

WEBVTT

NOTE duration:"00:58:39.3000000"

NOTE recognizability:0.780

NOTE language:en-us

NOTE Confidence: 0.778104054

00:00:00.000 --> 00:00:01.150 In person and on video.

NOTE Confidence: 0.648595576666667

00:00:02.630 --> 00:00:03.698 Recording his progress.

NOTE Confidence: 0.4673736

00:00:05.770 --> 00:00:08.028 And so we have a treat

NOTE Confidence: 0.835702823333333

00:00:08.030 --> 00:00:10.795 today. We're going to hear from both

NOTE Confidence: 0.835702823333333

00:00:10.795 --> 00:00:12.920 Jordan Slusher and Pat spouse Nick.

NOTE Confidence: 0.835702823333333

00:00:12.920 --> 00:00:14.372 We're going to tell us about

NOTE Confidence: 0.835702823333333

00:00:14.372 --> 00:00:15.760 different aspects of the study

NOTE Confidence: 0.835702823333333

00:00:15.760 --> 00:00:17.995 that they did together with Cyril

NOTE Confidence: 0.835702823333333

00:00:17.995 --> 00:00:19.930 D'souza and others on psilocybin,

NOTE Confidence: 0.835702823333333

00:00:19.930 --> 00:00:21.214 the treatment of depression.

NOTE Confidence: 0.835702823333333

00:00:21.214 --> 00:00:23.513 This may well have been the first

NOTE Confidence: 0.835702823333333

00:00:23.513 --> 00:00:25.088 silybin study that was started

NOTE Confidence: 0.835702823333333

00:00:25.088 --> 00:00:27.460 at Yale annuals, Emmanuelle.

NOTE Confidence: 0.835702823333333

00:00:27.460 --> 00:00:29.100 Yes, on this one.
NOTE Confidence: 0.8357028233333333

00:00:29.100 --> 00:00:32.990 That was the the trailblazing. Hey.
NOTE Confidence: 0.859382772

00:00:34.390 --> 00:00:35.360 So we're going to hear
NOTE Confidence: 0.767899969411765

00:00:35.370 --> 00:00:36.545 some some clinical results from
NOTE Confidence: 0.767899969411765

00:00:36.545 --> 00:00:37.952 EEG and some background and it's
NOTE Confidence: 0.767899969411765

00:00:37.952 --> 00:00:39.080 great to have you guys here.
NOTE Confidence: 0.823559532

00:00:39.760 --> 00:00:42.130 Thanks Chris for inviting us.
NOTE Confidence: 0.823559532

00:00:42.130 --> 00:00:43.522 Great to be here and thank
NOTE Confidence: 0.823559532

00:00:43.522 --> 00:00:44.770 you all for being here.
NOTE Confidence: 0.823559532

00:00:44.770 --> 00:00:48.502 It's really fun to be finally
NOTE Confidence: 0.823559532

00:00:48.502 --> 00:00:50.606 presenting this work. Doctor,
NOTE Confidence: 0.823559532

00:00:50.606 --> 00:00:52.730 this is a smiling it's been a long road
NOTE Confidence: 0.823559532

00:00:52.788 --> 00:00:57.250 to get here 7 about seven years or so.
NOTE Confidence: 0.823559532

00:00:57.250 --> 00:00:59.578 And so just great to finally be at
NOTE Confidence: 0.823559532

00:00:59.578 --> 00:01:02.039 a place of presenting the results,
NOTE Confidence: 0.823559532

00:01:02.040 --> 00:01:05.435 having had at least one of our

NOTE Confidence: 0.823559532

00:01:05.435 --> 00:01:07.978 papers accepted for publication.

NOTE Confidence: 0.823559532

00:01:07.978 --> 00:01:11.408 So let's dive in here.

NOTE Confidence: 0.690985494

00:01:11.600 --> 00:01:14.000 And I should, I should thank Jordan and

NOTE Confidence: 0.690985494

00:01:14.000 --> 00:01:17.096 Cyril too, because they did the hard work.

NOTE Confidence: 0.690985494

00:01:17.100 --> 00:01:19.487 I just put EEG electrodes on people.

NOTE Confidence: 0.780839607857143

00:01:21.660 --> 00:01:23.580 Definitely A-Team science approach and

NOTE Confidence: 0.780839607857143

00:01:23.580 --> 00:01:26.717 was a been a labor of love for sure.

NOTE Confidence: 0.79799104

00:01:29.060 --> 00:01:34.317 So Steve in this study was called suicide

NOTE Confidence: 0.79799104

00:01:34.317 --> 00:01:36.662 and induced neuroplasticity and the

NOTE Confidence: 0.79799104

00:01:36.662 --> 00:01:38.957 treatment of major depressive disorder.

NOTE Confidence: 0.79799104

00:01:38.960 --> 00:01:42.570 And happy representing Patrick today.

NOTE Confidence: 0.79799104

00:01:42.570 --> 00:01:44.970 As far as disclosures for myself,

NOTE Confidence: 0.79799104

00:01:44.970 --> 00:01:46.578 really nothing relevant to the talk.

NOTE Confidence: 0.79799104

00:01:46.580 --> 00:01:49.590 The research we're presenting was funded by

NOTE Confidence: 0.79799104

00:01:49.590 --> 00:01:52.581 the Hefter Research Institute and I serve

NOTE Confidence: 0.79799104

00:01:52.581 --> 00:01:55.470 as a consultant with you Sona and ZYBAN,
NOTE Confidence: 0.79799104

00:01:55.470 --> 00:01:56.798 which both are involved
NOTE Confidence: 0.79799104

00:01:56.798 --> 00:01:58.126 in solar sybian research,
NOTE Confidence: 0.79799104

00:01:58.130 --> 00:02:00.400 but not with this study.
NOTE Confidence: 0.79799104

00:02:00.400 --> 00:02:02.320 And as far as where we're going to go today,
NOTE Confidence: 0.79799104

00:02:02.320 --> 00:02:04.189 I'm going to just give a lightning
NOTE Confidence: 0.79799104

00:02:04.189 --> 00:02:05.470 fast overview of suicide.
NOTE Confidence: 0.79799104

00:02:05.470 --> 00:02:07.810 Ben Pression talked about the study
NOTE Confidence: 0.79799104

00:02:07.810 --> 00:02:10.620 design and methods of this study and
NOTE Confidence: 0.79799104

00:02:10.620 --> 00:02:13.122 I'll share the clinical results of the
NOTE Confidence: 0.79799104

00:02:13.122 --> 00:02:15.630 study and then I'll pass it to Patrick to
NOTE Confidence: 0.79799104

00:02:15.630 --> 00:02:17.807 talk about the EEG methods and results.
NOTE Confidence: 0.79799104

00:02:17.810 --> 00:02:19.376 If there's time at the end,
NOTE Confidence: 0.79799104

00:02:19.380 --> 00:02:21.995 I'll touch briefly on psychological
NOTE Confidence: 0.79799104

00:02:21.995 --> 00:02:24.610 flexibility and we'll have a
NOTE Confidence: 0.79799104

00:02:24.693 --> 00:02:26.897 little time for discussion.

NOTE Confidence: 0.79799104

00:02:26.900 --> 00:02:28.252 So just real quick,

NOTE Confidence: 0.79799104

00:02:28.252 --> 00:02:30.280 have you guys had talked specifically

NOTE Confidence: 0.79799104

00:02:30.341 --> 00:02:31.289 on suicide then?

NOTE Confidence: 0.670069492

00:02:31.660 --> 00:02:33.380 Yeah, but the attendance varies.

NOTE Confidence: 0.670069492

00:02:33.380 --> 00:02:34.927 Yeah, fluctuates. I think it's worth the

NOTE Confidence: 0.679274317583333

00:02:35.260 --> 00:02:37.850 really briefly, Sivan is is a member

NOTE Confidence: 0.679274317583333

00:02:37.850 --> 00:02:40.359 of the classical psychedelic family.

NOTE Confidence: 0.679274317583333

00:02:40.360 --> 00:02:44.070 It's a serotonin 2A agonist.

NOTE Confidence: 0.679274317583333

00:02:44.070 --> 00:02:47.608 Particular. Chemical occurs naturally

NOTE Confidence: 0.679274317583333

00:02:47.608 --> 00:02:49.388 in silicide mushroom species which

NOTE Confidence: 0.679274317583333

00:02:49.388 --> 00:02:50.959 are widespread around the globe,

NOTE Confidence: 0.679274317583333

00:02:50.960 --> 00:02:53.340 and psilocybin mushrooms have

NOTE Confidence: 0.679274317583333

00:02:53.340 --> 00:02:55.720 been used for millennia.

NOTE Confidence: 0.679274317583333

00:02:55.720 --> 00:02:58.352 Actually, at the bottom right you can

NOTE Confidence: 0.679274317583333

00:02:58.352 --> 00:03:00.718 see mushroom statues from Meso America,

NOTE Confidence: 0.679274317583333

00:03:00.720 --> 00:03:02.900 Middle America, Guatemala specifically
NOTE Confidence: 0.679274317583333

00:03:02.900 --> 00:03:05.910 that date back about 2500 years.
NOTE Confidence: 0.679274317583333

00:03:05.910 --> 00:03:08.400 As far As for Western science,
NOTE Confidence: 0.679274317583333

00:03:08.400 --> 00:03:10.782 it is first isolated from the
NOTE Confidence: 0.679274317583333

00:03:10.782 --> 00:03:12.580 mushrooms by Albert Hoffman in
NOTE Confidence: 0.679274317583333

00:03:12.580 --> 00:03:16.486 1957 and there was research with.
NOTE Confidence: 0.679274317583333

00:03:16.490 --> 00:03:19.269 The side then back in the early
NOTE Confidence: 0.679274317583333

00:03:19.269 --> 00:03:20.875 phase of psychedelic research
NOTE Confidence: 0.679274317583333

00:03:20.875 --> 00:03:23.587 in the West in the 50s and 60s.
NOTE Confidence: 0.679274317583333

00:03:23.590 --> 00:03:25.780 Not going to talk about that.
NOTE Confidence: 0.679274317583333

00:03:25.780 --> 00:03:28.706 More recently it has been the preferred
NOTE Confidence: 0.679274317583333

00:03:28.706 --> 00:03:31.708 psychedelic for most of the clinical studies,
NOTE Confidence: 0.679274317583333

00:03:31.710 --> 00:03:35.046 of which there is increasing many
NOTE Confidence: 0.679274317583333

00:03:35.046 --> 00:03:37.270 increasing numbers across different
NOTE Confidence: 0.679274317583333

00:03:37.351 --> 00:03:40.380 mental disorders as well as neurological
NOTE Confidence: 0.679274317583333

00:03:40.380 --> 00:03:42.120 disorders and increasing risk,

NOTE Confidence: 0.679274317583333
00:03:42.120 --> 00:03:45.220 potentially psychosomatic illness for sure.
NOTE Confidence: 0.679274317583333
00:03:45.220 --> 00:03:47.868 Depression, addictions,
NOTE Confidence: 0.679274317583333
00:03:47.868 --> 00:03:51.840 OCD increasingly and.
NOTE Confidence: 0.679274317583333
00:03:51.840 --> 00:03:53.193 Was headache disorders,
NOTE Confidence: 0.679274317583333
00:03:53.193 --> 00:03:55.448 you're Yale are getting more
NOTE Confidence: 0.679274317583333
00:03:55.448 --> 00:03:57.628 attention with the Sobin, please,
NOTE Confidence: 0.679274317583333
00:03:57.628 --> 00:04:01.852 as far As for the mental health conditions?
NOTE Confidence: 0.679274317583333
00:04:01.860 --> 00:04:03.940 The studies with suicide, then?
NOTE Confidence: 0.679274317583333
00:04:03.940 --> 00:04:05.692 Have used some sort of inside
NOTE Confidence: 0.679274317583333
00:04:05.692 --> 00:04:07.276 that assisted therapy model,
NOTE Confidence: 0.679274317583333
00:04:07.280 --> 00:04:08.273 which is which.
NOTE Confidence: 0.679274317583333
00:04:08.273 --> 00:04:09.597 There are many flavors,
NOTE Confidence: 0.679274317583333
00:04:09.600 --> 00:04:12.552 but the common elements generally include
NOTE Confidence: 0.679274317583333
00:04:12.552 --> 00:04:15.540 some attention to set and setting,
NOTE Confidence: 0.679274317583333
00:04:15.540 --> 00:04:17.430 meaning that mindset of the
NOTE Confidence: 0.679274317583333

00:04:17.430 --> 00:04:19.876 individual going in setting in which
NOTE Confidence: 0.679274317583333

00:04:19.876 --> 00:04:21.808 the medication is administered.
NOTE Confidence: 0.679274317583333

00:04:21.810 --> 00:04:22.914 And then the drug.
NOTE Confidence: 0.679274317583333

00:04:22.914 --> 00:04:25.080 So seeing that those are all important
NOTE Confidence: 0.679274317583333

00:04:25.080 --> 00:04:27.966 elements in determining the outcome and
NOTE Confidence: 0.679274317583333

00:04:27.966 --> 00:04:31.346 they followed essentially this three,
NOTE Confidence: 0.679274317583333

00:04:31.350 --> 00:04:33.807 three stage kind of model of using
NOTE Confidence: 0.679274317583333

00:04:33.807 --> 00:04:35.650 preparation support and integration,
NOTE Confidence: 0.679274317583333

00:04:35.650 --> 00:04:37.610 meaning preparation sessions leading
NOTE Confidence: 0.679274317583333

00:04:37.610 --> 00:04:40.060 up to the medication session,
NOTE Confidence: 0.679274317583333

00:04:40.060 --> 00:04:42.610 a supportive approach during medication
NOTE Confidence: 0.679274317583333

00:04:42.610 --> 00:04:45.160 administration and then follow up
NOTE Confidence: 0.679274317583333

00:04:45.230 --> 00:04:48.020 appointments sometimes called we call
NOTE Confidence: 0.679274317583333

00:04:48.020 --> 00:04:50.252 debriefing or integration sessions
NOTE Confidence: 0.679274317583333

00:04:50.260 --> 00:04:52.404 and of course there's been a lot of.
NOTE Confidence: 0.679274317583333

00:04:52.410 --> 00:04:54.495 Variety in what those sessions

NOTE Confidence: 0.679274317583333
00:04:54.495 --> 00:04:55.746 would look like,
NOTE Confidence: 0.679274317583333
00:04:55.750 --> 00:04:58.022 but have generally followed
NOTE Confidence: 0.679274317583333
00:04:58.022 --> 00:04:59.726 that three-part structure.
NOTE Confidence: 0.679274317583333
00:04:59.730 --> 00:05:02.845 As far as philosophy studies for depression,
NOTE Confidence: 0.679274317583333
00:05:02.850 --> 00:05:05.890 only going to mention do this very briefly,
NOTE Confidence: 0.679274317583333
00:05:05.890 --> 00:05:08.018 but this was really the state of
NOTE Confidence: 0.679274317583333
00:05:08.018 --> 00:05:09.986 the research when we were designing
NOTE Confidence: 0.679274317583333
00:05:09.986 --> 00:05:12.289 this study like 6-6 seven years ago.
NOTE Confidence: 0.679274317583333
00:05:12.290 --> 00:05:14.642 There was two trials that were
NOTE Confidence: 0.679274317583333
00:05:14.642 --> 00:05:17.129 published in 2016 looking at suicide
NOTE Confidence: 0.679274317583333
00:05:17.129 --> 00:05:19.229 and therapy in cancer patients
NOTE Confidence: 0.679274317583333
00:05:19.229 --> 00:05:21.410 who had depression and anxiety.
NOTE Confidence: 0.679274317583333
00:05:21.410 --> 00:05:23.858 And those were medium sized studies,
NOTE Confidence: 0.679274317583333
00:05:23.860 --> 00:05:27.150 about 100 participants and there was a
NOTE Confidence: 0.679274317583333
00:05:27.150 --> 00:05:30.439 lot of publicity generated from those.
NOTE Confidence: 0.679274317583333

00:05:30.440 --> 00:05:32.939 That is because the main finding sort
NOTE Confidence: 0.679274317583333

00:05:32.939 --> 00:05:35.157 of indicated these rapid acting and
NOTE Confidence: 0.679274317583333

00:05:35.157 --> 00:05:37.663 long lasting results from a single dose
NOTE Confidence: 0.679274317583333

00:05:37.727 --> 00:05:39.547 of psilocybin that were persisting
NOTE Confidence: 0.679274317583333

00:05:39.547 --> 00:05:42.402 up to about six months out and then
NOTE Confidence: 0.679274317583333

00:05:42.402 --> 00:05:44.466 later in follow up even longer.
NOTE Confidence: 0.679274317583333

00:05:44.470 --> 00:05:46.125 And so kind of generated
NOTE Confidence: 0.679274317583333

00:05:46.125 --> 00:05:47.449 this narrative around wow,
NOTE Confidence: 0.679274317583333

00:05:47.450 --> 00:05:48.546 you know,
NOTE Confidence: 0.679274317583333

00:05:48.546 --> 00:05:50.738 lasting effects from single
NOTE Confidence: 0.679274317583333

00:05:50.738 --> 00:05:52.930 doses of solar cylin.
NOTE Confidence: 0.679274317583333

00:05:52.930 --> 00:05:54.010 We talked about how the
NOTE Confidence: 0.679274317583333

00:05:54.010 --> 00:05:55.090 media picked up on that,
NOTE Confidence: 0.679274317583333

00:05:55.090 --> 00:05:58.700 but that was sort of the state of of that.
NOTE Confidence: 0.679274317583333

00:05:58.700 --> 00:06:00.470 And then right as we were
NOTE Confidence: 0.679274317583333

00:06:00.470 --> 00:06:01.750 really submitting this study,

NOTE Confidence: 0.679274317583333

00:06:01.750 --> 00:06:04.126 Robin card Harris published in 2016,

NOTE Confidence: 0.679274317583333

00:06:04.130 --> 00:06:06.851 this first Open label study of

NOTE Confidence: 0.679274317583333

00:06:06.851 --> 00:06:09.677 suicide then therapy in TRD or

NOTE Confidence: 0.679274317583333

00:06:09.677 --> 00:06:11.090 treatment refractory depression,

NOTE Confidence: 0.679274317583333

00:06:11.090 --> 00:06:13.780 very small open label study.

NOTE Confidence: 0.679274317583333

00:06:13.780 --> 00:06:15.365 And those were the individual

NOTE Confidence: 0.679274317583333

00:06:15.365 --> 00:06:16.950 patient results in the graph

NOTE Confidence: 0.86142712

00:06:17.011 --> 00:06:19.264 below. But just briefly you

NOTE Confidence: 0.86142712

00:06:19.264 --> 00:06:21.669 know showed robust effect that

NOTE Confidence: 0.86142712

00:06:21.669 --> 00:06:23.996 one week and that persisted to

NOTE Confidence: 0.86142712

00:06:23.996 --> 00:06:26.108 some degree for about 3 months.

NOTE Confidence: 0.86142712

00:06:26.110 --> 00:06:28.006 So again kind of.

NOTE Confidence: 0.86142712

00:06:28.006 --> 00:06:29.902 Providing some preliminary excitement

NOTE Confidence: 0.86142712

00:06:29.902 --> 00:06:32.790 around the potential of this therapy.

NOTE Confidence: 0.86142712

00:06:32.790 --> 00:06:35.275 Since then there's been a number of

NOTE Confidence: 0.86142712

00:06:35.275 --> 00:06:37.650 better studies that have gone on
NOTE Confidence: 0.86142712

00:06:37.650 --> 00:06:41.080 at Hopkins in back in London and
NOTE Confidence: 0.86142712

00:06:41.080 --> 00:06:43.976 increasingly now we have phase two
NOTE Confidence: 0.86142712

00:06:43.976 --> 00:06:46.866 level studies from Zona that will
NOTE Confidence: 0.86142712

00:06:46.866 --> 00:06:49.582 be published soon and one that was
NOTE Confidence: 0.86142712

00:06:49.582 --> 00:06:50.902 published from Compass Pathways in
NOTE Confidence: 0.86142712

00:06:50.902 --> 00:06:52.470 New England Journal just recently.
NOTE Confidence: 0.86142712

00:06:52.470 --> 00:06:54.358 I don't have time to dive into those
NOTE Confidence: 0.86142712

00:06:54.358 --> 00:06:56.530 because I want to spend time on our study,
NOTE Confidence: 0.86142712

00:06:56.530 --> 00:06:57.649 but you know.
NOTE Confidence: 0.86142712

00:06:57.649 --> 00:06:58.768 One of the.
NOTE Confidence: 0.86142712

00:06:58.770 --> 00:07:00.402 The brief summary that led into
NOTE Confidence: 0.86142712

00:07:00.402 --> 00:07:02.066 the design of this study was
NOTE Confidence: 0.86142712

00:07:02.066 --> 00:07:03.738 that there was intriguing data
NOTE Confidence: 0.86142712

00:07:03.738 --> 00:07:05.958 supporting suicidal therapy as a
NOTE Confidence: 0.86142712

00:07:05.958 --> 00:07:08.050 promising approach for depression,

NOTE Confidence: 0.86142712

00:07:08.050 --> 00:07:10.040 rapid acting, and sustained effects

NOTE Confidence: 0.86142712

00:07:10.040 --> 00:07:12.650 from limited numbers of doses of doses.

