WEBVTT

00:00:00.000 --> 00:00:00.240 I'm

00:00:03.280 --> 00:00:04.480 thank you everyone for coming

00:00:04.480 --> 00:00:05.440 to the Psychedelic Seminar.

00:00:05.440 --> 00:00:07.120 This is the first time this year

00:00:07.120 --> 00:00:08.509 we've had in person speakers.

00:00:08.509 --> 00:00:11.000 So thank you so much for being here.

00:00:11.000 --> 00:00:13.520 We are scheduled, we have,

00:00:13.520 --> 00:00:15.320 we have November and December scheduled.

00:00:15.320 --> 00:00:17.035 Jessica, do you have the the dates

00:00:17.035 --> 00:00:18.560 of November and December handy?

00:00:18.560 --> 00:00:20.440 It's typically the third Friday of the month.

00:00:23.320 --> 00:00:27.024 We're looking at November 17th talking

00:00:27.024 --> 00:00:28.880 about psychedelics and addiction.

00:00:28.880 --> 00:00:31.132 And then December 15th,

NOTE Confidence: 0.5532113

00:00:31.132 --> 00:00:34.510 I believe will be Jerry Sanacora.

NOTE Confidence: 0.42947567

00:00:35.590 --> 00:00:36.734 Yeah, Jerry and Ben will talk about the

NOTE Confidence: 0.42947567

00:00:36.734 --> 00:00:38.846 you saw in a depression study and the

NOTE Confidence: 0.42947567

00:00:38.846 --> 00:00:40.150 psychedelics and addiction. Who is that?

NOTE Confidence: 0.42947567

00:00:46.350 --> 00:00:47.510 It's cocaine from Alabama.

NOTE Confidence: 0.42947567

00:00:47.510 --> 00:00:48.670 I'm thinking on that.

NOTE Confidence: 0.42947567

00:00:49.110 --> 00:00:50.343 I know I can. Let me think of the

NOTE Confidence: 0.31732166

00:00:56.620 --> 00:00:58.340 anyway those those should

NOTE Confidence: 0.31732166

00:00:58.340 --> 00:01:02.255 be good and then we're working on thanks

NOTE Confidence: 0.31732166

00:01:02.255 --> 00:01:05.095 to Julian Orutzi who I saw on here.

NOTE Confidence: 0.31732166

00:01:05.100 --> 00:01:06.508 We're putting together something

NOTE Confidence: 0.31732166

00:01:06.508 --> 00:01:09.015 in in February that I think will

NOTE Confidence: 0.31732166

00:01:09.015 --> 00:01:11.019 be really interesting which is a

NOTE Confidence: 0.31732166

00:01:11.019 --> 00:01:13.259 discussion panel of the regulatory

NOTE Confidence: 0.31732166

00:01:13.259 --> 00:01:15.020 framework surrounding psychedelics.

00:01:15.020 --> 00:01:17.001 The Department of Health and Human Services

00:01:17.001 --> 00:01:18.580 is putting together draft guidance,

00:01:18.580 --> 00:01:21.524 not for the FDA put out draft guidance,

00:01:21.530 --> 00:01:22.650 you know, real guidance a couple of

00:01:22.650 --> 00:01:25.420 months ago, but this is HHS guidance

00:01:25.420 --> 00:01:27.649 about clinical use and that that

00:01:27.649 --> 00:01:29.167 should be coming out in November.

00:01:29.170 --> 00:01:30.595 Then there'll be a commentary

00:01:30.595 --> 00:01:32.343 period and it'll be finalized by

00:01:32.343 --> 00:01:34.145 February and we'll have a number

00:01:34.145 --> 00:01:36.170 of of this academic discussions,

00:01:36.170 --> 00:01:37.858 but also to people from HHS who are

00:01:37.858 --> 00:01:39.849 like in the process of developing this.

00:01:39.850 --> 00:01:42.406 So I think it'll be a really interesting both

00:01:42.406 --> 00:01:44.047 informational and and discussion session.

00:01:44.050 --> 00:01:45.408 We're going to do that in person.

NOTE Confidence: 0.31732166

00:01:45.410 --> 00:01:46.942 I expect that it'll be, you know,

NOTE Confidence: 0.31732166

00:01:46.942 --> 00:01:48.538 we'll advertise and I expect it'll

NOTE Confidence: 0.31732166

00:01:48.538 --> 00:01:50.377 be popular beyond our local community

NOTE Confidence: 0.31732166

00:01:50.380 --> 00:01:51.814 in the TAC Auditorium and it'll

NOTE Confidence: 0.31732166

00:01:51.814 --> 00:01:53.379 be a bit longer than usual.

NOTE Confidence: 0.31732166

00:01:53.380 --> 00:01:54.458 So keep an eye out for that.

NOTE Confidence: 0.31732166

00:01:54.460 --> 00:01:57.340 That's in the the third,

NOTE Confidence: 0.31732166

00:01:57.340 --> 00:01:58.300 the 3rd, February,

NOTE Confidence: 0.31732166

00:01:58.300 --> 00:02:01.019 3rd Friday in February.

NOTE Confidence: 0.37012887

00:02:01.220 --> 00:02:02.908 So Chris, in November,

NOTE Confidence: 0.37012887

00:02:02.908 --> 00:02:04.580 it's Peter Hendricks. Thank you.

NOTE Confidence: 0.37012887

00:02:07.140 --> 00:02:10.100 All right. So

NOTE Confidence: 0.37012887

00:02:10.620 --> 00:02:12.724 with that, I'll turn it over to Jerry

NOTE Confidence: 0.37012887

00:02:12.724 --> 00:02:14.699 Sanacora to introduce today's speaker.

NOTE Confidence: 0.37012887

00:02:15.020 --> 00:02:16.340 Great. Thank you.

NOTE Confidence: 0.37012887

00:02:16.340 --> 00:02:18.780 Well, I'm really happy to have Luanne here.

NOTE Confidence: 0.37012887

00:02:18.780 --> 00:02:21.762 We managed to become friends and

NOTE Confidence: 0.37012887

00:02:21.762 --> 00:02:24.670 collaborators over the past few years.

NOTE Confidence: 0.37012887

00:02:24.670 --> 00:02:27.154 I I got to know Moana's work actually from

NOTE Confidence: 0.37012887

00:02:27.154 --> 00:02:28.918 reading some of the stuff in ketamine.

NOTE Confidence: 0.37012887

00:02:28.918 --> 00:02:31.214 But then really started to read a

NOTE Confidence: 0.37012887

00:02:31.214 --> 00:02:34.690 lot of of your other work and how you

NOTE Confidence: 0.37012887

00:02:34.690 --> 00:02:38.670 incorporate the practice of placebo or

NOTE Confidence: 0.37012887

00:02:38.670 --> 00:02:42.309 the study of placebo into all of medicine.

NOTE Confidence: 0.37012887

00:02:42.309 --> 00:02:44.787 And you know starting with pain.

NOTE Confidence: 0.37012887

00:02:44.790 --> 00:02:46.833 I know you did your training back in Italy

NOTE Confidence: 0.37012887

00:02:46.833 --> 00:02:48.670 with Benedetti was one of the sort of,

NOTE Confidence: 0.37012887

00:02:48.670 --> 00:02:50.070 I don't want to say the father's,

NOTE Confidence: 0.37012887

00:02:50.070 --> 00:02:52.494 but one of the big names and placebo

NOTE Confidence: 0.37012887

00:02:52.494 --> 00:02:54.469 research one of the biggest names.

NOTE Confidence: 0.37012887

00:02:54.470 --> 00:02:56.648 But you've really managed to continue

NOTE Confidence: 0.37012887

00:02:56.648 --> 00:02:59.149 that line of research largely in pain.

NOTE Confidence: 0.37012887

00:02:59.150 --> 00:03:01.118 But now I know your interests

NOTE Confidence: 0.37012887

00:03:01.118 --> 00:03:02.102 as a psychiatrist,

NOTE Confidence: 0.37012887

00:03:02.110 --> 00:03:04.250 also very interested in spreading

NOTE Confidence: 0.37012887

00:03:04.250 --> 00:03:07.830 out into a range of other illnesses.

NOTE Confidence: 0.37012887

00:03:07.830 --> 00:03:12.950 And I think some of our discussions

NOTE Confidence: 0.37012887

00:03:12.950 --> 00:03:16.640 have really highlighted how

NOTE Confidence: 0.37012887

00:03:16.640 --> 00:03:18.780 you're looking at placebo.

NOTE Confidence: 0.37012887

00:03:18.780 --> 00:03:21.812 Not just as this sort of

NOTE Confidence: 0.37012887

00:03:21.812 --> 00:03:23.596 pejorative negative thing like,

NOTE Confidence: 0.37012887

00:03:23.600 --> 00:03:25.556 oh, this is the placebo response,

NOTE Confidence: 0.37012887

00:03:25.560 --> 00:03:28.240 but how the some of the core components

NOTE Confidence: 0.37012887

00:03:28.240 --> 00:03:30.995 of placebo would be playing a major role.

NOTE Confidence: 0.37012887

00:03:31.000 --> 00:03:33.200 Especially when we start thinking

NOTE Confidence: 0.37012887

00:03:33.200 --> 00:03:36.160 about the effects of psychedelics,

00:03:36.160 --> 00:03:38.680 how psychedelics can actually

00:03:38.680 --> 00:03:40.790 obviously be influenced by things

00:03:40.790 --> 00:03:42.478 like expectancy and conditioning,

00:03:42.480 --> 00:03:45.100 but also how they may actually have an

00:03:45.100 --> 00:03:46.842 impact on expectancy and conditioning.

00:03:46.842 --> 00:03:48.432 So comes this very interesting

00:03:48.432 --> 00:03:49.810 way of thinking about it,

00:03:49.810 --> 00:03:52.738 and I think Glenn has raised it to another

00:03:52.738 --> 00:03:54.370 level in the way of thinking about it.

00:03:54.370 --> 00:03:56.290 Not just so straightforward like,

00:03:56.290 --> 00:03:57.530 oh, this could all be

00:03:57.530 --> 00:03:58.522 explained just by expectancy,

00:03:58.530 --> 00:04:00.246 but actually thinking about the interaction.

00:04:00.250 --> 00:04:02.194 So really interesting about

00:04:02.194 --> 00:04:04.330 hearing more what you have to say.

00:04:04.330 --> 00:04:04.930 Thanks a lot.

NOTE Confidence: 0.35778156

00:04:05.720 --> 00:04:07.239 Thank you very much for having me.

NOTE Confidence: 0.35778156

00:04:07.240 --> 00:04:10.040 And thank you for making this visit

NOTE Confidence: 0.35778156

00:04:10.040 --> 00:04:12.040 very insightful and thoughtful

NOTE Confidence: 0.35778156

00:04:12.040 --> 00:04:13.504 and wonderful conversation with

NOTE Confidence: 0.35778156

00:04:13.504 --> 00:04:16.040 all the people I met so far.

NOTE Confidence: 0.35778156

00:04:16.040 --> 00:04:19.596 So I gave us title to Chris,

NOTE Confidence: 0.35778156

00:04:19.600 --> 00:04:22.795 Jessica mind over Monaco's because

NOTE Confidence: 0.35778156

00:04:22.795 --> 00:04:26.580 sometime Placib effects bring a lot

NOTE Confidence: 0.35778156

00:04:26.580 --> 00:04:29.278 of negative connotates and people tend

NOTE Confidence: 0.35778156

00:04:29.278 --> 00:04:31.870 to believe that this Marilla bias

NOTE Confidence: 0.35778156

00:04:31.942 --> 00:04:34.609 you know when in reality we started

NOTE Confidence: 0.35778156

00:04:34.609 --> 00:04:37.030 this year because underlying changes

NOTE Confidence: 0.35778156

00:04:37.030 --> 00:04:39.430 across symptoms across disease.

NOTE Confidence: 0.35778156

00:04:39.430 --> 00:04:41.590 And today I wanted to explain a little

NOTE Confidence: 0.35778156

00:04:41.590 --> 00:04:44.110 bit of neurobiology aspects of placebo,

NOTE Confidence: 0.35778156

00:04:44.110 --> 00:04:47.080 but also some implication towards

NOTE Confidence: 0.35778156

00:04:47.080 --> 00:04:50.445 the end about psychedelic and how

NOTE Confidence: 0.35778156

00:04:50.445 --> 00:04:53.210 this kind of knowledge can inform us.

NOTE Confidence: 0.35778156

00:04:53.210 --> 00:04:56.090 And I have to say that folks here

NOTE Confidence: 0.35778156

00:04:56.090 --> 00:04:58.610 at Yale brought me to these fields

NOTE Confidence: 0.35778156

00:04:58.610 --> 00:05:00.790 and in particular Jerry's and Akora.

NOTE Confidence: 0.35778156

00:05:00.790 --> 00:05:01.570 So thank you.

NOTE Confidence: 0.32298335

00:05:03.770 --> 00:05:03.880 So

NOTE Confidence: 0.32298335

00:05:10.440 --> 00:05:11.120 Preston,

NOTE Confidence: 0.2988057

00:05:15.210 --> 00:05:17.884 let's talk about what placebo effects are,

NOTE Confidence: 0.2988057

00:05:17.890 --> 00:05:19.194 which are the mechanism.

NOTE Confidence: 0.2988057

00:05:19.194 --> 00:05:21.522 And obviously I will talk about chronic

NOTE Confidence: 0.2988057

00:05:21.522 --> 00:05:23.720 pain because it's the main area of

NOTE Confidence: 0.2988057

00:05:23.720 --> 00:05:25.690 research we haven't been tackling.

NOTE Confidence: 0.2988057

00:05:25.690 --> 00:05:28.210 But I hope what I will show to you

NOTE Confidence: 0.2988057

00:05:28.210 --> 00:05:31.130 can be translated into psychiatry.

NOTE Confidence: 0.2988057

00:05:31.130 --> 00:05:33.626 And finally we can talk and tackle a

NOTE Confidence: 0.2988057

00:05:33.626 --> 00:05:36.043 little bit the show psychedelics and

NOTE Confidence: 0.2988057

00:05:36.043 --> 00:05:38.629 how Placip when treatment responses can

NOTE Confidence: 0.2988057

00:05:38.703 --> 00:05:41.209 interact and which are the controls or

NOTE Confidence: 0.2988057

00:05:41.209 --> 00:05:45.283 the design when we study psychedelics

NOTE Confidence: 0.2988057

00:05:45.283 --> 00:05:47.348 or antidepressants and so on.

