE Confidence: 0.97961164

00:34:34.665 --> 00:34:35.705 a lot of self selection,
NOTE Confidence: 0.97961164

00:34:35.705 --> 00:34:37.965 expectancy effects, and mixed outcomes.
NOTE Confidence: 0.97487324

00:34:38.505 --> 00:34:39.565 So as clinicians,
NOTE Confidence: 0.99126697

00:34:39.864 --> 00:34:40.825 I think the tone we
NOTE Confidence: 0.99126697

00:34:40.825 --> 00:34:41.785 should carry back to the
NOTE Confidence: 0.99126697

00:34:41.785 --> 00:34:42.285 clinic
NOTE Confidence: 0.9741463

00:34:42.590 --> 00:34:44.270 if asked about this is,
NOTE Confidence: 0.9741463

00:34:44.270 --> 00:34:45.790 you know, don't dismiss the
NOTE Confidence: 0.9741463

00:34:45.790 --> 00:34:47.230 signals, but don't let the
NOTE Confidence: 0.9741463

00:34:47.230 --> 00:34:48.530 signals become conclusions.

NOTE Confidence: 0.943943
00:34:49.390 --> 00:34:50.690 I think the better responses,
NOTE Confidence: 0.943943
00:34:50.830 --> 00:34:52.290 better trials, better endpoints,
NOTE Confidence: 0.97007203
00:34:52.910 --> 00:34:54.130 better safety measurement.
NOTE Confidence: 0.9272143
00:34:57.704 --> 00:34:58.664 So these are the human
NOTE Confidence: 0.9272143
00:34:58.664 --> 00:34:59.164 data.
NOTE Confidence: 0.910918
00:34:59.864 --> 00:35:00.904 As you as you can
NOTE Confidence: 0.910918
00:35:00.904 --> 00:35:02.105 see, the evidence base is
NOTE Confidence: 0.910918
00:35:02.105 --> 00:35:03.085 early and heterogeneous.
NOTE Confidence: 0.91686696
00:35:04.265 --> 00:35:05.545 The strongest signal show up
NOTE Confidence: 0.91686696
00:35:05.545 --> 00:35:07.724 in cancer, palliative context,
NOTE Confidence: 0.9823972
00:35:08.344 --> 00:35:09.839 headache, and then a couple
NOTE Confidence: 0.9823972
00:35:09.839 --> 00:35:11.219 of examples in nociplastic
NOTE Confidence: 0.9783263
00:35:11.599 --> 00:35:13.219 pain or, fibromyalgia.
NOTE Confidence: 0.95351654
00:35:13.839 --> 00:35:14.799 And I'll show you some
NOTE Confidence: 0.95351654
00:35:14.799 --> 00:35:15.779 of those examples,
NOTE Confidence: 0.89953136

00:35:16.719 --> 00:35:18.719 starting with, migraine headaches. So
NOTE Confidence: 0.89953136

00:35:18.719 --> 00:35:20.180 this was an exploratory
NOTE Confidence: 0.88575554

00:35:20.480 --> 00:35:22.420 double blind placebo controlled crossover
NOTE Confidence: 0.88575554

00:35:22.480 --> 00:35:24.435 study. At two sessions separated
NOTE Confidence: 0.88575554

00:35:24.435 --> 00:35:25.655 by fourteen days.
NOTE Confidence: 0.9671369

00:35:26.435 --> 00:35:28.055 Placebo was given first
NOTE Confidence: 0.95573664

00:35:28.355 --> 00:35:30.135 to avoid long term carryover.
NOTE Confidence: 0.9501739

00:35:30.435 --> 00:35:32.035 Contaminating placebo, we just heard
NOTE Confidence: 0.9501739

00:35:32.035 --> 00:35:33.155 from Chris. These drugs may
NOTE Confidence: 0.9501739

00:35:33.155 --> 00:35:34.615 have protracted effects.
NOTE Confidence: 0.99746495

00:35:35.369 --> 00:35:36.029 The dose was
NOTE Confidence: 0.97635704

00:35:36.650 --> 00:35:37.710 around ten milligrams,
NOTE Confidence: 0.8398974

00:35:39.049 --> 00:35:39.549 orally,
NOTE Confidence: 0.96719325

00:35:40.250 --> 00:35:42.109 and there were ten, participants
NOTE Confidence: 0.96719325

00:35:42.170 --> 00:35:43.609 in this study. They were
NOTE Confidence: 0.96719325

00:35:43.609 --> 00:35:44.089 given,

NOTE Confidence: 0.96432275
00:35:44.650 --> 00:35:45.930 diaries to keep track of
NOTE Confidence: 0.96432275
00:35:45.930 --> 00:35:47.769 the frequency and intensity of
NOTE Confidence: 0.96432275
00:35:47.769 --> 00:35:48.509 their migraine,
NOTE Confidence: 0.989112
00:35:48.969 --> 00:35:49.469 attacks.
NOTE Confidence: 0.99291724
00:35:49.849 --> 00:35:50.750 In the left,
NOTE Confidence: 0.98305386
00:35:51.635 --> 00:35:53.075 this graph shows a reduction
NOTE Confidence: 0.98305386
00:35:53.075 --> 00:35:54.535 in weekly migraine days,
NOTE Confidence: 0.96631175
00:35:55.075 --> 00:35:56.355 and it was significantly greater
NOTE Confidence: 0.96631175
00:35:56.355 --> 00:35:57.895 after psilocybin than placebo.
NOTE Confidence: 0.9993458
00:35:58.675 --> 00:35:59.655 And on the right,
NOTE Confidence: 0.99292475
00:36:00.035 --> 00:36:00.915 you see the time to
NOTE Confidence: 0.99292475
00:36:00.915 --> 00:36:02.355 the second migraine attack was
NOTE Confidence: 0.99292475
00:36:02.355 --> 00:36:03.494 longer after psilocybin.
NOTE Confidence: 0.9268193
00:36:04.515 --> 00:36:05.714 The first attack there there
NOTE Confidence: 0.9268193
00:36:05.714 --> 00:36:06.435 was a trend for the
NOTE Confidence: 0.9268193

00:36:06.435 --> 00:36:08.090 first attack as well.
NOTE Confidence: 0.91474646

00:36:08.870 --> 00:36:10.310 And interestingly, this is a
NOTE Confidence: 0.91474646

00:36:10.310 --> 00:36:12.170 this is a what's conventionally
NOTE Confidence: 0.91474646

00:36:12.230 --> 00:36:12.730 called
NOTE Confidence: 0.8826042

00:36:13.910 --> 00:36:14.470 it it used to be
NOTE Confidence: 0.8826042

00:36:14.470 --> 00:36:15.610 called a sub hallucinogenic
NOTE Confidence: 0.97372556

00:36:15.910 --> 00:36:16.410 dose,
NOTE Confidence: 0.907723

00:36:17.030 --> 00:36:18.790 or minimally hallucinogenic dose. People
NOTE Confidence: 0.907723

00:36:18.790 --> 00:36:20.150 don't use that terminology anymore,
NOTE Confidence: 0.907723

00:36:20.150 --> 00:36:21.270 so instead, we just call
NOTE Confidence: 0.907723

00:36:21.270 --> 00:36:22.090 it low dose,
NOTE Confidence: 0.98077166

00:36:22.685 --> 00:36:23.805 meaning it's not a dose
NOTE Confidence: 0.98077166

00:36:23.805 --> 00:36:25.744 that will produce a trip.
NOTE Confidence: 0.99504554

00:36:27.325 --> 00:36:28.864 The interesting part is,
NOTE Confidence: 0.95657545

00:36:29.325 --> 00:36:30.765 the migraine improvement did not
NOTE Confidence: 0.95657545

00:36:30.765 --> 00:36:32.605 correlate with the intensity of

NOTE Confidence: 0.95657545

00:36:32.605 --> 00:36:35.085 the the psychedelic effects. So

NOTE Confidence: 0.95657545

00:36:35.085 --> 00:36:35.585 the

NOTE Confidence: 0.99703044

00:36:35.885 --> 00:36:37.105 the benefit was

NOTE Confidence: 0.93116426

00:36:37.430 --> 00:36:38.550 dissociable from,

NOTE Confidence: 0.9977217

00:36:39.430 --> 00:36:40.570 whatever minimally,

NOTE Confidence: 0.9744252

00:36:41.030 --> 00:36:42.550 psychedelic experience they had with

NOTE Confidence: 0.9744252

00:36:42.550 --> 00:36:44.470 this ten milligram dose. And

NOTE Confidence: 0.9744252

00:36:44.470 --> 00:36:45.750 while while migraine is a

NOTE Confidence: 0.9744252

00:36:45.750 --> 00:36:46.250 specific,

NOTE Confidence: 0.90014625

00:36:47.270 --> 00:36:49.190 headache disorder with limited general

NOTE Confidence: 0.90014625

00:36:49.190 --> 00:36:49.690 generalizability

NOTE Confidence: 0.9206316

00:36:50.070 --> 00:36:51.190 for other types of chronic

NOTE Confidence: 0.9206316

00:36:51.190 --> 00:36:52.065 pain, This is a good

NOTE Confidence: 0.9206316

00:36:52.065 --> 00:36:53.585 example of a control signal

NOTE Confidence: 0.9206316

00:36:53.585 --> 00:36:55.265 after limited dosing for a

NOTE Confidence: 0.9206316

00:36:55.265 --> 00:36:56.645 merit debilitating disorder.
NOTE Confidence: 0.96583927

00:36:58.464 --> 00:37:00.385 This other study emphasizes feasibility
NOTE Confidence: 0.96583927

00:37:00.385 --> 00:37:02.545 and safety, and functional outcomes.
NOTE Confidence: 0.96583927

00:37:02.545 --> 00:37:03.585 This is the this is
NOTE Confidence: 0.96583927

00:37:03.585 --> 00:37:04.964 fibromyalgia, the prototypical,
NOTE Confidence: 0.9268509

00:37:06.145 --> 00:37:06.645 nociplastic,
NOTE Confidence: 0.99846506

00:37:07.960 --> 00:37:09.020 chronic pain condition.
NOTE Confidence: 0.96822625

00:37:09.800 --> 00:37:11.000 So it it's often framed
NOTE Confidence: 0.96822625

00:37:11.000 --> 00:37:12.540 as the as the prototypical
NOTE Confidence: 0.96822625

00:37:12.680 --> 00:37:14.520 nociplastic condition because it's associated
NOTE Confidence: 0.96822625

00:37:14.520 --> 00:37:15.260 with pain,
NOTE Confidence: 0.9674233

00:37:16.200 --> 00:37:18.200 sleep, mood, cognition dysfunction, and
NOTE Confidence: 0.9674233

00:37:18.200 --> 00:37:19.739 there are limited effective treatments.
NOTE Confidence: 0.9844717

00:37:20.165 --> 00:37:21.525 The design was open label.
NOTE Confidence: 0.9844717

00:37:21.525 --> 00:37:22.565 There were five people in
NOTE Confidence: 0.9844717

00:37:22.565 --> 00:37:23.844 this study, and they first

NOTE Confidence: 0.9844717
00:37:23.844 --> 00:37:25.705 got fifteen milligrams of psilocybin,
NOTE Confidence: 0.96370906
00:37:26.405 --> 00:37:27.685 then they got twenty five.
NOTE Confidence: 0.96370906
00:37:27.685 --> 00:37:28.885 So twenty five, it it
NOTE Confidence: 0.96370906
00:37:28.885 --> 00:37:30.665 is considered a psychedelic dose.
NOTE Confidence: 0.99538016
00:37:31.205 --> 00:37:32.325 This is separated by two
NOTE Confidence: 0.99538016
00:37:32.325 --> 00:37:34.165 weeks. The primary outcomes were
NOTE Confidence: 0.99538016
00:37:34.165 --> 00:37:35.065 safety related.
NOTE Confidence: 0.89489764
00:37:35.780 --> 00:37:37.619 There were transient changes in
NOTE Confidence: 0.89489764
00:37:37.619 --> 00:37:39.000 blood pressure to heart rate,
NOTE Confidence: 0.9573377
00:37:39.619 --> 00:37:40.900 during the dosing session that
NOTE Confidence: 0.9573377
00:37:40.900 --> 00:37:42.340 were normalized by the end
NOTE Confidence: 0.9573377
00:37:42.340 --> 00:37:43.619 of the session. There were
NOTE Confidence: 0.9573377
00:37:43.619 --> 00:37:44.680 no series AEs.
NOTE Confidence: 0.97733736
00:37:45.859 --> 00:37:46.900 Four out of five people
NOTE Confidence: 0.97733736
00:37:46.900 --> 00:37:47.400 reported,
NOTE Confidence: 0.9940849