NOTE Confidence: 0.86142712

00:07:12.650 --> 00:07:13.918 There were very significant

NOTE Confidence: 0.86142712

00:07:13.918 --> 00:07:15.186 limitations to those studies,

NOTE Confidence: 0.86142712

00:07:15.190 --> 00:07:16.950 including small sample sizes,

NOTE Confidence: 0.86142712

00:07:16.950 --> 00:07:18.710 lack of placebo controls,

NOTE Confidence: 0.86142712

00:07:18.710 --> 00:07:21.094 or for blinding, functional,

NOTE Confidence: 0.86142712

00:07:21.094 --> 00:07:21.690 unblinding,

NOTE Confidence: 0.86142712

00:07:21.690 --> 00:07:23.974 suspected and significant expectancy

NOTE Confidence: 0.86142712

00:07:23.974 --> 00:07:26.258 effects increasingly as the

NOTE Confidence: 0.86142712

00:07:26.258 --> 00:07:28.850 media also continued to hide.

NOTE Confidence: 0.86142712

00:07:28.850 --> 00:07:32.330 Couples therapy and the big one,

NOTE Confidence: 0.86142712

00:07:32.330 --> 00:07:32.796 you know,

NOTE Confidence: 0.86142712

00:07:32.796 --> 00:07:34.660 the big question is also if we're seeing

NOTE Confidence: 0.86142712

00:07:34.710 --> 00:07:36.810 these long lasting effects from single doses,

NOTE Confidence: 0.86142712

00:07:36.810 --> 00:07:38.042 how is this working?
NOTE Confidence: 0.86142712

00:07:38.042 --> 00:07:40.519 What are the mechanisms of action those are?
NOTE Confidence: 0.86142712

00:07:40.520 --> 00:07:42.560 Were and still are to a large degree,
NOTE Confidence: 0.86142712

00:07:42.560 --> 00:07:44.860 still unclear.
NOTE Confidence: 0.86142712

00:07:44.860 --> 00:07:46.888 So that led into US cooking
NOTE Confidence: 0.86142712

00:07:46.888 --> 00:07:48.240 up this this study.
NOTE Confidence: 0.86142712

00:07:48.240 --> 00:07:51.188 So Sabin induced neuroplasticity.
NOTE Confidence: 0.86142712

00:07:51.190 --> 00:07:55.026 And just to introduce the study aims,
NOTE Confidence: 0.86142712

00:07:55.030 --> 00:07:56.908 it was primarily a mechanistic study.
NOTE Confidence: 0.86142712

00:07:56.910 --> 00:07:59.310 This is a exploratory and
NOTE Confidence: 0.86142712

00:07:59.310 --> 00:08:00.750 relatively small study.
NOTE Confidence: 0.86142712

00:08:00.750 --> 00:08:02.615 The things we were interested
NOTE Confidence: 0.86142712

00:08:02.615 --> 00:08:04.608 in looking at were neuropathy,
NOTE Confidence: 0.86142712

00:08:04.608 --> 00:08:07.098 effects of could neuroplasticity be
NOTE Confidence: 0.86142712

00:08:07.098 --> 00:08:09.517 an explanatory mechanism and Patrick
NOTE Confidence: 0.86142712

00:08:09.517 --> 00:08:11.641 will share about the EEG paradigm

NOTE Confidence: 0.86142712

00:08:11.641 --> 00:08:14.608 that we used to look at that possibility.

NOTE Confidence: 0.86142712

00:08:14.610 --> 00:08:17.396 And I was interested in this idea

NOTE Confidence: 0.86142712

00:08:17.396 --> 00:08:18.590 about psychological flexibility,

NOTE Confidence: 0.86142712

00:08:18.590 --> 00:08:20.380 which is baked into acceptance

NOTE Confidence: 0.86142712

00:08:20.380 --> 00:08:21.096 and commitment.

NOTE Confidence: 0.86142712

00:08:21.100 --> 00:08:23.240 RP as another more psychological

NOTE Confidence: 0.86142712

00:08:23.240 --> 00:08:25.380 mechanism of action and we

NOTE Confidence: 0.86142712

00:08:25.457 --> 00:08:27.487 collected some data on that.

NOTE Confidence: 0.86142712

00:08:27.490 --> 00:08:29.812 And of course as secondary measures

NOTE Confidence: 0.86142712

00:08:29.812 --> 00:08:31.867 we did collect efficacy measures

NOTE Confidence: 0.86142712

00:08:31.867 --> 00:08:34.501 for depression and being quite so

NOTE Confidence: 0.86142712

00:08:34.501 --> 00:08:36.612 a clinician administered and self

NOTE Confidence: 0.86142712

00:08:36.612 --> 00:08:38.417 rated measure looked at anxiety

NOTE Confidence: 0.86142712

00:08:38.417 --> 00:08:42.060 and quality of life as well as well

NOTE Confidence: 0.86142712

00:08:42.060 --> 00:08:44.620 as some basic safety outcomes.

NOTE Confidence: 0.86142712

00:08:44.620 --> 00:08:45.880 As far as our methods,
NOTE Confidence: 0.86142712

00:08:45.880 --> 00:08:48.142 this was we recruited adults with
NOTE Confidence: 0.86142712

00:08:48.142 --> 00:08:49.650 moderate to severe depression
NOTE Confidence: 0.86142712

00:08:49.650 --> 00:08:51.530 and they had to have had one or
NOTE Confidence: 0.86142712

00:08:51.530 --> 00:08:52.520 more treatment failures,
NOTE Confidence: 0.86142712

00:08:52.520 --> 00:08:54.368 so not technically TRD,
NOTE Confidence: 0.86142712

00:08:54.368 --> 00:08:56.678 although most of them had
NOTE Confidence: 0.86142712

00:08:56.678 --> 00:08:58.897 probably met criteria for TRD,
NOTE Confidence: 0.86142712

00:08:58.900 --> 00:09:01.138 they had to be offered antidepressants
NOTE Confidence: 0.86142712

00:09:01.138 --> 00:09:04.075 at the time of inclusion and
NOTE Confidence: 0.86142712

00:09:04.075 --> 00:09:06.495 study and major exclusion.
NOTE Confidence: 0.86142712

00:09:06.500 --> 00:09:07.890 Pretty typical for most of
NOTE Confidence: 0.86142712

00:09:07.890 --> 00:09:09.280 the studies in the field.
NOTE Confidence: 0.86142712

00:09:09.280 --> 00:09:11.320 Personal family history of psychotic
NOTE Confidence: 0.86142712

00:09:11.320 --> 00:09:13.360 or bipolar disorders or uncontrolled
NOTE Confidence: 0.86142712

00:09:13.417 --> 00:09:15.147 medical issues and we excluded.

NOTE Confidence: 0.86142712

00:09:15.150 --> 00:09:17.880 Anyone who had a past year use

NOTE Confidence: 0.86142712

00:09:17.880 --> 00:09:18.660 of psychedelics.

NOTE Confidence: 0.86142712

00:09:18.660 --> 00:09:23.817 And we aim to enroll 18 subjects or targets.

NOTE Confidence: 0.86142712

00:09:23.820 --> 00:09:25.110 And as far as the design,

NOTE Confidence: 0.86142712

00:09:25.110 --> 00:09:26.534 which I'll show you on the next slide,

NOTE Confidence: 0.86142712

00:09:26.540 --> 00:09:29.192 this was a placebo control within

NOTE Confidence: 0.86142712

00:09:29.192 --> 00:09:32.032 subject fixed order design with enhanced

NOTE Confidence: 0.86142712

00:09:32.032 --> 00:09:35.014 blinding procedures and it's a mouthful,

NOTE Confidence: 0.86142712

00:09:35.020 --> 00:09:37.456 I'll show you what that looked like.

NOTE Confidence: 0.807343185714286

00:09:37.460 --> 00:09:38.906 So our participants

NOTE Confidence: 0.807343185714286

00:09:38.906 --> 00:09:41.573 enrolled in the study here.

NOTE Confidence: 0.807343185714286

00:09:41.573 --> 00:09:44.426 At screening, they underwent an

NOTE Confidence: 0.807343185714286

00:09:44.426 --> 00:09:46.274 initial psychotherapy session and

NOTE Confidence: 0.807343185714286

00:09:46.274 --> 00:09:48.918 then all the participants received

NOTE Confidence: 0.807343185714286

00:09:48.918 --> 00:09:51.278 an initial placebo session.

NOTE Confidence: 0.807343185714286

00:09:51.280 --> 00:09:52.540 And then four weeks later,
NOTE Confidence: 0.807343185714286

00:09:52.540 --> 00:09:54.676 was there still a cybin session.
NOTE Confidence: 0.807343185714286

00:09:54.680 --> 00:09:56.656 However, they were not aware of the fact
NOTE Confidence: 0.807343185714286

00:09:56.656 --> 00:09:58.699 that it would be in that fixed order.
NOTE Confidence: 0.807343185714286

00:09:58.700 --> 00:10:01.214 They were told that there were
NOTE Confidence: 0.807343185714286

00:10:01.214 --> 00:10:02.890 three possible study conditions.
NOTE Confidence: 0.807343185714286

00:10:02.890 --> 00:10:05.669 A placebo in lower dose of Zoloft,
NOTE Confidence: 0.807343185714286

00:10:05.670 --> 00:10:08.838 cybin at .1 milligrams per kilogram and a
NOTE Confidence: 0.807343185714286

00:10:08.838 --> 00:10:11.959 higher dose of .3 milligrams per kilogram.
NOTE Confidence: 0.807343185714286

00:10:11.960 --> 00:10:13.280 And so the the middle,
NOTE Confidence: 0.807343185714286

00:10:13.280 --> 00:10:15.786 the low dose was actually never administered
NOTE Confidence: 0.807343185714286

00:10:15.786 --> 00:10:17.479 although participants received the placebo.
NOTE Confidence: 0.807343185714286

00:10:17.480 --> 00:10:20.525 And then the higher .3 milligram dose
NOTE Confidence: 0.807343185714286

00:10:20.525 --> 00:10:23.480 of soliciting 4 weeks later and the
NOTE Confidence: 0.807343185714286

00:10:23.480 --> 00:10:25.790 blue heads there indicate where we did
NOTE Confidence: 0.807343185714286

00:10:25.790 --> 00:10:28.620 EG which is was one day and two weeks

NOTE Confidence: 0.807343185714286

00:10:28.620 --> 00:10:31.087 after each of the dosing sessions and

NOTE Confidence: 0.807343185714286

00:10:31.087 --> 00:10:33.966 then the yellow and yellow you can see.

NOTE Confidence: 0.807343185714286

00:10:33.966 --> 00:10:35.414 We collected our depression

NOTE Confidence: 0.807343185714286

00:10:35.414 --> 00:10:37.898 measures all the way out to 16

NOTE Confidence: 0.807343185714286

00:10:37.898 --> 00:10:39.558 weeks after that initial session,

NOTE Confidence: 0.807343185714286

00:10:39.560 --> 00:10:42.956 or three-week three months after Silybin.

NOTE Confidence: 0.807343185714286

00:10:42.960 --> 00:10:45.540 And there was psychotherapy

NOTE Confidence: 0.807343185714286

00:10:45.540 --> 00:10:48.765 throughout the intervention as well.

NOTE Confidence: 0.807343185714286

00:10:48.770 --> 00:10:49.540 All right.

NOTE Confidence: 0.834338039090909

00:10:51.760 --> 00:10:53.992 Keep on moving unless there's any

NOTE Confidence: 0.834338039090909

00:10:53.992 --> 00:10:55.970 burning questions about the design.

NOTE Confidence: 0.92365517

00:10:59.290 --> 00:11:02.215 So I'm going to jump in and share some

NOTE Confidence: 0.92365517

00:11:02.215 --> 00:11:05.569 of the clinical study results first here

NOTE Confidence: 0.92365517

00:11:05.570 --> 00:11:08.174 and just really briefly show you our

NOTE Confidence: 0.92365517

00:11:08.174 --> 00:11:10.498 consort diagram and just make the point

NOTE Confidence: 0.92365517

00:11:10.498 --> 00:11:12.714 that we assess a lot of individuals
NOTE Confidence: 0.92365517

00:11:12.714 --> 00:11:15.694 for this study recruitment is a big
NOTE Confidence: 0.92365517

00:11:15.694 --> 00:11:18.662 deal and these studies assessed in
NOTE Confidence: 0.92365517

00:11:18.662 --> 00:11:23.500 a 949 patients to enroll 22 and had
NOTE Confidence: 0.92365517

00:11:23.500 --> 00:11:26.470 fifteen complete two both test days,
NOTE Confidence: 0.92365517

00:11:26.470 --> 00:11:29.878 19 completed the first Test day and so.
NOTE Confidence: 0.92365517

00:11:29.880 --> 00:11:32.043 For the purposes of our EEG and
NOTE Confidence: 0.92365517

00:11:32.043 --> 00:11:32.970 primary depression outcomes,
NOTE Confidence: 0.92365517

00:11:32.970 --> 00:11:35.207 we analyze all everyone who completed
NOTE Confidence: 0.92365517

00:11:35.207 --> 00:11:36.936 at least one of the tests says.
NOTE Confidence: 0.834063004545454

00:11:39.570 --> 00:11:41.484 Alright, I'm just going to share
NOTE Confidence: 0.834063004545454

00:11:41.484 --> 00:11:43.210 initially actually the blinding success.
NOTE Confidence: 0.834063004545454

00:11:43.210 --> 00:11:44.848 And I'm going to present this in
NOTE Confidence: 0.834063004545454

00:11:44.848 --> 00:11:46.570 part because I think it's really
NOTE Confidence: 0.834063004545454

00:11:46.570 --> 00:11:48.185 important when thinking about actually
NOTE Confidence: 0.834063004545454

00:11:48.185 --> 00:11:49.946 the rest of the efficacy results

NOTE Confidence: 0.834063004545454

00:11:49.946 --> 00:11:51.984 and also because this is just a

NOTE Confidence: 0.834063004545454

00:11:51.984 --> 00:11:54.708 glaring blind spot in the literature,

NOTE Confidence: 0.834063004545454

00:11:54.710 --> 00:11:56.574 not only the psychedelics,

NOTE Confidence: 0.834063004545454

00:11:56.574 --> 00:11:59.310 but really been looking even more

NOTE Confidence: 0.834063004545454

00:11:59.310 --> 00:12:01.560 recently just across amical trials

NOTE Confidence: 0.834063004545454

00:12:01.560 --> 00:12:04.117 that say they're blinded but actually

NOTE Confidence: 0.834063004545454

00:12:04.117 --> 00:12:07.609 do not present any data related to how

NOTE Confidence: 0.834063004545454

00:12:07.609 --> 00:12:09.755 successive the blinding and this is.

NOTE Confidence: 0.834063004545454

00:12:09.755 --> 00:12:11.285 Even more of a heightened issue

NOTE Confidence: 0.834063004545454

00:12:11.285 --> 00:12:12.559 and psychedelic arena.

NOTE Confidence: 0.834063004545454

00:12:12.560 --> 00:12:16.662 So actually proud to show the data

NOTE Confidence: 0.834063004545454

00:12:16.662 --> 00:12:19.538 that we collected at least on that.

NOTE Confidence: 0.834063004545454

00:12:19.540 --> 00:12:21.046 So as far as you know,

NOTE Confidence: 0.834063004545454

00:12:21.050 --> 00:12:23.178 and we we asked the only the participants.

NOTE Confidence: 0.834063004545454

00:12:23.180 --> 00:12:24.360 We didn't ask the therapist,

NOTE Confidence: 0.834063004545454

00:12:24.360 --> 00:12:25.925 which would have been even
NOTE Confidence: 0.834063004545454

00:12:25.925 --> 00:12:27.840 another layer we could have done.
NOTE Confidence: 0.834063004545454

00:12:27.840 --> 00:12:30.000 But during the placebo session,
NOTE Confidence: 0.834063004545454

00:12:30.000 --> 00:12:32.280 about 80% of our participants
NOTE Confidence: 0.834063004545454

00:12:32.280 --> 00:12:34.560 correctly identified the placebo and
NOTE Confidence: 0.834063004545454

00:12:34.637 --> 00:12:37.059 the other four guests the low dose,
NOTE Confidence: 0.834063004545454

00:12:37.060 --> 00:12:39.270 there was some confusion there,
NOTE Confidence: 0.834063004545454

00:12:39.270 --> 00:12:42.238 but no one mistook the placebo for the
NOTE Confidence: 0.834063004545454

00:12:42.238 --> 00:12:45.440 higher dose and that was also true in
NOTE Confidence: 0.834063004545454

00:12:45.440 --> 00:12:48.479 the subsequent high dose silybin session.
NOTE Confidence: 0.834063004545454

00:12:48.480 --> 00:12:50.580 80% correctly guessed they had
NOTE Confidence: 0.834063004545454

00:12:50.580 --> 00:12:51.840 received that intervention.
NOTE Confidence: 0.834063004545454

00:12:51.840 --> 00:12:53.778 A few guests that they had
NOTE Confidence: 0.834063004545454

00:12:53.778 --> 00:12:55.660 received the lower dose silybin,
NOTE Confidence: 0.834063004545454

00:12:55.660 --> 00:12:57.730 but no one confused again but.
NOTE Confidence: 0.834063004545454

00:12:57.730 --> 00:13:01.270 Suicide, then for the placebo.

NOTE Confidence: 0.834063004545454

00:13:01.270 --> 00:13:03.776 So while it was not 100% failure,

NOTE Confidence: 0.834063004545454

00:13:03.776 --> 00:13:07.227 it also was not an overwhelming success

NOTE Confidence: 0.834063004545454

00:13:07.230 --> 00:13:10.170 as far as maintaining the blind.

NOTE Confidence: 0.834063004545454

00:13:10.170 --> 00:13:12.690 And so share a few thoughts of

NOTE Confidence: 0.834063004545454

00:13:12.690 --> 00:13:15.160 how that relates when you're yeah,

NOTE Confidence: 0.834063004545454

00:13:15.160 --> 00:13:16.854 I've just forgot about my question was

NOTE Confidence: 0.594650338

00:13:17.850 --> 00:13:19.960 were these subjects psychedelic, naive?

NOTE Confidence: 0.697269775

00:13:20.630 --> 00:13:23.786 No, actually about I have this

NOTE Confidence: 0.697269775

00:13:23.790 --> 00:13:26.303 at least over half were OK,

NOTE Confidence: 0.697269775

00:13:26.303 --> 00:13:28.468 but the criteria was passed.

NOTE Confidence: 0.697269775

00:13:28.470 --> 00:13:31.186 The year was an exclusion past year.

NOTE Confidence: 0.697269775

00:13:31.190 --> 00:13:34.378 Is there any suicide?

NOTE Confidence: 0.697269775

00:13:34.380 --> 00:13:37.205 Conclusion. Correct.

NOTE Confidence: 0.697269775

00:13:37.205 --> 00:13:40.250 And about half were naive and about

NOTE Confidence: 0.697269775

00:13:40.250 --> 00:13:42.783 the other half had a limited exposure,

NOTE Confidence: 0.697269775

00:13:42.783 --> 00:13:45.156 so it wasn't, we didn't need any
NOTE Confidence: 0.697269775

00:13:45.156 --> 00:13:48.390 one who I'd say was a psychonaut.
NOTE Confidence: 0.697269775

00:13:48.390 --> 00:13:50.022 But I think no one had
NOTE Confidence: 0.697269775

00:13:50.022 --> 00:13:52.760 more than seven lifetime,
NOTE Confidence: 0.845881666666667

00:13:52.830 --> 00:13:54.168 because whether or not they have,
NOTE Confidence: 0.845881666666667

00:13:54.170 --> 00:13:55.904 whether or not people have previous
NOTE Confidence: 0.845881666666667

00:13:55.904 --> 00:13:57.060 experience can influence their
NOTE Confidence: 0.845881666666667

00:13:57.109 --> 00:13:58.819 expectation and can influence blinding.
NOTE Confidence: 0.845881666666667

00:13:58.820 --> 00:14:00.200 And it's not going to make
NOTE Confidence: 0.845881666666667

00:14:00.200 --> 00:14:01.300 people think that saline is.
NOTE Confidence: 0.71908289

00:14:02.070 --> 00:14:03.318 You know a robust
NOTE Confidence: 0.861781182

00:14:03.330 --> 00:14:04.800 trip. And then my other question
NOTE Confidence: 0.861781182

00:14:04.800 --> 00:14:06.800 was do you can you speak for the
NOTE Confidence: 0.861781182

00:14:06.800 --> 00:14:08.240 Group A little bit about the
NOTE Confidence: 0.861781182

00:14:08.297 --> 00:14:09.967 dose .3 milligrams per kilogram,
NOTE Confidence: 0.861781182

00:14:09.970 --> 00:14:12.796 why weight dose instead of fixed

NOTE Confidence: 0.861781182

00:14:12.796 --> 00:14:14.950 and what is that dose mean?

NOTE Confidence: 0.861781182

00:14:14.950 --> 00:14:16.018 How do you like what is

NOTE Confidence: 0.861781182

00:14:16.018 --> 00:14:17.219 that a high dose of medium?