NOTE Confidence: 0.49085578

00:05:49.510 --> 00:05:52.330 So placebo and drug effects no

NOTE Confidence: 0.49085578

00:05:52.330 --> 00:05:54.630 matter which treatment we use.

NOTE Confidence: 0.49085578

00:05:54.630 --> 00:05:57.708 This can be for example opioids,

NOTE Confidence: 0.49085578

00:05:59.750 --> 00:06:01.670 surgical interventions or

NOTE Confidence: 0.49085578

00:06:01.670 --> 00:06:04.230 complementary and integrative medicine.

NOTE Confidence: 0.49085578

00:06:04.230 --> 00:06:07.572 There is some ways specific do

NOTE Confidence: 0.49085578

00:06:07.572 --> 00:06:09.384 I tend to dislike this word,

NOTE Confidence: 0.49085578

00:06:09.390 --> 00:06:12.258 pharmacodynamic component and the

NOTE Confidence: 0.49085578

00:06:12.258 --> 00:06:14.409 placebo psychosocial component.

NOTE Confidence: 0.49085578

00:06:14.410 --> 00:06:16.626 The placebo psychosocial component

NOTE Confidence: 0.49085578

00:06:16.626 --> 00:06:19.601 is the context around any treatment

NOTE Confidence: 0.49085578

00:06:19.601 --> 00:06:23.170 and at least when we talk about pain,

NOTE Confidence: 0.49085578

00:06:23.170 --> 00:06:25.906 the top down the descending pain

NOTE Confidence: 0.49085578

00:06:25.906 --> 00:06:28.807 modulator system can play a critical

NOTE Confidence: 0.49085578

00:06:28.807 --> 00:06:31.287 role in modulating pain outcomes

NOTE Confidence: 0.49085578

00:06:31.287 --> 00:06:34.122 sometimes more than the you know

NOTE Confidence: 0.49085578

00:06:34.122 --> 00:06:36.702 input not susceptive input coming

NOTE Confidence: 0.49085578

00:06:36.702 --> 00:06:38.250 from the periphery.

NOTE Confidence: 0.49085578

00:06:38.250 --> 00:06:41.850 And one of the first study we

NOTE Confidence: 0.49085578

00:06:41.850 --> 00:06:45.290 conduct while I was a PhD student in

NOTE Confidence: 0.49085578

00:06:45.290 --> 00:06:47.919 neuroscience was to try to understand

NOTE Confidence: 0.49085578

00:06:47.919 --> 00:06:50.860 how the context can change outcomes.

NOTE Confidence: 0.49085578

00:06:50.860 --> 00:06:53.668 So a very clinical simple observation

NOTE Confidence: 0.49085578

00:06:53.668 --> 00:06:56.383 where the same thing killer were

NOTE Confidence: 0.49085578

00:06:56.383 --> 00:06:59.036 given to a pump of infusion or

NOTE Confidence: 0.49085578

00:06:59.036 --> 00:07:01.688 with a physician a nurse at the

NOTE Confidence: 0.49085578

00:07:01.688 --> 00:07:03.724 bed decides telling patients now

NOTE Confidence: 0.49085578

00:07:03.724 --> 00:07:05.536 we're starting the treatment.

NOTE Confidence: 0.49085578

00:07:05.540 --> 00:07:07.058 When we wrote to this paper,

NOTE Confidence: 0.49085578

00:07:07.060 --> 00:07:09.910 we had called this hidden

NOTE Confidence: 0.49085578

00:07:09.910 --> 00:07:11.620 versus open administration,

NOTE Confidence: 0.49085578

00:07:11.620 --> 00:07:14.422 but the editors suggest over to

NOTE Confidence: 0.49085578

00:07:14.422 --> 00:07:16.980 versus covert but still hidden.

NOTE Confidence: 0.49085578

00:07:16.980 --> 00:07:19.155 Open paradox is very common

NOTE Confidence: 0.49085578

00:07:19.155 --> 00:07:20.895 in the placebo literature.

NOTE Confidence: 0.49085578

00:07:20.900 --> 00:07:24.540 So the Eden administration is this one.

NOTE Confidence: 0.49085578

00:07:24.540 --> 00:07:28.280 The open will be with physician,

NOTE Confidence: 0.49085578

00:07:28.280 --> 00:07:31.380 a nurse around the patient.

NOTE Confidence: 0.49085578

00:07:31.380 --> 00:07:33.576 And we were tackling the question,

NOTE Confidence: 0.49085578

00:07:33.580 --> 00:07:35.890 can we study Placib effects without

NOTE Confidence: 0.49085578

00:07:35.890 --> 00:07:37.968 any placebo, without tablets,

NOTE Confidence: 0.49085578

00:07:37.968 --> 00:07:39.930 without selling solution.

NOTE Confidence: 0.49085578

00:07:39.930 --> 00:07:42.415 And in this case we study patients

NOTE Confidence: 0.49085578

00:07:42.415 --> 00:07:44.890 who were you know in the hospital

NOTE Confidence: 0.49085578

00:07:44.890 --> 00:07:46.650 for removal of lung cancer.

NOTE Confidence: 0.49085578

00:07:46.650 --> 00:07:48.750 And the goal was to understand

NOTE Confidence: 0.49085578

00:07:48.750 --> 00:07:51.583 how we can improve the outcome by

NOTE Confidence: 0.49085578

00:07:51.583 --> 00:07:53.838 manipulating the route of administration

NOTE Confidence: 0.49085578

00:07:53.838 --> 00:07:56.528 and the context around the drug.

NOTE Confidence: 0.49085578

00:07:56.530 --> 00:07:58.672 For for those of you who are

NOTE Confidence: 0.49085578

00:07:58.672 --> 00:08:00.600 familiar with Penn Therapeutics,

NOTE Confidence: 0.49085578

00:08:00.600 --> 00:08:04.530 buprenorphine and Tramadol are opioids right.

NOTE Confidence: 0.49085578

00:08:04.530 --> 00:08:05.230 Keterolac,

NOTE Confidence: 0.49085578

00:08:05.230 --> 00:08:09.262 metamazole are non opioids and you

NOTE Confidence: 0.49085578

00:08:09.262 --> 00:08:12.922 can see that opioid treatment like

NOTE Confidence: 0.49085578

00:08:12.922 --> 00:08:15.338 buprenorphine can reduce clinical

NOTE Confidence: 0.49085578

00:08:15.338 --> 00:08:17.695 post operative pain significantly.

NOTE Confidence: 0.49085578

00:08:17.695 --> 00:08:21.510 But when we provide the same drug

NOTE Confidence: 0.49085578

00:08:21.510 --> 00:08:24.438 with the disclosure with the presence

NOTE Confidence: 0.49085578

00:08:24.438 --> 00:08:27.594 of the physician or the nurse there

NOTE Confidence: 0.49085578

00:08:27.594 --> 00:08:30.216 there is a optimization of the

NOTE Confidence: 0.49085578

00:08:30.216 --> 00:08:34.126 reduction of the pain For some drug

NOTE Confidence: 0.49085578

00:08:34.126 --> 00:08:36.765 this you know augmentation is even

NOTE Confidence: 0.49085578

00:08:36.765 --> 00:08:39.302 larger like tramadol if we merely

NOTE Confidence: 0.49085578

00:08:39.302 --> 00:08:42.050 use the gold standard to interpret

NOTE Confidence: 0.49085578

00:08:42.050 --> 00:08:44.432 clinical trial results merely the

NOTE Confidence: 0.49085578

00:08:44.432 --> 00:08:46.292 difference between hidden versus

NOTE Confidence: 0.49085578

00:08:46.292 --> 00:08:48.942 soap and represent to this specific

NOTE Confidence: 0.49085578

00:08:48.942 --> 00:08:51.288 component and all this part will

NOTE Confidence: 0.49085578

00:08:51.288 --> 00:08:53.460 be the placebo or psychosocial

NOTE Confidence: 0.49085578

00:08:53.460 --> 00:08:56.512 components and you can see that can

NOTE Confidence: 0.49085578

00:08:56.588 --> 00:08:58.880 be larger than the active drug.

NOTE Confidence: 0.49085578

00:08:58.880 --> 00:09:02.036 So the same for Cathedral Ecometamazole,

NOTE Confidence: 0.49085578

00:09:02.040 --> 00:09:04.260 but they're non opioids based,

NOTE Confidence: 0.49085578

00:09:04.260 --> 00:09:06.800 so the observation was poorly

NOTE Confidence: 0.49085578

00:09:06.800 --> 00:09:09.938 clinical and we state that open

NOTE Confidence: 0.49085578

00:09:09.938 --> 00:09:12.928 administration of a drug working

NOTE Confidence: 0.49085578

00:09:12.928 --> 00:09:15.320 through psychosocial context can

NOTE Confidence: 0.49085578

00:09:15.406 --> 00:09:18.136 be more beneficial for patients.

NOTE Confidence: 0.49085578

00:09:18.140 --> 00:09:20.018 What we did,

NOTE Confidence: 0.49085578

00:09:20.020 --> 00:09:22.420 we used the same paradigm with

NOTE Confidence: 0.49085578

00:09:22.420 --> 00:09:23.380 the ads department.

NOTE Confidence: 0.49085578

00:09:23.380 --> 00:09:24.980 Given that I'm talking to

NOTE Confidence: 0.49085578

00:09:24.980 --> 00:09:26.260 psychiatrists and psychologists,

NOTE Confidence: 0.49085578

00:09:26.260 --> 00:09:28.035 this can be more informative

NOTE Confidence: 0.49085578

00:09:28.035 --> 00:09:29.100 than pain treatment.

NOTE Confidence: 0.49085578

00:09:29.100 --> 00:09:32.089 So open injection of the adzipan again

NOTE Confidence: 0.49085578

00:09:32.089 --> 00:09:35.043 in patient who are cancer patient

NOTE Confidence: 0.49085578

00:09:35.043 --> 00:09:37.698 post operative setting can reduce

NOTE Confidence: 0.49085578

00:09:37.698 --> 00:09:40.620 situation and anxiety substantially.

NOTE Confidence: 0.49085578

00:09:40.620 --> 00:09:41.780 So when the same drug,

NOTE Confidence: 0.49085578

00:09:41.780 --> 00:09:44.580 same dose was given in a hidden way,

NOTE Confidence: 0.49085578

00:09:44.580 --> 00:09:45.876 there is no reduction.

NOTE Confidence: 0.49085578

00:09:45.876 --> 00:09:47.496 So the question here is,

NOTE Confidence: 0.49085578

00:09:47.500 --> 00:09:50.650 do we need somehow to have an

NOTE Confidence: 0.49085578

00:09:50.650 --> 00:09:54.248 expectancy for a drug to start to work?

NOTE Confidence: 0.2935229

00:09:54.250 --> 00:09:56.450 Also we try the opposite.

NOTE Confidence: 0.2935229

00:09:56.450 --> 00:09:58.150 We inform a patient,

NOTE Confidence: 0.2935229

00:09:58.150 --> 00:09:59.850 we interrupt the drug.

NOTE Confidence: 0.2935229

00:09:59.850 --> 00:10:02.615 So those who had the responded with

NOTE Confidence: 0.2935229

00:10:02.615 --> 00:10:04.808 the open administration of the azapam,

NOTE Confidence: 0.2935229

00:10:04.810 --> 00:10:07.090 when we're told now we are not injected,

NOTE Confidence: 0.2935229

00:10:07.090 --> 00:10:08.574 we stop the treatment.

NOTE Confidence: 0.2935229

00:10:08.574 --> 00:10:12.226 You can see that there is a worsening of

NOTE Confidence: 0.2935229

00:10:12.226 --> 00:10:15.362 anxiety and no change for the interruption.

NOTE Confidence: 0.2935229

00:10:15.370 --> 00:10:17.650 So with that, I hope I convince you.

NOTE Confidence: 0.53062505

00:10:21.840 --> 00:10:24.264 With that, I hope I convince

NOTE Confidence: 0.53062505

00:10:24.264 --> 00:10:27.052 you that somehow the open Eden

NOTE Confidence: 0.53062505

00:10:27.052 --> 00:10:30.196 administration can help us to study

NOTE Confidence: 0.53062505

00:10:30.196 --> 00:10:33.256 a drug by eliminating silencing,

NOTE Confidence: 0.53062505

00:10:33.256 --> 00:10:34.600 eliminating placebo.

NOTE Confidence: 0.53062505

00:10:34.600 --> 00:10:36.520 So ethical issue related

NOTE Confidence: 0.53062505

00:10:36.520 --> 00:10:37.960 to placebo treatment.

NOTE Confidence: 0.53062505

00:10:37.960 --> 00:10:40.830 But there is a way to silence

NOTE Confidence: 0.53062505

00:10:40.830 --> 00:10:42.312 expectations and I don't know,

NOTE Confidence: 0.53062505

00:10:42.312 --> 00:10:44.366 maybe we can use this kind of

NOTE Confidence: 0.53062505

00:10:44.366 --> 00:10:46.458 paradigm with further, you know,

NOTE Confidence: 0.53062505

17

00:10:46.458 --> 00:10:47.880 treatment and depressants

NOTE Confidence: 0.53062505

00:10:47.880 --> 00:10:50.250 that start working in acute

NOTE Confidence: 0.53062505

00:10:50.330 --> 00:10:52.590 like ketamine or psychedelics.

NOTE Confidence: 0.53062505

00:10:52.590 --> 00:10:57.189 This can be a paradigm to consider.

NOTE Confidence: 0.53062505

00:10:57.190 --> 00:10:59.662 The next step would be to talk a

NOTE Confidence: 0.53062505

00:10:59.662 --> 00:11:02.285 little bit more about how I start

NOTE Confidence: 0.53062505

00:11:02.285 --> 00:11:04.715 to be interested in this phenomenon.