00:37:47.780 --> 00:37:49.000 post dosing headaches.
NOTE Confidence: 0.95427036

00:37:49.944 --> 00:37:51.464 At one month post the
NOTE Confidence: 0.95427036

00:37:51.464 --> 00:37:52.285 second dose,
NOTE Confidence: 0.9898827

00:37:52.744 --> 00:37:54.344 there were clinically meaningful improvements
NOTE Confidence: 0.9898827

00:37:54.344 --> 00:37:55.724 in pain severity, interference,
NOTE Confidence: 0.79530615

00:37:56.105 --> 00:37:57.545 sleep disturbance, and they report
NOTE Confidence: 0.79530615

00:37:57.545 --> 00:37:58.664 a larger effect size of
NOTE Confidence: 0.79530615

00:37:58.664 --> 00:37:59.464 going to the f two
NOTE Confidence: 0.79530615

00:37:59.464 --> 00:38:00.125 and above.
NOTE Confidence: 0.901655

00:38:00.825 --> 00:38:02.664 Obviously, limitations include a tiny
NOTE Confidence: 0.901655

00:38:02.664 --> 00:38:04.505 sample, all the label, highly
NOTE Confidence: 0.901655

00:38:04.505 --> 00:38:05.005 selected.
NOTE Confidence: 0.74721813

00:38:05.680 --> 00:38:06.560 So this is best for
NOTE Confidence: 0.74721813

00:38:06.560 --> 00:38:07.940 this feasibility study.
NOTE Confidence: 0.94215494

00:38:08.239 --> 00:38:09.520 And, you know, together with
NOTE Confidence: 0.94215494

00:38:09.520 --> 00:38:11.200 the migraine model, this supports

NOTE Confidence: 0.94215494

00:38:11.200 --> 00:38:13.380 moving toward larger control trials

NOTE Confidence: 0.94215494

00:38:13.680 --> 00:38:14.420 that prioritize

NOTE Confidence: 0.9812993

00:38:14.800 --> 00:38:17.219 function and and, risk monitoring.

NOTE Confidence: 0.98625195

00:38:18.114 --> 00:38:19.475 And finally, for the pain

NOTE Confidence: 0.98625195

00:38:19.475 --> 00:38:20.835 part of the talk, I'd

NOTE Confidence: 0.98625195

00:38:20.835 --> 00:38:21.955 like to highlight a controlled

NOTE Confidence: 0.98625195

00:38:21.955 --> 00:38:23.735 human evidence of an analgesic

NOTE Confidence: 0.98625195

00:38:23.795 --> 00:38:25.395 signal. This is closer to

NOTE Confidence: 0.98625195

00:38:25.395 --> 00:38:26.275 my heart because it's a

NOTE Confidence: 0.98625195

00:38:26.275 --> 00:38:27.335 human lab study.

NOTE Confidence: 0.89845616

00:38:27.875 --> 00:38:29.335 And this was a randomized,

NOTE Confidence: 0.89845616

00:38:29.395 --> 00:38:30.935 double blind, placebo controlled,

NOTE Confidence: 0.9563147

00:38:31.280 --> 00:38:32.960 within subject crossover study. There

NOTE Confidence: 0.9563147

00:38:32.960 --> 00:38:33.920 were twenty five, in this

NOTE Confidence: 0.9563147

00:38:33.920 --> 00:38:34.980 case, healthy people.

NOTE Confidence: 0.90033656

00:38:35.359 --> 00:38:36.640 They received a low doses
NOTE Confidence: 0.90033656

00:38:36.640 --> 00:38:37.380 of LSD
NOTE Confidence: 0.97858274

00:38:37.760 --> 00:38:39.380 of five, ten, and twenty,
NOTE Confidence: 0.9993706

00:38:40.400 --> 00:38:40.900 micrograms
NOTE Confidence: 0.9769014

00:38:41.440 --> 00:38:42.900 per day versus placebo,
NOTE Confidence: 0.88345766

00:38:43.599 --> 00:38:44.739 each separate session.
NOTE Confidence: 0.9114544

00:38:45.040 --> 00:38:46.160 They did the cold pressor
NOTE Confidence: 0.9114544

00:38:46.160 --> 00:38:47.435 test, which is a pretty
NOTE Confidence: 0.9114544

00:38:47.435 --> 00:38:47.935 reliable,
NOTE Confidence: 0.99703443

00:38:49.114 --> 00:38:50.955 model for evoking the experience
NOTE Confidence: 0.99703443

00:38:50.955 --> 00:38:51.994 of pain using,
NOTE Confidence: 0.9386963

00:38:52.635 --> 00:38:54.235 a rapid onset and rapid
NOTE Confidence: 0.9386963

00:38:54.235 --> 00:38:56.315 offset, type of stimulation because
NOTE Confidence: 0.9386963

00:38:56.315 --> 00:38:58.075 you're you're looking at primarily
NOTE Confidence: 0.9386963

00:38:58.075 --> 00:38:59.215 unmyelinated fibers.
NOTE Confidence: 0.98003256

00:38:59.750 --> 00:39:00.630 And the the key result

NOTE Confidence: 0.98003256

00:39:00.630 --> 00:39:01.670 is that the highest dose

NOTE Confidence: 0.98003256

00:39:01.670 --> 00:39:02.650 of twenty micrograms

NOTE Confidence: 0.9152498

00:39:02.950 --> 00:39:04.469 was associated with increase in

NOTE Confidence: 0.9152498

00:39:04.469 --> 00:39:06.089 pain tolerance so people could

NOTE Confidence: 0.9152498

00:39:06.230 --> 00:39:07.270 stick their hand in this

NOTE Confidence: 0.9152498

00:39:07.270 --> 00:39:08.809 bath water for much longer.

NOTE Confidence: 0.7796179

00:39:09.430 --> 00:39:10.230 They also,

NOTE Confidence: 0.9825556

00:39:11.030 --> 00:39:11.530 reported,

NOTE Confidence: 0.99099064

00:39:11.989 --> 00:39:13.989 lower, ratings of painfulness and

NOTE Confidence: 0.99099064

00:39:13.989 --> 00:39:14.489 unpleasantness.

NOTE Confidence: 0.98337644

00:39:15.225 --> 00:39:16.745 There there were modest increases

NOTE Confidence: 0.98337644

00:39:16.745 --> 00:39:17.725 in blood pressure,

NOTE Confidence: 0.9921419

00:39:18.345 --> 00:39:19.305 but heart rate was not

NOTE Confidence: 0.9921419

00:39:19.305 --> 00:39:19.805 affected.

NOTE Confidence: 0.85457176

00:39:21.465 --> 00:39:23.005 And it it this supports

NOTE Confidence: 0.85457176

00:39:23.065 --> 00:39:25.545 biological plausibility for analgesic and

NOTE Confidence: 0.85457176

00:39:25.545 --> 00:39:26.045 hyprogesic

NOTE Confidence: 0.88523704

00:39:26.505 --> 00:39:27.005 effects,

NOTE Confidence: 0.9827673

00:39:28.080 --> 00:39:29.280 given that this model is

NOTE Confidence: 0.9827673

00:39:29.280 --> 00:39:31.060 believed to have predictive validity,

NOTE Confidence: 0.95234513

00:39:32.000 --> 00:39:33.680 for this clinical phenomenon. But,

NOTE Confidence: 0.95234513

00:39:33.680 --> 00:39:35.120 again, this is experimental pain

NOTE Confidence: 0.95234513

00:39:35.120 --> 00:39:36.800 in in healthy volunteers, not

NOTE Confidence: 0.95234513

00:39:36.800 --> 00:39:38.500 chronic pain, and not comorbid

NOTE Confidence: 0.95234513

00:39:38.640 --> 00:39:39.380 with OUD.

NOTE Confidence: 0.97919804

00:39:40.605 --> 00:39:41.344 Okay. But,

NOTE Confidence: 0.99791384

00:39:42.285 --> 00:39:43.344 what about OUD?

NOTE Confidence: 0.8912252

00:39:44.525 --> 00:39:45.725 What has this has this

NOTE Confidence: 0.8912252

00:39:45.805 --> 00:39:46.844 any of this been tested

NOTE Confidence: 0.8912252

00:39:46.844 --> 00:39:48.045 in OUD? And the candid

NOTE Confidence: 0.8912252

00:39:48.045 --> 00:39:49.485 answer is not enough. Not

NOTE Confidence: 0.8912252

00:39:49.485 --> 00:39:50.305 enough yet,

NOTE Confidence: 0.99772656

00:39:50.685 --> 00:39:52.145 but the data is emerging.

NOTE Confidence: 0.9461743

00:39:52.980 --> 00:39:55.860 Historically, there's LSD psychotherapy work,

NOTE Confidence: 0.9228128

00:39:56.820 --> 00:39:58.260 in chronic heroin use from

NOTE Confidence: 0.9228128

00:39:58.260 --> 00:39:59.540 the seventies. Chris had his

NOTE Confidence: 0.9228128

00:39:59.540 --> 00:40:01.060 line about that. That is

NOTE Confidence: 0.9228128

00:40:01.060 --> 00:40:02.900 import important proof of concept,

NOTE Confidence: 0.9228128

00:40:02.900 --> 00:40:04.200 but it is not modern

NOTE Confidence: 0.9228128

00:40:04.260 --> 00:40:06.040 MOUD era care.

NOTE Confidence: 0.9703121

00:40:06.515 --> 00:40:07.875 In more in modern work,

NOTE Confidence: 0.9703121

00:40:07.875 --> 00:40:09.415 we have early safety data,

NOTE Confidence: 0.80999696

00:40:09.955 --> 00:40:11.255 which is small but reassuring.

NOTE Confidence: 0.96854144

00:40:11.795 --> 00:40:13.015 And now we have registered

NOTE Confidence: 0.96854144

00:40:13.075 --> 00:40:15.335 trials underway that explicitly

NOTE Confidence: 0.9428719

00:40:16.035 --> 00:40:17.815 ask safety and efficacy questions

NOTE Confidence: 0.9428719

00:40:17.875 --> 00:40:19.255 in people with MOUD,
NOTE Confidence: 0.9848553

00:40:19.555 --> 00:40:20.935 primarily in phase two.
NOTE Confidence: 0.875635

00:40:21.980 --> 00:40:23.280 Now do the side effects
NOTE Confidence: 0.875635

00:40:23.339 --> 00:40:24.460 look different in people with
NOTE Confidence: 0.875635

00:40:24.460 --> 00:40:25.280 the o u d?
NOTE Confidence: 0.8204396

00:40:25.739 --> 00:40:26.719 Probably, yes.
NOTE Confidence: 0.99501544

00:40:27.500 --> 00:40:28.619 But we don't have enough
NOTE Confidence: 0.99501544

00:40:28.619 --> 00:40:29.440 data to say.
NOTE Confidence: 0.9757684

00:40:29.819 --> 00:40:31.180 And I say probably, yes,
NOTE Confidence: 0.9757684

00:40:31.180 --> 00:40:32.540 because what we do know
NOTE Confidence: 0.9757684

00:40:32.540 --> 00:40:34.079 is that the baseline vulnerability
NOTE Confidence: 0.9298466

00:40:34.460 --> 00:40:35.520 is often higher.
NOTE Confidence: 0.92443234

00:40:36.165 --> 00:40:37.925 Both psychiatric and and medical
NOTE Confidence: 0.92443234

00:40:37.925 --> 00:40:38.425 comorbidity,
NOTE Confidence: 0.98776674

00:40:38.885 --> 00:40:40.344 trauma exposure, polysubstance
NOTE Confidence: 0.9325117

00:40:40.645 --> 00:40:41.145 use.