NOTE Confidence: 0.667546590285714

00:14:17.830 --> 00:14:21.662 Thanks. So .3 is I guess can often

NOTE Confidence: 0.667546590285714

00:14:21.662 --> 00:14:24.758 considered a medium to high dose?

NOTE Confidence: 0.667546590285714

00:14:24.760 --> 00:14:28.432 Um, so definitely a dose that is will

NOTE Confidence: 0.667546590285714

00:14:28.432 --> 00:14:31.148 produce generally pronounced subjective

NOTE Confidence: 0.667546590285714

00:14:31.148 --> 00:14:34.960 psychedelic effects .1 being a lower

NOTE Confidence: 0.667546590285714

00:14:34.960 --> 00:14:37.311 threshold dose like where maybe

NOTE Confidence: 0.667546590285714

00:14:37.311 --> 00:14:38.817 not quite a microdose where there,

NOTE Confidence: 0.667546590285714

00:14:38.820 --> 00:14:41.442 but definitely not like robust psychedelic

NOTE Confidence: 0.667546590285714

00:14:41.442 --> 00:14:44.150 effects .3 and weight based dosing.

NOTE Confidence: 0.667546590285714

00:14:44.150 --> 00:14:46.342 At the time we designed this was kind

NOTE Confidence: 0.667546590285714

00:14:46.342 --> 00:14:48.636 of the standard and there's been a

NOTE Confidence: 0.667546590285714

00:14:48.636 --> 00:14:51.010 shift more recently to use fixed dose

NOTE Confidence: 0.7308617

00:14:51.120 --> 00:14:52.405 wait. Those dosing is a
NOTE Confidence: 0.7308617

00:14:52.405 --> 00:14:53.880 pain in the **** it is,
NOTE Confidence: 0.849464075

00:14:53.890 --> 00:14:54.703 it requires compounding.
NOTE Confidence: 0.849464075

00:14:54.703 --> 00:14:56.600 So I think probably as these drugs
NOTE Confidence: 0.849464075

00:14:56.649 --> 00:14:58.119 are getting closer to phase two,
NOTE Confidence: 0.849464075

00:14:58.120 --> 00:14:59.560 phase three and they're seeing
NOTE Confidence: 0.849464075

00:14:59.560 --> 00:15:01.036 that writing, you know,
NOTE Confidence: 0.849464075

00:15:01.036 --> 00:15:03.724 the actual scale of the suit.
NOTE Confidence: 0.849464075

00:15:03.730 --> 00:15:04.825 Towards fixed dosing.
NOTE Confidence: 0.849464075

00:15:04.825 --> 00:15:07.380 And I think there's some data also
NOTE Confidence: 0.849464075

00:15:07.447 --> 00:15:10.240 that perhaps body size is not a
NOTE Confidence: 0.849464075

00:15:10.240 --> 00:15:12.250 huge predictor of the robustness
NOTE Confidence: 0.849464075

00:15:12.333 --> 00:15:14.873 of the psychedelic effects as
NOTE Confidence: 0.849464075

00:15:14.873 --> 00:15:16.905 much as other idiosyncratic,
NOTE Confidence: 0.849464075

00:15:16.910 --> 00:15:21.160 you know, brain chemistry factors.
NOTE Confidence: 0.849464075

00:15:21.160 --> 00:15:23.256 But that was .3 was the dose also

NOTE Confidence: 0.849464075

00:15:23.256 --> 00:15:25.410 generally the dose used in those cancer

NOTE Confidence: 0.849464075

00:15:25.410 --> 00:15:27.480 trials that showed those early effects.

NOTE Confidence: 0.849464075

00:15:27.480 --> 00:15:29.454 So we just kind of adopted that.

NOTE Confidence: 0.855824623333333

00:15:31.450 --> 00:15:32.320 I'm just curious,

NOTE Confidence: 0.792869614

00:15:32.330 --> 00:15:35.940 during screening it was like 900 out of the

NOTE Confidence: 0.792869614

00:15:35.940 --> 00:15:39.550 949 were ineligible for in person screening.

NOTE Confidence: 0.792869614

00:15:39.550 --> 00:15:41.358 Was that was there like a common reason?

NOTE Confidence: 0.80276241875

00:15:42.840 --> 00:15:44.840 There was so many reasons that we did

NOTE Confidence: 0.51899023

00:15:45.540 --> 00:15:48.108 have it all in the paper,

NOTE Confidence: 0.760919241111111

00:15:48.120 --> 00:15:50.368 but so many you know speaks to the

NOTE Confidence: 0.760919241111111

00:15:50.368 --> 00:15:52.165 difficulty of recruitment and and

NOTE Confidence: 0.760919241111111

00:15:52.165 --> 00:15:54.110 also how restrictive the product.

NOTE Confidence: 0.760919241111111

00:15:54.110 --> 00:15:56.550 Most of these protocols actually

NOTE Confidence: 0.760919241111111

00:15:56.550 --> 00:15:58.636 are as far as you know having to

NOTE Confidence: 0.760919241111111

00:15:58.636 --> 00:16:00.888 have had one fit like at least one

NOTE Confidence: 0.760919241111111

00:16:00.888 --> 00:16:02.393 failed medication trial and then
NOTE Confidence: 0.7609192411111111

00:16:02.451 --> 00:16:04.180 being able to come off of that.
NOTE Confidence: 0.7609192411111111

00:16:04.180 --> 00:16:06.812 And we require people to be in active
NOTE Confidence: 0.7609192411111111

00:16:06.812 --> 00:16:08.464 treatment at the time of enrollment
NOTE Confidence: 0.7609192411111111

00:16:08.464 --> 00:16:10.570 and they have to be in the area and be
NOTE Confidence: 0.7609192411111111

00:16:10.570 --> 00:16:12.089 able to come for all these sessions.
NOTE Confidence: 0.7609192411111111

00:16:12.090 --> 00:16:14.790 So it's. So many logistical and
NOTE Confidence: 0.7609192411111111

00:16:14.790 --> 00:16:17.410 just factors why people couldn't.
NOTE Confidence: 0.7609192411111111

00:16:17.410 --> 00:16:18.510 Participate.
NOTE Confidence: 0.7609192411111111

00:16:18.510 --> 00:16:20.214 I'm going to be able to come off of,
NOTE Confidence: 0.7609192411111111

00:16:20.220 --> 00:16:21.480 especially having to be able
NOTE Confidence: 0.7609192411111111

00:16:21.480 --> 00:16:22.740 to come off of antidepressants,
NOTE Confidence: 0.7609192411111111

00:16:22.740 --> 00:16:24.908 but having to have had a recent trial
NOTE Confidence: 0.7609192411111111

00:16:24.908 --> 00:16:27.189 in the current depressive episode?
NOTE Confidence: 0.7609192411111111

00:16:27.190 --> 00:16:29.280 Very tricky.
NOTE Confidence: 0.7609192411111111

00:16:29.280 --> 00:16:31.356 So it's a lot of factors.

NOTE Confidence: 0.7428451175

00:16:33.590 --> 00:16:35.732 So let me having shared those binding

NOTE Confidence: 0.7428451175

00:16:35.732 --> 00:16:37.720 results, I'll show you the results

NOTE Confidence: 0.7428451175

00:16:37.720 --> 00:16:40.963 from the handy which is our is our

NOTE Confidence: 0.7428451175

00:16:40.963 --> 00:16:42.943 primary depression outcome widely

NOTE Confidence: 0.7428451175

00:16:42.943 --> 00:16:44.910 used clinician administered scale.

NOTE Confidence: 0.7428451175

00:16:44.910 --> 00:16:46.870 So just let me just walk you through it here.

NOTE Confidence: 0.7428451175

00:16:46.870 --> 00:16:49.418 So from the left, people came in

NOTE Confidence: 0.7428451175

00:16:49.418 --> 00:16:52.049 with about a handy of about 23.

NOTE Confidence: 0.7428451175

00:16:52.050 --> 00:16:54.306 Are you upper moderate depression and

NOTE Confidence: 0.7428451175

00:16:54.306 --> 00:16:57.601 after the placebo they had a notable and

NOTE Confidence: 0.7428451175

00:16:57.601 --> 00:16:58.897 significant statistically significant

NOTE Confidence: 0.7428451175

00:16:58.897 --> 00:17:01.388 drop in their depression which actually

NOTE Confidence: 0.7428451175

00:17:01.388 --> 00:17:05.580 persisted all the way out for four weeks.

NOTE Confidence: 0.7428451175

00:17:05.580 --> 00:17:08.916 Drop was around five points on the handy

NOTE Confidence: 0.7428451175

00:17:08.920 --> 00:17:11.686 and then have their silibin session

NOTE Confidence: 0.7428451175

00:17:11.686 --> 00:17:14.515 and improved again with a significant
NOTE Confidence: 0.7428451175

00:17:14.515 --> 00:17:17.672 drop a little bit larger in magnitude,
NOTE Confidence: 0.7428451175

00:17:17.680 --> 00:17:20.000 6 to 8 points.
NOTE Confidence: 0.7428451175

00:17:20.000 --> 00:17:22.556 Roughly the difference however between.
NOTE Confidence: 0.7428451175

00:17:22.556 --> 00:17:25.520 The magnitude of change here pre
NOTE Confidence: 0.7428451175

00:17:25.603 --> 00:17:28.220 postal cybin and pre post placebo this
NOTE Confidence: 0.7428451175

00:17:28.220 --> 00:17:30.396 it was not a significant difference
NOTE Confidence: 0.7428451175

00:17:30.396 --> 00:17:32.886 from this change to this change.
NOTE Confidence: 0.7428451175

00:17:32.890 --> 00:17:33.251 However,
NOTE Confidence: 0.7428451175

00:17:33.251 --> 00:17:36.139 the effect size in this case would be
NOTE Confidence: 0.7428451175

00:17:36.139 --> 00:17:39.718 crime looking at was larger postal cybin.
NOTE Confidence: 0.7428451175

00:17:39.718 --> 00:17:40.330 Anything,
NOTE Confidence: 0.7428451175

00:17:40.330 --> 00:17:42.076 just a couple of things that
NOTE Confidence: 0.7428451175

00:17:42.076 --> 00:17:43.240 are interesting thinking about
NOTE Confidence: 0.7428451175

00:17:43.290 --> 00:17:44.720 also the blinding results is,
NOTE Confidence: 0.7428451175

00:17:44.720 --> 00:17:46.220 is that people came in,

NOTE Confidence: 0.7428451175

00:17:46.220 --> 00:17:48.890 they had the placebo session most

NOTE Confidence: 0.7428451175

00:17:48.890 --> 00:17:51.563 actually realized they got placebo and

NOTE Confidence: 0.7428451175

00:17:51.563 --> 00:17:54.165 instead of you know maybe getting worse

NOTE Confidence: 0.7428451175

00:17:54.165 --> 00:17:56.380 or having an osebo response actually

NOTE Confidence: 0.7428451175

00:17:56.380 --> 00:17:58.879 continue to improve and so you might

NOTE Confidence: 0.7428451175

00:17:58.879 --> 00:18:01.196 think what what was going on there.

NOTE Confidence: 0.7428451175

00:18:01.200 --> 00:18:03.566 At least two ideas are we're one

NOTE Confidence: 0.7428451175

00:18:03.566 --> 00:18:05.401 they were receiving therapy and

NOTE Confidence: 0.7428451175

00:18:05.401 --> 00:18:07.663 so having some therapy effects but

NOTE Confidence: 0.7428451175

00:18:07.663 --> 00:18:09.979 another big one I think related to.

NOTE Confidence: 0.7428451175

00:18:09.980 --> 00:18:11.954 Expectancy was that they knew that

NOTE Confidence: 0.7428451175

00:18:11.954 --> 00:18:14.071 they had this other session coming

NOTE Confidence: 0.7428451175

00:18:14.071 --> 00:18:16.267 up and we're engaging in therapy.

NOTE Confidence: 0.7428451175

00:18:16.270 --> 00:18:18.846 So there was and I think we encouraged

NOTE Confidence: 0.7428451175

00:18:18.846 --> 00:18:20.545 the generally hopeful attitude and

NOTE Confidence: 0.7428451175

00:18:20.545 --> 00:18:22.859 thinking of this as one big journey.
NOTE Confidence: 0.7428451175

00:18:22.859 --> 00:18:25.162 So I think that's that is interesting
NOTE Confidence: 0.7428451175

00:18:25.162 --> 00:18:27.135 because we'll see probably in a few
NOTE Confidence: 0.7428451175

00:18:27.135 --> 00:18:29.110 weeks the results of the USONA study.
NOTE Confidence: 0.7428451175

00:18:29.110 --> 00:18:30.910 That was a single dose study
NOTE Confidence: 0.7428451175

00:18:30.910 --> 00:18:32.609 where if you didn't get it,
NOTE Confidence: 0.7428451175

00:18:32.610 --> 00:18:34.808 you had no hope of another session.
NOTE Confidence: 0.7428451175

00:18:34.810 --> 00:18:37.642 So you know be quite different
NOTE Confidence: 0.7428451175

00:18:37.642 --> 00:18:40.310 effects from the placebo session.
NOTE Confidence: 0.7428451175

00:18:40.310 --> 00:18:42.872 I would imagine and then just the
NOTE Confidence: 0.7428451175

00:18:42.872 --> 00:18:45.101 other caveat here is that there
NOTE Confidence: 0.7428451175

00:18:45.101 --> 00:18:47.506 was a carryover effect that we we
NOTE Confidence: 0.7428451175

00:18:47.506 --> 00:18:48.986 had anticipated that four weeks
NOTE Confidence: 0.7428451175

00:18:48.986 --> 00:18:50.729 would be enough to wash out,
NOTE Confidence: 0.7428451175

00:18:50.730 --> 00:18:52.722 but we did have carryover effects
NOTE Confidence: 0.7428451175

00:18:52.722 --> 00:18:54.920 into the second part of the study.

NOTE Confidence: 0.684396168

00:18:55.150 --> 00:18:57.340 They're getting weekly therapy throughout,

NOTE Confidence: 0.789768468571428

00:18:57.450 --> 00:18:59.907 not exactly weekly, but it was two.

NOTE Confidence: 0.789768468571428

00:18:59.910 --> 00:19:01.812 They would get therapy the day

NOTE Confidence: 0.789768468571428

00:19:01.812 --> 00:19:04.145 after and a week after the each

NOTE Confidence: 0.789768468571428

00:19:04.145 --> 00:19:06.131 of the sessions and then there

NOTE Confidence: 0.789768468571428

00:19:06.131 --> 00:19:08.455 was a few follow-up sessions after

NOTE Confidence: 0.789768468571428

00:19:08.455 --> 00:19:10.690 week six after that final. That

NOTE Confidence: 0.810139407777778

00:19:10.700 --> 00:19:11.755 may have helped may have

NOTE Confidence: 0.810139407777778

00:19:11.755 --> 00:19:12.599 contributed to carry over.

NOTE Confidence: 0.810139407777778

00:19:12.600 --> 00:19:15.897 But as you point out the anticipation

NOTE Confidence: 0.810139407777778

00:19:15.897 --> 00:19:18.677 of males that combination of and

NOTE Confidence: 0.810139407777778

00:19:18.677 --> 00:19:20.459 there's no therapy between the day

NOTE Confidence: 0.810139407777778

00:19:20.459 --> 00:19:22.462 before the W zero day before dosing

NOTE Confidence: 0.810139407777778

00:19:22.462 --> 00:19:24.316 and W 0 day after dose correct.

NOTE Confidence: 0.810139407777778

00:19:24.316 --> 00:19:25.944 The only thing that happens

NOTE Confidence: 0.810139407777778

00:19:25.944 --> 00:19:27.370 there is that correct
NOTE Confidence: 0.6839231714

00:19:27.740 --> 00:19:30.266 session with two with the therapists
NOTE Confidence: 0.6839231714

00:19:30.266 --> 00:19:31.950 anesthesiologists in the room
NOTE Confidence: 0.650365727272727

00:19:32.120 --> 00:19:33.765 that the therapy that happened to concurrent
NOTE Confidence: 0.650365727272727

00:19:33.765 --> 00:19:37.980 with the dosing session. Yes exactly.
NOTE Confidence: 0.896122124

00:19:37.980 --> 00:19:40.640 So, you know, I think someone's
NOTE Confidence: 0.896122124

00:19:40.640 --> 00:19:41.820 trying to say something.
NOTE Confidence: 0.799550146666667

00:19:44.270 --> 00:19:46.729 Was there someone? And it's just.
NOTE Confidence: 0.644932135714286

00:19:49.690 --> 00:19:51.566 Just said a lot of that contact,
NOTE Confidence: 0.644932135714286

00:19:51.570 --> 00:19:53.400 probably more than standard of character.
NOTE Confidence: 0.644932135714286

00:19:53.400 --> 00:19:55.829 Yeah. So, you know, I think it's,
NOTE Confidence: 0.644932135714286

00:19:55.830 --> 00:19:58.310 it's one thing I've.
NOTE Confidence: 0.644932135714286

00:19:58.310 --> 00:20:00.172 So of course suicide then at least
NOTE Confidence: 0.644932135714286

00:20:00.172 --> 00:20:02.640 for this primary outcome not not a
NOTE Confidence: 0.644932135714286

00:20:02.640 --> 00:20:03.849 statistically significant difference
NOTE Confidence: 0.644932135714286

00:20:03.850 --> 00:20:06.279 though if you look from a clinical

NOTE Confidence: 0.644932135714286

00:20:06.279 --> 00:20:08.485 standpoint from the beginning to end

NOTE Confidence: 0.644932135714286

00:20:08.485 --> 00:20:10.340 pretty significant drops with the

NOTE Confidence: 0.644932135714286

00:20:10.412 --> 00:20:13.100 combined the effect sizes as well as

NOTE Confidence: 0.644932135714286

00:20:13.100 --> 00:20:15.139 the overall intervention pretty large.

NOTE Confidence: 0.644932135714286

00:20:15.140 --> 00:20:18.124 And again this was not designed as an

NOTE Confidence: 0.644932135714286

00:20:18.124 --> 00:20:20.911 efficacy study with such a small and but

NOTE Confidence: 0.644932135714286

00:20:20.911 --> 00:20:23.920 just another piece on the clinical results.

NOTE Confidence: 0.644932135714286

00:20:23.920 --> 00:20:26.020 You know we also look at rates

NOTE Confidence: 0.644932135714286

00:20:26.020 --> 00:20:27.834 of response and remission for

NOTE Confidence: 0.644932135714286

00:20:27.834 --> 00:20:29.749 those who completed both sessions.

NOTE Confidence: 0.644932135714286

00:20:29.750 --> 00:20:32.094 And just also show here that after placebo

NOTE Confidence: 0.644932135714286

00:20:32.094 --> 00:20:34.177 you know a little bit of response,

NOTE Confidence: 0.644932135714286

00:20:34.180 --> 00:20:37.060 but 20% response rate which really

NOTE Confidence: 0.644932135714286

00:20:37.060 --> 00:20:40.850 jumps up after this whole sabin sessions

NOTE Confidence: 0.644932135714286

00:20:40.850 --> 00:20:44.090 with responses lasting up to that.

NOTE Confidence: 0.644932135714286

00:20:44.090 --> 00:20:46.310 This was our primary MDM point
NOTE Confidence: 0.644932135714286

00:20:46.310 --> 00:20:47.790 endpoint at Week 6.
NOTE Confidence: 0.6533123634

00:20:48.610 --> 00:20:51.400 Was the response to that response rate is a
NOTE Confidence: 0.6533123634

00:20:51.400 --> 00:20:54.378 50% improvement relative to what baseline?
NOTE Confidence: 0.902700276

00:20:55.680 --> 00:20:58.030 Actually, for this is actually
NOTE Confidence: 0.902700276

00:20:58.030 --> 00:21:01.230 relative to the day before. Each dose.
NOTE Confidence: 0.780790006923077

00:21:01.300 --> 00:21:02.880 OK. So the psilocybin response
NOTE Confidence: 0.780790006923077

00:21:02.880 --> 00:21:05.402 there is relative to a day before
NOTE Confidence: 0.780790006923077

00:21:05.402 --> 00:21:07.649 psilocybin, not three weeks a week.
NOTE Confidence: 0.47373462

00:21:08.660 --> 00:21:11.258 Yeah. Jordan, I know the
NOTE Confidence: 0.47373462

00:21:11.258 --> 00:21:12.286 numbers are really small,
NOTE Confidence: 0.9198734533333333

00:21:12.290 --> 00:21:16.526 but the people that did not
NOTE Confidence: 0.9198734533333333

00:21:16.526 --> 00:21:18.980 accurately guess their. Assignment.
NOTE Confidence: 0.9198734533333333

00:21:18.980 --> 00:21:20.630 Was there any difference there?
NOTE Confidence: 0.9198734533333333

00:21:20.630 --> 00:21:24.598 Were they? Were they the big
NOTE Confidence: 0.9198734533333333

00:21:24.598 --> 00:21:26.866 responders and non responders?