NOTE Confidence: 0.53062505

00:11:04.720 --> 00:11:07.920 So we were studying Parkinson's

NOTE Confidence: 0.53062505

00:11:07.920 --> 00:11:10.572 disorder and this was a special

NOTE Confidence: 0.53062505

00:11:10.572 --> 00:11:13.089 setting that for someone who had the

NOTE Confidence: 0.53062505

00:11:13.089 --> 00:11:15.798 Finnish MDM practising for about one year.

NOTE Confidence: 0.53062505

00:11:15.800 --> 00:11:18.880 It was something very comfortable,

NOTE Confidence: 0.53062505

00:11:18.880 --> 00:11:22.044 you know to go back to intraperative

NOTE Confidence: 0.53062505

00:11:22.044 --> 00:11:25.064 room and study a changes that occurred

NOTE Confidence: 0.53062505

00:11:25.064 --> 00:11:27.560 at the level of neuronal discharge.

NOTE Confidence: 0.53062505

00:11:27.560 --> 00:11:30.008 So patients who do not respond

NOTE Confidence: 0.53062505

00:11:30.008 --> 00:11:31.860 to the classical cocktail of

NOTE Confidence: 0.53062505

00:11:31.860 --> 00:11:33.672 dopamine agonist and antagonist

NOTE Confidence: 0.53062505

00:11:33.672 --> 00:11:35.937 to receive DP brain stimulation.

NOTE Confidence: 0.53062505

00:11:35.940 --> 00:11:39.820 DP brain stimulation consists of

NOTE Confidence: 0.53062505

00:11:39.820 --> 00:11:42.820 implanting on electrodes and sub

NOTE Confidence: 0.53062505

00:11:42.820 --> 00:11:47.150 thalamic nuclide and a battery

NOTE Confidence: 0.53062505

00:11:47.150 --> 00:11:50.558 eventually so that we have series of

NOTE Confidence: 0.53062505

00:11:50.558 --> 00:11:53.665 stimulation 12 to this patient managed

NOTE Confidence: 0.53062505

00:11:53.665 --> 00:11:56.226 their symptoms mostly for those who

NOTE Confidence: 0.53062505

00:11:56.226 --> 00:11:58.080 are not familiar but here everyone

NOTE Confidence: 0.53062505

00:11:58.136 --> 00:11:59.990 we are talking the same language.

NOTE Confidence: 0.53062505

00:11:59.990 --> 00:12:02.186 You know these patients have rigidity,

NOTE Confidence: 0.53062505

00:12:02.190 --> 00:12:03.450 tremor,

NOTE Confidence: 0.53062505

00:12:03.450 --> 00:12:06.168 bradykinesia as main Parkinson's

NOTE Confidence: 0.53062505

00:12:06.168 --> 00:12:08.526 symptom together with a lot

NOTE Confidence: 0.53062505

00:12:08.526 --> 00:12:09.870 of psychiatric problems.

NOTE Confidence: 0.53062505

00:12:09.870 --> 00:12:13.710 Here we try a pharmacological conditioning,

NOTE Confidence: 0.53062505

00:12:13.710 --> 00:12:14.826 so I work all of us.

NOTE Confidence: 0.53062505

00:12:14.830 --> 00:12:17.441 So to give a little of relief

NOTE Confidence: 0.53062505

00:12:17.441 --> 00:12:19.630 during the surgical implantation,

NOTE Confidence: 0.53062505

00:12:19.630 --> 00:12:22.310 this is a longer you know surgical procedure.

NOTE Confidence: 0.53062505

00:12:22.310 --> 00:12:24.578 We start early in the morning and

NOTE Confidence: 0.53062505

00:12:24.578 --> 00:12:27.378 then six 7-8 hour of intervention.

NOTE Confidence: 0.53062505

00:12:27.378 --> 00:12:31.360 So before the day of the surgery we

NOTE Confidence: 0.53062505

00:12:31.360 --> 00:12:33.256 condition patient with Apomorphine

NOTE Confidence: 0.53062505

00:12:33.256 --> 00:12:35.390 day one day 2 day three.

NOTE Confidence: 0.53062505

00:12:35.390 --> 00:12:37.950 Apomorphine is a dopamine agonist

NOTE Confidence: 0.53062505

00:12:37.950 --> 00:12:40.465 and producer reduction of the

NOTE Confidence: 0.53062505

00:12:40.465 --> 00:12:43.410 three symptoms I mentioned to you.

NOTE Confidence: 0.53062505

00:12:43.410 --> 00:12:46.525 But the time life is very short,

NOTE Confidence: 0.53062505

00:12:46.530 --> 00:12:49.320 the volume prover about 20 minutes

NOTE Confidence: 0.53062505

00:12:49.320 --> 00:12:51.690 some for maximum one hour.

NOTE Confidence: 0.53062505

00:12:51.690 --> 00:12:54.876 Therefore we were in the intraoperative

NOTE Confidence: 0.53062505

00:12:54.876 --> 00:12:59.393 room and the gun was to replace the

NOTE Confidence: 0.53062505

00:12:59.393 --> 00:13:02.498 drug Upomorphine with saline solution

NOTE Confidence: 0.53062505

00:13:02.498 --> 00:13:06.092 being injected subcutaneously while we

NOTE Confidence: 0.53062505

00:13:06.092 --> 00:13:08.497 were recording the neuronal activities

NOTE Confidence: 0.53062505

00:13:08.497 --> 00:13:11.418 from this this part of the brain.

NOTE Confidence: 0.53062505

00:13:11.420 --> 00:13:14.619 So for those who are not familiar,

NOTE Confidence: 0.53062505

00:13:14.620 --> 00:13:18.067 we are designed very well in terms of human

NOTE Confidence: 0.53062505

00:13:18.067 --> 00:13:20.915 being or also monkeys and other animals.

NOTE Confidence: 0.53062505

00:13:20.915 --> 00:13:24.890 So there is a zona incerta and then the

NOTE Confidence: 0.53062505

00:13:24.890 --> 00:13:27.783 supratalamic nucleus and then again a

NOTE Confidence: 0.53062505

00:13:27.783 --> 00:13:30.555 silent area before the substancia negra.

NOTE Confidence: 0.53062505

00:13:30.560 --> 00:13:34.480 So our goal in terms of neurophysiologists,

NOTE Confidence: 0.53062505

00:13:34.480 --> 00:13:36.982 surgeons was to identify this part

NOTE Confidence: 0.53062505

00:13:36.982 --> 00:13:39.775 of the brain and in order to make

NOTE Confidence: 0.53062505

00:13:39.775 --> 00:13:42.363 sure that we were there we record

NOTE Confidence: 0.53062505

00:13:42.363 --> 00:13:44.319 the several neuronal activities,

NOTE Confidence: 0.53062505

00:13:44.320 --> 00:13:48.152 many and so we had over 100 you

NOTE Confidence: 0.53062505

00:13:48.152 --> 00:13:50.923 know recordings and usually you

NOTE Confidence: 0.53062505

00:13:50.923 --> 00:13:53.195 see the typical firing.

NOTE Confidence: 0.53062505

00:13:53.200 --> 00:13:56.427 So and also this first activity where

NOTE Confidence: 0.53062505

00:13:56.427 --> 00:13:59.700 the spike become close to one another,

NOTE Confidence: 0.53062505

00:13:59.700 --> 00:14:02.300 so we counterbalance the nuclear

NOTE Confidence: 0.53062505

00:14:02.300 --> 00:14:04.900 serving gas control and the

NOTE Confidence: 0.53062505

00:14:04.996 --> 00:14:07.340 nuclear serving gas target.

NOTE Confidence: 0.53062505

00:14:07.340 --> 00:14:10.420 So the goal was to see if some

NOTE Confidence: 0.53062505

00:14:10.420 --> 00:14:12.396 other suggestion of improvement

NOTE Confidence: 0.53062505

00:14:12.396 --> 00:14:14.628 along with the administration

NOTE Confidence: 0.53062505

00:14:14.628 --> 00:14:16.860 of selling solution can

NOTE Confidence: 0.31534237

00:14:16.943 --> 00:14:19.493 change the pattern of firing

NOTE Confidence: 0.31534237

00:14:19.493 --> 00:14:21.533 in the Subitalamic nuclear.

NOTE Confidence: 0.31534237

00:14:21.540 --> 00:14:26.140 And you can see that it's a very small area.

NOTE Confidence: 0.31534237

00:14:26.140 --> 00:14:30.790 This is smaller than a bin in humans and

NOTE Confidence: 0.31534237

00:14:30.790 --> 00:14:34.640 was very you know unique cast contest.

NOTE Confidence: 0.31534237

00:14:34.640 --> 00:14:37.214 So what we were interested was

NOTE Confidence: 0.31534237

00:14:37.214 --> 00:14:40.079 the self report by the patient.

NOTE Confidence: 0.31534237

00:14:40.080 --> 00:14:42.900 A neurologist entered into the surgical

NOTE Confidence: 0.31534237

00:14:42.900 --> 00:14:46.660 room and in a blind way assess rigidity

NOTE Confidence: 0.31534237

00:14:46.660 --> 00:14:50.080 and the scale that they use is the

NOTE Confidence: 0.31534237

00:14:50.080 --> 00:14:54.119 UPD RS4 point scale to assess rigidity

NOTE Confidence: 0.31534237

00:14:54.120 --> 00:14:59.060 and you can see here the circles and

NOTE Confidence: 0.31534237

00:14:59.060 --> 00:15:01.550 then we also measured the firing.

NOTE Confidence: 0.31534237

00:15:01.550 --> 00:15:04.702 So these are only two examples of the

NOTE Confidence: 0.31534237

00:15:04.702 --> 00:15:07.622 many patients involved that but mostly all

NOTE Confidence: 0.31534237

00:15:07.622 --> 00:15:10.908 the neurons that we were able to record.

NOTE Confidence: 0.31534237

00:15:10.910 --> 00:15:13.892 We found congruency between what patient

NOTE Confidence: 0.31534237

00:15:13.892 --> 00:15:16.367 experience the reduction of clinical

NOTE Confidence: 0.31534237

00:15:16.367 --> 00:15:18.821 symptoms and the reduction of the

NOTE Confidence: 0.31534237

00:15:18.821 --> 00:15:22.028 firing at the level of subitalamic area.

NOTE Confidence: 0.31534237

00:15:22.030 --> 00:15:23.944 But there were also patients who

NOTE Confidence: 0.31534237

00:15:23.944 --> 00:15:26.074 didn't improve and for those patients

NOTE Confidence: 0.31534237

00:15:26.074 --> 00:15:27.259 who didn't improve,

NOTE Confidence: 0.31534237

00:15:27.260 --> 00:15:29.380 they didn't experience a benefit.

NOTE Confidence: 0.31534237

00:15:29.380 --> 00:15:32.296 The neurologist didn't detect any change.

NOTE Confidence: 0.31534237

00:15:32.300 --> 00:15:35.348 And so it when we compared the neuronal

NOTE Confidence: 0.31534237

00:15:35.348 --> 00:15:38.017 discharge before and after selling solution,

NOTE Confidence: 0.31534237

00:15:38.020 --> 00:15:41.692 we found in a changes that was you know

NOTE Confidence: 0.31534237

00:15:41.700 --> 00:15:45.095 important study to me for two reasons.

NOTE Confidence: 0.31534237

00:15:45.100 --> 00:15:47.556 First was a sort of epiphany you hear

NOTE Confidence: 0.31534237

00:15:47.556 --> 00:15:50.248 the spike and then when you go back

NOTE Confidence: 0.31534237

00:15:50.248 --> 00:15:52.452 towards these neurons and see this

NOTE Confidence: 0.31534237

00:15:52.452 --> 00:15:54.858 change associated with plasymbi fats 10.

NOTE Confidence: 0.31534237

00:15:54.860 --> 00:15:55.806 Last one,

NOTE Confidence: 0.31534237

00:15:55.806 --> 00:15:59.208 there is something here more than a bias,

NOTE Confidence: 0.31534237

00:15:59.208 --> 00:16:01.470 more than another effects as many

NOTE Confidence: 0.31534237

00:16:01.546 --> 00:16:04.060 people try to think about placebo,

NOTE Confidence: 0.31534237

00:16:04.060 --> 00:16:06.265 but also this question why some people

NOTE Confidence: 0.31534237

00:16:06.265 --> 00:16:08.820 respond and some other people don't respond.

NOTE Confidence: 0.31534237

00:16:08.820 --> 00:16:11.140 It's still an open question and the main

NOTE Confidence: 0.31534237

00:16:11.140 --> 00:16:13.537 line of the research in my lab today.

NOTE Confidence: 0.7061442

00:16:20.440 --> 00:16:23.205 So from this sort of pioneering studies

NOTE Confidence: 0.7061442

00:16:23.205 --> 00:16:25.877 that was running when I start my PhD,

NOTE Confidence: 0.7061442

00:16:25.880 --> 00:16:28.808 we continue and I decided to

NOTE Confidence: 0.7061442

00:16:28.808 --> 00:16:31.280 transition from Parkinson to pain.

NOTE Confidence: 0.7061442

00:16:31.280 --> 00:16:34.772 But the simple reason that I had so many

NOTE Confidence: 0.7061442

00:16:34.772 --> 00:16:37.064 questions Parkinson patients are very

NOTE Confidence: 0.7061442

00:16:37.064 --> 00:16:39.920 difficult to be studied the disease,

NOTE Confidence: 0.7061442

00:16:39.920 --> 00:16:42.320 it's difficult to model enough controls.

NOTE Confidence: 0.7061442

00:16:42.320 --> 00:16:44.800 You don't make people becoming,

NOTE Confidence: 0.7061442

00:16:44.800 --> 00:16:48.250 you know, parkinsonian patient and

NOTE Confidence: 0.7061442

00:16:48.250 --> 00:16:50.980 also the amount of surgical procedure

NOTE Confidence: 0.7061442

00:16:50.980 --> 00:16:53.860 we were conducting was 2/3 per months.

NOTE Confidence: 0.7061442

00:16:53.860 --> 00:16:57.580 So I was literally too slow to finish a PhD.

NOTE Confidence: 0.7061442

00:16:57.580 --> 00:16:59.360 That's also not good.

NOTE Confidence: 0.7061442

00:16:59.360 --> 00:17:01.585 That's model to understand other

NOTE Confidence: 0.7061442

00:17:01.585 --> 00:17:03.419 questions related to placebo.