NOTE Confidence: 0.99291253
00:40:41.525 --> 00:40:43.125 So our safety approach must
NOTE Confidence: 0.99291253
00:40:43.125 --> 00:40:44.025 be more intentional,
NOTE Confidence: 0.9979673
00:40:45.045 --> 00:40:46.405 and our follow-up needs to
NOTE Confidence: 0.9979673
00:40:46.405 --> 00:40:47.225 to be real.
NOTE Confidence: 0.9637266
00:40:48.500 --> 00:40:50.599 This table summarizes the human
NOTE Confidence: 0.9637266
00:40:50.739 --> 00:40:53.060 OUD evidence and highlights why
NOTE Confidence: 0.9637266
00:40:53.060 --> 00:40:55.000 safety and real world risk
NOTE Confidence: 0.9637266
00:40:55.060 --> 00:40:57.140 must be accounted for in
NOTE Confidence: 0.9637266
00:40:57.140 --> 00:40:58.520 in in the study design.
NOTE Confidence: 0.9637266
00:40:58.739 --> 00:41:00.020 The big picture is OUD
NOTE Confidence: 0.9637266
00:41:00.020 --> 00:41:01.160 evidence is thinner
NOTE Confidence: 0.94628364
00:41:01.540 --> 00:41:02.680 than the pain evidence,
NOTE Confidence: 0.99259126
00:41:03.204 --> 00:41:04.724 and and the studies vary
NOTE Confidence: 0.99259126
00:41:04.724 --> 00:41:06.025 widely by setting,
NOTE Confidence: 0.9365066
00:41:06.565 --> 00:41:08.025 dosing, and and outcomes.
NOTE Confidence: 0.94613534

00:41:09.525 --> 00:41:10.885 There is enough signal to
NOTE Confidence: 0.94613534

00:41:10.885 --> 00:41:13.285 justify modern trials in OUD
NOTE Confidence: 0.94613534

00:41:13.285 --> 00:41:14.665 and pain, in my opinion,
NOTE Confidence: 0.9395436

00:41:15.125 --> 00:41:16.484 but the risks we actually
NOTE Confidence: 0.9395436

00:41:16.484 --> 00:41:17.704 care about overdose
NOTE Confidence: 0.9075976

00:41:18.430 --> 00:41:19.969 risk of polysubstance use,
NOTE Confidence: 0.99469393

00:41:20.670 --> 00:41:21.570 in some cases,
NOTE Confidence: 0.9928267

00:41:22.190 --> 00:41:23.090 cardiac arrhythmia,
NOTE Confidence: 0.8025155

00:41:24.430 --> 00:41:24.930 and,
NOTE Confidence: 0.96460986

00:41:26.190 --> 00:41:27.730 pain interference function
NOTE Confidence: 0.9351499

00:41:28.190 --> 00:41:29.870 have to be built into,
NOTE Confidence: 0.9351499

00:41:30.110 --> 00:41:31.489 design and and measurement.
NOTE Confidence: 0.9606596

00:41:32.664 --> 00:41:33.625 This slide shows some of
NOTE Confidence: 0.9606596

00:41:33.625 --> 00:41:35.724 the historical control OUD signal.
NOTE Confidence: 0.9898856

00:41:36.505 --> 00:41:37.724 So this was a randomized
NOTE Confidence: 0.9898856

00:41:37.864 --> 00:41:38.364 incarcerated,

NOTE Confidence: 0.97859526
00:41:39.545 --> 00:41:40.825 randomized trial in which they
NOTE Confidence: 0.97859526
00:41:40.984 --> 00:41:41.964 people were incarcerated
NOTE Confidence: 0.923579
00:41:42.904 --> 00:41:44.025 in, they they had a
NOTE Confidence: 0.923579
00:41:44.025 --> 00:41:46.424 residential psychedelic therapy program versus
NOTE Confidence: 0.923579
00:41:46.424 --> 00:41:47.085 an outpatient
NOTE Confidence: 0.94429326
00:41:47.640 --> 00:41:49.739 abstinence program without MOUD.
NOTE Confidence: 0.99206257
00:41:50.520 --> 00:41:52.299 Both had intense monitoring.
NOTE Confidence: 0.99278307
00:41:52.920 --> 00:41:54.380 In the psychedelic arm,
NOTE Confidence: 0.96226484
00:41:54.839 --> 00:41:56.359 people received five weeks of
NOTE Confidence: 0.96226484
00:41:56.359 --> 00:41:56.859 preparatory
NOTE Confidence: 0.9990562
00:41:57.719 --> 00:41:58.219 psychotherapy
NOTE Confidence: 0.98215187
00:41:58.760 --> 00:41:59.500 that culminated
NOTE Confidence: 0.9427851
00:42:00.039 --> 00:42:01.579 in one very high dose,
NOTE Confidence: 0.99332315
00:42:02.154 --> 00:42:02.894 of LSD,
NOTE Confidence: 0.9228559
00:42:03.674 --> 00:42:04.875 administered in one session. The
NOTE Confidence: 0.9228559

00:42:04.875 --> 00:42:06.315 dose was three hundred to
NOTE Confidence: 0.9228559

00:42:06.315 --> 00:42:07.755 four fifty. So just to
NOTE Confidence: 0.9228559

00:42:07.755 --> 00:42:09.114 compare, this is over ten
NOTE Confidence: 0.9228559

00:42:09.114 --> 00:42:10.714 times higher than the human
NOTE Confidence: 0.9228559

00:42:10.714 --> 00:42:12.094 lab study I just showed,
NOTE Confidence: 0.85896516

00:42:12.875 --> 00:42:14.414 but what people call heroic
NOTE Confidence: 0.85896516

00:42:14.474 --> 00:42:15.535 dose of LSD.
NOTE Confidence: 0.91692346

00:42:16.730 --> 00:42:17.930 Twenty five percent what the
NOTE Confidence: 0.91692346

00:42:17.930 --> 00:42:18.969 graph shows is that twenty
NOTE Confidence: 0.91692346

00:42:18.969 --> 00:42:20.829 five percent maintained verified
NOTE Confidence: 0.9847414

00:42:21.130 --> 00:42:21.630 abstinence
NOTE Confidence: 0.9987912

00:42:21.930 --> 00:42:22.829 for a year
NOTE Confidence: 0.960148

00:42:23.609 --> 00:42:25.469 versus in in the, LSD
NOTE Confidence: 0.960148

00:42:25.530 --> 00:42:26.890 group as opposed to five
NOTE Confidence: 0.960148

00:42:26.890 --> 00:42:28.430 percent in the control group.
NOTE Confidence: 0.960148

00:42:28.489 --> 00:42:29.290 And you see some of

NOTE Confidence: 0.960148
00:42:29.290 --> 00:42:30.809 the patient quotes on the
NOTE Confidence: 0.960148
00:42:30.809 --> 00:42:31.309 right.
NOTE Confidence: 0.89406854
00:42:33.525 --> 00:42:34.744 This patient describes,
NOTE Confidence: 0.9727018
00:42:35.364 --> 00:42:36.744 heroin as an escape.
NOTE Confidence: 0.9293374
00:42:37.685 --> 00:42:39.125 The overall theme is the
NOTE Confidence: 0.9293374
00:42:39.125 --> 00:42:40.505 LSD as a confrontation
NOTE Confidence: 0.9972536
00:42:40.885 --> 00:42:41.945 or reorientation.
NOTE Confidence: 0.962967
00:42:42.965 --> 00:42:44.580 So, again, this is not
NOTE Confidence: 0.962967
00:42:44.580 --> 00:42:45.240 a modern,
NOTE Confidence: 0.8778737
00:42:45.940 --> 00:42:47.460 clinical trial. People were not
NOTE Confidence: 0.8778737
00:42:47.460 --> 00:42:48.500 getting m o u d.
NOTE Confidence: 0.8778737
00:42:48.500 --> 00:42:49.560 This is not blinded.
NOTE Confidence: 0.944246
00:42:50.260 --> 00:42:52.100 Still, it's durable behavior change
NOTE Confidence: 0.944246
00:42:52.100 --> 00:42:52.600 signal,
NOTE Confidence: 0.98500246
00:42:53.460 --> 00:42:54.680 that is motivating
NOTE Confidence: 0.98017335

00:42:55.140 --> 00:42:55.640 modern
NOTE Confidence: 0.9009246

00:42:55.940 --> 00:42:57.795 and safer trials in people
NOTE Confidence: 0.9009246

00:42:57.795 --> 00:42:59.474 with, people receiving m o
NOTE Confidence: 0.9009246

00:42:59.474 --> 00:43:00.135 u d.
NOTE Confidence: 0.9086654

00:43:01.075 --> 00:43:01.954 And here I'd like to
NOTE Confidence: 0.9086654

00:43:01.954 --> 00:43:03.515 make the safety point. I
NOTE Confidence: 0.9086654

00:43:03.555 --> 00:43:04.055 Ibogaine
NOTE Confidence: 0.9913065

00:43:04.434 --> 00:43:06.194 illustrates this well. This was
NOTE Confidence: 0.9913065

00:43:06.194 --> 00:43:08.055 an open label observational study
NOTE Confidence: 0.98365325

00:43:08.594 --> 00:43:10.194 in four people receiving m
NOTE Confidence: 0.98365325

00:43:10.194 --> 00:43:11.395 o u d. On the
NOTE Confidence: 0.98365325

00:43:11.395 --> 00:43:11.895 left,
NOTE Confidence: 0.9539677

00:43:12.420 --> 00:43:13.140 you see,
NOTE Confidence: 0.96833575

00:43:13.619 --> 00:43:15.400 the figure show shows prolongation
NOTE Confidence: 0.7456566

00:43:16.420 --> 00:43:16.920 prolongation
NOTE Confidence: 0.96853346

00:43:17.219 --> 00:43:18.819 proportion of subjects with a

NOTE Confidence: 0.96853346
00:43:18.819 --> 00:43:19.319 QTC
NOTE Confidence: 0.99841475
00:43:20.099 --> 00:43:22.200 time exceeding four fifty milliseconds
NOTE Confidence: 0.99841475
00:43:22.339 --> 00:43:23.560 or five hundred milliseconds
NOTE Confidence: 0.98161614
00:43:24.655 --> 00:43:25.615 in the first twenty four
NOTE Confidence: 0.98161614
00:43:25.615 --> 00:43:27.395 hours period after Ibogaine.
NOTE Confidence: 0.9247246
00:43:28.415 --> 00:43:29.455 And and there's a clear
NOTE Confidence: 0.9247246
00:43:29.455 --> 00:43:31.135 signal there. The in on
NOTE Confidence: 0.9247246
00:43:31.135 --> 00:43:32.735 average, the QPC was prolonged
NOTE Confidence: 0.9247246
00:43:32.735 --> 00:43:33.935 by around a hundred ninety
NOTE Confidence: 0.9247246
00:43:33.935 --> 00:43:35.155 five to a hundred milliseconds.
NOTE Confidence: 0.99719644
00:43:36.095 --> 00:43:36.575 And,
NOTE Confidence: 0.89903754
00:43:37.055 --> 00:43:39.215 Ibogaine, especially the metabolite of
NOTE Confidence: 0.89903754
00:43:39.215 --> 00:43:40.275 Ibogaine or Ibogaine
NOTE Confidence: 0.93510044
00:43:40.680 --> 00:43:41.180 blocks,
NOTE Confidence: 0.86129284
00:43:42.119 --> 00:43:43.180 potassium channels.
NOTE Confidence: 0.99805534

00:43:43.560 --> 00:43:44.940 So it delays ventricular
NOTE Confidence: 0.9588133

00:43:45.319 --> 00:43:45.819 repolarization.
NOTE Confidence: 0.9887605

00:43:47.400 --> 00:43:48.780 It's it's a very promiscuous
NOTE Confidence: 0.9887605

00:43:48.839 --> 00:43:49.339 drug.
NOTE Confidence: 0.91991174

00:43:50.520 --> 00:43:52.599 On on on the right,
NOTE Confidence: 0.91991174

00:43:52.599 --> 00:43:54.599 you see, another consequence of
NOTE Confidence: 0.91991174

00:43:54.599 --> 00:43:55.980 this receptor promastridium
NOTE Confidence: 0.9625461

00:43:57.295 --> 00:43:57.955 of, Ibogaine,
NOTE Confidence: 0.933902

00:43:58.735 --> 00:43:59.855 which is ataxia. It's a
NOTE Confidence: 0.933902

00:43:59.855 --> 00:44:01.395 spaghetti block with individual
NOTE Confidence: 0.9725592

00:44:01.695 --> 00:44:03.215 level data, and you see
NOTE Confidence: 0.9725592

00:44:03.215 --> 00:44:03.715 that
NOTE Confidence: 0.9800764

00:44:04.015 --> 00:44:06.435 people experience attack ataxia primarily
NOTE Confidence: 0.9800764

00:44:06.495 --> 00:44:07.455 in the first two to
NOTE Confidence: 0.9800764

00:44:07.455 --> 00:44:08.195 six hours
NOTE Confidence: 0.94153976

00:44:08.910 --> 00:44:10.369 after getting Ibogaine.