NOTE Confidence: 0.9198734533333333
00:21:26.870 --> 00:21:28.550 So we have numbers are so small,
NOTE Confidence: 0.9198734533333333
00:21:28.550 --> 00:21:29.894 we just have to be a
NOTE Confidence: 0.9198734533333333
00:21:29.894 --> 00:21:31.060 qualitative look at it. But
NOTE Confidence: 0.8296332727777778
00:21:31.130 --> 00:21:33.450 yeah, the the the one that was the
NOTE Confidence: 0.8296332727777778
00:21:33.450 --> 00:21:35.114 biggest outlier was actually it
NOTE Confidence: 0.8296332727777778
00:21:35.114 --> 00:21:36.819 was our very first participant.
NOTE Confidence: 0.8296332727777778
00:21:36.820 --> 00:21:40.800 He had a very robust he detected
NOTE Confidence: 0.8296332727777778
00:21:40.800 --> 00:21:44.028 effects from the placebo session and
NOTE Confidence: 0.8296332727777778
00:21:44.028 --> 00:21:46.180 had very significant antidepressant
NOTE Confidence: 0.8296332727777778
00:21:46.261 --> 00:21:48.764 response from the placebo session
NOTE Confidence: 0.8296332727777778
00:21:48.764 --> 00:21:51.620 as far as the other ones.
NOTE Confidence: 0.8296332727777778
00:21:51.620 --> 00:21:52.872 Sort of less memorable.
NOTE Confidence: 0.8296332727777778
00:21:52.872 --> 00:21:54.750 I think they were just unsure,
NOTE Confidence: 0.8296332727777778
00:21:54.750 --> 00:21:57.270 you know, which.
NOTE Confidence: 0.8296332727777778
00:21:57.270 --> 00:21:58.705 Because that was the participant
NOTE Confidence: 0.8296332727777778

00:21:58.705 --> 00:22:00.750 that sticks out the most in my mind.
NOTE Confidence: 0.7812621

00:22:07.330 --> 00:22:08.060 All right.
NOTE Confidence: 0.839552949444444

00:22:11.340 --> 00:22:13.560 So as far as just you know the other thing
NOTE Confidence: 0.839552949444444

00:22:13.620 --> 00:22:15.900 that I mentioned at the beginning was this,
NOTE Confidence: 0.839552949444444

00:22:15.900 --> 00:22:17.778 this whole narrative around the duration
NOTE Confidence: 0.839552949444444

00:22:17.778 --> 00:22:19.719 of response from a single dose.
NOTE Confidence: 0.839552949444444

00:22:19.720 --> 00:22:21.498 And so that was something we were
NOTE Confidence: 0.839552949444444

00:22:21.498 --> 00:22:22.999 interested in looking at and we look,
NOTE Confidence: 0.839552949444444

00:22:23.000 --> 00:22:25.367 we look at that best looking at the quiz,
NOTE Confidence: 0.839552949444444

00:22:25.370 --> 00:22:27.356 the self rated measure of depression
NOTE Confidence: 0.839552949444444

00:22:27.356 --> 00:22:29.194 that we collected because unlike the
NOTE Confidence: 0.839552949444444

00:22:29.194 --> 00:22:31.085 hand D which was just out to week six,
NOTE Confidence: 0.839552949444444

00:22:31.090 --> 00:22:32.842 we did collect this all the way out
NOTE Confidence: 0.839552949444444

00:22:32.842 --> 00:22:34.845 to week sixteen or three months after
NOTE Confidence: 0.839552949444444

00:22:34.845 --> 00:22:36.805 the suicide then dosing session.
NOTE Confidence: 0.839552949444444

00:22:36.805 --> 00:22:38.800 And So what I'm just highlighting

NOTE Confidence: 0.839552949444444

00:22:38.800 --> 00:22:41.986 in this box here is that relative to

NOTE Confidence: 0.839552949444444

00:22:41.986 --> 00:22:46.359 the pre sobin baseline from one one

NOTE Confidence: 0.839552949444444

00:22:46.359 --> 00:22:48.690 day after the dose there was that

NOTE Confidence: 0.839552949444444

00:22:48.769 --> 00:22:51.157 a significant drop similar to what

NOTE Confidence: 0.839552949444444

00:22:51.157 --> 00:22:54.608 the Hamdy and that response remains

NOTE Confidence: 0.839552949444444

00:22:54.608 --> 00:22:57.256 statistically significant for two

NOTE Confidence: 0.839552949444444

00:22:57.256 --> 00:23:00.512 months and then at three months that

NOTE Confidence: 0.839552949444444

00:23:00.512 --> 00:23:03.280 difference was no longer significant.

NOTE Confidence: 0.839552949444444

00:23:03.280 --> 00:23:05.387 However, they were at this point they

NOTE Confidence: 0.839552949444444

00:23:05.387 --> 00:23:07.220 were still significantly better than their.

NOTE Confidence: 0.839552949444444

00:23:07.220 --> 00:23:09.290 Initial baseline prior to placebo,

NOTE Confidence: 0.839552949444444

00:23:09.290 --> 00:23:11.408 but you know again small numbers,

NOTE Confidence: 0.839552949444444

00:23:11.410 --> 00:23:14.480 but I to me this was both.

NOTE Confidence: 0.839552949444444

00:23:14.480 --> 00:23:15.500 And encouraging,

NOTE Confidence: 0.839552949444444

00:23:15.500 --> 00:23:19.070 but also maybe perhaps more realistic result

NOTE Confidence: 0.839552949444444

00:23:19.152 --> 00:23:22.197 of seeing a two-month about a two-month.

NOTE Confidence: 0.839552949444444

00:23:22.200 --> 00:23:24.444 Response and duration from the single

NOTE Confidence: 0.839552949444444

00:23:24.444 --> 00:23:27.134 dose of suicide then at least the

NOTE Confidence: 0.839552949444444

00:23:27.134 --> 00:23:29.004 combination of everything that came

NOTE Confidence: 0.839552949444444

00:23:29.004 --> 00:23:31.398 before it and then the solar sybian does.

NOTE Confidence: 0.839552949444444

00:23:31.400 --> 00:23:34.104 So perhaps that you know I I mentioned

NOTE Confidence: 0.839552949444444

00:23:34.104 --> 00:23:36.090 that because I'm a bit skeptical

NOTE Confidence: 0.839552949444444

00:23:36.090 --> 00:23:38.160 of the single dose is going to

NOTE Confidence: 0.839552949444444

00:23:38.160 --> 00:23:41.303 cure people who've had 20 years of

NOTE Confidence: 0.839552949444444

00:23:41.303 --> 00:23:43.092 depression narrative and perhaps

NOTE Confidence: 0.839552949444444

00:23:43.092 --> 00:23:45.956 this is what we might see a little

NOTE Confidence: 0.839552949444444

00:23:45.956 --> 00:23:48.299 more realistic moving forward.

NOTE Confidence: 0.839552949444444

00:23:48.300 --> 00:23:48.806 All right.

NOTE Confidence: 0.839552949444444

00:23:48.806 --> 00:23:50.324 Before I wrap up this section,

NOTE Confidence: 0.839552949444444

00:23:50.330 --> 00:23:52.591 I'll just show you also some interesting

NOTE Confidence: 0.839552949444444

00:23:52.591 --> 00:23:54.990 results from our quality of life measure,

NOTE Confidence: 0.839552949444444

00:23:54.990 --> 00:23:58.510 which was the Rand 36 it had

NOTE Confidence: 0.839552949444444

00:23:58.510 --> 00:24:00.860 contains 8 health related domains.

NOTE Confidence: 0.839552949444444

00:24:00.860 --> 00:24:02.788 And I think this is important in depression

NOTE Confidence: 0.839552949444444

00:24:02.788 --> 00:24:04.416 studies not just to look at symptoms,

NOTE Confidence: 0.839552949444444

00:24:04.420 --> 00:24:06.660 but also the collect some idea of how

NOTE Confidence: 0.839552949444444

00:24:06.660 --> 00:24:08.980 people are actually doing in their life.

NOTE Confidence: 0.839552949444444

00:24:08.980 --> 00:24:10.684 And we collected qualitative data as

NOTE Confidence: 0.839552949444444

00:24:10.684 --> 00:24:12.879 well that I'm not going to show here,

NOTE Confidence: 0.839552949444444

00:24:12.880 --> 00:24:14.096 I haven't analyzed yet,

NOTE Confidence: 0.839552949444444

00:24:14.096 --> 00:24:16.879 but as far as from these eight domains,

NOTE Confidence: 0.839552949444444

00:24:16.880 --> 00:24:17.428 so actually.

NOTE Confidence: 0.839552949444444

00:24:17.428 --> 00:24:19.402 Out of seven, out of the eight,

NOTE Confidence: 0.839552949444444

00:24:19.402 --> 00:24:20.842 we saw significant time effect,

NOTE Confidence: 0.839552949444444

00:24:20.850 --> 00:24:22.490 meaning people significantly improved

NOTE Confidence: 0.839552949444444

00:24:22.490 --> 00:24:24.540 from their initial baseline over

NOTE Confidence: 0.839552949444444

00:24:24.540 --> 00:24:26.448 the course of the whole study.
NOTE Confidence: 0.839552949444444

00:24:26.450 --> 00:24:28.390 And in these three, sorry,
NOTE Confidence: 0.839552949444444

00:24:28.390 --> 00:24:31.126 4 domains on the left now in green,
NOTE Confidence: 0.839552949444444

00:24:31.130 --> 00:24:34.016 that we actually did see a
NOTE Confidence: 0.839552949444444

00:24:34.016 --> 00:24:35.459 statistically significant improvement
NOTE Confidence: 0.839552949444444

00:24:35.459 --> 00:24:38.106 post silybin compared to post SIBO.
NOTE Confidence: 0.839552949444444

00:24:38.110 --> 00:24:40.230 So unlike the depression measures,
NOTE Confidence: 0.839552949444444

00:24:40.230 --> 00:24:42.310 this was statistically significant.
NOTE Confidence: 0.839552949444444

00:24:42.310 --> 00:24:45.430 Still cybin and these are pretty
NOTE Confidence: 0.839552949444444

00:24:45.507 --> 00:24:48.487 relevant domains that role limitations.
NOTE Confidence: 0.839552949444444

00:24:48.490 --> 00:24:50.290 Due to emotional problems and emotional
NOTE Confidence: 0.839552949444444

00:24:50.290 --> 00:24:51.658 well-being, social functioning.
NOTE Confidence: 0.839552949444444

00:24:51.658 --> 00:24:53.260 And general Health,
NOTE Confidence: 0.839552949444444

00:24:53.260 --> 00:24:55.460 we didn't see it for energy and fatigue.
NOTE Confidence: 0.839552949444444

00:24:55.460 --> 00:24:57.300 And just to show you what those results
NOTE Confidence: 0.839552949444444

00:24:57.300 --> 00:24:59.556 for us look like with something like this,

NOTE Confidence: 0.839552949444444

00:24:59.560 --> 00:25:01.145 this is for role limitations

NOTE Confidence: 0.839552949444444

00:25:01.145 --> 00:25:02.413 due to emotional problems,

NOTE Confidence: 0.839552949444444

00:25:02.420 --> 00:25:04.388 increase in scores, improvements.

NOTE Confidence: 0.839552949444444

00:25:04.388 --> 00:25:07.980 And so we we did see pretty

NOTE Confidence: 0.839552949444444

00:25:07.980 --> 00:25:09.548 significant jumps after the

NOTE Confidence: 0.839552949444444

00:25:09.548 --> 00:25:11.900 suicide and actually and this is

NOTE Confidence: 0.725588814166667

00:25:11.967 --> 00:25:13.818 2 weeks. After the Silybin session

NOTE Confidence: 0.725588814166667

00:25:13.818 --> 00:25:16.377 and then we collected it at the end

NOTE Confidence: 0.725588814166667

00:25:16.377 --> 00:25:18.808 of study and that improvement was

NOTE Confidence: 0.725588814166667

00:25:18.808 --> 00:25:21.218 still significant three months later.

NOTE Confidence: 0.725588814166667

00:25:21.220 --> 00:25:23.418 And that was true for these other

NOTE Confidence: 0.725588814166667

00:25:23.418 --> 00:25:25.526 domains and the emotional well-being

NOTE Confidence: 0.725588814166667

00:25:25.526 --> 00:25:28.168 and social functioning as well.

NOTE Confidence: 0.725588814166667

00:25:28.168 --> 00:25:30.990 So that is. And perhaps promising results.

NOTE Confidence: 0.725588814166667

00:25:30.990 --> 00:25:33.650 So just to sum up that before I

NOTE Confidence: 0.725588814166667

00:25:33.650 --> 00:25:36.016 pass it over to Patrick from this,
NOTE Confidence: 0.725588814166667

00:25:36.016 --> 00:25:38.764 we did see significant improvements in
NOTE Confidence: 0.725588814166667

00:25:38.764 --> 00:25:40.735 depression following both the placebo
NOTE Confidence: 0.725588814166667

00:25:40.735 --> 00:25:42.800 and the sobin without a statistically
NOTE Confidence: 0.725588814166667

00:25:42.800 --> 00:25:44.600 significant difference between the two.
NOTE Confidence: 0.725588814166667

00:25:44.600 --> 00:25:46.274 However, we did see larger effect
NOTE Confidence: 0.725588814166667

00:25:46.274 --> 00:25:48.102 sizes and higher rates of response
NOTE Confidence: 0.725588814166667

00:25:48.102 --> 00:25:49.089 and remission postal,
NOTE Confidence: 0.725588814166667

00:25:49.090 --> 00:25:52.940 cybin and after the SILIBIN dosing session,
NOTE Confidence: 0.725588814166667

00:25:52.940 --> 00:25:55.055 the decreases in depression remains
NOTE Confidence: 0.725588814166667

00:25:55.055 --> 00:25:58.186 significant for two months and we saw
NOTE Confidence: 0.725588814166667

00:25:58.186 --> 00:26:00.070 significant and lasting improvements.
NOTE Confidence: 0.725588814166667

00:26:00.070 --> 00:26:02.545 In several mood related quality
NOTE Confidence: 0.725588814166667

00:26:02.545 --> 00:26:04.030 of life domains.
NOTE Confidence: 0.725588814166667

00:26:04.030 --> 00:26:06.322 Again, the limitations that I touched
NOTE Confidence: 0.725588814166667

00:26:06.322 --> 00:26:08.703 on for this section against small

NOTE Confidence: 0.725588814166667

00:26:08.703 --> 00:26:11.419 sample size for for an efficacy study.

NOTE Confidence: 0.725588814166667

00:26:11.420 --> 00:26:13.574 Any study we did have carryover

NOTE Confidence: 0.725588814166667

00:26:13.574 --> 00:26:15.576 effects that may have limited

NOTE Confidence: 0.725588814166667

00:26:15.576 --> 00:26:17.512 detecting that that difference.

NOTE Confidence: 0.725588814166667

00:26:17.512 --> 00:26:20.338 We had limited success with blinding

NOTE Confidence: 0.725588814166667

00:26:20.338 --> 00:26:22.360 and clear expectancy effects

NOTE Confidence: 0.725588814166667

00:26:22.360 --> 00:26:24.870 at play and therapy effects,

NOTE Confidence: 0.725588814166667

00:26:24.870 --> 00:26:27.236 and you know we can't separate in

NOTE Confidence: 0.725588814166667

00:26:27.236 --> 00:26:29.225 this model the therapy effects

NOTE Confidence: 0.725588814166667

00:26:29.225 --> 00:26:31.485 from the actual drug effects.

NOTE Confidence: 0.725588814166667

00:26:31.490 --> 00:26:33.580 Discuss more in the discussion.

NOTE Confidence: 0.725588814166667

00:26:33.580 --> 00:26:34.660 So with that,

NOTE Confidence: 0.725588814166667

00:26:34.660 --> 00:26:36.820 I'm going to stop my share

NOTE Confidence: 0.725588814166667

00:26:36.820 --> 00:26:39.230 and pass it over to Patrick.

NOTE Confidence: 0.899043302

00:26:43.400 --> 00:26:44.850 All right. Thank you, Jordan.

NOTE Confidence: 0.81063434

00:26:54.920 --> 00:26:56.940 Can everyone see my
NOTE Confidence: 0.81063434

00:26:56.940 --> 00:26:58.850 opening slide? Looks good.
NOTE Confidence: 0.61868894

00:27:00.350 --> 00:27:03.080 Alright. Great pointer.
NOTE Confidence: 0.9178268333333333

00:27:05.190 --> 00:27:06.180 So now we want to talk
NOTE Confidence: 0.857683730769231

00:27:06.190 --> 00:27:08.598 a little bit what are the potential
NOTE Confidence: 0.857683730769231

00:27:08.598 --> 00:27:10.717 neural mechanisms of the antidepressant
NOTE Confidence: 0.857683730769231

00:27:10.717 --> 00:27:14.678 effect that Jordan just outlined.
NOTE Confidence: 0.857683730769231

00:27:14.680 --> 00:27:16.280 And so we're really in the
NOTE Confidence: 0.857683730769231

00:27:16.280 --> 00:27:18.268 middle of a paradigm shift.
NOTE Confidence: 0.8055909025

00:27:22.250 --> 00:27:25.690 In the sense that there's this idea that
NOTE Confidence: 0.8055909025

00:27:25.690 --> 00:27:28.060 psychedelics are psychoplasma begins,
NOTE Confidence: 0.8055909025

00:27:28.060 --> 00:27:31.420 so they induced a neuroplastic state,
NOTE Confidence: 0.8055909025

00:27:31.420 --> 00:27:34.680 which might open a therapeutic
NOTE Confidence: 0.8055909025

00:27:34.680 --> 00:27:36.636 window for therapy.
NOTE Confidence: 0.8055909025

00:27:36.640 --> 00:27:40.840 And it's a paradigm shift because it
NOTE Confidence: 0.8055909025

00:27:40.840 --> 00:27:44.288 goes beyond the standard, you know,

NOTE Confidence: 0.8055909025
00:27:44.288 --> 00:27:46.536 trying to manipulate neurochemistry
NOTE Confidence: 0.8055909025
00:27:46.536 --> 00:27:51.002 with via mono Amiens, Prozac and Zoloft.
NOTE Confidence: 0.8055909025
00:27:51.002 --> 00:27:54.018 And whatnot and instead.
NOTE Confidence: 0.8055909025
00:27:54.020 --> 00:27:56.618 Try to selectively modulate and change
NOTE Confidence: 0.8055909025
00:27:56.618 --> 00:27:58.841 neural circuits that are implicated
NOTE Confidence: 0.8055909025
00:27:58.841 --> 00:28:01.774 in depression and anxiety and OCD and
NOTE Confidence: 0.8055909025
00:28:01.774 --> 00:28:04.130 other things as well in addiction.
NOTE Confidence: 0.707514135
00:28:07.660 --> 00:28:10.036 So I'll start with what's neuroplasticity.
NOTE Confidence: 0.707514135
00:28:10.040 --> 00:28:12.550 So neuroplasticity refers to the
NOTE Confidence: 0.707514135
00:28:12.550 --> 00:28:14.056 activity dependent modification
NOTE Confidence: 0.707514135
00:28:14.056 --> 00:28:16.620 of cement synaptic transmission,
NOTE Confidence: 0.707514135
00:28:16.620 --> 00:28:19.086 which is thought to be one of the neural
NOTE Confidence: 0.707514135
00:28:19.086 --> 00:28:20.657 substrates of learning and memory.
NOTE Confidence: 0.707514135
00:28:20.660 --> 00:28:21.959 In some sense,
NOTE Confidence: 0.707514135
00:28:21.959 --> 00:28:24.124 I think neuroplasticity plasticity is
NOTE Confidence: 0.707514135

00:28:24.124 --> 00:28:26.540 redundant because the brain is so dynamic.

NOTE Confidence: 0.707514135

00:28:26.540 --> 00:28:28.660 Our environments are constantly

NOTE Confidence: 0.707514135

00:28:28.660 --> 00:28:31.310 changing and relationships are changing.

NOTE Confidence: 0.707514135

00:28:31.310 --> 00:28:32.864 And so the brain is so dynamic,

NOTE Confidence: 0.707514135

00:28:32.870 --> 00:28:35.038 so it's always plastic,

NOTE Confidence: 0.707514135

00:28:35.038 --> 00:28:38.290 but we use the term neuroplasticity.

NOTE Confidence: 0.707514135

00:28:38.290 --> 00:28:40.710 And this idea goes back

NOTE Confidence: 0.707514135

00:28:40.710 --> 00:28:43.246 to Donald Hebb from 1949.

NOTE Confidence: 0.707514135

00:28:43.246 --> 00:28:47.850 And this quote of his is is so

NOTE Confidence: 0.707514135

00:28:47.850 --> 00:28:51.090 iconic and really I think prophetic.

NOTE Confidence: 0.707514135

00:28:51.090 --> 00:28:56.054 So Donald Hebb said in 1949 when an Axon

NOTE Confidence: 0.707514135

00:28:56.054 --> 00:29:00.746 of cell A is near enough to excite a cell B.

NOTE Confidence: 0.707514135

00:29:00.750 --> 00:29:02.310 And repeatedly or persistently

NOTE Confidence: 0.707514135

00:29:02.310 --> 00:29:03.870 takes part in firing,

NOTE Confidence: 0.707514135

00:29:03.870 --> 00:29:04.968 firing it.