NOTE Confidence: 0.7061442

00:17:03.420 --> 00:17:06.057 So I thought pain can be a good model.

NOTE Confidence: 0.7061442

00:17:06.060 --> 00:17:08.900 We can work with pain with health control.

NOTE Confidence: 0.7061442

00:17:08.900 --> 00:17:10.220 So we have animal models.

NOTE Confidence: 0.7061442

00:17:10.220 --> 00:17:13.256 So we have chronic pain patients.

NOTE Confidence: 0.7061442

00:17:13.260 --> 00:17:16.820 So we started to do a variety of studies to

NOTE Confidence: 0.7061442

00:17:16.910 --> 00:17:19.153 understand some psychological questions.

NOTE Confidence: 0.7061442

00:17:19.153 --> 00:17:21.979 What can treat the ablazific effect,

NOTE Confidence: 0.7061442

00:17:21.980 --> 00:17:23.200 expectations,

NOTE Confidence: 0.7061442

00:17:23.200 --> 00:17:25.640 verbal suggestions,

NOTE Confidence: 0.7061442

00:17:25.640 --> 00:17:26.860 conditioning.

NOTE Confidence: 0.7061442

00:17:26.860 --> 00:17:31.672 And I really continue the line of

NOTE Confidence: 0.7061442

00:17:31.672 --> 00:17:33.364 research like hypomorphine where

NOTE Confidence: 0.7061442

00:17:33.364 --> 00:17:35.426 we were giving the administration

NOTE Confidence: 0.7061442

00:17:35.426 --> 00:17:38.548 of medications and you can do the

NOTE Confidence: 0.7061442

00:17:38.548 --> 00:17:41.250 same thing with pain by reduction

NOTE Confidence: 0.7061442

00:17:41.250 --> 00:17:43.873 of pain intensity you can simulate

NOTE Confidence: 0.7061442

00:17:43.873 --> 00:17:46.078 a benefit without giving 12

NOTE Confidence: 0.7061442

00:17:46.078 --> 00:17:47.830 participants morphine for example.

NOTE Confidence: 0.7061442

00:17:47.830 --> 00:17:50.188 Although we did this so too.

NOTE Confidence: 0.7061442

00:17:50.190 --> 00:17:53.746 So currently there is a sort of

NOTE Confidence: 0.7061442

00:17:53.746 --> 00:17:56.350 understanding that verbal suggestion,

NOTE Confidence: 0.7061442

00:17:56.350 --> 00:17:58.870 this is a wonderful antidepressant.

NOTE Confidence: 0.7061442

00:17:58.870 --> 00:18:01.246 Your depression can improve

NOTE Confidence: 0.7061442

00:18:01.246 --> 00:18:03.028 therapeutic prior experience.

NOTE Confidence: 0.7061442

00:18:03.030 --> 00:18:06.126 How many of your patients come and say I

NOTE Confidence: 0.7061442

00:18:06.126 --> 00:18:09.304 like this drug because I benefit from it?

NOTE Confidence: 0.7061442

00:18:09.310 --> 00:18:11.900 Observation from other people and

NOTE Confidence: 0.7061442

00:18:11.900 --> 00:18:15.164 contextual effects like the Open Eden

NOTE Confidence: 0.7061442

00:18:15.164 --> 00:18:18.134 paradigm and of course interpersonal

NOTE Confidence: 0.7061442

00:18:18.134 --> 00:18:22.090 interaction can trigger placebo effects.

NOTE Confidence: 0.7061442

00:18:22.090 --> 00:18:24.190 Expectancy is something that

NOTE Confidence: 0.7061442

00:18:24.190 --> 00:18:26.290 continue to intrigue us,

NOTE Confidence: 0.7061442

00:18:26.290 --> 00:18:28.810 and when we talk about expectancy,

NOTE Confidence: 0.7061442

00:18:28.810 --> 00:18:31.346 we can refer to something that we can

NOTE Confidence: 0.7061442

00:18:31.346 --> 00:18:33.609 measure and we call it expectations.

NOTE Confidence: 0.7061442

00:18:33.610 --> 00:18:37.165 With a scale from zero to 100 for example,

NOTE Confidence: 0.7061442

00:18:37.170 --> 00:18:39.140 how much benefit you have

NOTE Confidence: 0.7061442

00:18:39.140 --> 00:18:42.140 expect from zero to maximum?

NOTE Confidence: 0.7061442

00:18:42.140 --> 00:18:43.860 But also there are expectancy

NOTE Confidence: 0.7061442

00:18:43.860 --> 00:18:45.580 that we study in animals,

NOTE Confidence: 0.7061442

00:18:45.580 --> 00:18:48.300 we study in non human model or sometimes

NOTE Confidence: 0.7061442

00:18:48.300 --> 00:18:51.149 we are not even able to model in

NOTE Confidence: 0.7061442

00:18:51.149 --> 00:18:53.049 humans because can not necessarily

NOTE Confidence: 0.7061442

00:18:53.049 --> 00:18:55.659 be captured by a simple scale.

NOTE Confidence: 0.7061442

00:18:55.660 --> 00:18:57.774 How much do you expect to improve?

NOTE Confidence: 0.7061442

00:18:57.780 --> 00:19:00.216 And it is when we do modeling

NOTE Confidence: 0.7061442

00:19:00.220 --> 00:19:03.490 other brain imaging approach to

NOTE Confidence: 0.7061442

00:19:03.490 --> 00:19:06.106 understand how expectancy can

NOTE Confidence: 0.7061442

00:19:06.106 --> 00:19:09.097 modulate drug and Placid beefast.

NOTE Confidence: 0.7061442

00:19:09.100 --> 00:19:11.182 An interesting aspect is that at

NOTE Confidence: 0.7061442

00:19:11.182 --> 00:19:13.787 least for pain as you can see on

NOTE Confidence: 0.7061442

00:19:13.787 --> 00:19:15.980 this part of the graph is that

NOTE Confidence: 0.58686125

00:19:18.060 --> 00:19:20.727 you know the descending component in the

NOTE Confidence: 0.58686125

00:19:20.727 --> 00:19:23.712 dotted line in blue can be so relevant

NOTE Confidence: 0.58686125

00:19:23.712 --> 00:19:25.982 make pain disappear in some patient

NOTE Confidence: 0.58686125

00:19:25.982 --> 00:19:28.538 at least in the placebo responders.

NOTE Confidence: 0.58686125

00:19:28.540 --> 00:19:31.004 And so they're all of the descending

NOTE Confidence: 0.58686125

00:19:31.004 --> 00:19:33.662 pathway is so relevant to when we

NOTE Confidence: 0.58686125

00:19:33.662 --> 00:19:36.400 study placebo effects in pain to the

NOTE Confidence: 0.58686125

00:19:36.400 --> 00:19:38.450 point that the ascending component,

NOTE Confidence: 0.58686125

00:19:38.450 --> 00:19:41.610 it can become less prevalent

NOTE Confidence: 0.58686125

00:19:41.610 --> 00:19:42.966 from the part of the brain,

NOTE Confidence: 0.58686125

00:19:42.970 --> 00:19:44.606 at least for pain,

NOTE Confidence: 0.58686125

00:19:44.606 --> 00:19:46.651 that are critical in modulating

NOTE Confidence: 0.58686125

00:19:46.651 --> 00:19:50.159 placip effects are the frontal area.

NOTE Confidence: 0.58686125

00:19:50.159 --> 00:19:53.131 So ventromedia dorsolateral prefrontal

NOTE Confidence: 0.58686125

00:19:53.131 --> 00:19:56.070 cortex where ventromedia prefrontal

NOTE Confidence: 0.58686125

00:19:56.070 --> 00:19:59.834 cortex has been associated to the

NOTE Confidence: 0.58686125

00:19:59.834 --> 00:20:03.354 decision process versus the dorsolateral

NOTE Confidence: 0.58686125

00:20:03.354 --> 00:20:07.430 prefrontal cortex being more involved in.

NOTE Confidence: 0.58686125

00:20:07.430 --> 00:20:09.830 Maintaining A placebo effects and of

NOTE Confidence: 0.58686125

00:20:09.830 --> 00:20:12.353 course the nuclear compounds and then

NOTE Confidence: 0.58686125

00:20:12.353 --> 00:20:14.503 trastriatom become so critical because

NOTE Confidence: 0.58686125

00:20:14.503 --> 00:20:16.908 especially in patients seeking a reward,

NOTE Confidence: 0.58686125

00:20:16.910 --> 00:20:19.110 the seeking reduction of Parkinson's

NOTE Confidence: 0.58686125

00:20:19.110 --> 00:20:21.310 symptom or pain or depression.

NOTE Confidence: 0.58686125

00:20:21.310 --> 00:20:24.630 Mathematica. It's a big deal.

NOTE Confidence: 0.26277643

00:20:27.950 --> 00:20:32.350 So, and of course there are some genetic

NOTE Confidence: 0.26277643

00:20:32.350 --> 00:20:35.600 factors that can serve us predictors

NOTE Confidence: 0.26277643

00:20:35.600 --> 00:20:37.280 to see those people who respond and

NOTE Confidence: 0.26277643

00:20:37.280 --> 00:20:38.880 those people who don't respond.

NOTE Confidence: 0.5063826

00:20:44.440 --> 00:20:44.880 So

NOTE Confidence: 0.5063826

00:20:47.560 --> 00:20:50.280 if expectancy are so relevant,

NOTE Confidence: 0.5063826

00:20:50.280 --> 00:20:52.145 then we thought it's time

NOTE Confidence: 0.5063826

00:20:52.145 --> 00:20:54.664 to try to understand how we

NOTE Confidence: 0.5063826

00:20:54.664 --> 00:20:56.398 can manipulate expectations.

NOTE Confidence: 0.5063826

00:20:56.400 --> 00:20:58.590 When we study pain in health

NOTE Confidence: 0.5063826

00:20:58.590 --> 00:21:00.640 controls and placebo nocibo effects,

NOTE Confidence: 0.5063826

00:21:00.640 --> 00:21:03.332 usually we use thermal stimulation which

NOTE Confidence: 0.5063826

00:21:03.332 --> 00:21:05.384 is the thermal stimulation that has

NOTE Confidence: 0.4575084

00:21:05.390 --> 00:21:06.950 been used at first labs.

NOTE Confidence: 0.4575084

00:21:07.470 --> 00:21:11.870 And in this case we use visual cue

NOTE Confidence: 0.4575084

00:21:11.870 --> 00:21:15.470 red during the anticipatory phase.

NOTE Confidence: 0.4575084

00:21:15.470 --> 00:21:18.314 And then when the painful stimulation

NOTE Confidence: 0.4575084

00:21:18.314 --> 00:21:21.830 was used, you can see that we had the

NOTE Confidence: 0.4575084

00:21:21.830 --> 00:21:24.402 emotional component fearful phase.

NOTE Confidence: 0.4575084

00:21:24.402 --> 00:21:29.261 With yellow we had neutral phase and with

NOTE Confidence: 0.4575084

00:21:29.261 --> 00:21:33.520 green epiphase the most critical component

NOTE Confidence: 0.4575084

00:21:33.520 --> 00:21:36.738 was for us to create an experience of

NOTE Confidence: 0.4575084

00:21:36.738 --> 00:21:39.580 eye pain and low pain and control pain.

NOTE Confidence: 0.4575084

00:21:39.580 --> 00:21:42.009 So this is a visual analogue scale

NOTE Confidence: 0.4575084

00:21:42.009 --> 00:21:44.937 and we raise the intensity of the

NOTE Confidence: 0.4575084

00:21:44.937 --> 00:21:48.520 thermal stimulation to 8050 or 12 day.

NOTE Confidence: 0.4575084

00:21:48.520 --> 00:21:51.295 One participant received many stimulation

NOTE Confidence: 0.4575084

00:21:51.295 --> 00:21:54.660 seeks to be precise and that allow us

NOTE Confidence: 0.4575084

00:21:54.660 --> 00:21:57.940 to create an experience of eye pain,

NOTE Confidence: 0.4575084

00:21:57.940 --> 00:22:01.160 low pain as compared to moderate pain

NOTE Confidence: 0.4575084

00:22:01.160 --> 00:22:05.324 day 2 in the scanner we set all the

NOTE Confidence: 0.4575084

00:22:05.324 --> 00:22:08.123 intensity out to the same level and

NOTE Confidence: 0.4575084

00:22:08.123 --> 00:22:10.703 operationally we define a change in

NOTE Confidence: 0.4575084

00:22:10.703 --> 00:22:14.398 the red pair stimulation and green pair

NOTE Confidence: 0.4575084

00:22:14.398 --> 00:22:17.872 stimulation as placebo and nocible effects.

NOTE Confidence: 0.4575084

00:22:17.880 --> 00:22:19.816 We want to see how the

NOTE Confidence: 0.4575084

00:22:19.816 --> 00:22:21.640 prior experience day one,

NOTE Confidence: 0.4575084

00:22:21.640 --> 00:22:23.392 but also the anticipation,

NOTE Confidence: 0.4575084

00:22:23.392 --> 00:22:26.553 the expectation of higher low pain would

NOTE Confidence: 0.4575084

00:22:26.553 --> 00:22:29.759 have changed when we mismatch the conditions.

NOTE Confidence: 0.4575084

00:22:29.760 --> 00:22:32.840 That is why we use two visual stimulation,

NOTE Confidence: 0.4575084

00:22:32.840 --> 00:22:35.160 you know 2 cures.

NOTE Confidence: 0.4575084

00:22:35.160 --> 00:22:37.880 And so when participants receive

NOTE Confidence: 0.4575084

00:22:37.880 --> 00:22:41.360 identical stimulation in a match patient,

NOTE Confidence: 0.4575084

00:22:41.360 --> 00:22:44.125 you can see that same identical level

NOTE Confidence: 0.4575084

00:22:44.125 --> 00:22:46.680 of tumor stimulation produce lower pain.

NOTE Confidence: 0.4575084

00:22:46.680 --> 00:22:50.016 This is their circle report as compared to

NOTE Confidence: 0.4575084

00:22:50.016 --> 00:22:53.478 our control in dire pain when they expect IP.