NOTE Confidence: 0.94712865

00:44:11.230 --> 00:44:12.109 And and, you know, it

NOTE Confidence: 0.94712865

00:44:12.109 --> 00:44:13.329 has a lot of cerebellar

NOTE Confidence: 0.94712865

00:44:13.390 --> 00:44:14.670 and vestibular effects. It's an

NOTE Confidence: 0.94712865

00:44:14.670 --> 00:44:15.650 NDMA antagonist.

NOTE Confidence: 0.9109265

00:44:16.270 --> 00:44:17.230 Also, it has some effect

NOTE Confidence: 0.9109265

00:44:17.230 --> 00:44:18.369 on sodium channels.

NOTE Confidence: 0.99282104

00:44:18.750 --> 00:44:20.109 So the the message here

NOTE Confidence: 0.99282104

00:44:20.109 --> 00:44:20.670 is that,

NOTE Confidence: 0.89501077

00:44:21.405 --> 00:44:23.025 especially for people getting methadone,

NOTE Confidence: 0.9725147

00:44:23.485 --> 00:44:25.005 the arrhythmia risk is real

NOTE Confidence: 0.9725147

00:44:25.005 --> 00:44:25.745 with Ibogaine.

NOTE Confidence: 0.9469413

00:44:26.125 --> 00:44:26.625 So,

NOTE Confidence: 0.95245963

00:44:27.325 --> 00:44:29.185 strict medical monitoring is required.

NOTE Confidence: 0.97479385

00:44:29.565 --> 00:44:30.445 And and we have to

NOTE Confidence: 0.97479385

00:44:30.445 --> 00:44:32.525 be cautious to, generalize. Most

NOTE Confidence: 0.97479385

00:44:32.525 --> 00:44:33.805 of these studies are done
NOTE Confidence: 0.97479385

00:44:33.805 --> 00:44:35.165 in Central America or South
NOTE Confidence: 0.97479385

00:44:35.165 --> 00:44:36.465 America, and they're observational.
NOTE Confidence: 0.9391548

00:44:37.700 --> 00:44:39.380 There are companies working in,
NOTE Confidence: 0.98383176

00:44:40.019 --> 00:44:41.380 tweaking the ibogaine molecule to
NOTE Confidence: 0.98383176

00:44:41.380 --> 00:44:42.420 avoid some of these effects,
NOTE Confidence: 0.98383176

00:44:42.420 --> 00:44:43.940 but we we have yet
NOTE Confidence: 0.98383176

00:44:43.940 --> 00:44:44.420 to see,
NOTE Confidence: 0.9988068

00:44:44.819 --> 00:44:46.260 high quality data with those
NOTE Confidence: 0.9988068

00:44:46.260 --> 00:44:46.760 compounds.
NOTE Confidence: 0.6880954

00:44:48.180 --> 00:44:48.920 And here's
NOTE Confidence: 0.95942116

00:44:50.105 --> 00:44:51.065 one of the few modern
NOTE Confidence: 0.95942116

00:44:51.065 --> 00:44:53.045 data points on psychedelics in
NOTE Confidence: 0.95942116

00:44:53.065 --> 00:44:53.545 an,
NOTE Confidence: 0.73760104

00:44:54.025 --> 00:44:55.085 NYUD context.
NOTE Confidence: 0.944778

00:44:56.025 --> 00:44:57.545 The question here was, can

NOTE Confidence: 0.944778

00:44:57.545 --> 00:44:59.145 salsalvin be given safely to

NOTE Confidence: 0.944778

00:44:59.145 --> 00:45:00.444 people who are getting buprenorphine?

NOTE Confidence: 0.99466497

00:45:00.904 --> 00:45:01.944 And this was an open

NOTE Confidence: 0.99466497

00:45:01.944 --> 00:45:03.005 label case series.

NOTE Confidence: 0.85499144

00:45:05.730 --> 00:45:07.430 People were getting buprenorphine naloxone.

NOTE Confidence: 0.95433754

00:45:07.730 --> 00:45:09.570 They completed two psilocybin sessions

NOTE Confidence: 0.95433754

00:45:09.570 --> 00:45:11.090 in a supportive setting. There

NOTE Confidence: 0.95433754

00:45:11.090 --> 00:45:12.390 were no serious AEs,

NOTE Confidence: 0.98043346

00:45:13.250 --> 00:45:14.290 and and no evidence of

NOTE Confidence: 0.98043346

00:45:14.290 --> 00:45:15.430 psilocybin compromising,

NOTE Confidence: 0.98669255

00:45:16.610 --> 00:45:18.530 the effectiveness of buprenorphine in

NOTE Confidence: 0.98669255

00:45:18.530 --> 00:45:19.270 any way.

NOTE Confidence: 0.9661605

00:45:19.575 --> 00:45:20.775 The n is very small.

NOTE Confidence: 0.9661605

00:45:20.775 --> 00:45:22.455 There's only two people, so

NOTE Confidence: 0.9661605

00:45:22.455 --> 00:45:23.255 take that with a grain

NOTE Confidence: 0.9661605

00:45:23.255 --> 00:45:23.915 of salt.
NOTE Confidence: 0.9746103

00:45:25.015 --> 00:45:27.195 The figure shows subjective effects,
NOTE Confidence: 0.89503473

00:45:27.655 --> 00:45:29.114 looking broadly consistent
NOTE Confidence: 0.96390116

00:45:29.494 --> 00:45:31.515 consistent with previous psilocybin
NOTE Confidence: 0.6955875

00:45:31.815 --> 00:45:32.315 studies.
NOTE Confidence: 0.9974131

00:45:32.820 --> 00:45:33.800 And, you know, supporting
NOTE Confidence: 0.98667383

00:45:34.100 --> 00:45:35.160 feasibility without
NOTE Confidence: 0.88082033

00:45:35.700 --> 00:45:37.620 over claiming out outcomes, which
NOTE Confidence: 0.88082033

00:45:37.620 --> 00:45:38.600 the paper doesn't,
NOTE Confidence: 0.99288183

00:45:39.300 --> 00:45:40.520 given the tiny sample.
NOTE Confidence: 0.9779752

00:45:42.260 --> 00:45:43.640 And here we see epidemiology
NOTE Confidence: 0.96509385

00:45:43.940 --> 00:45:45.239 epidemiology as
NOTE Confidence: 0.94411045

00:45:45.915 --> 00:45:47.835 additional early signal. This is
NOTE Confidence: 0.94411045

00:45:47.835 --> 00:45:50.155 an SDOH data from forty
NOTE Confidence: 0.94411045

00:45:50.155 --> 00:45:51.455 five thousand adults.
NOTE Confidence: 0.9139591

00:45:51.915 --> 00:45:53.355 The authors here examine the

NOTE Confidence: 0.9139591

00:45:53.355 --> 00:45:55.295 relationship between history of nonmedical

NOTE Confidence: 0.9139591

00:45:55.435 --> 00:45:56.415 opioid use

NOTE Confidence: 0.9392267

00:45:57.035 --> 00:45:59.355 and lifetime classic psychedelic use.

NOTE Confidence: 0.9392267

00:45:59.355 --> 00:45:59.855 So,

NOTE Confidence: 0.84900385

00:46:00.250 --> 00:46:01.610 think about the first quadrant,

NOTE Confidence: 0.84900385

00:46:01.610 --> 00:46:02.489 think about on the first

NOTE Confidence: 0.84900385

00:46:02.489 --> 00:46:03.630 slides Chris shows.

NOTE Confidence: 0.95198596

00:46:04.810 --> 00:46:06.190 Those are the classic psychedelics.

NOTE Confidence: 0.9627713

00:46:06.730 --> 00:46:07.850 And and the results show

NOTE Confidence: 0.9627713

00:46:07.850 --> 00:46:09.610 that psychedelic use was associated

NOTE Confidence: 0.9627713

00:46:09.610 --> 00:46:11.290 with reduced risk of past

NOTE Confidence: 0.9627713

00:46:11.290 --> 00:46:13.290 year, opioid dependence, and opioid

NOTE Confidence: 0.9627713

00:46:13.290 --> 00:46:14.570 abuse. This is DSM four

NOTE Confidence: 0.9627713

00:46:14.570 --> 00:46:15.070 criteria.

NOTE Confidence: 0.9917994

00:46:15.455 --> 00:46:16.735 The paper came out around

NOTE Confidence: 0.9917994

00:46:16.735 --> 00:46:18.094 three years ago, but the
NOTE Confidence: 0.9917994

00:46:18.094 --> 00:46:19.855 data itself is from twenty
NOTE Confidence: 0.9917994

00:46:19.855 --> 00:46:21.455 thirteen, I believe. So it's,
NOTE Confidence: 0.9917994

00:46:21.695 --> 00:46:22.275 the DSM,
NOTE Confidence: 0.99698997

00:46:22.975 --> 00:46:23.475 four.
NOTE Confidence: 0.9357336

00:46:24.415 --> 00:46:25.695 And a couple caveats, it's
NOTE Confidence: 0.9357336

00:46:25.695 --> 00:46:26.895 cross sectional, so we cannot
NOTE Confidence: 0.9357336

00:46:26.895 --> 00:46:27.795 infer causality.
NOTE Confidence: 0.9373468

00:46:28.094 --> 00:46:30.755 There's unmeasured confounding, very likely.
NOTE Confidence: 0.9373468

00:46:31.050 --> 00:46:32.010 The point here is that
NOTE Confidence: 0.9373468

00:46:32.010 --> 00:46:34.010 the signal doesn't come it's
NOTE Confidence: 0.9373468

00:46:34.010 --> 00:46:35.770 not confined, just the small
NOTE Confidence: 0.9373468

00:46:35.770 --> 00:46:36.750 clinical cohorts.
NOTE Confidence: 0.970592

00:46:38.010 --> 00:46:39.050 You know, these large scale
NOTE Confidence: 0.970592

00:46:39.050 --> 00:46:41.310 epidemiological studies also lend support
NOTE Confidence: 0.99335647

00:46:41.930 --> 00:46:43.710 to hypothesis driven,

NOTE Confidence: 0.99948424
00:46:44.090 --> 00:46:45.070 clinical trials.
NOTE Confidence: 0.9494886
00:46:46.114 --> 00:46:47.155 Now let me also give
NOTE Confidence: 0.9494886
00:46:47.155 --> 00:46:48.055 you a preclinical
NOTE Confidence: 0.9992094
00:46:48.515 --> 00:46:49.015 snapshot
NOTE Confidence: 0.9943301
00:46:49.635 --> 00:46:51.075 as plausibility for what we
NOTE Confidence: 0.9943301
00:46:51.075 --> 00:46:52.035 should test and what we
NOTE Confidence: 0.9943301
00:46:52.035 --> 00:46:52.775 should measure.
NOTE Confidence: 0.8982248
00:46:53.474 --> 00:46:54.835 On the left, you have,
NOTE Confidence: 0.8982248
00:46:54.994 --> 00:46:56.035 paper that came out last
NOTE Confidence: 0.8982248
00:46:56.035 --> 00:46:57.974 year, Nature Neuroscience paper.
NOTE Confidence: 0.93248963
00:46:58.400 --> 00:47:00.000 They looked at two standard
NOTE Confidence: 0.93248963
00:47:00.000 --> 00:47:01.600 chronic pain models. One of
NOTE Confidence: 0.93248963
00:47:01.600 --> 00:47:03.840 neuropathic pain, called spare nerve
NOTE Confidence: 0.93248963
00:47:03.840 --> 00:47:05.380 injury and another of inflammatory
NOTE Confidence: 0.93248963
00:47:05.520 --> 00:47:07.060 pain called the CFA model.
NOTE Confidence: 0.9840117