NOTE Confidence: 0.707514135

00:29:04.968 --> 00:29:07.713 Some growth process for metabolic

NOTE Confidence: 0.707514135

00:29:07.713 --> 00:29:11.125 change takes place in one of both

NOTE Confidence: 0.707514135

00:29:11.125 --> 00:29:13.960 cells such that a efficiency as one

NOTE Confidence: 0.707514135

00:29:13.960 --> 00:29:16.585 of the cells firing B is increased.

NOTE Confidence: 0.707514135

00:29:16.590 --> 00:29:19.461 So a simply simple way to say that is

NOTE Confidence: 0.707514135

00:29:19.461 --> 00:29:22.169 sales or networks that fire together,

NOTE Confidence: 0.707514135

00:29:22.170 --> 00:29:23.282 wire together,

NOTE Confidence: 0.707514135

00:29:23.282 --> 00:29:26.618 that's these the essence of neuroplasticity.

NOTE Confidence: 0.707514135

00:29:26.620 --> 00:29:28.978 This is really important in the

NOTE Confidence: 0.707514135

00:29:28.978 --> 00:29:30.550 context of depression because

NOTE Confidence: 0.707514135

00:29:30.622 --> 00:29:32.300 enhancing neuroplasticity,

NOTE Confidence: 0.707514135

00:29:32.300 --> 00:29:33.972 for example through psychedelics,

NOTE Confidence: 0.707514135

00:29:33.972 --> 00:29:37.003 could up again open up this therapeutic

NOTE Confidence: 0.707514135

00:29:37.003 --> 00:29:38.787 window in which traditional

NOTE Confidence: 0.707514135

00:29:38.787 --> 00:29:41.582 therapies such as CBT and others

NOTE Confidence: 0.707514135

00:29:41.582 --> 00:29:43.558 could prove more efficacious,

NOTE Confidence: 0.707514135

00:29:43.560 --> 00:29:46.652 and indeed deficits and
NOTE Confidence: 0.707514135

00:29:46.652 --> 00:29:47.900 markers of neuroplasticity,
NOTE Confidence: 0.707514135

00:29:47.900 --> 00:29:50.020 for instance a peripheral BDNF,
NOTE Confidence: 0.707514135

00:29:50.020 --> 00:29:51.990 have been observed and depression.
NOTE Confidence: 0.81021771125

00:29:54.990 --> 00:29:59.974 So this review paper just came out showing.
NOTE Confidence: 0.81021771125

00:29:59.980 --> 00:30:02.780 Some of the work that's been done
NOTE Confidence: 0.81021771125

00:30:02.780 --> 00:30:06.103 in the context of psychedelics on
NOTE Confidence: 0.81021771125

00:30:06.103 --> 00:30:08.819 different measures of neuroplasticity.
NOTE Confidence: 0.81021771125

00:30:08.820 --> 00:30:12.110 And there's several measures that.
NOTE Confidence: 0.81021771125

00:30:12.110 --> 00:30:13.978 Have been used, including.
NOTE Confidence: 0.743717016666667

00:30:16.290 --> 00:30:19.188 Immediate early genes,
NOTE Confidence: 0.743717016666667

00:30:19.190 --> 00:30:22.454 upregulation of other plastic
NOTE Confidence: 0.743717016666667

00:30:22.454 --> 00:30:25.450 plasticity genes, spinal genesis,
NOTE Confidence: 0.743717016666667

00:30:25.450 --> 00:30:28.170 neurogenesis, density of synapses.
NOTE Confidence: 0.743717016666667

00:30:28.170 --> 00:30:29.526 One thing that to note here,
NOTE Confidence: 0.743717016666667

00:30:29.530 --> 00:30:31.630 which may come up in discussion later,

NOTE Confidence: 0.743717016666667
00:30:31.630 --> 00:30:35.890 is that each of these different
NOTE Confidence: 0.743717016666667
00:30:35.890 --> 00:30:37.730 measures of neuroplasticity looked
NOTE Confidence: 0.743717016666667
00:30:37.730 --> 00:30:40.490 to have a different time course.
NOTE Confidence: 0.743717016666667
00:30:40.490 --> 00:30:42.356 So of course the immediate early
NOTE Confidence: 0.743717016666667
00:30:42.356 --> 00:30:43.904 genes are early, you know,
NOTE Confidence: 0.743717016666667
00:30:43.904 --> 00:30:45.746 within an hour of administration of.
NOTE Confidence: 0.743717016666667
00:30:45.750 --> 00:30:47.366 Of the second relic,
NOTE Confidence: 0.743717016666667
00:30:47.366 --> 00:30:49.386 whereas some of the morphological
NOTE Confidence: 0.743717016666667
00:30:49.386 --> 00:30:51.228 changes tend to happen later.
NOTE Confidence: 0.733548463333333
00:30:54.580 --> 00:30:56.988 You asked in the chat if you
NOTE Confidence: 0.733548463333333
00:30:56.988 --> 00:30:58.703 get neuroplastic changes after
NOTE Confidence: 0.733548463333333
00:30:58.703 --> 00:31:01.650 conventional, like monoaminergic.
NOTE Confidence: 0.733548463333333
00:31:01.650 --> 00:31:03.780 Antidepressants, the answer is yes.
NOTE Confidence: 0.685931305
00:31:06.050 --> 00:31:08.216 And with ketamine and with ECT.
NOTE Confidence: 0.84035224
00:31:09.860 --> 00:31:14.454 Correct. In with TMS I believe as well.
NOTE Confidence: 0.84035224

00:31:14.460 --> 00:31:16.812 Umm, but you know the the change of
NOTE Confidence: 0.84035224

00:31:16.812 --> 00:31:18.377 psychedelics are pretty rapid and
NOTE Confidence: 0.84035224

00:31:18.377 --> 00:31:20.512 they they can be pretty long lasting.
NOTE Confidence: 0.84035224

00:31:20.520 --> 00:31:24.214 And for like the typical, you know,
NOTE Confidence: 0.84035224

00:31:24.214 --> 00:31:27.316 SSRI's, it may take months for
NOTE Confidence: 0.84035224

00:31:27.316 --> 00:31:30.439 these types of changes to occur.
NOTE Confidence: 0.84035224

00:31:30.440 --> 00:31:32.939 In a really elegant study for from
NOTE Confidence: 0.84035224

00:31:32.939 --> 00:31:35.345 some of our colleagues right here
NOTE Confidence: 0.84035224

00:31:35.345 --> 00:31:38.729 at Yale shall it all showed that a
NOTE Confidence: 0.84035224

00:31:38.729 --> 00:31:40.986 single dose of silybin increased spine
NOTE Confidence: 0.84035224

00:31:40.986 --> 00:31:43.614 density in the media prefrontal cortex.
NOTE Confidence: 0.84035224

00:31:43.614 --> 00:31:46.349 It immediately related stress related
NOTE Confidence: 0.84035224

00:31:46.349 --> 00:31:48.498 behavioral deficits using learned
NOTE Confidence: 0.84035224

00:31:48.498 --> 00:31:51.102 helplessness paradigm which is a standard
NOTE Confidence: 0.84035224

00:31:51.102 --> 00:31:54.275 animal model of depression and also
NOTE Confidence: 0.84035224

00:31:54.275 --> 00:31:56.679 also promoted excitatory neurotransmission.

NOTE Confidence: 0.84035224
00:31:56.680 --> 00:31:58.576 So it was really elegant in
NOTE Confidence: 0.84035224
00:31:58.576 --> 00:32:00.410 the sense that it showed.
NOTE Confidence: 0.84035224
00:32:00.410 --> 00:32:02.490 Silas Sylvan could induce
NOTE Confidence: 0.84035224
00:32:02.490 --> 00:32:03.530 morphological changes,
NOTE Confidence: 0.84035224
00:32:03.530 --> 00:32:04.690 structural changes,
NOTE Confidence: 0.84035224
00:32:04.690 --> 00:32:07.590 behavioral changes related to depression,
NOTE Confidence: 0.84035224
00:32:07.590 --> 00:32:08.720 and.
NOTE Confidence: 0.703882562
00:32:10.900 --> 00:32:14.050 Excitatory neurotransmission
NOTE Confidence: 0.703882562
00:32:14.050 --> 00:32:17.200 via electrophysiology.
NOTE Confidence: 0.703882562
00:32:17.200 --> 00:32:20.596 So going back to this plot I showed earlier,
NOTE Confidence: 0.703882562
00:32:20.596 --> 00:32:22.984 one thing to note is this, this,
NOTE Confidence: 0.703882562
00:32:22.984 --> 00:32:26.536 this middle row here is it's in yellow.
NOTE Confidence: 0.703882562
00:32:26.540 --> 00:32:28.320 These are the human studies.
NOTE Confidence: 0.703882562
00:32:28.320 --> 00:32:30.560 And what you can see is most of
NOTE Confidence: 0.703882562
00:32:30.560 --> 00:32:32.953 the human studies have really just
NOTE Confidence: 0.703882562

00:32:32.953 --> 00:32:35.153 looked at peripheral BDNF levels,
NOTE Confidence: 0.703882562

00:32:35.160 --> 00:32:37.070 which are thought to be
NOTE Confidence: 0.703882562

00:32:37.070 --> 00:32:38.216 related to neuroplasticity.
NOTE Confidence: 0.703882562

00:32:38.220 --> 00:32:39.840 And there have been several
NOTE Confidence: 0.703882562

00:32:39.840 --> 00:32:41.136 negative findings as well.
NOTE Confidence: 0.703882562

00:32:41.140 --> 00:32:42.460 But there's a question of,
NOTE Confidence: 0.703882562

00:32:42.460 --> 00:32:44.445 you know, do BDNF levels
NOTE Confidence: 0.703882562

00:32:44.445 --> 00:32:46.430 peripherally reflect being the be.
NOTE Confidence: 0.703882562

00:32:46.430 --> 00:32:49.850 Enough levels in the brain.
NOTE Confidence: 0.703882562

00:32:49.850 --> 00:32:50.930 Which is not highlighted here.
NOTE Confidence: 0.703882562

00:32:50.930 --> 00:32:53.023 There have been some F MRI studies
NOTE Confidence: 0.703882562

00:32:53.023 --> 00:32:54.457 look at functional connectivity
NOTE Confidence: 0.703882562

00:32:54.457 --> 00:32:56.812 in the context of psychedelics
NOTE Confidence: 0.703882562

00:32:56.812 --> 00:32:58.225 showing increased connectivity,
NOTE Confidence: 0.703882562

00:32:58.230 --> 00:33:00.384 but what this really does show
NOTE Confidence: 0.703882562

00:33:00.384 --> 00:33:02.350 is there's a possibility of data

NOTE Confidence: 0.703882562

00:33:02.350 --> 00:33:04.790 using sort of brain measures,

NOTE Confidence: 0.703882562

00:33:04.790 --> 00:33:05.796 especially electrophysiological,

NOTE Confidence: 0.703882562

00:33:05.796 --> 00:33:08.311 in the context of psychedelics

NOTE Confidence: 0.703882562

00:33:08.311 --> 00:33:09.317 and depression.

NOTE Confidence: 0.8438104575

00:33:12.690 --> 00:33:16.980 So how can we non invasively

NOTE Confidence: 0.8438104575

00:33:16.980 --> 00:33:18.410 assess neuroplasticity?

NOTE Confidence: 0.8438104575

00:33:18.410 --> 00:33:21.042 In humans, and one way we could do

NOTE Confidence: 0.8438104575

00:33:21.042 --> 00:33:24.099 it is with long term potentiation.

NOTE Confidence: 0.8438104575

00:33:24.100 --> 00:33:25.876 So one form of synaptic plasticity

NOTE Confidence: 0.8438104575

00:33:25.876 --> 00:33:27.630 is the ability of synapses,

NOTE Confidence: 0.8438104575

00:33:27.630 --> 00:33:29.494 as I mentioned earlier,

NOTE Confidence: 0.8438104575

00:33:29.494 --> 00:33:32.290 to strengthen overtime in response to

NOTE Confidence: 0.8438104575

00:33:32.373 --> 00:33:35.505 increases or decreases in their activity.

NOTE Confidence: 0.8438104575

00:33:35.510 --> 00:33:37.380 The type of synaptic plasticity

NOTE Confidence: 0.8438104575

00:33:37.380 --> 00:33:38.876 that's typically measured is

NOTE Confidence: 0.8438104575

00:33:38.876 --> 00:33:40.590 called long term potentiation,
NOTE Confidence: 0.8438104575

00:33:40.590 --> 00:33:43.416 which is a persistent increase in
NOTE Confidence: 0.8438104575

00:33:43.416 --> 00:33:45.918 synaptic strength followed flood following
NOTE Confidence: 0.8438104575

00:33:45.918 --> 00:33:48.628 high frequency pre synaptic tetanic
NOTE Confidence: 0.8438104575

00:33:48.628 --> 00:33:51.590 stimulation typically at about 100 Hertz.
NOTE Confidence: 0.8438104575

00:33:51.590 --> 00:33:53.380 And it is really this is to be a neural
NOTE Confidence: 0.8438104575

00:33:53.427 --> 00:33:55.360 substrate of learning and memory.
NOTE Confidence: 0.8438104575

00:33:55.360 --> 00:33:57.445 So high frequency Titanic stimulation
NOTE Confidence: 0.8438104575

00:33:57.445 --> 00:34:00.092 of the presynaptic cell will increase
NOTE Confidence: 0.8438104575

00:34:00.092 --> 00:34:02.567 excitability in the postsynaptic cell.
NOTE Confidence: 0.8438104575

00:34:02.570 --> 00:34:04.509 This has been one of the quintessential
NOTE Confidence: 0.8438104575

00:34:04.509 --> 00:34:05.860 models of neuroplasticity going back.
NOTE Confidence: 0.8438104575

00:34:05.860 --> 00:34:07.690 Decades,
NOTE Confidence: 0.8438104575

00:34:07.690 --> 00:34:09.715 and while it's traditionally been
NOTE Confidence: 0.8438104575

00:34:09.715 --> 00:34:11.335 studied in slice preparations,
NOTE Confidence: 0.8438104575

00:34:11.340 --> 00:34:14.746 and it has been done in humans using

NOTE Confidence: 0.8438104575

00:34:14.746 --> 00:34:17.926 exercise tissue some surgical patients,

NOTE Confidence: 0.8438104575

00:34:17.930 --> 00:34:20.960 it's now possible to index LTP

NOTE Confidence: 0.8438104575

00:34:20.960 --> 00:34:23.644 and humans non invasively using

NOTE Confidence: 0.8438104575

00:34:23.644 --> 00:34:25.876 sensory stimulation and EG.

NOTE Confidence: 0.755103465714286

00:34:30.160 --> 00:34:33.219 So this, so this is what the,

NOTE Confidence: 0.755103465714286

00:34:33.220 --> 00:34:35.590 the, the typical paradigm that I'm

NOTE Confidence: 0.755103465714286

00:34:35.590 --> 00:34:37.696 Speaking of entails. And in fact

NOTE Confidence: 0.755103465714286

00:34:37.696 --> 00:34:40.080 this is the very paradigm we used.

NOTE Confidence: 0.755103465714286

00:34:40.080 --> 00:34:42.056 So it's good to pay attention to this.

NOTE Confidence: 0.755103465714286

00:34:42.060 --> 00:34:45.380 So, so we chose this paradigm adapted from

NOTE Confidence: 0.755103465714286

00:34:45.380 --> 00:34:50.480 clap at all 2005 and it's an auditory.

NOTE Confidence: 0.755103465714286

00:34:50.480 --> 00:34:53.699 Sensory LTP paradigm.

NOTE Confidence: 0.755103465714286

00:34:53.700 --> 00:34:55.284 Losing my point here.

NOTE Confidence: 0.755103465714286

00:34:55.284 --> 00:34:58.029 So the way it typically works is

NOTE Confidence: 0.755103465714286

00:34:58.029 --> 00:35:00.935 you have a pre tetanus period where

NOTE Confidence: 0.755103465714286

00:35:00.935 --> 00:35:03.696 you present roughly 120 tone pips.
NOTE Confidence: 0.755103465714286

00:35:03.696 --> 00:35:05.956 They're just 1000 Hertz tones,
NOTE Confidence: 0.755103465714286

00:35:05.960 --> 00:35:08.912 50 milliseconds each and what they
NOTE Confidence: 0.755103465714286

00:35:08.912 --> 00:35:11.851 do is they induce an auditory
NOTE Confidence: 0.755103465714286

00:35:11.851 --> 00:35:14.896 ERP or the way we have analyzed
NOTE Confidence: 0.755103465714286

00:35:14.896 --> 00:35:18.177 it an event related oscillation.
NOTE Confidence: 0.755103465714286

00:35:18.180 --> 00:35:21.438 So this is standard ERP stuff.
NOTE Confidence: 0.755103465714286

00:35:21.440 --> 00:35:22.564 You present a tone,
NOTE Confidence: 0.755103465714286

00:35:22.564 --> 00:35:25.222 you get an ERP or you get an
NOTE Confidence: 0.755103465714286

00:35:25.222 --> 00:35:26.578 event related oscillation.
NOTE Confidence: 0.755103465714286

00:35:26.580 --> 00:35:30.094 And then we do 2 minutes of
NOTE Confidence: 0.755103465714286

00:35:30.094 --> 00:35:32.860 a tetanus at 13 Hertz,
NOTE Confidence: 0.755103465714286

00:35:32.860 --> 00:35:34.612 which has been shown to be
NOTE Confidence: 0.755103465714286

00:35:34.612 --> 00:35:36.240 optimal for the auditory cortex.
NOTE Confidence: 0.755103465714286

00:35:36.240 --> 00:35:38.690 And then we redo the the test
NOTE Confidence: 0.755103465714286

00:35:38.690 --> 00:35:40.918 phase with the same types of

NOTE Confidence: 0.755103465714286
00:35:40.918 --> 00:35:43.480 tone tips as in the pre tetanus.
NOTE Confidence: 0.755103465714286
00:35:43.480 --> 00:35:46.288 And what you can see here is an
NOTE Confidence: 0.755103465714286
00:35:46.288 --> 00:35:49.199 increase in event related oscillations
NOTE Confidence: 0.755103465714286
00:35:49.200 --> 00:35:51.080 particularly in the Theta range.
NOTE Confidence: 0.755103465714286
00:35:51.080 --> 00:35:52.418 And these are actually our data.
NOTE Confidence: 0.755103465714286
00:35:52.420 --> 00:35:54.930 These are about 9 control
NOTE Confidence: 0.755103465714286
00:35:54.930 --> 00:35:57.440 subjects that we used to.
NOTE Confidence: 0.755103465714286
00:35:57.440 --> 00:35:58.142 Deposit the paradigm.
NOTE Confidence: 0.755103465714286
00:35:58.142 --> 00:35:59.780 So this is what you should see
NOTE Confidence: 0.755103465714286
00:35:59.830 --> 00:36:01.528 in a normal individual.
NOTE Confidence: 0.755103465714286
00:36:01.530 --> 00:36:03.108 So is there any questions on,
NOTE Confidence: 0.755103465714286
00:36:03.110 --> 00:36:04.040 on the paradigm
NOTE Confidence: 0.71263241
00:36:05.130 --> 00:36:06.810 ERP is event related potential.
NOTE Confidence: 0.71263241
00:36:06.810 --> 00:36:08.728 So that's like the reliable EG squiggle
NOTE Confidence: 0.71263241
00:36:08.728 --> 00:36:10.678 that comes after a sense risk stimulus,
NOTE Confidence: 0.812873504375

00:36:11.030 --> 00:36:13.116 right. And that's what's typically done with
NOTE Confidence: 0.812873504375

00:36:13.116 --> 00:36:15.197 with this paradigm and we did that as well.
NOTE Confidence: 0.812873504375

00:36:15.200 --> 00:36:16.646 I'm not going to show that,
NOTE Confidence: 0.812873504375

00:36:16.650 --> 00:36:18.744 but I chose event related oscillations
NOTE Confidence: 0.812873504375

00:36:18.744 --> 00:36:20.887 because you really get the same
NOTE Confidence: 0.812873504375

00:36:20.887 --> 00:36:22.602 information but you get added
NOTE Confidence: 0.812873504375

00:36:22.602 --> 00:36:24.176 information about the frequency
NOTE Confidence: 0.812873504375

00:36:24.176 --> 00:36:26.100 characteristics of the response.
NOTE Confidence: 0.812873504375

00:36:26.100 --> 00:36:27.932 Does that make sense? Yeah, yeah.
NOTE Confidence: 0.812873504375

00:36:27.932 --> 00:36:29.180 When you look at an ERP,
NOTE Confidence: 0.812873504375

00:36:29.180 --> 00:36:31.094 you, you really have no idea
NOTE Confidence: 0.812873504375

00:36:31.094 --> 00:36:32.620 what frequency that ERP is.
NOTE Confidence: 0.665498465714286

00:36:34.090 --> 00:36:35.630 Once, but at the time it didn't.
NOTE Confidence: 0.916462891666667

00:36:37.550 --> 00:36:38.618 I'm sorry, I didn't catch that.
NOTE Confidence: 0.76222267

00:36:43.830 --> 00:36:45.162 Someone asking you a question if
NOTE Confidence: 0.76222267

00:36:45.162 --> 00:36:46.900 someone who had need wasn't muted.

NOTE Confidence: 0.84193569

00:36:50.920 --> 00:36:53.139 How long does it last this posted?