NOTE Confidence: 0.4575084

00:22:53.480 --> 00:22:56.574 So what we expect can drive moderate

NOTE Confidence: 0.4575084

00:22:56.574 --> 00:22:59.603 level of pain to become high or

NOTE Confidence: 0.4575084

00:22:59.603 --> 00:23:02.587 low and that is what you know we've

NOTE Confidence: 0.4575084

00:23:02.587 --> 00:23:05.550 got nocebo and placebo response.

NOTE Confidence: 0.4575084

00:23:05.550 --> 00:23:07.150 However when we mismatch,

NOTE Confidence: 0.4575084

00:23:07.150 --> 00:23:09.150 so we manipulate the expectation,

NOTE Confidence: 0.4575084

00:23:09.150 --> 00:23:11.298 we manipulate the events and I

NOTE Confidence: 0.4575084

00:23:11.298 --> 00:23:14.557 bet that all of us had experienced

NOTE Confidence: 0.4575084

00:23:14.557 --> 00:23:16.306 violation of expectations.

NOTE Confidence: 0.4575084

00:23:16.310 --> 00:23:18.308 You know, you go towards something,

NOTE Confidence: 0.4575084

00:23:18.310 --> 00:23:19.810 you expect something and

NOTE Confidence: 0.4575084

00:23:19.810 --> 00:23:21.310 you get something else.

NOTE Confidence: 0.4575084

00:23:21.310 --> 00:23:23.270 And this is the story of many patients.

NOTE Confidence: 0.4575084

00:23:23.270 --> 00:23:24.960 They went to the clinic,

NOTE Confidence: 0.4575084

00:23:24.960 --> 00:23:27.676 they want to be healed and treated,

NOTE Confidence: 0.4575084

00:23:27.680 --> 00:23:29.560 but eventually their depression

NOTE Confidence: 0.4575084

00:23:29.560 --> 00:23:31.440 or symptom doesn't change.

NOTE Confidence: 0.4575084

00:23:31.440 --> 00:23:33.612 Every time we see a violation

NOTE Confidence: 0.4575084

00:23:33.612 --> 00:23:35.726 of expectation that can trigger

NOTE Confidence: 0.4575084

00:23:35.726 --> 00:23:37.517 a neurobiological response.

NOTE Confidence: 0.4575084

00:23:37.520 --> 00:23:40.691 And we can call this nausea if it's

NOTE Confidence: 0.4575084

00:23:40.691 --> 00:23:42.199 a worsening in symptoms.

NOTE Confidence: 0.4575084

00:23:42.200 --> 00:23:45.625 So nausea effects didn't disappear

NOTE Confidence: 0.4575084

00:23:45.625 --> 00:23:48.959 when mismatched cues were presented,

NOTE Confidence: 0.4575084

00:23:48.959 --> 00:23:52.877 but mismatched cues abolish plessive effects.

NOTE Confidence: 0.4575084

00:23:52.880 --> 00:23:54.520 So I was asked today,

NOTE Confidence: 0.4575084

00:23:54.520 --> 00:23:57.328 how can we somehow reduce placebo

NOTE Confidence: 0.4575084

00:23:57.328 --> 00:23:59.200 responses in clinical trials?

NOTE Confidence: 0.4575084

00:23:59.200 --> 00:24:01.840 One strategy will be to create

NOTE Confidence: 0.4575084

00:24:01.840 --> 00:24:04.564 mismatch of expectations and that can

NOTE Confidence: 0.4575084

00:24:04.564 --> 00:24:07.372 somehow help to reduce the placebo

NOTE Confidence: 0.4575084

00:24:07.372 --> 00:24:09.984 component and focus purely on the

NOTE Confidence: 0.4575084

00:24:09.984 --> 00:24:12.039 drug that we are studying.

NOTE Confidence: 0.4575084

00:24:12.040 --> 00:24:14.515 And of course, so if you are a physician,

NOTE Confidence: 0.4575084

00:24:14.520 --> 00:24:17.160 you may want to amplify

NOTE Confidence: 0.4575084

00:24:17.160 --> 00:24:18.540 the placebo component.

NOTE Confidence: 0.4575084

00:24:18.540 --> 00:24:19.920 So it depends.

NOTE Confidence: 0.734735

00:24:20.450 --> 00:24:22.250 Can I ask you so all of this,

NOTE Confidence: 0.734735

00:24:22.250 --> 00:24:23.810 the beautiful studies you've shown us

NOTE Confidence: 0.734735

00:24:23.810 --> 00:24:27.082 are all acute acute change in anxiety,

NOTE Confidence: 0.734735

00:24:27.082 --> 00:24:28.896 acute change in pain, right.

NOTE Confidence: 0.734735

00:24:28.896 --> 00:24:30.200 Whereas clinically what's relevant

NOTE Confidence: 0.734735

00:24:30.200 --> 00:24:32.430 is in including in a drug trial

NOTE Confidence: 0.734735

00:24:32.430 --> 00:24:34.050 as you were just referring to.

NOTE Confidence: 0.734735

00:24:34.050 --> 00:24:36.095 What's relevant is chronic effects

NOTE Confidence: 0.734735

00:24:36.095 --> 00:24:38.788 and it's not obvious that those are

NOTE Confidence: 0.734735

00:24:38.788 --> 00:24:40.734 going to be through the same mechanism

NOTE Confidence: 0.734735

00:24:40.734 --> 00:24:42.089 or have the same characteristics.

NOTE Confidence: 0.54941934

00:24:42.330 --> 00:24:44.418 So the study I chose and we do in

NOTE Confidence: 0.54941934

00:24:44.418 --> 00:24:46.410 the lab are mostly one session,

NOTE Confidence: 0.54941934

00:24:46.410 --> 00:24:48.340 although now we are studying

NOTE Confidence: 0.54941934

37

00:24:48.340 --> 00:24:50.270 chronic pain patient who have

NOTE Confidence: 0.54941934

00:24:50.343 --> 00:24:52.299 long lasting effects and we call

NOTE Confidence: 0.54941934

00:24:52.299 --> 00:24:54.610 them back to the lab after six,

NOTE Confidence: 0.54941934

00:24:54.610 --> 00:24:56.962 one year time to see if they

NOTE Confidence: 0.54941934

00:24:56.962 --> 00:24:57.970 continue to benefit.

NOTE Confidence: 0.54941934

00:24:57.970 --> 00:25:01.710 And I mean we don't study

NOTE Confidence: 0.54941934

00:25:01.710 --> 00:25:03.290 a report or don't publish,

NOTE Confidence: 0.54941934

00:25:03.290 --> 00:25:05.684 but we have some of our patients

NOTE Confidence: 0.54941934

00:25:05.684 --> 00:25:07.984 who improve with this kind of sham

NOTE Confidence: 0.54941934

00:25:07.984 --> 00:25:10.168 electrodes and they went to buy

NOTE Confidence: 0.54941934

00:25:10.168 --> 00:25:12.059 because their pain was solved.

NOTE Confidence: 0.54941934

00:25:12.060 --> 00:25:14.860 So and of course there are many

NOTE Confidence: 0.54941934

00:25:14.860 --> 00:25:17.379 clinical trials show that the placebo

NOTE Confidence: 0.54941934

00:25:17.380 --> 00:25:19.528 component lasts over time And we

NOTE Confidence: 0.54941934

00:25:19.528 --> 00:25:22.192 know also from the failure of many

NOTE Confidence: 0.54941934

00:25:22.192 --> 00:25:24.818 trials the reason why we look at

NOTE Confidence: 0.54941934

00:25:24.818 --> 00:25:26.460 this response with cross-sectional

NOTE Confidence: 0.54941934

00:25:26.460 --> 00:25:29.580 studies mostly for you know brain

NOTE Confidence: 0.54941934

00:25:29.580 --> 00:25:31.140 imaging mechanistic approach.

NOTE Confidence: 0.54941934

00:25:31.140 --> 00:25:34.086 But that doesn't mean and that

NOTE Confidence: 0.54941934

00:25:34.086 --> 00:25:36.590 placebo effects extinguish over time

NOTE Confidence: 0.54941934

00:25:36.590 --> 00:25:39.308 or patient who have chronic disease

NOTE Confidence: 0.54941934

00:25:39.310 --> 00:25:41.470 actual experience placebo effects.

NOTE Confidence: 0.3972127

00:25:42.150 --> 00:25:44.075 And I guess the question I'm wondering

NOTE Confidence: 0.3972127

00:25:44.075 --> 00:25:45.748 if clearly there are long lasting

NOTE Confidence: 0.3972127

00:25:45.750 --> 00:25:47.566 placebo effects and we've all seen them,

NOTE Confidence: 0.3972127

00:25:47.566 --> 00:25:49.630 are the mechanisms of the later phase or

NOTE Confidence: 0.3972127

00:25:49.630 --> 00:25:51.950 the persistence of the placebo the same

NOTE Confidence: 0.3972127

00:25:52.110 --> 00:25:54.000 as the mechanisms of the CUE

NOTE Confidence: 0.3972127

00:25:54.000 --> 00:25:54.945 driven immediate environment?

NOTE Confidence: 0.3972127

00:25:54.950 --> 00:25:56.525 That's the question I was asking and

NOTE Confidence: 0.3972127

00:25:56.525 --> 00:25:57.590 it's an experimentally difficult

NOTE Confidence: 0.3972127

00:25:58.750 --> 00:26:00.290 question and there are other

NOTE Confidence: 0.3972127

00:26:00.290 --> 00:26:01.830 groups that are studying this.

NOTE Confidence: 0.3972127

00:26:01.830 --> 00:26:05.430 For example Vanya Caparia is interested

NOTE Confidence: 0.3972127

00:26:05.430 --> 00:26:08.805 in brain imaging and long lasting

NOTE Confidence: 0.3972127

00:26:08.805 --> 00:26:11.763 effect of placebo and the mechanism

NOTE Confidence: 0.3972127

00:26:11.763 --> 00:26:14.349 that he has been publishing are

NOTE Confidence: 0.3972127

00:26:14.349 --> 00:26:16.939 primarily related to the reward the

NOTE Confidence: 0.3972127

00:26:16.939 --> 00:26:19.517 system and there are similarity in

NOTE Confidence: 0.3972127

00:26:19.517 --> 00:26:22.013 terms of our expectation can trigger

NOTE Confidence: 0.3972127

00:26:22.013 --> 00:26:24.202 uplasi effects in chronic pain

NOTE Confidence: 0.3972127

00:26:24.202 --> 00:26:26.066 patients in particular osteoarthritis.

NOTE Confidence: 0.3972127

00:26:26.070 --> 00:26:29.514 For his line of research we are

NOTE Confidence: 0.3972127

00:26:29.514 --> 00:26:33.384 doing that in for a facial pain and

NOTE Confidence: 0.3972127

00:26:33.384 --> 00:26:35.568 yes the goal is to try to see how

NOTE Confidence: 0.3972127

00:26:35.568 --> 00:26:37.968 long we can maintain these effects

NOTE Confidence: 0.3972127

00:26:37.968 --> 00:26:39.396 and translate therapeutically.

NOTE Confidence: 0.3972127

00:26:39.400 --> 00:26:42.721 We are not there yet but that is one

NOTE Confidence: 0.3972127

00:26:42.721 --> 00:26:46.120 of the question we try to address.

NOTE Confidence: 0.3972127

00:26:46.120 --> 00:26:48.800 Another aspects that is relevant

NOTE Confidence: 0.3972127

00:26:48.800 --> 00:26:52.091 especially when we talk about clinical

NOTE Confidence: 0.3972127

00:26:52.091 --> 00:26:55.146 situations is the negative component

NOTE Confidence: 0.3972127

00:26:55.146 --> 00:26:58.349 Nasib effects because Nasib effects

NOTE Confidence: 0.3972127

00:26:58.349 --> 00:27:01.443 somehow amplify negative you know and

NOTE Confidence: 0.3972127

00:27:01.443 --> 00:27:04.090 worsening of symptoms in this case

NOTE Confidence: 0.3972127

00:27:04.090 --> 00:27:08.360 we show in a very you know simple way

NOTE Confidence: 0.3972127

00:27:08.360 --> 00:27:11.124 for time restriction that Nosibo the

NOTE Confidence: 0.3972127

00:27:11.124 --> 00:27:14.088 negative or component of placebo effects.

NOTE Confidence: 0.3972127

00:27:14.090 --> 00:27:16.470 Actually with pharmacological study,

NOTE Confidence: 0.3972127

00:27:16.470 --> 00:27:20.710 we know that work through the engagement

NOTE Confidence: 0.3972127

00:27:20.710 --> 00:27:23.860 of the coagcystokines systems in

NOTE Confidence: 0.3972127

00:27:23.860 --> 00:27:26.822 particular A&amp;B receptors with studying

NOTE Confidence: 0.3972127

00:27:26.822 --> 00:27:29.737 both animal models and humans,

NOTE Confidence: 0.3972127

00:27:29.740 --> 00:27:32.788 there is a change in the new opioids

NOTE Confidence: 0.3972127

00:27:32.788 --> 00:27:34.987 availability as well as the release

NOTE Confidence: 0.3972127

00:27:34.987 --> 00:27:36.692 of D2 and D3 dopamine.

NOTE Confidence: 0.3972127

00:27:36.700 --> 00:27:39.689 So this nocebo component can be even

NOTE Confidence: 0.3972127

00:27:39.689 --> 00:27:41.464 clinically speaking more relevant

NOTE Confidence: 0.3972127

00:27:41.464 --> 00:27:43.984 because every time we see worsening

NOTE Confidence: 0.3972127

00:27:43.984 --> 00:27:46.579 in symptom pain or other symptoms.

NOTE Confidence: 0.3972127

00:27:46.580 --> 00:27:49.040 There is also an engagement of

NOTE Confidence: 0.3972127

00:27:49.040 --> 00:27:51.300 circles that are not parallel to

NOTE Confidence: 0.3972127

00:27:51.300 --> 00:27:52.380 the placebo mechanism,

NOTE Confidence: 0.3972127

00:27:52.380 --> 00:27:54.536 at least in terms of brain imaging,

NOTE Confidence: 0.3972127

00:27:54.540 --> 00:27:56.184 but yet it can,

NOTE Confidence: 0.3972127

00:27:56.184 --> 00:27:57.006 you know,

NOTE Confidence: 0.3972127

00:27:57.010 --> 00:27:59.460 be triggered by expectation and

NOTE Confidence: 0.3972127

00:27:59.460 --> 00:28:00.930 similar psychological mechanisms.