00:47:07.760 --> 00:47:09.040 And the the key point
NOTE Confidence: 0.9840117

00:47:09.040 --> 00:47:10.739 is that once these animals
NOTE Confidence: 0.9840117

00:47:10.800 --> 00:47:12.255 have chronic pain, they have,
NOTE Confidence: 0.9840117

00:47:12.494 --> 00:47:13.555 mechanical hypersensitivity.
NOTE Confidence: 0.9959597

00:47:14.654 --> 00:47:15.614 And a single dose of
NOTE Confidence: 0.9959597

00:47:15.614 --> 00:47:16.114 psilocybin
NOTE Confidence: 0.903058

00:47:16.734 --> 00:47:18.815 produces a rapid improvement by
NOTE Confidence: 0.903058

00:47:18.815 --> 00:47:19.855 the next day. So you
NOTE Confidence: 0.903058

00:47:19.855 --> 00:47:21.694 see the psilocybin administered here
NOTE Confidence: 0.903058

00:47:21.694 --> 00:47:22.755 here in a normalization
NOTE Confidence: 0.9467945

00:47:24.094 --> 00:47:25.394 of, mechanical
NOTE Confidence: 0.88815403

00:47:25.775 --> 00:47:26.275 hypersensitivity,
NOTE Confidence: 0.9994136

00:47:27.980 --> 00:47:29.599 across the follow-up window
NOTE Confidence: 0.9139665

00:47:30.619 --> 00:47:31.839 on the order of weeks.
NOTE Confidence: 0.9360628

00:47:32.380 --> 00:47:33.420 And I'm showing this animal
NOTE Confidence: 0.9360628

00:47:33.420 --> 00:47:34.160 data because

NOTE Confidence: 0.95200205
00:47:34.539 --> 00:47:35.359 it supports,
NOTE Confidence: 0.90351945
00:47:35.739 --> 00:47:37.099 I believe, an an important
NOTE Confidence: 0.90351945
00:47:37.099 --> 00:47:38.079 clinical idea,
NOTE Confidence: 0.9812378
00:47:38.460 --> 00:47:39.660 which we may be looking
NOTE Confidence: 0.9812378
00:47:39.660 --> 00:47:41.435 at a time limited window
NOTE Confidence: 0.9812378
00:47:41.435 --> 00:47:43.135 of change rather than daily
NOTE Confidence: 0.9812378
00:47:43.275 --> 00:47:43.775 symptomatic
NOTE Confidence: 0.9973066
00:47:44.235 --> 00:47:44.735 dosing.
NOTE Confidence: 0.93658245
00:47:45.275 --> 00:47:46.895 So human trials should prioritize
NOTE Confidence: 0.9786593
00:47:47.195 --> 00:47:49.195 durability and function and not
NOTE Confidence: 0.9786593
00:47:49.195 --> 00:47:51.215 just same day pain ratings.
NOTE Confidence: 0.9149283
00:47:52.089 --> 00:47:53.210 And on the right, we,
NOTE Confidence: 0.9149283
00:47:53.369 --> 00:47:55.130 there's a a molecular psychiatry
NOTE Confidence: 0.9149283
00:47:55.130 --> 00:47:56.670 paper also from last year.
NOTE Confidence: 0.9149283
00:47:56.809 --> 00:47:58.510 Actually, it's twenty twenty four.
NOTE Confidence: 0.8772028

00:48:00.489 --> 00:48:01.609 And this was a heroin,
NOTE Confidence: 0.8772028

00:48:01.770 --> 00:48:03.230 self administration study.
NOTE Confidence: 0.7433468

00:48:03.530 --> 00:48:04.910 And and and here, psilocybin
NOTE Confidence: 0.8651307

00:48:05.210 --> 00:48:05.710 blunted
NOTE Confidence: 0.91606176

00:48:06.385 --> 00:48:08.145 cue induced heroin seeking, which
NOTE Confidence: 0.91606176

00:48:08.145 --> 00:48:09.045 is believed
NOTE Confidence: 0.95138335

00:48:09.585 --> 00:48:10.725 to model relapse.
NOTE Confidence: 0.99765474

00:48:11.745 --> 00:48:13.285 And in this pattern of
NOTE Confidence: 0.88206905

00:48:13.585 --> 00:48:15.045 effects on relapse vulnerability
NOTE Confidence: 0.9177929

00:48:15.585 --> 00:48:16.864 maps onto what we care
NOTE Confidence: 0.9177929

00:48:16.864 --> 00:48:17.605 about clinically.
NOTE Confidence: 0.9087343

00:48:18.719 --> 00:48:19.940 So I I think explanations,
NOTE Confidence: 0.9087343

00:48:20.000 --> 00:48:21.200 we should treat these as
NOTE Confidence: 0.9087343

00:48:21.200 --> 00:48:22.420 directional signs.
NOTE Confidence: 0.88010496

00:48:22.800 --> 00:48:24.960 In pain, measure interference and
NOTE Confidence: 0.88010496

00:48:24.960 --> 00:48:25.460 function

NOTE Confidence: 0.9431223

00:48:25.760 --> 00:48:26.800 over a longer period than

NOTE Confidence: 0.9431223

00:48:26.800 --> 00:48:27.680 you normally would with the

NOTE Confidence: 0.9431223

00:48:27.680 --> 00:48:28.660 traditional analgesic.

NOTE Confidence: 0.9022816

00:48:28.960 --> 00:48:30.880 In OUD, measure cue, stress,

NOTE Confidence: 0.9022816

00:48:30.880 --> 00:48:33.125 pain, provoke, craving, and relapse

NOTE Confidence: 0.9022816

00:48:33.344 --> 00:48:34.965 risk along with safety.

NOTE Confidence: 0.93490297

00:48:36.385 --> 00:48:37.585 And there's also momentum in

NOTE Confidence: 0.93490297

00:48:37.585 --> 00:48:39.105 clinical research. So these are

NOTE Confidence: 0.93490297

00:48:39.105 --> 00:48:40.864 the registered studies. There are

NOTE Confidence: 0.93490297

00:48:40.864 --> 00:48:43.045 studies looking psilocybin assisted therapy,

NOTE Confidence: 0.96957064

00:48:44.145 --> 00:48:46.320 to help taper long term

NOTE Confidence: 0.96957064

00:48:46.320 --> 00:48:48.020 opioid therapy for for pain.

NOTE Confidence: 0.9981888

00:48:48.480 --> 00:48:48.980 Also,

NOTE Confidence: 0.8666196

00:48:50.880 --> 00:48:52.820 safety interaction work with buprenorphine

NOTE Confidence: 0.8666196

00:48:53.040 --> 00:48:54.900 expanding on the preliminary data

NOTE Confidence: 0.8853418

00:48:55.280 --> 00:48:57.120 I showed earlier. And also
NOTE Confidence: 0.8853418

00:48:57.120 --> 00:48:58.320 plan studies in people on
NOTE Confidence: 0.8853418

00:48:58.320 --> 00:48:58.820 methadone,
NOTE Confidence: 0.9895609

00:49:00.405 --> 00:49:02.485 where medication and and cardiac
NOTE Confidence: 0.9895609

00:49:02.485 --> 00:49:04.265 monitoring matter matters the most.
NOTE Confidence: 0.9895609

00:49:04.405 --> 00:49:05.605 So the the science is
NOTE Confidence: 0.9895609

00:49:05.605 --> 00:49:07.445 finally moving from idea to
NOTE Confidence: 0.9895609

00:49:07.445 --> 00:49:08.185 to program.
NOTE Confidence: 0.94129837

00:49:10.325 --> 00:49:12.085 And, you know, the patients
NOTE Confidence: 0.94129837

00:49:12.085 --> 00:49:13.125 are already living in this
NOTE Confidence: 0.94129837

00:49:13.125 --> 00:49:14.005 reality. I don't know if
NOTE Confidence: 0.94129837

00:49:14.005 --> 00:49:15.205 you have patients who ask
NOTE Confidence: 0.94129837

00:49:15.205 --> 00:49:16.140 about this, but,
NOTE Confidence: 0.97295856

00:49:16.619 --> 00:49:17.819 I I have patients who
NOTE Confidence: 0.97295856

00:49:17.819 --> 00:49:19.420 have asked about states like
NOTE Confidence: 0.97295856

00:49:19.420 --> 00:49:19.920 Oregon.

NOTE Confidence: 0.97428304

00:49:20.940 --> 00:49:22.779 And, you know, sometimes people

NOTE Confidence: 0.97428304

00:49:22.779 --> 00:49:23.680 assume that,

NOTE Confidence: 0.9732589

00:49:24.940 --> 00:49:26.400 states that have programs

NOTE Confidence: 0.96243864

00:49:26.859 --> 00:49:28.779 that facilitate facilitate access to

NOTE Confidence: 0.96243864

00:49:28.779 --> 00:49:29.279 psychedelics,

NOTE Confidence: 0.92354226

00:49:29.819 --> 00:49:30.719 such as psilocybin,

NOTE Confidence: 0.92418605

00:49:33.494 --> 00:49:34.695 It is the same phenomenon

NOTE Confidence: 0.92418605

00:49:34.695 --> 00:49:36.295 we saw with cannabinoids, right?

NOTE Confidence: 0.92418605

00:49:36.295 --> 00:49:37.435 State level indication

NOTE Confidence: 0.8073092

00:49:38.055 --> 00:49:39.734 is different than an FDA

NOTE Confidence: 0.8073092

00:49:39.734 --> 00:49:40.635 approved indication.

NOTE Confidence: 0.9544108

00:49:41.494 --> 00:49:43.655 The states have regulated access

NOTE Confidence: 0.9544108

00:49:43.655 --> 00:49:44.155 frameworks.

NOTE Confidence: 0.94402

00:49:44.520 --> 00:49:45.800 A clinical trial on the

NOTE Confidence: 0.94402

00:49:45.800 --> 00:49:46.920 other hand which is how

NOTE Confidence: 0.94402

00:49:46.920 --> 00:49:48.380 you obtain a date approval
NOTE Confidence: 0.8741951

00:49:48.840 --> 00:49:50.700 you have diagnosis based enrollment,
NOTE Confidence: 0.9845959

00:49:51.160 --> 00:49:52.140 medical monitoring,
NOTE Confidence: 0.98728263

00:49:52.600 --> 00:49:53.820 you have defined endpoints,
NOTE Confidence: 0.9394841

00:49:54.280 --> 00:49:56.120 you have systematic adverse event
NOTE Confidence: 0.9394841

00:49:56.120 --> 00:49:56.620 tracking,
NOTE Confidence: 0.96501493

00:49:57.355 --> 00:49:58.875 And and here's why that
NOTE Confidence: 0.96501493

00:49:58.875 --> 00:49:59.695 gap matters.
NOTE Confidence: 0.9965277

00:50:00.075 --> 00:50:00.895 If psilocybin
NOTE Confidence: 0.9779831

00:50:01.355 --> 00:50:03.355 were to receive FDA approval
NOTE Confidence: 0.9779831

00:50:03.355 --> 00:50:04.635 for any indication, which is
NOTE Confidence: 0.9779831

00:50:04.635 --> 00:50:05.614 likely to happen
NOTE Confidence: 0.97761697

00:50:05.915 --> 00:50:07.195 in the next several months
NOTE Confidence: 0.97761697

00:50:07.195 --> 00:50:08.495 to a year for depression,
NOTE Confidence: 0.95048404

00:50:09.515 --> 00:50:10.495 it would become,
NOTE Confidence: 0.85531557

00:50:11.170 --> 00:50:12.710 you you know, legally prescribable

NOTE Confidence: 0.8300892
00:50:13.010 --> 00:50:13.750 off label,
NOTE Confidence: 0.9593369
00:50:14.130 --> 00:50:16.530 including for people with OUD
NOTE Confidence: 0.9593369
00:50:16.530 --> 00:50:18.469 or even pain well before
NOTE Confidence: 0.988959
00:50:19.010 --> 00:50:20.070 we have mature
NOTE Confidence: 0.998065
00:50:20.370 --> 00:50:22.130 efficacy and safety data in
NOTE Confidence: 0.998065
00:50:22.130 --> 00:50:22.870 those populations.
NOTE Confidence: 0.99429953
00:50:23.489 --> 00:50:25.250 So if if access expands
NOTE Confidence: 0.99429953
00:50:25.250 --> 00:50:26.230 faster than evidence,
NOTE Confidence: 0.9591513
00:50:26.844 --> 00:50:28.685 the earliest adopters may be
NOTE Confidence: 0.9591513
00:50:28.685 --> 00:50:29.725 the the people who are
NOTE Confidence: 0.9591513
00:50:29.725 --> 00:50:31.805 most vulnerable. And those people
NOTE Confidence: 0.9591513
00:50:31.805 --> 00:50:32.925 are often those with pain,
NOTE Confidence: 0.9591513
00:50:32.925 --> 00:50:35.105 OED, trauma histories, and polysubstance
NOTE Confidence: 0.9933286
00:50:35.405 --> 00:50:36.925 exposure. So we really need
NOTE Confidence: 0.9933286
00:50:36.925 --> 00:50:38.285 high quality data in in
NOTE Confidence: 0.9933286