NOTE Confidence: 0.84193569

00:36:53.140 --> 00:36:54.952 And it's like this increase in

NOTE Confidence: 0.84193569

00:36:54.952 --> 00:36:57.010 the data band after the auditory.

NOTE Confidence: 0.813057208571428

00:36:59.360 --> 00:37:02.950 How long does the entire task take? How how

NOTE Confidence: 0.88674987

00:37:02.960 --> 00:37:04.955 long do you observe this this effect

NOTE Confidence: 0.88674987

00:37:04.955 --> 00:37:06.920 and and when does it come back?

NOTE Confidence: 0.88674987

00:37:06.920 --> 00:37:09.016 Does it come back to know to the

NOTE Confidence: 0.88674987

00:37:09.016 --> 00:37:10.358 President state after a while?

NOTE Confidence: 0.88674987

00:37:10.360 --> 00:37:12.808 And if yes, after how long?

NOTE Confidence: 0.687597596

00:37:13.380 --> 00:37:14.860 That's a really good question.

NOTE Confidence: 0.687597596

00:37:14.860 --> 00:37:16.258 So we did not test that.

NOTE Confidence: 0.687597596

00:37:16.260 --> 00:37:18.936 But in the original plat study,

NOTE Confidence: 0.687597596

00:37:18.940 --> 00:37:21.796 they observed it up to six

NOTE Confidence: 0.687597596

00:37:21.796 --> 00:37:24.600 hours after after the tetanus.

NOTE Confidence: 0.687597596

00:37:24.600 --> 00:37:27.396 So they observed this increase in,

NOTE Confidence: 0.687597596

00:37:27.400 --> 00:37:29.262 in their case they did ERP's,
NOTE Confidence: 0.687597596

00:37:29.262 --> 00:37:31.236 but they observed it six hours after.
NOTE Confidence: 0.687597596

00:37:31.240 --> 00:37:32.890 They didn't go beyond that.
NOTE Confidence: 0.687597596

00:37:32.890 --> 00:37:35.230 Um, probably just for logistical
NOTE Confidence: 0.687597596

00:37:35.230 --> 00:37:37.102 reasons and subject burden.
NOTE Confidence: 0.687597596

00:37:37.110 --> 00:37:38.664 So it could last longer than that.
NOTE Confidence: 0.687597596

00:37:38.670 --> 00:37:40.404 But they did observe it six
NOTE Confidence: 0.687597596

00:37:40.404 --> 00:37:41.560 hours after the tetanus.
NOTE Confidence: 0.703249597647059

00:37:42.820 --> 00:37:44.550 And maybe you can get in Vivo LP in the
NOTE Confidence: 0.703249597647059

00:37:44.597 --> 00:37:46.326 hippocampus that lasts a month or more.
NOTE Confidence: 0.703249597647059

00:37:46.330 --> 00:37:48.298 So in principle it can last a very
NOTE Confidence: 0.703249597647059

00:37:48.300 --> 00:37:50.080 long time whether that would happen
NOTE Confidence: 0.703249597647059

00:37:50.080 --> 00:37:51.940 in this paradigm, but in principle.
NOTE Confidence: 0.867193963333333

00:37:55.660 --> 00:37:58.200 So this is just a
NOTE Confidence: 0.867193963333333

00:37:58.200 --> 00:38:00.232 reiteration of Jordan slide.
NOTE Confidence: 0.867193963333333

00:38:00.240 --> 00:38:02.322 So just to remind everyone that

NOTE Confidence: 0.867193963333333

00:38:02.322 --> 00:38:05.740 we did EG 24 hours after placebo,

NOTE Confidence: 0.867193963333333

00:38:05.740 --> 00:38:07.232 the first placebo session.

NOTE Confidence: 0.867193963333333

00:38:07.232 --> 00:38:09.470 We did it two weeks after

NOTE Confidence: 0.867193963333333

00:38:09.544 --> 00:38:10.978 the placebo session,

NOTE Confidence: 0.867193963333333

00:38:10.980 --> 00:38:12.748 then we did a 24 hours after the

NOTE Confidence: 0.867193963333333

00:38:12.748 --> 00:38:14.703 style of seven session and then two

NOTE Confidence: 0.867193963333333

00:38:14.703 --> 00:38:16.650 weeks after the Salah seven session.

NOTE Confidence: 0.624813704

00:38:19.140 --> 00:38:21.440 General EEG methods pretty standard.

NOTE Confidence: 0.624813704

00:38:21.440 --> 00:38:23.696 We use the Compton medics and M6 to

NOTE Confidence: 0.624813704

00:38:23.696 --> 00:38:25.617 four channel nurse scan EEG system.

NOTE Confidence: 0.624813704

00:38:25.620 --> 00:38:28.371 Umm. This good to note that all

NOTE Confidence: 0.624813704

00:38:28.371 --> 00:38:30.382 stimuli presented at 80 decibels

NOTE Confidence: 0.624813704

00:38:30.382 --> 00:38:33.028 SPL which is standard and it's kind

NOTE Confidence: 0.624813704

00:38:33.028 --> 00:38:36.061 of the same decimal level as as

NOTE Confidence: 0.624813704

00:38:36.061 --> 00:38:38.228 you know conversation sample rate

NOTE Confidence: 0.624813704

00:38:38.228 --> 00:38:40.418 of 1000 Hertz, bandpass filter,
NOTE Confidence: 0.624813704

00:38:40.420 --> 00:38:42.916 notch filter to get rid of line noise,
NOTE Confidence: 0.624813704

00:38:42.920 --> 00:38:43.678 standard preprocessing,
NOTE Confidence: 0.624813704

00:38:43.678 --> 00:38:46.331 getting rid of bad trials and ocular
NOTE Confidence: 0.624813704

00:38:46.331 --> 00:38:48.479 correction and all data was analyzed using.
NOTE Confidence: 0.624813704

00:38:48.480 --> 00:38:50.620 Brain products and less for 2.0.
NOTE Confidence: 0.961913575

00:38:52.940 --> 00:38:57.256 OK. So this is the event related
NOTE Confidence: 0.961913575

00:38:57.256 --> 00:38:59.216 oscillations across all the conditions.
NOTE Confidence: 0.961913575

00:38:59.220 --> 00:39:00.936 So the first thing to pay
NOTE Confidence: 0.961913575

00:39:00.936 --> 00:39:02.719 attention to is the top left.
NOTE Confidence: 0.961913575

00:39:02.720 --> 00:39:06.208 So this is the day after placebo and
NOTE Confidence: 0.961913575

00:39:06.208 --> 00:39:09.918 what you can see is we observe no
NOTE Confidence: 0.961913575

00:39:09.918 --> 00:39:13.099 LTP pre tetanus versus post tetanus.
NOTE Confidence: 0.961913575

00:39:13.100 --> 00:39:14.932 So they related oscillations
NOTE Confidence: 0.961913575

00:39:14.932 --> 00:39:17.222 in the Theta band identical.
NOTE Confidence: 0.813215812727273

00:39:19.330 --> 00:39:22.150 Suggesting that perhaps in this depressed

NOTE Confidence: 0.813215812727273
00:39:22.150 --> 00:39:24.370 population they have impaired LTP.
NOTE Confidence: 0.813215812727273
00:39:24.370 --> 00:39:26.600 But that's speculative at this
NOTE Confidence: 0.813215812727273
00:39:26.600 --> 00:39:28.359 point because we did see it in our,
NOTE Confidence: 0.813215812727273
00:39:28.360 --> 00:39:31.810 at least our pilot control study.
NOTE Confidence: 0.813215812727273
00:39:31.810 --> 00:39:35.248 Likewise, 2 weeks after placebo, same thing.
NOTE Confidence: 0.813215812727273
00:39:35.248 --> 00:39:41.090 No, no LTP from pre tetanus to post tetanus.
NOTE Confidence: 0.813215812727273
00:39:41.090 --> 00:39:42.580 Moving on to Silo Sybian,
NOTE Confidence: 0.813215812727273
00:39:42.580 --> 00:39:44.968 so 24 hours after Silas Sabin.
NOTE Confidence: 0.813215812727273
00:39:44.970 --> 00:39:47.705 Again no change from pre
NOTE Confidence: 0.813215812727273
00:39:47.705 --> 00:39:49.893 tetanus to post tetanus.
NOTE Confidence: 0.813215812727273
00:39:49.900 --> 00:39:53.050 And the other thing to note is the amplitude
NOTE Confidence: 0.813215812727273
00:39:53.050 --> 00:39:55.668 or the power of the Theta responses
NOTE Confidence: 0.813215812727273
00:39:55.668 --> 00:39:58.768 were the same in all these conditions.
NOTE Confidence: 0.813215812727273
00:39:58.770 --> 00:40:00.905 The thing that was we weren't expecting,
NOTE Confidence: 0.813215812727273
00:40:00.910 --> 00:40:03.352 which is really the interesting thing
NOTE Confidence: 0.813215812727273

00:40:03.352 --> 00:40:06.538 of this study is we found we we
NOTE Confidence: 0.813215812727273

00:40:06.538 --> 00:40:08.752 didn't see pre tetanus versus post
NOTE Confidence: 0.813215812727273

00:40:08.837 --> 00:40:11.627 tetanus 2 weeks after silaban either,
NOTE Confidence: 0.813215812727273

00:40:11.630 --> 00:40:14.708 but we saw an almost doubling
NOTE Confidence: 0.813215812727273

00:40:14.708 --> 00:40:18.049 of data power just in general.
NOTE Confidence: 0.813215812727273

00:40:18.050 --> 00:40:19.653 And these are just the bar graphs
NOTE Confidence: 0.813215812727273

00:40:19.653 --> 00:40:23.380 showing what I just showed, so.
NOTE Confidence: 0.813215812727273

00:40:23.380 --> 00:40:24.478 The difference?
NOTE Confidence: 0.813215812727273

00:40:24.478 --> 00:40:27.223 Pre tetanus post tetanus 24
NOTE Confidence: 0.813215812727273

00:40:27.223 --> 00:40:30.079 hours after two weeks after,
NOTE Confidence: 0.813215812727273

00:40:30.080 --> 00:40:33.056 maybe a little bit two weeks after here.
NOTE Confidence: 0.813215812727273

00:40:33.060 --> 00:40:34.551 Not significant though.
NOTE Confidence: 0.813215812727273

00:40:34.551 --> 00:40:37.533 Nothing the day after Silas Syben.
NOTE Confidence: 0.813215812727273

00:40:37.540 --> 00:40:40.956 And then you see this doubling of data
NOTE Confidence: 0.813215812727273

00:40:40.956 --> 00:40:44.039 power two weeks after Silas Simon.
NOTE Confidence: 0.813215812727273

00:40:44.040 --> 00:40:46.756 And the really intriguing part of this

NOTE Confidence: 0.813215812727273

00:40:46.756 --> 00:40:49.756 study is that we found that change

NOTE Confidence: 0.813215812727273

00:40:49.756 --> 00:40:53.224 in AMD scores after Salas Livin.

NOTE Confidence: 0.813215812727273

00:40:53.230 --> 00:40:55.046 Negatively correlated with change

NOTE Confidence: 0.813215812727273

00:40:55.046 --> 00:40:56.408 in Theta power.

NOTE Confidence: 0.813215812727273

00:40:56.410 --> 00:40:59.090 So an easy way to to say this is those

NOTE Confidence: 0.813215812727273

00:40:59.168 --> 00:41:01.218 individuals that had the greatest

NOTE Confidence: 0.813215812727273

00:41:01.218 --> 00:41:04.189 decrease in their hand D scores had

NOTE Confidence: 0.813215812727273

00:41:04.189 --> 00:41:07.157 the greatest increase in their Theta power.

NOTE Confidence: 0.806098537857143

00:41:13.370 --> 00:41:15.874 Sorry, was it computed at the brain level

NOTE Confidence: 0.806098537857143

00:41:15.874 --> 00:41:18.710 or on specific clusters of electrodes?

NOTE Confidence: 0.75650941

00:41:19.890 --> 00:41:22.034 That's a good question.

NOTE Confidence: 0.75650941

00:41:22.034 --> 00:41:25.061 We used electrode FCZ umm because

NOTE Confidence: 0.75650941

00:41:25.061 --> 00:41:27.789 that's we typically we do that a lot.

NOTE Confidence: 0.75650941

00:41:27.790 --> 00:41:30.429 That's just where the signal was maximal,

NOTE Confidence: 0.75650941

00:41:30.430 --> 00:41:32.100 which is typical for auditory

NOTE Confidence: 0.75650941

00:41:32.100 --> 00:41:34.666 stimuli to have the front of central
NOTE Confidence: 0.75650941

00:41:34.666 --> 00:41:36.326 electrodes have Max responses.
NOTE Confidence: 0.75650941

00:41:36.330 --> 00:41:39.060 So we just competed this at FCZ.
NOTE Confidence: 0.838166102222222

00:41:41.680 --> 00:41:44.638 Patrick, the the because of the
NOTE Confidence: 0.838166102222222

00:41:44.638 --> 00:41:47.046 fixed order here, you can't.
NOTE Confidence: 0.838166102222222

00:41:47.046 --> 00:41:50.287 Am I right that you can't disambiguate
NOTE Confidence: 0.838166102222222

00:41:50.287 --> 00:41:53.224 whether the increase in power that you
NOTE Confidence: 0.838166102222222

00:41:53.224 --> 00:41:56.086 see pre tetanus at 2 weeks is related
NOTE Confidence: 0.838166102222222

00:41:56.086 --> 00:41:58.242 to the tetanus given at one day?
NOTE Confidence: 0.664559324

00:42:02.460 --> 00:42:04.320 Well, this correlation has changed.
NOTE Confidence: 0.664559324

00:42:04.320 --> 00:42:07.650 This I I should specify this
NOTE Confidence: 0.664559324

00:42:07.650 --> 00:42:11.480 correlation is change from.
NOTE Confidence: 0.664559324

00:42:11.480 --> 00:42:13.580 24 hours post silacci ibin
NOTE Confidence: 0.664559324

00:42:13.580 --> 00:42:15.428 to two weeks psilocybin.
NOTE Confidence: 0.760934485333333

00:42:15.860 --> 00:42:17.967 I'm sorry but I've been just in
NOTE Confidence: 0.760934485333333

00:42:17.967 --> 00:42:20.566 the EG if you go back one slide.

NOTE Confidence: 0.760934485333333
00:42:20.570 --> 00:42:21.836 So I don't know if this
NOTE Confidence: 0.760934485333333
00:42:21.836 --> 00:42:22.734 makes any sense or not,
NOTE Confidence: 0.760934485333333
00:42:22.734 --> 00:42:24.316 but this is just where my mind is going.
NOTE Confidence: 0.760934485333333
00:42:24.316 --> 00:42:25.690 So you're giving a tetanus one
NOTE Confidence: 0.760934485333333
00:42:25.745 --> 00:42:28.280 day after psilocybin, right?
NOTE Confidence: 0.760934485333333
00:42:28.280 --> 00:42:30.824 And you see no change in power one
NOTE Confidence: 0.760934485333333
00:42:30.824 --> 00:42:32.870 hour after that tetanus, right?
NOTE Confidence: 0.788279707058824
00:42:33.990 --> 00:42:35.394 It's shorter than that.
NOTE Confidence: 0.788279707058824
00:42:35.394 --> 00:42:37.909 It it it's it's about it's about
NOTE Confidence: 0.788279707058824
00:42:37.909 --> 00:42:39.895 8 minutes of the tone pips,
NOTE Confidence: 0.788279707058824
00:42:39.900 --> 00:42:42.732 2 minutes of tetanus and then
NOTE Confidence: 0.788279707058824
00:42:42.732 --> 00:42:45.177 another two another 8 minutes
NOTE Confidence: 0.788279707058824
00:42:45.177 --> 00:42:47.628 of the does it make sense?
NOTE Confidence: 0.632368769090909
00:42:49.020 --> 00:42:50.994 Only no enhancement of LTP immediately
NOTE Confidence: 0.632368769090909
00:42:50.994 --> 00:42:53.303 within minutes after the tenants, correct?
NOTE Confidence: 0.632368769090909

00:42:53.303 --> 00:42:55.662 But suppose you got an enhancement
NOTE Confidence: 0.632368769090909

00:42:55.662 --> 00:42:58.260 of LTP an hour after the tetanus.
NOTE Confidence: 0.839599677142857

00:43:01.050 --> 00:43:03.346 See that in your week four data?
NOTE Confidence: 0.839599677142857

00:43:03.350 --> 00:43:05.890 Because you're looking too soon.
NOTE Confidence: 0.839599677142857

00:43:05.890 --> 00:43:08.968 And that could be the cause.
NOTE Confidence: 0.839599677142857

00:43:08.970 --> 00:43:11.022 Of the increase that you see at 2 weeks,
NOTE Confidence: 0.839599677142857

00:43:11.030 --> 00:43:14.210 it could be long lasting LTP.
NOTE Confidence: 0.839599677142857

00:43:14.210 --> 00:43:18.725 Obviously enhanced could be long lasting LTP.
NOTE Confidence: 0.839599677142857

00:43:18.730 --> 00:43:21.980 From the Week 4 stimulus, right. You
NOTE Confidence: 0.828642926363636

00:43:21.990 --> 00:43:23.525 know that's a really interesting
NOTE Confidence: 0.828642926363636

00:43:23.525 --> 00:43:24.753 interpretation that I didn't
NOTE Confidence: 0.828642926363636

00:43:24.753 --> 00:43:26.998 think of. Yeah, so you don't
NOTE Confidence: 0.801743842

00:43:27.010 --> 00:43:28.590 that we didn't see any change
NOTE Confidence: 0.801743842

00:43:28.590 --> 00:43:31.389 from that initial week 02 weeks.
NOTE Confidence: 0.801743842

00:43:31.390 --> 00:43:33.980 I would clearly it would be 4 weeks
NOTE Confidence: 0.560522518333333

00:43:33.990 --> 00:43:35.724 and you have a silybin effect, right.

NOTE Confidence: 0.560522518333333
00:43:35.724 --> 00:43:38.342 So it could either be that psilocybin
NOTE Confidence: 0.560522518333333
00:43:38.342 --> 00:43:40.315 is enhancing Theta in a completely
NOTE Confidence: 0.560522518333333
00:43:40.315 --> 00:43:42.240 non contingent way that you know two
NOTE Confidence: 0.560522518333333
00:43:42.297 --> 00:43:44.103 weeks after psilocybin you have an
NOTE Confidence: 0.560522518333333
00:43:44.103 --> 00:43:46.002 increased in the Theta that's induced
NOTE Confidence: 0.560522518333333
00:43:46.002 --> 00:43:47.904 by these auditory pips full stop,
NOTE Confidence: 0.560522518333333
00:43:47.910 --> 00:43:49.947 has nothing to do with the tetanus.
NOTE Confidence: 0.560522518333333
00:43:49.950 --> 00:43:54.950 Or it could be that it is psilocybin
NOTE Confidence: 0.560522518333333
00:43:54.950 --> 00:43:57.740 increases plasticity it increases.
NOTE Confidence: 0.560522518333333
00:43:57.740 --> 00:44:00.316 Plasticity produce in a long lasting way,
NOTE Confidence: 0.560522518333333
00:44:00.320 --> 00:44:03.210 it's just that you don't see it at 8 minutes.
NOTE Confidence: 0.560522518333333
00:44:03.210 --> 00:44:05.030 You see it sometime hours or days
NOTE Confidence: 0.560522518333333
00:44:05.030 --> 00:44:07.169 after and it persists for two weeks.
NOTE Confidence: 0.560522518333333
00:44:07.170 --> 00:44:08.220 And because of the fixed story,
NOTE Confidence: 0.560522518333333
00:44:08.220 --> 00:44:10.210 you can't, you can't disambiguate
NOTE Confidence: 0.560522518333333

00:44:10.210 --> 00:44:11.190 those from this design.
NOTE Confidence: 0.5605225183333333

00:44:11.190 --> 00:44:13.017 But it's it's just this may be
NOTE Confidence: 0.5605225183333333

00:44:13.017 --> 00:44:13.975 a plasticity effect, right?
NOTE Confidence: 0.5605225183333333

00:44:13.975 --> 00:44:15.375 This may be a result of your tetanus.
NOTE Confidence: 0.5605225183333333

00:44:15.380 --> 00:44:17.277 It's just taking just manifesting much later.
NOTE Confidence: 0.739229506

00:44:18.380 --> 00:44:19.500 What it it's a great,
NOTE Confidence: 0.739229506

00:44:19.500 --> 00:44:20.308 it's a great point.
NOTE Confidence: 0.739229506

00:44:20.308 --> 00:44:21.520 I didn't think of that interpretation.
NOTE Confidence: 0.739229506

00:44:21.520 --> 00:44:23.560 I think either way it's a plasticity effect.
NOTE Confidence: 0.739229506

00:44:23.560 --> 00:44:27.176 It could be like you said the places
NOTE Confidence: 0.739229506

00:44:27.180 --> 00:44:29.430 plasticity effect from the tetanus
NOTE Confidence: 0.739229506

00:44:29.430 --> 00:44:32.659 just takes longer to kick in for back.
NOTE Confidence: 0.739229506

00:44:32.660 --> 00:44:36.386 Lack of a better phrase or.
NOTE Confidence: 0.739229506

00:44:36.390 --> 00:44:38.077 The way we've thought about it with
NOTE Confidence: 0.739229506

00:44:38.077 --> 00:44:39.590 this paper is in in revision.
NOTE Confidence: 0.739229506

00:44:39.590 --> 00:44:41.702 So the way we framed it is we

NOTE Confidence: 0.739229506

00:44:41.702 --> 00:44:43.753 think this increase in Theta in

NOTE Confidence: 0.739229506

00:44:43.753 --> 00:44:45.931 general is sort of a qualitatively

NOTE Confidence: 0.739229506

00:44:46.003 --> 00:44:47.919 different type of plasticity.