NOTE Confidence: 0.49906704

00:28:06.560 --> 00:28:08.996 So to tackle the question about

NOTE Confidence: 0.49906704

00:28:08.996 --> 00:28:11.480 Placib effects in chronic conditions,

NOTE Confidence: 0.49906704

00:28:14.240 --> 00:28:17.696 we study chronic or facial pain

NOTE Confidence: 0.49906704

00:28:17.696 --> 00:28:20.000 and temporal mandibular disorders

NOTE Confidence: 0.49906704

00:28:20.000 --> 00:28:21.740 because after about had decades

NOTE Confidence: 0.49906704

00:28:21.740 --> 00:28:23.480 of studies in earth controls,

NOTE Confidence: 0.49906704

00:28:23.480 --> 00:28:25.676 we were wondering what if we

NOTE Confidence: 0.49906704

00:28:25.676 --> 00:28:27.140 study chronic pain patients,

NOTE Confidence: 0.49906704

00:28:27.140 --> 00:28:30.059 they do show the same placebo effects,

NOTE Confidence: 0.49906704

00:28:30.060 --> 00:28:32.856 this sort of huge change in

NOTE Confidence: 0.49906704

00:28:32.856 --> 00:28:35.745 the pain reports and you know

NOTE Confidence: 0.49906704

00:28:35.745 --> 00:28:38.220 affective component of the pain.

NOTE Confidence: 0.49906704

00:28:38.220 --> 00:28:41.196 So we brought in patients for

NOTE Confidence: 0.49906704

00:28:41.196 --> 00:28:43.998 in depth clinical screening of

NOTE Confidence: 0.49906704

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00:28:43.998 --> 00:28:46.389 temporomandibular pain at UMB where

NOTE Confidence: 0.49906704

00:28:46.389 --> 00:28:47.954 the Brothman or official clinic

NOTE Confidence: 0.49906704

00:28:47.954 --> 00:28:50.124 that is one of the major clinic

NOTE Confidence: 0.49906704

00:28:50.124 --> 00:28:52.090 for this condition in the states.

NOTE Confidence: 0.49906704

00:28:52.090 --> 00:28:54.841 And then we did the same manipulation

NOTE Confidence: 0.49906704

00:28:54.841 --> 00:28:57.090 individual calibration of pen sensitivity,

NOTE Confidence: 0.49906704

00:28:57.090 --> 00:28:59.526 we call this quantitative sensory test.

NOTE Confidence: 0.49906704

00:28:59.530 --> 00:29:01.610 We assess baseline expectation

NOTE Confidence: 0.49906704

00:29:01.610 --> 00:29:04.730 and we expose them to conditioning

NOTE Confidence: 0.49906704

00:29:04.810 --> 00:29:08.400 with 24 trials where we you know

NOTE Confidence: 0.49906704

00:29:08.400 --> 00:29:11.120 we're in a pseudorandom way,

NOTE Confidence: 0.49906704

00:29:11.120 --> 00:29:12.948 deliver eye painful and

NOTE Confidence: 0.49906704

00:29:12.948 --> 00:29:14.319 low painful stimulation.

NOTE Confidence: 0.49906704

00:29:14.320 --> 00:29:16.693 And we told them that every time

NOTE Confidence: 0.49906704

00:29:16.693 --> 00:29:18.480 this sham electrodes was active,

NOTE Confidence: 0.49906704

00:29:18.480 --> 00:29:21.144 the painful stimulation was the same

NOTE Confidence: 0.49906704

00:29:21.144 --> 00:29:23.680 but eventually they perceive less pain.

NOTE Confidence: 0.49906704

00:29:23.680 --> 00:29:26.752 The idea is to avoid to create a

NOTE Confidence: 0.49906704

00:29:26.752 --> 00:29:29.016 conditioning with morphine or other

NOTE Confidence: 0.49906704

00:29:29.016 --> 00:29:31.366 painkillers rather expose them to

NOTE Confidence: 0.49906704

00:29:31.366 --> 00:29:34.124 low intensity stimulations and after

NOTE Confidence: 0.49906704

00:29:34.124 --> 00:29:37.550 that we reassess expectation and your

NOTE Confidence: 0.49906704

00:29:37.633 --> 00:29:41.056 expectation improve if you have a benefit.

NOTE Confidence: 0.49906704

00:29:41.060 --> 00:29:43.900 We call this reinforced expectation

NOTE Confidence: 0.49906704

00:29:43.900 --> 00:29:46.448 and then we test for placebo first

NOTE Confidence: 0.49906704

00:29:46.448 --> 00:29:49.155 testing phase where we use identical eye

NOTE Confidence: 0.49906704

00:29:49.155 --> 00:29:51.465 level log thermal stimulation to see

NOTE Confidence: 0.49906704

00:29:51.533 --> 00:29:54.081 if somehow there is a placebo response

NOTE Confidence: 0.49906704

00:29:54.081 --> 00:29:59.100 in chronic pain patient with this condition.

NOTE Confidence: 0.49906704

00:29:59.100 --> 00:30:02.228 These are the data and you can see

NOTE Confidence: 0.49906704

00:30:02.228 --> 00:30:05.100 that we match people for race,

NOTE Confidence: 0.49906704

00:30:05.100 --> 00:30:07.119 age and sex.

NOTE Confidence: 0.49906704

00:30:07.119 --> 00:30:09.844 The distribution of placebo

NOTE Confidence: 0.49906704

00:30:09.844 --> 00:30:12.660 response assessed several time,

NOTE Confidence: 0.49906704

00:30:12.660 --> 00:30:15.623 you know trial by trial are identical.

NOTE Confidence: 0.49906704

00:30:15.623 --> 00:30:18.761 So no matter if people had

NOTE Confidence: 0.49906704

00:30:18.761 --> 00:30:22.019 chronic pain or no chronic pain,

NOTE Confidence: 0.49906704

00:30:22.020 --> 00:30:25.700 there was some placebo analgesia.

NOTE Confidence: 0.49906704

00:30:25.700 --> 00:30:28.730 When we compare the proportion of

NOTE Confidence: 0.49906704

00:30:28.730 --> 00:30:30.926 placebo responders with permutation

NOTE Confidence: 0.49906704

00:30:30.926 --> 00:30:35.060 test to see some who are the placebo

NOTE Confidence: 0.49906704

00:30:35.060 --> 00:30:38.239 responders and for our you know the

NOTE Confidence: 0.49906704

00:30:38.239 --> 00:30:40.686 proportion of responders in TMD

NOTE Confidence: 0.49906704

00:30:40.686 --> 00:30:43.764 where the 53 percentage of placebo

NOTE Confidence: 0.49906704

00:30:43.764 --> 00:30:45.942 responders that was significantly

NOTE Confidence: 0.49906704

00:30:45.942 --> 00:30:49.128 lower but still quite high than

NOTE Confidence: 0.49906704

00:30:49.128 --> 00:30:52.272 pain free people 67.8 percentage.

NOTE Confidence: 0.49906704

00:30:52.272 --> 00:30:56.628 But this numbers make clinical trials

NOTE Confidence: 0.49906704

00:30:56.628 --> 00:30:59.700 fail because with this proportion of

NOTE Confidence: 0.49906704

00:30:59.700 --> 00:31:02.040 placebo responsivity is extremely high.

NOTE Confidence: 0.49906704

00:31:02.040 --> 00:31:04.988 But if we talk about patient benefits,

NOTE Confidence: 0.49906704

00:31:04.988 --> 00:31:07.712 that can be actually good because

NOTE Confidence: 0.49906704

00:31:07.712 --> 00:31:11.252 if we look at the number needed

NOTE Confidence: 0.49906704

00:31:11.252 --> 00:31:13.292 to treat anticonvulsionant and

NOTE Confidence: 0.49906704

00:31:13.292 --> 00:31:15.674 opioids vary from 1.7 to 3.

NOTE Confidence: 0.49906704

00:31:15.674 --> 00:31:17.822 And when we look at our

NOTE Confidence: 0.49906704

00:31:17.822 --> 00:31:19.158 depression in the lab,

NOTE Confidence: 0.49906704

00:31:19.160 --> 00:31:22.280 you can see that the NNT

NOTE Confidence: 0.49906704

00:31:22.280 --> 00:31:25.750 for TMD it's about 1.8.

NOTE Confidence: 0.49906704

00:31:25.750 --> 00:31:27.760 So suggesting that protein effects

NOTE Confidence: 0.49906704

00:31:27.760 --> 00:31:30.176 are real can be important in

NOTE Confidence: 0.49906704

00:31:30.176 --> 00:31:32.186 chronic pain patient and even with

NOTE Confidence: 0.49906704

00:31:32.186 --> 00:31:34.669 an empty the desired and controls.

NOTE Confidence: 0.3284985

00:31:37.510 --> 00:31:39.030 Do you want to maybe just go through

NOTE Confidence: 0.3284985

00:31:39.030 --> 00:31:40.668 that a little bit because I'm not

NOTE Confidence: 0.3284985

00:31:40.668 --> 00:31:42.106 sure people fully get the number

NOTE Confidence: 0.3284985

00:31:42.106 --> 00:31:43.879 needed to treat and what it would

NOTE Confidence: 0.3284985

00:31:43.879 --> 00:31:45.589 be compared to an active medicine,

NOTE Confidence: 0.3284985

00:31:46.830 --> 00:31:51.415 yes. So the number needed to treat

NOTE Confidence: 0.3284985

00:31:51.415 --> 00:31:54.990 is one of the way to assess it.

NOTE Confidence: 0.3284985

00:31:54.990 --> 00:31:56.854 But treatment is efficacious.

NOTE Confidence: 0.3284985

00:31:56.854 --> 00:32:00.866 So when we run a clinical trial that is

NOTE Confidence: 0.3284985

00:32:00.866 --> 00:32:04.199 the number that the index and then T and

NOTE Confidence: 0.3284985

00:32:04.199 --> 00:32:07.174 so for opioids and anticonvulsion and it

NOTE Confidence: 0.3284985

00:32:07.174 --> 00:32:10.359 has been published in the literature,

NOTE Confidence: 0.3284985

00:32:10.360 --> 00:32:13.684 this critical number is 1.7 for

NOTE Confidence: 0.3284985

00:32:13.684 --> 00:32:16.439 anticonvulsion and and opioids is 3.

NOTE Confidence: 0.3284985

00:32:16.440 --> 00:32:19.160 And the reason why we want to somehow

NOTE Confidence: 0.3284985

00:32:19.160 --> 00:32:21.530 compare for our placebo manipulation was

NOTE Confidence: 0.3284985

00:32:21.530 --> 00:32:24.440 to try to understand where we stand.

NOTE Confidence: 0.3284985

00:32:24.440 --> 00:32:27.275 And so you can see that it's within the

NOTE Confidence: 0.3284985

00:32:27.275 --> 00:32:30.408 range of current use pain therapeutics

NOTE Confidence: 0.3284985

00:32:30.408 --> 00:32:34.320 for neuropathic pain or chronic pain.

NOTE Confidence: 0.3284985

00:32:34.320 --> 00:32:36.960 And the fact that even manipulation

NOTE Confidence: 0.3284985

00:32:36.960 --> 00:32:39.824 in the lab, the reduction can change

NOTE Confidence: 0.3284985

00:32:39.824 --> 00:32:41.754 the mindset of a patient.

NOTE Confidence: 0.3284985

00:32:41.760 --> 00:32:44.704 And that is why I call this stock

NOTE Confidence: 0.3284985

00:32:44.704 --> 00:32:47.353 mind over molecules even you know

NOTE Confidence: 0.3284985

00:32:47.353 --> 00:32:51.110 the exposure to low pain that can be

NOTE Confidence: 0.3284985

00:32:51.110 --> 00:32:54.050 translated in improvements or mode for

NOTE Confidence: 0.3284985

00:32:54.050 --> 00:32:56.523 antidepressant can be so important

NOTE Confidence: 0.3284985

00:32:56.523 --> 00:32:58.898 in manipulating the expectation and

NOTE Confidence: 0.3284985

00:32:58.898 --> 00:33:03.090 trigger somehow this you know index

NOTE Confidence: 0.3284985

00:33:03.090 --> 00:33:06.870 to help us eventually to validate

NOTE Confidence: 0.3284985

00:33:06.870 --> 00:33:08.620 the drug or treat patients.

NOTE Confidence: 0.24997637

00:33:08.620 --> 00:33:10.340 So would you conceive of this number

NOTE Confidence: 0.24997637

00:33:10.340 --> 00:33:11.940 needed to treat number is essentially

NOTE Confidence: 0.24997637

00:33:11.940 --> 00:33:13.572 an effect size of treatments and

NOTE Confidence: 0.24997637

00:33:13.572 --> 00:33:15.404 what you're saying is the effect size

NOTE Confidence: 0.24997637

00:33:15.404 --> 00:33:18.260 of yes is the same as it's a that's

NOTE Confidence: 0.24997637

00:33:18.260 --> 00:33:19.820 that's amazing. Yes that's

NOTE Confidence: 0.24997637

00:33:19.820 --> 00:33:21.140 a that's a big point Yeah.

NOTE Confidence: 0.24997637

00:33:21.620 --> 00:33:23.460 Yes it's it's thriller.

NOTE Confidence: 0.24997637

00:33:25.740 --> 00:33:26.780 So the other thing,

NOTE Confidence: 0.24997637

00:33:29.460 --> 00:33:34.498 when I move from an age University

NOTE Confidence: 0.24997637

00:33:34.498 --> 00:33:37.338 of Maryland in Baltimore, I realised

NOTE Confidence: 0.24997637

00:33:37.338 --> 00:33:39.326 first that my lab was very diverse.

NOTE Confidence: 0.24997637

00:33:39.330 --> 00:33:41.730 I had a PhD student of

NOTE Confidence: 0.24997637

00:33:41.730 --> 00:33:43.330 American black white patients,

NOTE Confidence: 0.24997637

00:33:43.330 --> 00:33:46.130 but also the patients were quite diverse.