00:50:38.285 --> 00:50:39.885 the populations that we actually
NOTE Confidence: 0.9933286

00:50:39.885 --> 00:50:40.385 treat.
NOTE Confidence: 0.97039706

00:50:42.569 --> 00:50:43.930 So what should we measure
NOTE Confidence: 0.97039706

00:50:43.930 --> 00:50:46.089 to mitigate OUD risk? Because
NOTE Confidence: 0.97039706

00:50:46.089 --> 00:50:47.150 this population has
NOTE Confidence: 0.9166127

00:50:47.450 --> 00:50:49.049 higher baseline rates of trauma,
NOTE Confidence: 0.9166127

00:50:49.049 --> 00:50:50.270 anxiety, mood disorders,
NOTE Confidence: 0.8731899

00:50:51.369 --> 00:50:53.289 including both depression and bipolar
NOTE Confidence: 0.8731899

00:50:53.289 --> 00:50:56.109 disorder, suicidality and polysubstance use,
NOTE Confidence: 0.98797566

00:50:57.094 --> 00:50:58.295 We need to assess those
NOTE Confidence: 0.98797566

00:50:58.295 --> 00:50:59.335 medically. We need to look
NOTE Confidence: 0.98797566

00:50:59.335 --> 00:51:00.954 at cardiac arrhythmia risk,
NOTE Confidence: 0.99816775

00:51:01.335 --> 00:51:02.155 sleep deprivation,
NOTE Confidence: 0.99742365

00:51:02.535 --> 00:51:03.515 autonomic instability,
NOTE Confidence: 0.93013984

00:51:04.694 --> 00:51:06.694 medication lists, DDI, drug drug
NOTE Confidence: 0.93013984

00:51:06.694 --> 00:51:07.194 interactions.

NOTE Confidence: 0.7756566
00:51:07.815 --> 00:51:09.494 And there's also general a
NOTE Confidence: 0.7756566
00:51:09.494 --> 00:51:10.315 gender analyzability
NOTE Confidence: 0.98218477
00:51:10.614 --> 00:51:11.114 issue.
NOTE Confidence: 0.97983885
00:51:11.540 --> 00:51:13.320 Many psychedelic studies,
NOTE Confidence: 0.97717637
00:51:14.099 --> 00:51:15.780 exclude the very patients we're
NOTE Confidence: 0.97717637
00:51:15.780 --> 00:51:16.520 talking about.
NOTE Confidence: 0.9917438
00:51:17.140 --> 00:51:18.500 So that doesn't mean we
NOTE Confidence: 0.9917438
00:51:18.500 --> 00:51:19.880 shouldn't study them.
NOTE Confidence: 0.96945685
00:51:20.180 --> 00:51:21.800 We can study this safely,
NOTE Confidence: 0.96945685
00:51:22.020 --> 00:51:23.219 but only if we measure
NOTE Confidence: 0.96945685
00:51:23.219 --> 00:51:25.219 risk as rigorously as we
NOTE Confidence: 0.96945685
00:51:25.219 --> 00:51:26.119 measure benefit.
NOTE Confidence: 0.93279445
00:51:29.204 --> 00:51:30.484 This slide is basically the
NOTE Confidence: 0.93279445
00:51:30.484 --> 00:51:32.405 approach or should I say
NOTE Confidence: 0.93279445
00:51:32.405 --> 00:51:34.105 the philosophy of our lab.
NOTE Confidence: 0.9329421

00:51:34.645 --> 00:51:35.844 If we want to understand
NOTE Confidence: 0.9329421

00:51:35.844 --> 00:51:37.364 pain, especially pain in people
NOTE Confidence: 0.9329421

00:51:37.364 --> 00:51:38.105 with SUD,
NOTE Confidence: 0.9671323

00:51:38.805 --> 00:51:39.925 we have to bridge two
NOTE Confidence: 0.9671323

00:51:39.925 --> 00:51:40.425 worlds.
NOTE Confidence: 0.97868395

00:51:41.260 --> 00:51:42.140 On the left is what
NOTE Confidence: 0.97868395

00:51:42.140 --> 00:51:42.860 we can do in the
NOTE Confidence: 0.97868395

00:51:42.860 --> 00:51:44.780 lab, controlled pain testing. So
NOTE Confidence: 0.97868395

00:51:44.780 --> 00:51:45.440 we use,
NOTE Confidence: 0.763624

00:51:46.300 --> 00:51:47.660 quantitation sort of testing or
NOTE Confidence: 0.763624

00:51:47.660 --> 00:51:48.160 QST
NOTE Confidence: 0.929625

00:51:48.460 --> 00:51:50.060 to probe mechanisms like central
NOTE Confidence: 0.929625

00:51:50.060 --> 00:51:50.560 sensitization.
NOTE Confidence: 0.9394664

00:51:51.500 --> 00:51:53.180 We pair that with pharma
NOTE Confidence: 0.9394664

00:51:53.260 --> 00:51:53.760 PKPD,
NOTE Confidence: 0.98254037

00:51:54.060 --> 00:51:54.560 pharmacokinetics,

NOTE Confidence: 0.9490117

00:51:55.375 --> 00:51:56.155 and pharmacodynamics

NOTE Confidence: 0.97274846

00:51:56.614 --> 00:51:58.635 modeling when drugs are involved

NOTE Confidence: 0.93392897

00:51:59.094 --> 00:52:00.055 so that we're not just

NOTE Confidence: 0.93392897

00:52:00.055 --> 00:52:01.494 asking did pain change, but

NOTE Confidence: 0.93392897

00:52:01.494 --> 00:52:03.255 also how did the system

NOTE Confidence: 0.93392897

00:52:03.255 --> 00:52:04.455 respond to this drug and

NOTE Confidence: 0.93392897

00:52:04.455 --> 00:52:05.755 at what level of exposure.

NOTE Confidence: 0.9985138

00:52:06.055 --> 00:52:07.114 And on the right,

NOTE Confidence: 0.9461208

00:52:07.610 --> 00:52:08.890 in the real world, this

NOTE Confidence: 0.9461208

00:52:08.890 --> 00:52:10.170 is where pain actually drives

NOTE Confidence: 0.9461208

00:52:10.170 --> 00:52:12.330 disability and relapse risk. That's

NOTE Confidence: 0.9461208

00:52:12.330 --> 00:52:13.050 why we use,

NOTE Confidence: 0.9033699

00:52:13.530 --> 00:52:15.070 experience sampling or EMA.

NOTE Confidence: 0.84825516

00:52:15.690 --> 00:52:17.950 So smartphone based assessments, accelerometers

NOTE Confidence: 0.8910561

00:52:18.250 --> 00:52:20.430 to capture pain intensity, interference,

NOTE Confidence: 0.8910561

00:52:20.650 --> 00:52:21.825 mood function,
NOTE Confidence: 0.9136289

00:52:22.364 --> 00:52:24.045 in real time, not just
NOTE Confidence: 0.9136289

00:52:24.045 --> 00:52:25.905 as a monthly clinic visit.
NOTE Confidence: 0.99081093

00:52:26.525 --> 00:52:27.405 And and the reason we
NOTE Confidence: 0.99081093

00:52:27.405 --> 00:52:28.685 do both is lab measures
NOTE Confidence: 0.99081093

00:52:28.685 --> 00:52:30.065 give mechanistic precision,
NOTE Confidence: 0.88986087

00:52:30.445 --> 00:52:31.325 but they miss the lived
NOTE Confidence: 0.88986087

00:52:31.325 --> 00:52:32.844 experience. And the real world
NOTE Confidence: 0.88986087

00:52:32.844 --> 00:52:33.344 measures,
NOTE Confidence: 0.98659295

00:52:34.605 --> 00:52:36.030 they capture what matters to
NOTE Confidence: 0.98659295

00:52:36.190 --> 00:52:37.230 patients, but they can be
NOTE Confidence: 0.98659295

00:52:37.230 --> 00:52:37.969 very noisy.
NOTE Confidence: 0.9684895

00:52:38.350 --> 00:52:39.469 When you combine them, we
NOTE Confidence: 0.9684895

00:52:39.469 --> 00:52:41.250 can test a stronger question,
NOTE Confidence: 0.9300393

00:52:41.630 --> 00:52:42.850 which is does an intervention
NOTE Confidence: 0.9300393

00:52:42.910 --> 00:52:44.190 move the mechanisms that we

NOTE Confidence: 0.9300393
00:52:44.190 --> 00:52:45.489 care about as scientists,
NOTE Confidence: 0.91317165
00:52:45.790 --> 00:52:47.230 and does that translate into
NOTE Confidence: 0.91317165
00:52:47.230 --> 00:52:48.670 better function and less the
NOTE Confidence: 0.91317165
00:52:48.670 --> 00:52:49.950 day less day to day
NOTE Confidence: 0.91317165
00:52:49.950 --> 00:52:50.450 suffering?
NOTE Confidence: 0.9965312
00:52:50.835 --> 00:52:52.114 And this is the bridge
NOTE Confidence: 0.9965312
00:52:52.114 --> 00:52:53.895 that we're trying to build.
NOTE Confidence: 0.99199516
00:52:54.515 --> 00:52:55.474 And I'll end with one
NOTE Confidence: 0.99199516
00:52:55.474 --> 00:52:57.094 concrete example of that approach,
NOTE Confidence: 0.99199516
00:52:57.155 --> 00:52:57.635 which is,
NOTE Confidence: 0.89531034
00:52:58.195 --> 00:52:59.234 we're going through the JIT
NOTE Confidence: 0.89531034
00:52:59.234 --> 00:53:00.435 process right now for this.
NOTE Confidence: 0.89531034
00:53:00.435 --> 00:53:02.195 So this is, an NIH
NOTE Confidence: 0.89531034
00:53:02.195 --> 00:53:03.234 grant, the National Center of
NOTE Confidence: 0.89531034
00:53:03.234 --> 00:53:04.775 Culinary Integrator Health.
NOTE Confidence: 0.89255935

00:53:05.360 --> 00:53:06.320 And we're going to test
NOTE Confidence: 0.89255935

00:53:06.320 --> 00:53:07.600 psilocybin as a nudge on
NOTE Confidence: 0.89255935

00:53:07.600 --> 00:53:09.219 the treatment of physical therapy
NOTE Confidence: 0.89255935

00:53:09.440 --> 00:53:10.900 to chronic low back pain.
NOTE Confidence: 0.98784965

00:53:11.360 --> 00:53:12.500 The reason to test
NOTE Confidence: 0.9596004

00:53:12.880 --> 00:53:14.739 to pair psilocybin with PT
NOTE Confidence: 0.9596004

00:53:14.960 --> 00:53:15.840 is that PT is an
NOTE Confidence: 0.9596004

00:53:15.840 --> 00:53:18.080 evidence based, intervention for chronic
NOTE Confidence: 0.9596004

00:53:18.080 --> 00:53:19.120 low back pain, but many
NOTE Confidence: 0.9596004

00:53:19.120 --> 00:53:20.340 patients can't fully
NOTE Confidence: 0.95961326

00:53:20.964 --> 00:53:22.805 engage with it because pain,
NOTE Confidence: 0.95961326

00:53:22.805 --> 00:53:24.344 fear of movement, and avoidance
NOTE Confidence: 0.95961326

00:53:24.405 --> 00:53:25.305 get in the way.
NOTE Confidence: 0.9760173

00:53:25.765 --> 00:53:27.125 And the hypothesis here isn't
NOTE Confidence: 0.9760173