NOTE Confidence: 0.760532966190476

00:44:50.700 --> 00:44:53.024 But yeah, in the mechanisms of synaptic

NOTE Confidence: 0.760532966190476

00:44:53.024 --> 00:44:54.986 plasticity the they were qualitatively

NOTE Confidence: 0.760532966190476

00:44:54.986 --> 00:44:56.806 different mechanisms involved in

NOTE Confidence: 0.760532966190476

00:44:56.806 --> 00:44:59.140 short term plasticity lasting minutes.

NOTE Confidence: 0.760532966190476

00:44:59.140 --> 00:45:00.904 Then there are in plasticity that

NOTE Confidence: 0.760532966190476

00:45:00.904 --> 00:45:02.891 lasts hours or days they're completely

NOTE Confidence: 0.760532966190476

00:45:02.891 --> 00:45:04.756 and you can dissociate them.

NOTE Confidence: 0.760532966190476

00:45:04.760 --> 00:45:05.288 That's actually.

NOTE Confidence: 0.760532966190476

00:45:05.288 --> 00:45:07.816 This is actually what I did my PhD thesis

NOTE Confidence: 0.760532966190476

00:45:07.816 --> 00:45:09.988 on was blocking long lasting plasticity

NOTE Confidence: 0.760532966190476

00:45:09.988 --> 00:45:11.959 without affecting short term plasticity.

NOTE Confidence: 0.760532966190476

00:45:11.960 --> 00:45:14.354 You can also enhance long lasting plasticity

NOTE Confidence: 0.760532966190476

00:45:14.354 --> 00:45:17.300 without affecting short term plasticity.
NOTE Confidence: 0.760532966190476

00:45:17.300 --> 00:45:19.616 So depending on the mechanisms whereby.
NOTE Confidence: 0.760532966190476

00:45:19.620 --> 00:45:21.528 Hillside and is acting on plasticity.
NOTE Confidence: 0.760532966190476

00:45:21.530 --> 00:45:23.402 It it's it's very plausible that
NOTE Confidence: 0.760532966190476

00:45:23.402 --> 00:45:25.841 it could have not have a short term
NOTE Confidence: 0.760532966190476

00:45:25.841 --> 00:45:28.030 effect but have a long term effect.
NOTE Confidence: 0.760532966190476

00:45:28.030 --> 00:45:30.590 So I think that's an important your date.
NOTE Confidence: 0.760532966190476

00:45:30.590 --> 00:45:31.850 This is a discussion point is not
NOTE Confidence: 0.760532966190476

00:45:31.850 --> 00:45:32.828 something your data can speak to,
NOTE Confidence: 0.760532966190476

00:45:32.830 --> 00:45:33.990 but it's an important possibility
NOTE Confidence: 0.760532966190476

00:45:33.990 --> 00:45:36.125 to to think, to think about when
NOTE Confidence: 0.760532966190476

00:45:36.125 --> 00:45:37.590 looking at future studies.
NOTE Confidence: 0.760532966190476

00:45:37.590 --> 00:45:40.285 If this were a non contingent effect,
NOTE Confidence: 0.760532966190476

00:45:40.290 --> 00:45:41.530 meaning if this had nothing
NOTE Confidence: 0.760532966190476

00:45:41.530 --> 00:45:42.770 to do with the tetanus,
NOTE Confidence: 0.760532966190476

00:45:42.770 --> 00:45:45.008 it would be startling to me.

NOTE Confidence: 0.760532966190476
00:45:45.010 --> 00:45:46.914 If you do you do you see any
NOTE Confidence: 0.760532966190476
00:45:46.914 --> 00:45:48.858 effects in Theta in resting Theta?
NOTE Confidence: 0.760532966190476
00:45:48.860 --> 00:45:51.667 If you just look at your resting
NOTE Confidence: 0.760532966190476
00:45:51.667 --> 00:45:54.968 EEG if this were a non contingent.
NOTE Confidence: 0.760532966190476
00:45:54.970 --> 00:45:57.440 Change in brain wiring that
NOTE Confidence: 0.760532966190476
00:45:57.440 --> 00:45:59.416 causes enhanced Theta power.
NOTE Confidence: 0.760532966190476
00:45:59.420 --> 00:46:02.980 You should see something in your resting age.
NOTE Confidence: 0.760532966190476
00:46:02.980 --> 00:46:05.167 And if you only see it with your stimulation,
NOTE Confidence: 0.760532966190476
00:46:05.170 --> 00:46:06.958 then that makes it sound like
NOTE Confidence: 0.760532966190476
00:46:06.958 --> 00:46:08.600 it's a circuit specific effect,
NOTE Confidence: 0.760532966190476
00:46:08.600 --> 00:46:10.769 which makes it to my mind more likely to
NOTE Confidence: 0.760532966190476
00:46:10.769 --> 00:46:13.210 be a late effect of your of your tetanus.
NOTE Confidence: 0.840154716666667
00:46:14.330 --> 00:46:15.805 Yeah, we didn't see anything
NOTE Confidence: 0.840154716666667
00:46:15.805 --> 00:46:16.985 in the resting Theta.
NOTE Confidence: 0.840154716666667
00:46:16.990 --> 00:46:19.566 In fact if you did so this
NOTE Confidence: 0.840154716666667

00:46:19.566 --> 00:46:21.190 this dashed line here,
NOTE Confidence: 0.840154716666667

00:46:21.190 --> 00:46:22.339 that's stimulus onset.
NOTE Confidence: 0.840154716666667

00:46:22.339 --> 00:46:25.410 So if you saw differences in resting data,
NOTE Confidence: 0.840154716666667

00:46:25.410 --> 00:46:26.964 you would actually see it in this,
NOTE Confidence: 0.840154716666667

00:46:26.970 --> 00:46:28.430 in this window here,
NOTE Confidence: 0.840154716666667

00:46:28.430 --> 00:46:31.910 this pre stimulus window, so.
NOTE Confidence: 0.840154716666667

00:46:31.910 --> 00:46:32.996 But this is a great point.
NOTE Confidence: 0.840154716666667

00:46:33.000 --> 00:46:36.295 It goes back to that plot I showed
NOTE Confidence: 0.840154716666667

00:46:36.295 --> 00:46:38.305 earlier with the different time courses,
NOTE Confidence: 0.840154716666667

00:46:38.310 --> 00:46:41.200 from the early, immediate early
NOTE Confidence: 0.840154716666667

00:46:41.200 --> 00:46:44.550 genes to the synaptogenesis and the.
NOTE Confidence: 0.840154716666667

00:46:44.550 --> 00:46:47.870 Increase in dendritic spines.
NOTE Confidence: 0.840154716666667

00:46:47.870 --> 00:46:50.005 The one study from I think it's
NOTE Confidence: 0.840154716666667

00:46:50.005 --> 00:46:52.326 Ravel at all showed that in pig
NOTE Confidence: 0.840154716666667

00:46:52.326 --> 00:46:54.450 brain a single dose of Cialis
NOTE Confidence: 0.840154716666667

00:46:54.450 --> 00:46:56.747 Cybin you don't see increases in

NOTE Confidence: 0.840154716666667
00:46:56.747 --> 00:46:58.479 synaptic density until about.
NOTE Confidence: 0.840154716666667
00:46:58.480 --> 00:46:59.881 Seven days after.
NOTE Confidence: 0.840154716666667
00:46:59.881 --> 00:47:02.683 And that also makes sense because
NOTE Confidence: 0.840154716666667
00:47:02.683 --> 00:47:05.951 the way what EG is measuring
NOTE Confidence: 0.840154716666667
00:47:05.951 --> 00:47:08.123 is thousands of postsynaptic
NOTE Confidence: 0.840154716666667
00:47:08.123 --> 00:47:10.538 potentials from pyramidal cells.
NOTE Confidence: 0.840154716666667
00:47:10.540 --> 00:47:13.738 So if you have increased spine
NOTE Confidence: 0.840154716666667
00:47:13.738 --> 00:47:15.337 density and synaptogenesis,
NOTE Confidence: 0.840154716666667
00:47:15.340 --> 00:47:17.800 you're going to see increase
NOTE Confidence: 0.840154716666667
00:47:17.800 --> 00:47:18.864 ERP's and increase power.
NOTE Confidence: 0.840154716666667
00:47:18.864 --> 00:47:20.460 So that's sort of the way
NOTE Confidence: 0.840154716666667
00:47:20.516 --> 00:47:21.680 we're thinking about it.
NOTE Confidence: 0.745830042666667
00:47:25.980 --> 00:47:27.440 So just in summary,
NOTE Confidence: 0.745830042666667
00:47:27.440 --> 00:47:29.630 EG long interpretation was not observed
NOTE Confidence: 0.745830042666667
00:47:29.695 --> 00:47:31.800 in this sample depressed subjects,
NOTE Confidence: 0.745830042666667

00:47:31.800 --> 00:47:36.112 we did it observe increased Theta power which
NOTE Confidence: 0.745830042666667

00:47:36.112 --> 00:47:39.410 correlated with decreases in depression.
NOTE Confidence: 0.745830042666667

00:47:39.410 --> 00:47:41.672 This increased Theta power post Silas
NOTE Confidence: 0.745830042666667

00:47:41.672 --> 00:47:43.180 statement is objective evidence
NOTE Confidence: 0.745830042666667

00:47:43.238 --> 00:47:44.483 of sustained electrophysiological
NOTE Confidence: 0.745830042666667

00:47:44.483 --> 00:47:46.973 changes in the brain produced by
NOTE Confidence: 0.745830042666667

00:47:46.973 --> 00:47:49.358 Psylocybe bin and given the correlation
NOTE Confidence: 0.745830042666667

00:47:49.358 --> 00:47:50.504 with decreased depression,
NOTE Confidence: 0.745830042666667

00:47:50.510 --> 00:47:52.856 this may represent a biomarker response
NOTE Confidence: 0.745830042666667

00:47:52.856 --> 00:47:55.260 to Silas cyber couple limitations.
NOTE Confidence: 0.745830042666667

00:47:55.260 --> 00:47:57.612 We didn't have a control group to
NOTE Confidence: 0.745830042666667

00:47:57.612 --> 00:47:59.790 compare the EEG LTE LTP outcome.
NOTE Confidence: 0.745830042666667

00:47:59.790 --> 00:48:01.210 We do have pilot data,
NOTE Confidence: 0.745830042666667

00:48:01.210 --> 00:48:03.968 but we don't have the longitudinal 4
NOTE Confidence: 0.745830042666667

00:48:03.968 --> 00:48:06.930 test days with with control subjects,
NOTE Confidence: 0.745830042666667

00:48:06.930 --> 00:48:09.418 so it's unclear if if that lack of.

NOTE Confidence: 0.745830042666667
00:48:09.420 --> 00:48:11.996 LP was it because that these are depressed
NOTE Confidence: 0.745830042666667
00:48:11.996 --> 00:48:14.347 people and that's impaired in general.
NOTE Confidence: 0.745830042666667
00:48:14.350 --> 00:48:16.569 So that's an area of future study.
NOTE Confidence: 0.745830042666667
00:48:16.570 --> 00:48:19.566 We didn't have any baseline EEG measures,
NOTE Confidence: 0.745830042666667
00:48:19.570 --> 00:48:21.970 you know, before the.
NOTE Confidence: 0.745830042666667
00:48:21.970 --> 00:48:22.714 The sequence started,
NOTE Confidence: 0.745830042666667
00:48:22.714 --> 00:48:24.670 but I think because there's a placebo arm,
NOTE Confidence: 0.745830042666667
00:48:24.670 --> 00:48:27.526 I don't think that's a big limitation.
NOTE Confidence: 0.745830042666667
00:48:27.530 --> 00:48:28.638 I should mention that
NOTE Confidence: 0.745830042666667
00:48:28.638 --> 00:48:29.746 the effective data pile,
NOTE Confidence: 0.745830042666667
00:48:29.750 --> 00:48:32.207 we're actually at trend level at .07,
NOTE Confidence: 0.745830042666667
00:48:32.210 --> 00:48:33.638 so that's probably due
NOTE Confidence: 0.745830042666667
00:48:33.638 --> 00:48:35.423 to the small sample size.
NOTE Confidence: 0.745830042666667
00:48:35.430 --> 00:48:37.420 But we think these limitations
NOTE Confidence: 0.745830042666667
00:48:37.420 --> 00:48:39.012 notwithstanding these results complement
NOTE Confidence: 0.745830042666667

00:48:39.012 --> 00:48:41.354 the emerging notion that Silas Syben
NOTE Confidence: 0.745830042666667

00:48:41.354 --> 00:48:42.862 and perhaps other psychedelics,
NOTE Confidence: 0.745830042666667

00:48:42.870 --> 00:48:44.547 classical psychedelics can
NOTE Confidence: 0.745830042666667

00:48:44.547 --> 00:48:46.783 produce long-term alterations in
NOTE Confidence: 0.745830042666667

00:48:46.783 --> 00:48:48.914 neuroplasticity as assessed via
NOTE Confidence: 0.745830042666667

00:48:48.914 --> 00:48:51.224 electrophysiology or EEG in this case.
NOTE Confidence: 0.8139732

00:48:54.820 --> 00:48:56.222 All right. And that's what
NOTE Confidence: 0.8139732

00:48:56.222 --> 00:48:57.830 I ask from the EEG portion.
NOTE Confidence: 0.798996604

00:48:59.810 --> 00:49:00.866 Patrick, it's Jerry.
NOTE Confidence: 0.798996604

00:49:00.866 --> 00:49:03.330 So I understand your logic by not
NOTE Confidence: 0.798996604

00:49:03.402 --> 00:49:07.170 doing it before the placebo, but.
NOTE Confidence: 0.798996604

00:49:07.170 --> 00:49:09.450 The studies that I know and
NOTE Confidence: 0.798996604

00:49:09.450 --> 00:49:10.970 depression actually the best
NOTE Confidence: 0.798996604

00:49:11.044 --> 00:49:13.486 predictor is EG of placebo response.
NOTE Confidence: 0.798996604

00:49:13.490 --> 00:49:15.583 You know, the Lucia's data and others
NOTE Confidence: 0.798996604

00:49:15.583 --> 00:49:18.070 that that's a pretty powerful predictor.

NOTE Confidence: 0.798996604

00:49:18.070 --> 00:49:20.408 In fact, I think they're trying to

NOTE Confidence: 0.798996604

00:49:20.408 --> 00:49:22.169 develop whole methodologies of predicting

NOTE Confidence: 0.69431736

00:49:22.590 --> 00:49:24.565 predictor of what predictor of

NOTE Confidence: 0.69431736

00:49:24.565 --> 00:49:26.145 clinical response to antidepressant.

NOTE Confidence: 0.425537339285714

00:49:26.290 --> 00:49:30.609 Yeah, with with EG to to placebo.

NOTE Confidence: 0.79654087625

00:49:32.640 --> 00:49:35.216 But so the the thought was you weren't,

NOTE Confidence: 0.79654087625

00:49:35.220 --> 00:49:36.520 you weren't really interested in

NOTE Confidence: 0.79654087625

00:49:36.520 --> 00:49:37.820 the placebo response that's why

NOTE Confidence: 0.79654087625

00:49:37.866 --> 00:49:39.245 you didn't do it prior to placebo?

NOTE Confidence: 0.555509314285714

00:49:41.600 --> 00:49:45.968 But Jerry, EG what EEG measure and

NOTE Confidence: 0.763873339285714

00:49:45.980 --> 00:49:48.059 they they have, they're looking at alpha

NOTE Confidence: 0.763873339285714

00:49:48.059 --> 00:49:50.237 and gamma and a few other things in

NOTE Confidence: 0.763873339285714

00:49:50.237 --> 00:49:52.346 the resting part of it is proprietary,

NOTE Confidence: 0.763873339285714

00:49:52.346 --> 00:49:54.440 so you don't know exactly what.

NOTE Confidence: 0.763873339285714

00:49:54.440 --> 00:49:57.800 What the whole set of measures are,

NOTE Confidence: 0.763873339285714

00:49:57.800 --> 00:49:59.952 but and they're looking at resting and then

NOTE Confidence: 0.763873339285714

00:49:59.952 --> 00:50:01.716 they look at the change after placebo.

NOTE Confidence: 0.73806334

00:50:04.940 --> 00:50:06.900 Yeah, it's a fairpoint. I guess we

NOTE Confidence: 0.73806334

00:50:06.900 --> 00:50:08.100 were thinking about subject burden,

NOTE Confidence: 0.879723385

00:50:08.100 --> 00:50:10.452 but you know maybe in retrospect we we

NOTE Confidence: 0.879723385

00:50:10.452 --> 00:50:13.696 should have had a a baseline EEG before

NOTE Confidence: 0.879723385

00:50:13.696 --> 00:50:16.350 before placebo and the whole sequence.

NOTE Confidence: 0.743849627333333

00:50:16.360 --> 00:50:17.535 I can understand that that's

NOTE Confidence: 0.743849627333333

00:50:17.535 --> 00:50:18.710 a that's a pretty heavy

NOTE Confidence: 0.743849627333333

00:50:18.764 --> 00:50:20.079 burden on people right there.

NOTE Confidence: 0.743849627333333

00:50:20.080 --> 00:50:21.020 You want to minimize it,

NOTE Confidence: 0.743849627333333

00:50:21.020 --> 00:50:22.680 but that that was the reason

NOTE Confidence: 0.743849627333333

00:50:22.680 --> 00:50:25.500 we didn't do it subject burden.

NOTE Confidence: 0.621349538333333

00:50:28.590 --> 00:50:30.156 Yeah, these edges take, you know,

NOTE Confidence: 0.621349538333333

00:50:30.160 --> 00:50:31.260 these are very depressed people.

NOTE Confidence: 0.621349538333333

00:50:31.260 --> 00:50:33.570 They take about 3 hours.

NOTE Confidence: 0.621349538333333
00:50:33.570 --> 00:50:36.962 Our hour and a half set up hour
NOTE Confidence: 0.621349538333333
00:50:36.962 --> 00:50:41.030 of task and. No. Debriefing
NOTE Confidence: 0.638522108
00:50:41.120 --> 00:50:43.040 you're doing pre post stimulation.
NOTE Confidence: 0.638522108
00:50:43.040 --> 00:50:44.670 I think that's the lesson, the concerns.
NOTE Confidence: 0.3850543
00:50:49.400 --> 00:50:51.794 So do you have a couple more slides?
NOTE Confidence: 0.797025342857143
00:50:51.800 --> 00:50:53.438 But if there's that, I could show.
NOTE Confidence: 0.797025342857143
00:50:53.440 --> 00:50:55.280 But if there's other questions,
NOTE Confidence: 0.797025342857143
00:50:55.280 --> 00:50:57.521 you could do you now or I could wrap
NOTE Confidence: 0.797025342857143
00:50:57.521 --> 00:51:01.270 up my slides, but you would want to.
NOTE Confidence: 0.797025342857143
00:51:01.270 --> 00:51:04.010 Ask anything about the Lego piece.
NOTE Confidence: 0.905390387142857
00:51:06.100 --> 00:51:07.549 Can I ask you a quick question?
NOTE Confidence: 0.84455884
00:51:09.330 --> 00:51:13.220 Sure. Hi, this is Pasha. I'm MD,
NOTE Confidence: 0.657059395
00:51:13.230 --> 00:51:14.670 pH. D student in Alex Kwanzaa.
NOTE Confidence: 0.657059395
00:51:14.670 --> 00:51:15.980 So I actually did the ethers for
NOTE Confidence: 0.657059395
00:51:15.980 --> 00:51:17.486 the shall at all paper that you
NOTE Confidence: 0.657059395

00:51:17.486 --> 00:51:19.270 showed and I'm doing in vivo now.
NOTE Confidence: 0.657059395

00:51:19.270 --> 00:51:21.646 So we're trying to think of like more
NOTE Confidence: 0.657059395

00:51:21.650 --> 00:51:23.760 reverse translationally relevant.
NOTE Confidence: 0.919370516666667

00:51:24.470 --> 00:51:25.160 Did you look
NOTE Confidence: 0.909420536666667

00:51:25.170 --> 00:51:26.358 at any of the other bands?
NOTE Confidence: 0.859798971111111

00:51:26.370 --> 00:51:28.230 Because I know there's been
NOTE Confidence: 0.859798971111111

00:51:28.230 --> 00:51:29.718 some work in preclinical
NOTE Confidence: 0.77018512625

00:51:29.730 --> 00:51:30.550 and clinical for like
NOTE Confidence: 0.77018512625

00:51:30.550 --> 00:51:31.880 gamma bands and stuff, but
NOTE Confidence: 0.829025311

00:51:32.290 --> 00:51:34.200 and you said all of this was in the frontal
NOTE Confidence: 0.86529266

00:51:34.210 --> 00:51:36.730 cortical electrodes. Is that right?
NOTE Confidence: 0.871039796

00:51:37.630 --> 00:51:42.064 Yeah, but you know, these discrete
NOTE Confidence: 0.871039796

00:51:42.064 --> 00:51:45.020 auditory stimuli almost always.
NOTE Confidence: 0.871039796

00:51:45.020 --> 00:51:46.736 They they live in the Theta
NOTE Confidence: 0.871039796

00:51:46.736 --> 00:51:48.240 band between 4:00 and 8:00.
NOTE Confidence: 0.871039796

00:51:48.240 --> 00:51:49.330 You just, you just don't,

NOTE Confidence: 0.871039796

00:51:49.330 --> 00:51:51.682 you just don't say any evoked

NOTE Confidence: 0.871039796

00:51:51.682 --> 00:51:53.780 activity in the higher bands.