NOTE Confidence: 0.24997637

00:33:46.130 --> 00:33:47.930 So despite this not to begin

NOTE Confidence: 0.24997637

00:33:47.930 --> 00:33:49.850 a name of our everyone.

NOTE Confidence: 0.24997637

00:33:49.850 --> 00:33:52.671 I thought I needed to keep record

NOTE Confidence: 0.24997637

00:33:52.671 --> 00:33:57.234 because the data can be some biased

NOTE Confidence: 0.24997637

00:33:57.234 --> 00:34:01.114 by race and ethnicity and eventually

NOTE Confidence: 0.24997637

00:34:01.114 --> 00:34:03.984 you know our beautiful collegiality.

NOTE Confidence: 0.24997637

00:34:03.984 --> 00:34:07.806 It was environment with students a

NOTE Confidence: 0.24997637

00:34:07.806 --> 00:34:12.758 student of mine bogus Sago was you know

NOTE Confidence: 0.24997637

00:34:12.758 --> 00:34:15.716 very talent and Young came and say Lana,

NOTE Confidence: 0.24997637

00:34:15.716 --> 00:34:17.746 can I study race differences.

NOTE Confidence: 0.24997637

00:34:17.750 --> 00:34:19.906 That's a perfect we have the data.

NOTE Confidence: 0.24997637

00:34:19.910 --> 00:34:22.668 So we started diving into the data,

NOTE Confidence: 0.24997637

00:34:22.670 --> 00:34:23.910 see if somehow the race,

NOTE Confidence: 0.24997637

00:34:23.910 --> 00:34:26.115 ethnicity of the patient and

NOTE Confidence: 0.24997637

00:34:26.115 --> 00:34:28.320 the experimenter can change the

NOTE Confidence: 0.24997637

00:34:28.397 --> 00:34:30.527 money to the plus CB effects.

NOTE Confidence: 0.24997637

00:34:30.530 --> 00:34:32.290 And we have suffered that

NOTE Confidence: 0.24997637

00:34:32.290 --> 00:34:34.050 only for chronic pain patient.

NOTE Confidence: 0.24997637

00:34:34.050 --> 00:34:37.272 Same concordance of rays produce larger

NOTE Confidence: 0.24997637

00:34:37.272 --> 00:34:41.298 plus CB effects dark blue as compared

NOTE Confidence: 0.24997637

00:34:41.298 --> 00:34:44.480 to different experiment patient rays.

NOTE Confidence: 0.24997637

00:34:44.480 --> 00:34:47.260 But this doesn't become

NOTE Confidence: 0.24997637

00:34:47.260 --> 00:34:49.574 relevant for health controls.

NOTE Confidence: 0.24997637

00:34:49.574 --> 00:34:52.346 So we are still diving into

NOTE Confidence: 0.24997637

00:34:52.346 --> 00:34:54.650 this kind of differences.

NOTE Confidence: 0.24997637

00:34:54.650 --> 00:34:54.970 Why?

NOTE Confidence: 0.24997637

00:34:54.970 --> 00:34:56.890 And this is the disparities that

NOTE Confidence: 0.24997637

00:34:56.890 --> 00:34:59.290 we read in the literature and

NOTE Confidence: 0.24997637

00:34:59.290 --> 00:35:01.524 clinical practice when there are

NOTE Confidence: 0.24997637

00:35:01.524 --> 00:35:03.684 other groups earlier cram from

NOTE Confidence: 0.24997637

00:35:03.684 --> 00:35:06.499 Stanford that is studying this bias,

NOTE Confidence: 0.24997637

00:35:06.500 --> 00:35:08.817 something under the skin and so on.

NOTE Confidence: 0.24997637

00:35:08.820 --> 00:35:11.646 We are now tackling these questions

NOTE Confidence: 0.24997637

00:35:11.646 --> 00:35:13.059 with neurobiological measurements.

NOTE Confidence: 0.24997637

00:35:13.060 --> 00:35:17.260 Try to understand if it's an implicit bias,

NOTE Confidence: 0.24997637

00:35:17.260 --> 00:35:19.900 if it's related to immigration,

NOTE Confidence: 0.24997637

00:35:19.900 --> 00:35:21.612 media, where they live,

NOTE Confidence: 0.24997637

00:35:21.612 --> 00:35:22.896 where everything from,

NOTE Confidence: 0.24997637

00:35:22.900 --> 00:35:24.550 you know,

NOTE Confidence: 0.24997637

00:35:24.550 --> 00:35:28.546 social demographic position for the ancestry,

NOTE Confidence: 0.24997637

00:35:28.550 --> 00:35:31.546 because we are intrigued by this difference.

NOTE Confidence: 0.24997637

00:35:31.550 --> 00:35:31.790 Seems

NOTE Confidence: 0.25151125

00:35:31.790 --> 00:35:32.930 like the possibility that

NOTE Confidence: 0.25151125

00:35:32.930 --> 00:35:34.070 those effects in psychedelics

NOTE Confidence: 0.25151125

00:35:34.070 --> 00:35:35.790 is a bit more right.

NOTE Confidence: 0.25151125

00:35:35.950 --> 00:35:38.206 That's gonna be great.

NOTE Confidence: 0.25151125

00:35:38.206 --> 00:35:41.590 So definitely something to think about.

NOTE Confidence: 0.25151125

00:35:41.590 --> 00:35:44.038 But also chronic benefit is a

NOTE Confidence: 0.25151125

00:35:44.038 --> 00:35:46.425 disease for women in the sense

NOTE Confidence: 0.25151125

00:35:46.425 --> 00:35:48.350 that the prevalence of women

NOTE Confidence: 0.25151125

00:35:48.350 --> 00:35:50.865 affected by chronic pain is 3 to 1.

NOTE Confidence: 0.25151125

00:35:50.870 --> 00:35:54.294 So we were wondering within TMD,

NOTE Confidence: 0.25151125

00:35:54.294 --> 00:35:56.736 but no in health controls in

NOTE Confidence: 0.25151125

00:35:56.736 --> 00:35:59.639 T in TMD which is stronger,

NOTE Confidence: 0.25151125

00:35:59.640 --> 00:36:02.262 you know prevalence of the disease

NOTE Confidence: 0.25151125

00:36:02.262 --> 00:36:05.048 among women but also larger PLACIP

NOTE Confidence: 0.25151125

00:36:05.048 --> 00:36:07.952 effects in women and we don't see

NOTE Confidence: 0.25151125

00:36:07.952 --> 00:36:09.792 that again in health controls.

NOTE Confidence: 0.25151125

00:36:09.800 --> 00:36:12.824 So we dive into the data here and

NOTE Confidence: 0.25151125

00:36:12.824 --> 00:36:15.595 we measure very colorfully the

NOTE Confidence: 0.25151125

00:36:15.595 --> 00:36:18.770 menstrual cycle periods and the

NOTE Confidence: 0.25151125

00:36:18.770 --> 00:36:23.630 gonadal hormones Luter with the

NOTE Confidence: 0.25151125

00:36:23.630 --> 00:36:26.705 follicular phase register and versus

NOTE Confidence: 0.25151125

00:36:26.705 --> 00:36:30.560 estrogen And we found no effects of

NOTE Confidence: 0.25151125

00:36:30.560 --> 00:36:33.092 gonadal hormones for placebo effects.

NOTE Confidence: 0.25151125

00:36:33.092 --> 00:36:36.480 Yet we saw that the pain threshold

NOTE Confidence: 0.25151125

00:36:36.480 --> 00:36:39.720 out when we use the term and change

NOTE Confidence: 0.25151125

00:36:39.720 --> 00:36:42.232 in women based on the middle

NOTE Confidence: 0.25151125

00:36:42.232 --> 00:36:45.352 follicular or lutal phase as compared,

NOTE Confidence: 0.25151125

00:36:45.352 --> 00:36:46.264 you know,

NOTE Confidence: 0.25151125

00:36:46.264 --> 00:36:48.544 to the general understanding that

NOTE Confidence: 0.25151125

00:36:48.544 --> 00:36:50.449 men are more tolerant.

NOTE Confidence: 0.25151125

00:36:50.450 --> 00:36:53.138 So men are more tolerant than women

NOTE Confidence: 0.25151125

00:36:53.138 --> 00:36:57.008 only when a woman is in the looter phase.

NOTE Confidence: 0.25151125

00:36:57.010 --> 00:36:59.802 But also despite we didn't see any effects

NOTE Confidence: 0.25151125

00:36:59.802 --> 00:37:02.487 of gonadal hormones and placebo effects,

NOTE Confidence: 0.25151125

00:37:02.490 --> 00:37:05.647 we did the sea effects on expectations.

NOTE Confidence: 0.25151125

00:37:05.650 --> 00:37:07.790 But this effects didn't moderate

NOTE Confidence: 0.25151125

00:37:07.790 --> 00:37:09.930 mediate any change in placebo.

NOTE Confidence: 0.25151125

00:37:09.930 --> 00:37:12.482 That is why I tended to think that

NOTE Confidence: 0.25151125

00:37:12.482 --> 00:37:14.472 expectancy and expectations from a

NOTE Confidence: 0.25151125

00:37:14.472 --> 00:37:17.046 cognitive point of view is something

NOTE Confidence: 0.25151125

00:37:17.046 --> 00:37:18.850 different than PLACIP effects,

NOTE Confidence: 0.25151125

00:37:18.850 --> 00:37:21.566 at least when we use conditioning paradigm.

NOTE Confidence: 0.25151125

00:37:21.570 --> 00:37:24.658 So you can see that we found the

NOTE Confidence: 0.25151125

00:37:24.658 --> 00:37:26.825 difference in expectation of

NOTE Confidence: 0.25151125

00:37:26.825 --> 00:37:29.381 improvement when we compare men

NOTE Confidence: 0.25151125

00:37:29.381 --> 00:37:31.883 with women in with diluted face,

NOTE Confidence: 0.25151125

00:37:31.890 --> 00:37:35.194 but no in women in diluted face.

NOTE Confidence: 0.25151125

00:37:35.200 --> 00:37:37.200 And also of course there is a difference

NOTE Confidence: 0.25151125

00:37:37.200 --> 00:37:38.720 between the two places in women.

NOTE Confidence: 0.29335818

00:37:43.840 --> 00:37:46.598 And when we look at the concordance

56

NOTE Confidence: 0.29335818

00:37:46.600 --> 00:37:50.304 experimental where men or women,

NOTE Confidence: 0.29335818

00:37:50.304 --> 00:37:52.134 and I'm talking in terms

NOTE Confidence: 0.29335818

00:37:52.134 --> 00:37:54.546 of biological sex here,

NOTE Confidence: 0.29335818

00:37:54.546 --> 00:37:58.116 you can see that at least for now,

NOTE Confidence: 0.29335818

00:37:58.116 --> 00:38:01.000 we have not power to study gender effects.

NOTE Confidence: 0.29335818

00:38:01.000 --> 00:38:06.200 You can see that actually in women

NOTE Confidence: 0.29335818

00:38:06.200 --> 00:38:08.960 when we had a man experimenter,

NOTE Confidence: 0.29335818

00:38:08.960 --> 00:38:13.375 the effects in terms of placebo algea

NOTE Confidence: 0.29335818

00:38:13.375 --> 00:38:16.897 is different than when we had same sex.

NOTE Confidence: 0.29335818

00:38:16.897 --> 00:38:19.816 So same sex local Placib effects when

NOTE Confidence: 0.29335818

00:38:19.816 --> 00:38:23.439 a man experimenter was studying them,

NOTE Confidence: 0.29335818

00:38:23.440 --> 00:38:24.733 larger Placib effects.

NOTE Confidence: 0.29335818

00:38:24.733 --> 00:38:27.319 And again this is something that

NOTE Confidence: 0.29335818

00:38:27.319 --> 00:38:30.208 human wants to keep you know in mind

NOTE Confidence: 0.29335818

00:38:30.208 --> 00:38:32.410 when you study not just psychedelics

NOTE Confidence: 0.29335818

00:38:32.483 --> 00:38:34.808 but any antidepressants because you

NOTE Confidence: 0.29335818

00:38:34.808 --> 00:38:38.684 may observe this sort of participant

NOTE Confidence: 0.29335818

00:38:38.684 --> 00:38:43.100 experiment or sex biases or differences.

NOTE Confidence: 0.29335818

00:38:43.100 --> 00:38:43.540 Is there

NOTE Confidence: 0.39747304

00:38:43.540 --> 00:38:46.220 any That's a very cool finding fact

NOTE Confidence: 0.39747304

00:38:46.220 --> 00:38:47.978 that you know seems to be opposite in

NOTE Confidence: 0.39747304

00:38:48.140 --> 00:38:49.020 in men even though

NOTE Confidence: 0.39747304

00:38:50.340 --> 00:38:51.858 has that been done cross culturally?

NOTE Confidence: 0.39747304

00:38:52.340 --> 00:38:53.018 Sorry, I mean

NOTE Confidence: 0.39747304

00:38:54.500 --> 00:38:57.140 what is up battered good,

NOTE Confidence: 0.26573345

00:38:59.780 --> 00:39:01.872 this is the higher number

NOTE Confidence: 0.26573345

00:39:01.872 --> 00:39:03.656 more analgesia or less

NOTE Confidence: 0.26573345

00:39:04.060 --> 00:39:05.275 different more analgesia,

NOTE Confidence: 0.26573345

00:39:05.275 --> 00:39:08.380 this is higher and more analgesic

NOTE Confidence: 0.26573345

00:39:08.380 --> 00:39:11.419 improvement, larger plus.

NOTE Confidence: 0.26573345

00:39:11.420 --> 00:39:14.900 So a man experiment was triggering

NOTE Confidence: 0.26573345

00:39:14.900 --> 00:39:19.060 larger plus CB effects in our women TMD,

NOTE Confidence: 0.26573345

00:39:19.060 --> 00:39:21.724 but in men TMD patients we

NOTE Confidence: 0.26573345

00:39:21.724 --> 00:39:23.500 didn't see this effect.

NOTE Confidence: 0.40626156

00:39:25.370 --> 00:39:27.324 Sorry, sorry, no not at all.