00:53:27.125 --> 00:53:27.785 that psilocybin,
NOTE Confidence: 0.91055626

00:53:29.285 --> 00:53:30.405 will have a a a

NOTE Confidence: 0.91055626
00:53:30.405 --> 00:53:31.765 traditional ad hoc effect is
NOTE Confidence: 0.91055626
00:53:31.765 --> 00:53:33.045 that it will create a
NOTE Confidence: 0.91055626
00:53:33.045 --> 00:53:34.565 time limited window where people
NOTE Confidence: 0.91055626
00:53:34.565 --> 00:53:36.250 are more able to engage
NOTE Confidence: 0.91055626
00:53:36.250 --> 00:53:36.910 with movement,
NOTE Confidence: 0.9072786
00:53:37.370 --> 00:53:39.070 update their threat beliefs.
NOTE Confidence: 0.8943622
00:53:40.010 --> 00:53:41.290 So pain you know, motion
NOTE Confidence: 0.8943622
00:53:41.290 --> 00:53:42.890 is lotion, like physical therapist
NOTE Confidence: 0.8943622
00:53:42.890 --> 00:53:44.010 say, rather than pain is
NOTE Confidence: 0.8943622
00:53:44.010 --> 00:53:44.590 a threat,
NOTE Confidence: 0.95492876
00:53:44.970 --> 00:53:46.250 and, and do the work
NOTE Confidence: 0.95492876
00:53:46.250 --> 00:53:48.270 of of, of recovery. And,
NOTE Confidence: 0.97678095
00:53:49.464 --> 00:53:50.344 and, you know, this might
NOTE Confidence: 0.97678095
00:53:50.344 --> 00:53:51.385 be a if it does
NOTE Confidence: 0.97678095
00:53:51.385 --> 00:53:52.265 work, it could be a
NOTE Confidence: 0.97678095

00:53:52.265 --> 00:53:53.244 scalable concept,
NOTE Confidence: 0.9237502

00:53:54.265 --> 00:53:55.464 because it will work by
NOTE Confidence: 0.9237502

00:53:55.464 --> 00:53:55.964 strengthening,
NOTE Confidence: 0.99964994

00:53:56.585 --> 00:53:57.805 an existing clinical
NOTE Confidence: 0.98296344

00:53:58.265 --> 00:53:58.765 intervention,
NOTE Confidence: 0.939912

00:54:00.425 --> 00:54:02.025 backbone of PT rather than
NOTE Confidence: 0.939912

00:54:02.025 --> 00:54:03.645 building a stand alone psychedelic
NOTE Confidence: 0.939912

00:54:03.705 --> 00:54:04.205 intervention.
NOTE Confidence: 0.900354

00:54:04.830 --> 00:54:06.030 And this is the direction
NOTE Confidence: 0.900354

00:54:06.030 --> 00:54:07.489 that I'm I'm looking for,
NOTE Confidence: 0.900354

00:54:07.710 --> 00:54:09.570 a psychedelic science that's embedded
NOTE Confidence: 0.9915781

00:54:10.430 --> 00:54:11.489 in standard care,
NOTE Confidence: 0.9996119

00:54:12.030 --> 00:54:13.489 with measurable mechanisms
NOTE Confidence: 0.9956916

00:54:13.790 --> 00:54:15.010 and outcomes that
NOTE Confidence: 0.9891753

00:54:15.310 --> 00:54:15.810 clinicians,
NOTE Confidence: 0.9990033

00:54:16.510 --> 00:54:17.489 already trust.

NOTE Confidence: 0.9940214
00:54:18.795 --> 00:54:19.755 So I'll close with this
NOTE Confidence: 0.9940214
00:54:19.755 --> 00:54:21.535 mindset of responsible acceleration.
NOTE Confidence: 0.98847264
00:54:22.555 --> 00:54:23.935 That means that we take,
NOTE Confidence: 0.7968459
00:54:24.555 --> 00:54:25.375 risk seriously.
NOTE Confidence: 0.98745966
00:54:26.714 --> 00:54:27.775 We plan follow-up
NOTE Confidence: 0.9436344
00:54:28.315 --> 00:54:29.915 because benefit and risk don't
NOTE Confidence: 0.9436344
00:54:29.915 --> 00:54:31.455 end when the drug administration
NOTE Confidence: 0.9436344
00:54:31.675 --> 00:54:32.175 ends.
NOTE Confidence: 0.94813555
00:54:32.700 --> 00:54:33.900 It also means that we
NOTE Confidence: 0.94813555
00:54:33.900 --> 00:54:34.380 designed,
NOTE Confidence: 0.97723895
00:54:35.260 --> 00:54:36.780 clinical trials that include patients
NOTE Confidence: 0.97723895
00:54:36.780 --> 00:54:37.440 we actually
NOTE Confidence: 0.94757396
00:54:37.820 --> 00:54:38.320 treat,
NOTE Confidence: 0.92865294
00:54:38.940 --> 00:54:40.460 in both mechanistic studies and
NOTE Confidence: 0.92865294
00:54:40.460 --> 00:54:40.940 pragmatic,
NOTE Confidence: 0.9327455

00:54:41.420 --> 00:54:42.859 studies. So we can answer
NOTE Confidence: 0.9327455

00:54:42.859 --> 00:54:44.219 not just does it work,
NOTE Confidence: 0.9327455

00:54:44.219 --> 00:54:44.719 but
NOTE Confidence: 0.9220994

00:54:45.065 --> 00:54:46.505 for whom and wonder what
NOTE Confidence: 0.9220994

00:54:46.505 --> 00:54:48.105 conditions, and if so, at
NOTE Confidence: 0.9220994

00:54:48.105 --> 00:54:48.845 what cost,
NOTE Confidence: 0.91696

00:54:49.305 --> 00:54:51.085 and and what risk. So
NOTE Confidence: 0.91696

00:54:51.145 --> 00:54:52.745 so that we can replace
NOTE Confidence: 0.91696

00:54:52.745 --> 00:54:54.425 the uncertainty with data and
NOTE Confidence: 0.91696

00:54:54.425 --> 00:54:56.025 patients are enforced to choose
NOTE Confidence: 0.91696

00:54:56.025 --> 00:54:57.805 between unrelieved pain and OUD
NOTE Confidence: 0.941971

00:54:58.265 --> 00:54:59.965 or hype and speculation.
NOTE Confidence: 0.9394399

00:55:01.280 --> 00:55:02.580 Thanks again for the invitation,
NOTE Confidence: 0.9446965

00:55:03.040 --> 00:55:04.400 and the CNRU for being
NOTE Confidence: 0.9446965

00:55:04.400 --> 00:55:05.700 the home of our cannabinoids
NOTE Confidence: 0.9446965

00:55:05.760 --> 00:55:07.280 and now psychedelic studies and

NOTE Confidence: 0.9446965

00:55:07.280 --> 00:55:08.320 all the funders of this

NOTE Confidence: 0.9446965

00:55:08.320 --> 00:55:09.520 work. I'm happy to answer

NOTE Confidence: 0.9446965

00:55:09.520 --> 00:55:10.180 any questions.

NOTE Confidence: 0.99072874

00:55:12.080 --> 00:55:14.020 Thank you, JP. Wonderful overview.

NOTE Confidence: 0.99072874

00:55:14.160 --> 00:55:15.705 Thank you again, Chris, for

NOTE Confidence: 0.99072874

00:55:15.705 --> 00:55:17.165 your overview of psychedelics.

NOTE Confidence: 0.91193086

00:55:18.105 --> 00:55:18.985 I wanted to open it

NOTE Confidence: 0.91193086

00:55:18.985 --> 00:55:20.605 up for questions if anybody

NOTE Confidence: 0.94434124

00:55:21.065 --> 00:55:22.185 as we've got a couple

NOTE Confidence: 0.94434124

00:55:22.185 --> 00:55:22.844 of minutes.

NOTE Confidence: 0.9904537

00:55:23.705 --> 00:55:24.825 There's a question in the

NOTE Confidence: 0.9904537

00:55:24.825 --> 00:55:25.325 chat.

NOTE Confidence: 0.9813749

00:55:26.105 --> 00:55:27.405 Many for doctor,

NOTE Confidence: 0.9618758

00:55:27.785 --> 00:55:29.864 Dakino, many studies suggest that

NOTE Confidence: 0.9618758

00:55:29.864 --> 00:55:32.219 the psychedelic experience is important

NOTE Confidence: 0.9618758

00:55:32.219 --> 00:55:34.560 for therapeutic outcomes in depression

NOTE Confidence: 0.9618758

00:55:34.780 --> 00:55:35.920 and other psychiatric

NOTE Confidence: 0.98705345

00:55:36.540 --> 00:55:37.040 conditions.

NOTE Confidence: 0.95467293

00:55:37.500 --> 00:55:38.460 What do you make of

NOTE Confidence: 0.95467293

00:55:38.460 --> 00:55:40.060 one of the study finding

NOTE Confidence: 0.95467293

00:55:40.060 --> 00:55:41.280 that psychedelic intensity

NOTE Confidence: 0.9931168

00:55:41.820 --> 00:55:43.420 did not correlate with migraine

NOTE Confidence: 0.9931168

00:55:43.420 --> 00:55:43.920 improvement?

NOTE Confidence: 0.9638625

00:55:44.285 --> 00:55:45.245 Is this a signal that

NOTE Confidence: 0.9638625

00:55:45.245 --> 00:55:47.265 psychedelics work differently for pain

NOTE Confidence: 0.9638625

00:55:47.325 --> 00:55:48.945 than for psychiatric conditions?

NOTE Confidence: 0.80755794

00:55:50.525 --> 00:55:51.585 There's a pretty question.

NOTE Confidence: 0.9548907

00:55:52.045 --> 00:55:52.945 And this is,

NOTE Confidence: 0.97899836

00:55:53.405 --> 00:55:54.765 along with, you know, all

NOTE Confidence: 0.97899836

00:55:54.765 --> 00:55:56.844 the, all the methodological questions

NOTE Confidence: 0.97899836

00:55:56.844 --> 00:55:58.605 around blindness is probably one

NOTE Confidence: 0.97899836
00:55:58.605 --> 00:56:00.390 of the top two, top
NOTE Confidence: 0.97899836
00:56:00.390 --> 00:56:01.770 three questions in the field
NOTE Confidence: 0.901521
00:56:02.150 --> 00:56:03.530 to what degree the psychedelic
NOTE Confidence: 0.901521
00:56:03.670 --> 00:56:04.730 experiences matter.
NOTE Confidence: 0.97577673
00:56:06.630 --> 00:56:08.069 You know, many people think
NOTE Confidence: 0.97577673
00:56:08.069 --> 00:56:08.550 that,
NOTE Confidence: 0.93109906
00:56:09.030 --> 00:56:09.989 if you want to change
NOTE Confidence: 0.93109906
00:56:09.989 --> 00:56:10.650 the relationship,
NOTE Confidence: 0.970842
00:56:11.955 --> 00:56:13.315 with pain or with,
NOTE Confidence: 0.9323398
00:56:14.275 --> 00:56:15.955 opioid use and if you
NOTE Confidence: 0.9323398
00:56:15.955 --> 00:56:17.015 have these entrenched
NOTE Confidence: 0.9936733
00:56:17.475 --> 00:56:17.975 beliefs
NOTE Confidence: 0.92536974
00:56:18.515 --> 00:56:20.195 that the experience itself and
NOTE Confidence: 0.92536974
00:56:20.195 --> 00:56:21.255 going through it,
NOTE Confidence: 0.9391632
00:56:22.035 --> 00:56:23.245 might be important to,
NOTE Confidence: 0.96343225

00:56:24.320 --> 00:56:25.920 dissociate them. But I I
NOTE Confidence: 0.96343225

00:56:25.920 --> 00:56:26.880 I I have not seen
NOTE Confidence: 0.96343225

00:56:26.880 --> 00:56:28.160 convincing data yet. I think
NOTE Confidence: 0.96343225

00:56:28.160 --> 00:56:29.119 it I think we have
NOTE Confidence: 0.96343225

00:56:29.119 --> 00:56:30.739 to extrapolate thoughtfully.
NOTE Confidence: 0.9127843

00:56:31.600 --> 00:56:32.980 Like I said, migraine headaches
NOTE Confidence: 0.9127843