NOTE Confidence: 0.871039796

00:51:53.780 --> 00:51:57.600 Thank you. Had we done a more

NOTE Confidence: 0.871039796

00:51:57.600 --> 00:51:59.220 cognitive perceptual task,

NOTE Confidence: 0.871039796

00:51:59.220 --> 00:52:01.098 then certainly we would probably want

NOTE Confidence: 0.871039796

00:52:01.098 --> 00:52:03.619 to look at the other bands as well,

NOTE Confidence: 0.871039796

00:52:03.620 --> 00:52:05.720 but this is very simple sensory stimuli.

NOTE Confidence: 0.8919077333333333

00:52:06.480 --> 00:52:08.028 Patrick, did you look at the

NOTE Confidence: 0.41061586

00:52:08.560 --> 00:52:12.540 the affected VLT EEG correlates?

NOTE Confidence: 0.35781595

00:52:14.620 --> 00:52:18.770 The AV Lt. yeah, yeah.

NOTE Confidence: 0.847596637272727

00:52:18.770 --> 00:52:21.486 That's in process, So what I didn't

NOTE Confidence: 0.847596637272727

00:52:21.486 --> 00:52:23.638 mention to everyone is when you

NOTE Confidence: 0.847596637272727

00:52:23.638 --> 00:52:26.710 take all the the time to get people

NOTE Confidence: 0.847596637272727

00:52:26.803 --> 00:52:29.595 set up with the EG in the booth.

NOTE Confidence: 0.847596637272727

00:52:29.600 --> 00:52:31.812 This this task is about 12 minutes

NOTE Confidence: 0.847596637272727

00:52:31.812 --> 00:52:34.036 this LTP task, so you don't want
NOTE Confidence: 0.847596637272727

00:52:34.036 --> 00:52:36.689 to do all that set up and get.
NOTE Confidence: 0.847596637272727

00:52:36.690 --> 00:52:38.170 Just 10 minutes of data,
NOTE Confidence: 0.847596637272727

00:52:38.170 --> 00:52:39.074 12 minutes of data.
NOTE Confidence: 0.847596637272727

00:52:39.074 --> 00:52:40.932 So we have several other tasks that we're
NOTE Confidence: 0.847596637272727

00:52:40.932 --> 00:52:42.514 going to be looking at and hopefully
NOTE Confidence: 0.847596637272727

00:52:42.514 --> 00:52:44.330 we can have some follow up papers on.
NOTE Confidence: 0.847596637272727

00:52:44.330 --> 00:52:48.210 One is and EG version of the Gray
NOTE Confidence: 0.847596637272727

00:52:48.210 --> 00:52:50.430 auditory verbal learning task and
NOTE Confidence: 0.847596637272727

00:52:50.430 --> 00:52:53.009 we also have gamma driving P300.
NOTE Confidence: 0.847596637272727

00:52:53.009 --> 00:52:55.163 So there's other things that we
NOTE Confidence: 0.847596637272727

00:52:55.163 --> 00:52:57.639 can look at that might inform.
NOTE Confidence: 0.847596637272727

00:52:57.640 --> 00:52:58.820 Potential mechanisms.
NOTE Confidence: 0.816078085714286

00:53:06.440 --> 00:53:08.036 Well, we have a couple of minutes.
NOTE Confidence: 0.816078085714286

00:53:08.040 --> 00:53:11.688 I'll just quickly show a little bit of
NOTE Confidence: 0.816078085714286

00:53:11.688 --> 00:53:14.405 data related to psychological mechanisms

NOTE Confidence: 0.816078085714286

00:53:14.405 --> 00:53:18.325 and this was relates to in some ways

NOTE Confidence: 0.816078085714286

00:53:18.325 --> 00:53:20.455 what could be a psychological correlate

NOTE Confidence: 0.816078085714286

00:53:20.455 --> 00:53:23.168 of what we're seeing in terms of

NOTE Confidence: 0.816078085714286

00:53:23.168 --> 00:53:25.279 neuroplasticity are to equate the two,

NOTE Confidence: 0.816078085714286

00:53:25.280 --> 00:53:26.201 one being cellular,

NOTE Confidence: 0.816078085714286

00:53:26.201 --> 00:53:28.350 but in this other concept much more

NOTE Confidence: 0.816078085714286

00:53:28.415 --> 00:53:30.150 in the psychological realm but.

NOTE Confidence: 0.816078085714286

00:53:30.150 --> 00:53:32.664 Still going with that same general

NOTE Confidence: 0.816078085714286

00:53:32.664 --> 00:53:34.779 notion that psychedelics might open

NOTE Confidence: 0.816078085714286

00:53:34.779 --> 00:53:36.987 up this period of critical plasticity

NOTE Confidence: 0.816078085714286

00:53:36.987 --> 00:53:39.935 in which there may be more potential

NOTE Confidence: 0.816078085714286

00:53:39.935 --> 00:53:41.715 for psychological flexibility and

NOTE Confidence: 0.816078085714286

00:53:41.715 --> 00:53:43.945 other changes in people's lives.

NOTE Confidence: 0.816078085714286

00:53:43.945 --> 00:53:47.354 So we did use this therapy model using

NOTE Confidence: 0.816078085714286

00:53:47.354 --> 00:53:48.978 acceptance and commitment therapy,

NOTE Confidence: 0.816078085714286

00:53:48.980 --> 00:53:52.332 which explicitly targets psychological
NOTE Confidence: 0.816078085714286

00:53:52.332 --> 00:53:54.674 flexibility. That's the main mechanism.
NOTE Confidence: 0.816078085714286

00:53:54.674 --> 00:53:57.631 We've written some papers and I could give
NOTE Confidence: 0.816078085714286

00:53:57.631 --> 00:54:00.360 a whole talk about just this this model.
NOTE Confidence: 0.835869603333333

00:54:02.370 --> 00:54:05.258 But the basic idea was was that we
NOTE Confidence: 0.835869603333333

00:54:05.258 --> 00:54:07.046 saw conceptual and phenomenological
NOTE Confidence: 0.835869603333333

00:54:07.046 --> 00:54:09.516 overlaps between the components of
NOTE Confidence: 0.835869603333333

00:54:09.516 --> 00:54:12.770 act and the effects of solar cybin.
NOTE Confidence: 0.835869603333333

00:54:12.770 --> 00:54:14.933 And we thought that these two might
NOTE Confidence: 0.835869603333333

00:54:14.933 --> 00:54:17.222 synergize well together and that this
NOTE Confidence: 0.835869603333333

00:54:17.222 --> 00:54:19.038 increases in psychological flexibility
NOTE Confidence: 0.835869603333333

00:54:19.038 --> 00:54:21.186 which there there are measures
NOTE Confidence: 0.835869603333333

00:54:21.186 --> 00:54:23.328 for could maybe a key mediator.
NOTE Confidence: 0.835869603333333

00:54:23.330 --> 00:54:25.946 So we wanted to look at that and
NOTE Confidence: 0.835869603333333

00:54:25.946 --> 00:54:27.345 increasingly actually other investigators
NOTE Confidence: 0.835869603333333

00:54:27.345 --> 00:54:30.057 have picked up on this idea and this

NOTE Confidence: 0.8358696033333333
00:54:30.125 --> 00:54:32.429 is from now on Davis that did show it.
NOTE Confidence: 0.8358696033333333
00:54:32.430 --> 00:54:33.750 This is from survey data,
NOTE Confidence: 0.8358696033333333
00:54:33.750 --> 00:54:36.342 but did show that basic kind of model
NOTE Confidence: 0.8358696033333333
00:54:36.342 --> 00:54:38.909 of the acute psychedelic effects
NOTE Confidence: 0.8358696033333333
00:54:38.910 --> 00:54:41.600 feeding into increases in psychological
NOTE Confidence: 0.8358696033333333
00:54:41.600 --> 00:54:43.752 flexibility that that mediated.
NOTE Confidence: 0.8358696033333333
00:54:43.760 --> 00:54:44.552 Clinical improvements.
NOTE Confidence: 0.8358696033333333
00:54:44.552 --> 00:54:47.324 This far just quickly to show you
NOTE Confidence: 0.8358696033333333
00:54:47.324 --> 00:54:49.198 because I think it it was nice
NOTE Confidence: 0.8358696033333333
00:54:49.198 --> 00:54:50.700 data that we we did see.
NOTE Confidence: 0.8358696033333333
00:54:50.700 --> 00:54:52.000 So this is the AQ,
NOTE Confidence: 0.8358696033333333
00:54:52.000 --> 00:54:53.939 it's one of the primary measures that
NOTE Confidence: 0.8358696033333333
00:54:53.939 --> 00:54:56.788 was developed to look at the idea of
NOTE Confidence: 0.8358696033333333
00:54:56.788 --> 00:54:58.906 psychological flexibility decreases are
NOTE Confidence: 0.8358696033333333
00:54:58.906 --> 00:55:00.998 actually clinical improvements here.
NOTE Confidence: 0.8358696033333333

00:55:01.000 --> 00:55:03.772 So we did see a statistically
NOTE Confidence: 0.8358696033333333

00:55:03.772 --> 00:55:05.158 significant improvements in
NOTE Confidence: 0.8358696033333333

00:55:05.158 --> 00:55:06.523 psychological flexibility following
NOTE Confidence: 0.8358696033333333

00:55:06.523 --> 00:55:09.435 soybean but not after placebo and this
NOTE Confidence: 0.8358696033333333

00:55:09.435 --> 00:55:11.878 was a significant difference here.
NOTE Confidence: 0.8358696033333333

00:55:11.880 --> 00:55:14.052 We looked two weeks after Socmen
NOTE Confidence: 0.8358696033333333

00:55:14.052 --> 00:55:16.454 and again it did persist.
NOTE Confidence: 0.8358696033333333

00:55:16.454 --> 00:55:18.128 Three months later,
NOTE Confidence: 0.8358696033333333

00:55:18.130 --> 00:55:20.674 I do have some other measures that we
NOTE Confidence: 0.8358696033333333

00:55:20.674 --> 00:55:23.068 looked at that relate to this idea.
NOTE Confidence: 0.8358696033333333

00:55:23.070 --> 00:55:24.602 Especially mindfulness and there
NOTE Confidence: 0.8358696033333333

00:55:24.602 --> 00:55:26.134 were some significant changes
NOTE Confidence: 0.8358696033333333

00:55:26.134 --> 00:55:28.250 there as well as in value living.
NOTE Confidence: 0.8358696033333333

00:55:28.250 --> 00:55:29.058 And just to show,
NOTE Confidence: 0.8358696033333333

00:55:29.058 --> 00:55:30.830 you know the other thing that was Nice is,
NOTE Confidence: 0.8358696033333333

00:55:30.830 --> 00:55:32.462 is we also saw,

NOTE Confidence: 0.8358696033333333
00:55:32.462 --> 00:55:35.700 did see a correlation here between those
NOTE Confidence: 0.8358696033333333
00:55:35.700 --> 00:55:38.080 changes in psychological flexibility
NOTE Confidence: 0.8358696033333333
00:55:38.080 --> 00:55:41.590 and the actual clinical improvements.
NOTE Confidence: 0.8358696033333333
00:55:41.590 --> 00:55:43.490 So those things trending together
NOTE Confidence: 0.8358696033333333
00:55:43.490 --> 00:55:45.512 of course can't see causation,
NOTE Confidence: 0.8358696033333333
00:55:45.512 --> 00:55:48.022 but it was highly significant
NOTE Confidence: 0.8358696033333333
00:55:48.022 --> 00:55:50.606 correlation between those those two.
NOTE Confidence: 0.8358696033333333
00:55:50.606 --> 00:55:54.372 So, so just a promising direction here.
NOTE Confidence: 0.8358696033333333
00:55:54.380 --> 00:55:55.166 And you know,
NOTE Confidence: 0.8358696033333333
00:55:55.166 --> 00:55:56.214 it's interesting given the
NOTE Confidence: 0.8358696033333333
00:55:56.214 --> 00:55:58.185 small sample that we did see a
NOTE Confidence: 0.8358696033333333
00:55:58.185 --> 00:55:59.037 highly significant improvement,
NOTE Confidence: 0.8358696033333333
00:55:59.040 --> 00:55:59.418 sorry,
NOTE Confidence: 0.8358696033333333
00:55:59.418 --> 00:56:00.174 correlation here,
NOTE Confidence: 0.8358696033333333
00:56:00.174 --> 00:56:02.820 but we actually did not see a
NOTE Confidence: 0.8358696033333333

00:56:02.896 --> 00:56:05.560 statistically significant correlation,
NOTE Confidence: 0.8358696033333333

00:56:05.560 --> 00:56:07.924 really any correlation here between the
NOTE Confidence: 0.8358696033333333

00:56:07.924 --> 00:56:10.519 strength of the mystical experience and
NOTE Confidence: 0.8358696033333333

00:56:10.519 --> 00:56:12.894 the clinical improvements postal cybin,
NOTE Confidence: 0.8358696033333333

00:56:12.900 --> 00:56:14.208 which and that has,
NOTE Confidence: 0.8358696033333333

00:56:14.208 --> 00:56:16.781 you know typically been one of the
NOTE Confidence: 0.8358696033333333

00:56:16.781 --> 00:56:19.466 prominent explanatory mechanisms on the
NOTE Confidence: 0.8358696033333333

00:56:19.466 --> 00:56:21.614 more psychological experiential level.
NOTE Confidence: 0.8358696033333333

00:56:21.620 --> 00:56:22.710 So we didn't see that,
NOTE Confidence: 0.8358696033333333

00:56:22.710 --> 00:56:25.326 but we did see the correlations.
NOTE Confidence: 0.8358696033333333

00:56:25.330 --> 00:56:26.905 Both with the EEG measure
NOTE Confidence: 0.8358696033333333

00:56:26.905 --> 00:56:27.850 that Patrick shared,
NOTE Confidence: 0.8358696033333333

00:56:27.850 --> 00:56:31.630 as well as with psychological flexibility.
NOTE Confidence: 0.8358696033333333

00:56:31.630 --> 00:56:33.464 So that's just what I said there.
NOTE Confidence: 0.8358696033333333

00:56:33.470 --> 00:56:34.400 And so just to wrap up,
NOTE Confidence: 0.8358696033333333

00:56:34.400 --> 00:56:36.444 you know I think the study was

NOTE Confidence: 0.8358696033333333
00:56:36.444 --> 00:56:37.932 really a good demonstrator
NOTE Confidence: 0.8358696033333333
00:56:37.932 --> 00:56:40.108 of with psychedelic studies,
NOTE Confidence: 0.8358696033333333
00:56:40.110 --> 00:56:42.492 just how tricky these are from
NOTE Confidence: 0.8358696033333333
00:56:42.492 --> 00:56:43.683 a methodological standpoint.
NOTE Confidence: 0.8358696033333333
00:56:43.690 --> 00:56:45.748 And it's such a complex interplay
NOTE Confidence: 0.8358696033333333
00:56:45.748 --> 00:56:46.777 between expectancy effects,
NOTE Confidence: 0.8358696033333333
00:56:46.780 --> 00:56:48.640 therapy effects and drug and placebo
NOTE Confidence: 0.8358696033333333
00:56:48.640 --> 00:56:50.754 effects that we need to be really
NOTE Confidence: 0.8358696033333333
00:56:50.754 --> 00:56:52.658 mindful of as we design these trials.
NOTE Confidence: 0.8358696033333333
00:56:52.660 --> 00:56:55.300 I I do think given the robustness of
NOTE Confidence: 0.8358696033333333
00:56:55.300 --> 00:56:57.600 the clinical effects that we saw that
NOTE Confidence: 0.8358696033333333
00:56:57.600 --> 00:57:00.236 it does again add to the promise of
NOTE Confidence: 0.8358696033333333
00:57:00.236 --> 00:57:01.956 this overall treatment model both
NOTE Confidence: 0.8358696033333333
00:57:01.956 --> 00:57:03.939 suicide and therapy and potentially
NOTE Confidence: 0.8358696033333333
00:57:03.940 --> 00:57:06.200 with actions and psychological
NOTE Confidence: 0.8358696033333333

00:57:06.200 --> 00:57:08.361 flexibility as being important
NOTE Confidence: 0.8358696033333333

00:57:08.361 --> 00:57:10.666 potential ways of providing this
NOTE Confidence: 0.8358696033333333

00:57:10.666 --> 00:57:13.320 treatment to patients with depression.
NOTE Confidence: 0.8358696033333333

00:57:13.320 --> 00:57:16.182 And both of our these alterations
NOTE Confidence: 0.8358696033333333

00:57:16.182 --> 00:57:18.090 in neuroplasticity and changes
NOTE Confidence: 0.844311666

00:57:18.169 --> 00:57:20.257 in psychological flexibility may
NOTE Confidence: 0.844311666

00:57:20.257 --> 00:57:22.208 be important potential mechanisms.
NOTE Confidence: 0.844311666

00:57:22.208 --> 00:57:25.064 Of course psychedelic therapy for depression,
NOTE Confidence: 0.844311666

00:57:25.070 --> 00:57:27.692 but potentially again we we're seeing
NOTE Confidence: 0.844311666

00:57:27.692 --> 00:57:30.003 effects across many other mental
NOTE Confidence: 0.844311666

00:57:30.003 --> 00:57:33.405 disorders and and both of these are
NOTE Confidence: 0.844311666

00:57:33.405 --> 00:57:34.780 potentially transdiagnostic mechanisms
NOTE Confidence: 0.844311666

00:57:34.780 --> 00:57:37.602 and so I think that adds to the
NOTE Confidence: 0.844311666

00:57:37.602 --> 00:57:40.674 intrigue around both of those so.
NOTE Confidence: 0.844311666

00:57:40.680 --> 00:57:43.928 Lot of questions remain on how to deliver
NOTE Confidence: 0.844311666

00:57:43.928 --> 00:57:46.602 this treatment most effectively and discuss,

NOTE Confidence: 0.844311666

00:57:46.602 --> 00:57:48.779 but I think I'm just going to

NOTE Confidence: 0.844311666

00:57:48.779 --> 00:57:50.887 wrap up so we can discuss here.

NOTE Confidence: 0.844311666

00:57:50.890 --> 00:57:53.698 Again, just really want to thank

NOTE Confidence: 0.844311666

00:57:53.698 --> 00:57:56.279 Doctor D'souza for sticking with me

NOTE Confidence: 0.844311666

00:57:56.279 --> 00:57:58.512 and the study for the duration and

NOTE Confidence: 0.844311666

00:57:58.512 --> 00:58:01.219 taking it to the finish line as well

NOTE Confidence: 0.844311666

00:58:01.219 --> 00:58:03.569 as everyone who's been involved from.

NOTE Confidence: 0.844311666

00:58:03.570 --> 00:58:06.186 Of the synergy lab at the VA there

NOTE Confidence: 0.844311666

00:58:06.186 --> 00:58:08.551 and our whole team of therapists

NOTE Confidence: 0.844311666

00:58:08.551 --> 00:58:11.970 and and our funders as well as the

NOTE Confidence: 0.844311666

00:58:11.970 --> 00:58:14.070 study participants who were our

NOTE Confidence: 0.844311666

00:58:14.070 --> 00:58:16.554 best teachers in this never so.

NOTE Confidence: 0.844311666

00:58:16.554 --> 00:58:18.060 Thank you all.

NOTE Confidence: 0.688268853571429

00:58:20.470 --> 00:58:22.689 See if there's any. Great for discussion.

NOTE Confidence: 0.6656290075

00:58:24.480 --> 00:58:25.365 Thank you both.

NOTE Confidence: 0.6656290075

00:58:25.365 --> 00:58:26.620 It's really great to see this

NOTE Confidence: 0.6656290075

00:58:26.620 --> 00:58:27.760 come to fruition and there's

NOTE Confidence: 0.6656290075

00:58:27.760 --> 00:58:29.540 some nice results, you know,

NOTE Confidence: 0.6656290075

00:58:29.540 --> 00:58:30.560 small and limited study,

NOTE Confidence: 0.6656290075

00:58:30.560 --> 00:58:31.595 but given those limitations

NOTE Confidence: 0.6656290075

00:58:31.595 --> 00:58:32.765 have some nice stuff in there.

NOTE Confidence: 0.87008202

00:58:34.510 --> 00:58:35.758 So thank you.