00:56:33.119 --> 00:56:34.900 are, a specific ideology.
NOTE Confidence: 0.94462687

00:56:35.360 --> 00:56:36.640 It's unclear. I mean, they
NOTE Confidence: 0.94462687

00:56:36.640 --> 00:56:37.984 have central citizenization
NOTE Confidence: 0.9141208

00:56:38.285 --> 00:56:39.904 does happen in migraine headaches,
NOTE Confidence: 0.98590744

00:56:40.605 --> 00:56:41.105 but,
NOTE Confidence: 0.9076358

00:56:41.805 --> 00:56:43.244 it's hard to extrapolate that
NOTE Confidence: 0.9076358

00:56:43.244 --> 00:56:44.684 to chronic low back pain,
NOTE Confidence: 0.9076358

00:56:44.684 --> 00:56:46.444 which is a heterogeneous condition
NOTE Confidence: 0.9076358

00:56:46.444 --> 00:56:47.105 in itself.
NOTE Confidence: 0.9374589

00:56:48.204 --> 00:56:49.404 So so the the honest

NOTE Confidence: 0.9374589
00:56:49.404 --> 00:56:50.204 answer is, I don't know,
NOTE Confidence: 0.9374589
00:56:50.204 --> 00:56:51.244 as as more data becomes
NOTE Confidence: 0.9374589
00:56:51.244 --> 00:56:52.880 available, hopefully, we can, you
NOTE Confidence: 0.9374589
00:56:52.880 --> 00:56:54.960 know, harmonize those datasets and
NOTE Confidence: 0.9374589
00:56:54.960 --> 00:56:56.400 and see where it matters
NOTE Confidence: 0.9374589
00:56:56.400 --> 00:56:57.680 and where where it it
NOTE Confidence: 0.9374589
00:56:57.680 --> 00:56:58.180 doesn't.
NOTE Confidence: 0.9974771
00:56:58.640 --> 00:57:00.480 If if it doesn't matter
NOTE Confidence: 0.9974771
00:57:00.480 --> 00:57:02.080 as much from a clinical
NOTE Confidence: 0.9974771
00:57:02.080 --> 00:57:03.140 monitoring standpoint,
NOTE Confidence: 0.98077583
00:57:04.000 --> 00:57:05.620 that could be interesting because
NOTE Confidence: 0.88845724
00:57:06.000 --> 00:57:06.960 one of the main reasons
NOTE Confidence: 0.88845724
00:57:06.960 --> 00:57:08.295 why, you know, the you
NOTE Confidence: 0.88845724
00:57:08.295 --> 00:57:09.515 have to have two people
NOTE Confidence: 0.88845724
00:57:09.575 --> 00:57:10.694 when you when you administer
NOTE Confidence: 0.88845724

00:57:10.694 --> 00:57:12.135 these medications, the very intestinal
NOTE Confidence: 0.88845724

00:57:12.135 --> 00:57:13.835 abnormalities precisely because of phenomenological
NOTE Confidence: 0.995686

00:57:14.135 --> 00:57:14.635 effects.
NOTE Confidence: 0.955946

00:57:15.015 --> 00:57:15.815 So if it turns out
NOTE Confidence: 0.955946

00:57:15.815 --> 00:57:16.694 we can have some of
NOTE Confidence: 0.955946

00:57:16.694 --> 00:57:17.355 the benefit
NOTE Confidence: 0.9538613

00:57:17.815 --> 00:57:18.934 without having to go through
NOTE Confidence: 0.9538613

00:57:18.934 --> 00:57:19.595 that experience,
NOTE Confidence: 0.927495

00:57:21.760 --> 00:57:23.600 From building a service that's
NOTE Confidence: 0.927495

00:57:23.600 --> 00:57:25.120 able to administer these drugs,
NOTE Confidence: 0.927495

00:57:25.120 --> 00:57:26.100 that would be advantageous.
NOTE Confidence: 0.9734256

00:57:28.880 --> 00:57:29.840 I'll just throw in that
NOTE Confidence: 0.9734256

00:57:29.840 --> 00:57:30.740 I think it's premature
NOTE Confidence: 0.99633235

00:57:31.200 --> 00:57:33.380 to conclude that the specific
NOTE Confidence: 0.9478561

00:57:33.875 --> 00:57:35.234 characteristics of the of the
NOTE Confidence: 0.9478561

00:57:35.234 --> 00:57:36.535 of the phenom the phenomenological
NOTE Confidence: 0.9478561

00:57:36.755 --> 00:57:38.355 experience during the psychedelic dosing
NOTE Confidence: 0.9478561

00:57:38.355 --> 00:57:39.015 are necessary,
NOTE Confidence: 0.9870184

00:57:39.555 --> 00:57:41.234 but the therapeutic benefit there
NOTE Confidence: 0.9870184

00:57:41.234 --> 00:57:42.595 are these correlations. They're not
NOTE Confidence: 0.9870184

00:57:42.595 --> 00:57:43.714 seen in every study, but
NOTE Confidence: 0.9870184

00:57:43.714 --> 00:57:44.755 more often than not, there's
NOTE Confidence: 0.9870184

00:57:44.755 --> 00:57:46.214 a correlation between certain
NOTE Confidence: 0.9506553

00:57:46.820 --> 00:57:48.920 aspects of the experience, especially
NOTE Confidence: 0.9506553

00:57:49.060 --> 00:57:51.400 the religious mystical oceanic boundlessness
NOTE Confidence: 0.9506553

00:57:51.460 --> 00:57:53.640 ego dissolving aspects, which are
NOTE Confidence: 0.9506553

00:57:53.700 --> 00:57:55.220 operationalized in self report scales
NOTE Confidence: 0.9506553

00:57:55.220 --> 00:57:55.940 in a veranda in a
NOTE Confidence: 0.9506553

00:57:55.940 --> 00:57:57.140 variety of different ways, but
NOTE Confidence: 0.9506553

00:57:57.140 --> 00:57:58.440 very hard to grapple with.
NOTE Confidence: 0.9506553

00:57:58.660 --> 00:58:00.120 There are often these correlations.

NOTE Confidence: 0.9743665

00:58:00.635 --> 00:58:01.835 However, this is a classic

NOTE Confidence: 0.9743665

00:58:01.835 --> 00:58:02.954 example of correlation does not

NOTE Confidence: 0.9743665

00:58:02.954 --> 00:58:05.035 equal causation. The simplest explanation

NOTE Confidence: 0.9743665

00:58:05.035 --> 00:58:05.675 to that is just that

NOTE Confidence: 0.9743665

00:58:05.675 --> 00:58:06.714 it's a surrogate marker of

NOTE Confidence: 0.9743665

00:58:06.714 --> 00:58:08.075 the effect effective dose amount

NOTE Confidence: 0.9743665

00:58:08.075 --> 00:58:08.795 of drug that's in the

NOTE Confidence: 0.9743665

00:58:08.795 --> 00:58:09.295 brain.

NOTE Confidence: 0.96012676

00:58:09.755 --> 00:58:10.555 Right? You get the drug

NOTE Confidence: 0.96012676

00:58:10.555 --> 00:58:11.515 into the brain, you get

NOTE Confidence: 0.96012676

00:58:11.515 --> 00:58:13.029 therapeutic effect, and you get

NOTE Confidence: 0.96012676

00:58:13.029 --> 00:58:14.390 the psychological effects. And so

NOTE Confidence: 0.96012676

00:58:14.390 --> 00:58:15.190 it simply may be a

NOTE Confidence: 0.96012676

00:58:15.190 --> 00:58:16.309 marker that you got the

NOTE Confidence: 0.96012676

00:58:16.309 --> 00:58:17.670 drug there at an adequate

NOTE Confidence: 0.96012676

00:58:17.670 --> 00:58:18.170 dose.

NOTE Confidence: 0.9526097

00:58:18.789 --> 00:58:20.150 And it could be a

NOTE Confidence: 0.9526097

00:58:20.150 --> 00:58:21.750 marker of activity in in

NOTE Confidence: 0.9526097

00:58:21.750 --> 00:58:23.510 certain brain circuits that are

NOTE Confidence: 0.9526097

00:58:23.510 --> 00:58:24.010 are,

NOTE Confidence: 0.96468556

00:58:24.485 --> 00:58:25.865 you know, relevant to therapy

NOTE Confidence: 0.96468556

00:58:25.925 --> 00:58:27.305 and related to these,

NOTE Confidence: 0.95965695

00:58:28.405 --> 00:58:29.545 experiences. So

NOTE Confidence: 0.95280766

00:58:30.005 --> 00:58:31.545 might be necessary.

NOTE Confidence: 0.96210074

00:58:32.085 --> 00:58:33.605 What that means is an

NOTE Confidence: 0.96210074

00:58:33.605 --> 00:58:34.965 interesting question when you talk

NOTE Confidence: 0.96210074

00:58:34.965 --> 00:58:36.245 about causality happening at the

NOTE Confidence: 0.96210074

00:58:36.245 --> 00:58:37.365 psychological level and at the

NOTE Confidence: 0.96210074

00:58:37.365 --> 00:58:39.300 neural level simultaneously. That gets

NOTE Confidence: 0.96210074

00:58:39.300 --> 00:58:40.340 into deep waters. But it

NOTE Confidence: 0.96210074

00:58:40.340 --> 00:58:41.380 might might be it. I'm

NOTE Confidence: 0.96210074

00:58:41.380 --> 00:58:42.600 totally open to the possibility.

NOTE Confidence: 0.96210074

00:58:42.820 --> 00:58:44.120 I think it's pre premature

NOTE Confidence: 0.96210074

00:58:44.340 --> 00:58:45.460 from the existence of these

NOTE Confidence: 0.96210074

00:58:45.460 --> 00:58:45.960 correlations

NOTE Confidence: 0.9846456

00:58:46.660 --> 00:58:47.700 to use that as a

NOTE Confidence: 0.9846456

00:58:48.260 --> 00:58:49.300 to assume that or to

NOTE Confidence: 0.9846456

00:58:49.300 --> 00:58:50.200 conclude that.

NOTE Confidence: 0.91659105

00:58:52.805 --> 00:58:54.885 Preston, JP, doctor Pittenger, and

NOTE Confidence: 0.91659105

00:58:54.885 --> 00:58:55.704 doctor Dakino,

NOTE Confidence: 0.99820733

00:58:56.085 --> 00:58:57.305 thank you so much.

NOTE Confidence: 0.9880976

00:58:58.325 --> 00:59:00.005 Fascinating. It's clear there's a

NOTE Confidence: 0.9880976

00:59:00.005 --> 00:59:02.005 lot of opportunity here. If

NOTE Confidence: 0.9880976

00:59:02.005 --> 00:59:03.464 I were an early stage

NOTE Confidence: 0.9880976

00:59:03.685 --> 00:59:05.605 investigator, I'd certainly be thinking

NOTE Confidence: 0.9880976

00:59:05.605 --> 00:59:06.105 about

NOTE Confidence: 0.99765825

00:59:06.500 --> 00:59:07.859 including research on,
NOTE Confidence: 0.9428679

00:59:08.500 --> 00:59:10.579 psychedelics and the potential impact
NOTE Confidence: 0.9428679

00:59:10.579 --> 00:59:12.099 in both acute and chronic
NOTE Confidence: 0.9428679

00:59:12.099 --> 00:59:13.460 pain and then not to
NOTE Confidence: 0.9428679

00:59:13.460 --> 00:59:15.079 mention opioid use disorder.
NOTE Confidence: 0.9783774

00:59:16.020 --> 00:59:17.380 So thank you very much,
NOTE Confidence: 0.9783774

00:59:17.380 --> 00:59:19.720 and, thanks everybody for joining,
NOTE Confidence: 0.9783774

00:59:19.885 --> 00:59:20.605 and we look forward to
NOTE Confidence: 0.9783774

00:59:20.605 --> 00:59:21.645 seeing you next time. Take
NOTE Confidence: 0.9783774

00:59:21.645 --> 00:59:22.145 care.
NOTE Confidence: 0.97351176

00:59:22.845 --> 00:59:23.645 It's been a pleasure to
NOTE Confidence: 0.97351176

00:59:23.645 --> 00:59:24.525 be with you today. Thank
NOTE Confidence: 0.97351176

00:59:24.525 --> 00:59:25.905 you. Yep. Thanks.