NOTE Confidence: 0.40626156

00:39:27.324 --> 00:39:28.974 I'm wondering I I assume that I

NOTE Confidence: 0.40626156

00:39:28.974 --> 00:39:30.970 mean this is a recent paper but

NOTE Confidence: 0.40626156

00:39:31.050 --> 00:39:32.555 but thinking about this culturally

NOTE Confidence: 0.40626156

00:39:32.555 --> 00:39:34.488 like a different you know different

NOTE Confidence: 0.40626156

00:39:34.488 --> 00:39:36.626 expectations and gender roles could I'm

NOTE Confidence: 0.40626156

00:39:36.626 --> 00:39:38.649 glad that you asked that could influence

NOTE Confidence: 0.40626156

00:39:38.650 --> 00:39:42.070 because we have another PhD student

NOTE Confidence: 0.40626156

00:39:42.070 --> 00:39:46.289 now who is diving into spirituality

NOTE Confidence: 0.40626156

00:39:46.290 --> 00:39:49.314 and try to understand if somehow

NOTE Confidence: 0.40626156

00:39:49.314 --> 00:39:51.851 the interplay between sex race

NOTE Confidence: 0.40626156

00:39:51.851 --> 00:39:54.350 effects are you know dependent

NOTE Confidence: 0.40626156

00:39:54.350 --> 00:39:57.390 on spirituality and religiosity.

NOTE Confidence: 0.40626156

00:39:57.390 --> 00:39:59.922 So in terms of cultural difference

NOTE Confidence: 0.40626156

00:39:59.922 --> 00:40:03.118 we are tackling this in two way

NOTE Confidence: 0.40626156

00:40:03.118 --> 00:40:05.024 studying immigration and religiosity

NOTE Confidence: 0.40626156

00:40:05.024 --> 00:40:07.886 and spirituality to try to understand

NOTE Confidence: 0.40626156

00:40:07.886 --> 00:40:10.730 how this can influence both

NOTE Confidence: 0.40626156

00:40:10.730 --> 00:40:13.146 expectations and placing difference.

NOTE Confidence: 0.40626156

00:40:13.150 --> 00:40:15.750 I can tell you that we see difference

NOTE Confidence: 0.40626156

00:40:15.750 --> 00:40:20.176 for well this is sort of recorded

NOTE Confidence: 0.40626156

00:40:20.176 --> 00:40:22.220 then online but expectations.

NOTE Confidence: 0.40626156

00:40:22.220 --> 00:40:24.740 Somebody based on religiosity

NOTE Confidence: 0.40626156

00:40:24.740 --> 00:40:27.260 but no plessive effects,

NOTE Confidence: 0.40626156

00:40:27.260 --> 00:40:29.870 at least when we use our

NOTE Confidence: 0.40626156

00:40:29.870 --> 00:40:30.740 conditioning paradigm.

NOTE Confidence: 0.40626156

00:40:30.740 --> 00:40:30.940 So

NOTE Confidence: 0.28797182

00:40:31.020 --> 00:40:32.937 I mean if you go wait like in the

NOTE Confidence: 0.28797182

00:40:32.937 --> 00:40:34.576 1950s Jerome Frank out of your,

NOTE Confidence: 0.28797182

00:40:34.580 --> 00:40:36.995 I mean he really distilled it down

NOTE Confidence: 0.28797182

00:40:36.995 --> 00:40:39.960 to three things basically competence,

NOTE Confidence: 0.28797182

00:40:39.960 --> 00:40:42.580 compassion and connective saying.

NOTE Confidence: 0.28797182

00:40:42.580 --> 00:40:45.035 I mean you can imagine

NOTE Confidence: 0.28797182

00:40:45.035 --> 00:40:47.244 how those play a big role,

NOTE Confidence: 0.28797182

00:40:47.244 --> 00:40:48.774 you know the perceived competence,

NOTE Confidence: 0.28797182

00:40:48.780 --> 00:40:51.190 you know something

NOTE Confidence: 0.3393348

00:40:51.230 --> 00:40:54.030 that we do for all our experiments.

NOTE Confidence: 0.3393348

00:40:54.030 --> 00:40:57.180 At the end of the experiment we

NOTE Confidence: 0.3393348

00:40:57.180 --> 00:40:59.121 ask participants health controls

NOTE Confidence: 0.3393348

00:40:59.121 --> 00:41:02.212 or chronic pain patients to rate

NOTE Confidence: 0.3393348

00:41:02.212 --> 00:41:04.967 our experimenter a warm confident

NOTE Confidence: 0.3393348

00:41:04.967 --> 00:41:08.248 they were and so far we didn't see

NOTE Confidence: 0.3393348

00:41:08.248 --> 00:41:10.350 any significant effects on placebo.

NOTE Confidence: 0.3393348

00:41:11.270 --> 00:41:12.878 So this is not so it's not looking

NOTE Confidence: 0.3393348

00:41:12.878 --> 00:41:14.470 at you to explain this effect.

NOTE Confidence: 0.3393348

00:41:14.510 --> 00:41:17.597 Yes. We were not able to explain

NOTE Confidence: 0.3393348

00:41:17.597 --> 00:41:20.080 with warm competency or empathy.

NOTE Confidence: 0.4084049

00:41:28.200 --> 00:41:29.822 But I mentioned to you, you know,

NOTE Confidence: 0.4084049

00:41:29.822 --> 00:41:31.477 I'm very intrigued about phenotyping,

NOTE Confidence: 0.4084049

00:41:31.480 --> 00:41:34.320 placebo responder and non responders.

NOTE Confidence: 0.4084049

00:41:34.320 --> 00:41:37.560 This was a project led by Doctor Wang.

NOTE Confidence: 0.4084049

00:41:37.560 --> 00:41:40.020 Currently she is an assistant

NOTE Confidence: 0.4084049

00:41:40.020 --> 00:41:42.966 professor in our department at the

NOTE Confidence: 0.4084049

00:41:42.966 --> 00:41:45.354 time she was supposed to talk.

NOTE Confidence: 0.4084049

00:41:45.360 --> 00:41:51.408 So we use a very large scale of

NOTE Confidence: 0.4084049

00:41:51.410 --> 00:41:55.095 surveys for psychological factors or

NOTE Confidence: 0.4084049

00:41:55.095 --> 00:41:59.182 personality factors and so using our

NOTE Confidence: 0.4084049

00:41:59.182 --> 00:42:01.490 placebo responders, no responders.

NOTE Confidence: 0.5261186

00:42:03.610 --> 00:42:05.585 Instead of using median or

NOTE Confidence: 0.5261186

00:42:05.585 --> 00:42:07.165 average or standard deviation,

NOTE Confidence: 0.5261186

00:42:07.170 --> 00:42:10.768 we use permutation tests to account for,

NOTE Confidence: 0.5261186

00:42:10.770 --> 00:42:13.885 you know, trial by trial placebo effects.

NOTE Confidence: 0.5261186

00:42:13.890 --> 00:42:16.375 This is the time course you know

NOTE Confidence: 0.5261186

00:42:16.380 --> 00:42:20.460 and in blue placebo responders

NOTE Confidence: 0.5261186

00:42:20.460 --> 00:42:23.772 and the two different shape here

NOTE Confidence: 0.5261186

00:42:23.772 --> 00:42:25.980 represents TMD and controls.

NOTE Confidence: 0.5261186

00:42:25.980 --> 00:42:28.528 You can see that having a chronic

NOTE Confidence: 0.5261186

00:42:28.528 --> 00:42:30.869 disorders for pain that affect release

NOTE Confidence: 0.5261186

00:42:30.869 --> 00:42:33.613 of endogenic fluids and so on didn't

NOTE Confidence: 0.5261186

00:42:33.686 --> 00:42:36.332 really change the ability to experience

NOTE Confidence: 0.5261186

00:42:36.332 --> 00:42:38.850 a placebo response over time and

NOTE Confidence: 0.5261186

00:42:38.850 --> 00:42:41.475 the same dose were not responders no

NOTE Confidence: 0.5261186

00:42:41.475 --> 00:42:44.019 matter if they have pain or no pain.

NOTE Confidence: 0.5261186

00:42:44.020 --> 00:42:46.320 The trend is similar.

NOTE Confidence: 0.5261186

00:42:46.320 --> 00:42:48.770 So below 0 we consider

NOTE Confidence: 0.5261186

00:42:48.770 --> 00:42:50.240 this nocebo responders,

NOTE Confidence: 0.5261186

00:42:50.240 --> 00:42:52.529 you tell them that they will benefit

NOTE Confidence: 0.5261186

00:42:52.529 --> 00:42:54.805 and they get worse and that will

NOTE Confidence: 0.5261186

00:42:54.805 --> 00:42:56.870 be the next I think cut chapter

NOTE Confidence: 0.5261186

00:42:56.939 --> 00:42:59.004 in our lab to try to understand

NOTE Confidence: 0.5261186

00:42:59.004 --> 00:43:01.598 who are these people and why they

NOTE Confidence: 0.5261186

00:43:01.598 --> 00:43:03.238 respond to like paradoxically.

NOTE Confidence: 0.5261186

00:43:03.240 --> 00:43:05.752 So this is the large array of survey

NOTE Confidence: 0.5261186

00:43:05.752 --> 00:43:09.161 that we have been using in the lab and

NOTE Confidence: 0.5261186

00:43:09.161 --> 00:43:13.366 it's intriguing because across countries,

NOTE Confidence: 0.5261186

00:43:13.370 --> 00:43:14.917 I mean we are a small community

NOTE Confidence: 0.5261186

00:43:14.917 --> 00:43:16.130 of people working on placebo,

NOTE Confidence: 0.5261186

00:43:16.130 --> 00:43:17.146 relatively small.

NOTE Confidence: 0.5261186

00:43:17.146 --> 00:43:20.194 So we know that Manchester has

NOTE Confidence: 0.5261186

00:43:20.194 --> 00:43:23.490 data with optimist placity effects,

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NOTE Confidence: 0.5261186

00:43:23.490 --> 00:43:25.610 Toledo and and so on.

NOTE Confidence: 0.5261186

00:43:25.610 --> 00:43:29.102 So this was a collection of surveys that

NOTE Confidence: 0.5261186

00:43:29.102 --> 00:43:31.286 have been published in the literature.

NOTE Confidence: 0.5261186

00:43:31.290 --> 00:43:35.042 A single survey that a somehow was critical.

NOTE Confidence: 0.5261186

00:43:35.042 --> 00:43:37.046 Like how can a single survey

NOTE Confidence: 0.5261186

00:43:37.046 --> 00:43:38.792 predict plasive effects in one lab

NOTE Confidence: 0.5261186

00:43:38.792 --> 00:43:40.647 and then you move to Baltimore

NOTE Confidence: 0.5261186

00:43:40.647 --> 00:43:42.399 and doesn't predict anymore.

NOTE Confidence: 0.5261186

00:43:42.400 --> 00:43:44.400 Maybe because we are diverse

NOTE Confidence: 0.5261186

00:43:44.400 --> 00:43:48.600 so we use the NMH approach of

NOTE Confidence: 0.5261186

00:43:48.600 --> 00:43:50.400 distinguish the balance.

NOTE Confidence: 0.5261186

00:43:50.400 --> 00:43:51.080 So we did the

NOTE Confidence: 0.26479432

00:43:53.560 --> 00:43:58.880 PPCA to somehow create 4 domains

NOTE Confidence: 0.26479432

00:43:58.880 --> 00:44:02.576 of coming from all the 17 surveys

NOTE Confidence: 0.26479432

00:44:02.576 --> 00:44:05.165 for our 1000 questions that we do

NOTE Confidence: 0.26479432

00:44:05.165 --> 00:44:07.562 every time as part of the screening

NOTE Confidence: 0.26479432

00:44:07.562 --> 00:44:09.572 participant know that it's important

NOTE Confidence: 0.26479432

00:44:09.572 --> 00:44:12.434 they get to compensate for stay with

NOTE Confidence: 0.26479432

00:44:12.434 --> 00:44:14.793 us two hours to address all that.

NOTE Confidence: 0.26479432

00:44:14.800 --> 00:44:17.200 And so we define emotional distress,

NOTE Confidence: 0.26479432

00:44:17.200 --> 00:44:19.400 reward, the sickness, pain related,

NOTE Confidence: 0.26479432

00:44:19.400 --> 00:44:21.485 the fear catastrophizing,

NOTE Confidence: 0.26479432

00:44:21.485 --> 00:44:25.655 empathy and openness as critical violence

NOTE Confidence: 0.26479432

00:44:25.655 --> 00:44:29.718 to somehow study three different aspects.

NOTE Confidence: 0.26479432

00:44:29.718 --> 00:44:32.998 Expectation Learning index we call

NOTE Confidence: 0.26479432

00:44:32.998 --> 00:44:35.670 conditioning strengths that this can be

NOTE Confidence: 0.26479432

00:44:35.670 --> 00:44:40.188 called learning index or implacive effects.

NOTE Confidence: 0.26479432

00:44:40.190 --> 00:44:43.238 So our goal was OK based on this

NOTE Confidence: 0.26479432

00:44:43.238 --> 00:44:45.869 PCA approach and balance approach,

NOTE Confidence: 0.26479432

00:44:45.870 --> 00:44:49.686 how can this for violence help

NOTE Confidence: 0.26479432

00:44:49.686 --> 00:44:52.230 us to interpret expectation,

NOTE Confidence: 0.26479432

00:44:52.230 --> 00:44:54.042 conditioning and placive effects?

NOTE Confidence: 0.26479432

00:44:54.042 --> 00:44:56.760 The first question was do we

NOTE Confidence: 0.26479432

00:44:56.834 --> 00:44:59.462 see a difference between TMD and

NOTE Confidence: 0.26479432

00:44:59.462 --> 00:45:00.776 chronic pain patient?

NOTE Confidence: 0.26479432

00:45:00.780 --> 00:45:04.060 Yes, When it comes to reward the seeking

NOTE Confidence: 0.26479432

00:45:04.060 --> 00:45:06.538 chronic pain patients seek a reward.

NOTE Confidence: 0.26479432

00:45:06.540 --> 00:45:08.922 People who don't experience pain care

NOTE Confidence: 0.26479432

00:45:08.922 --> 00:45:11.820 less when you say this is analgesic

NOTE Confidence: 0.26479432

00:45:11.820 --> 00:45:14.179 and so expectation tended to be lower.

NOTE Confidence: 0.26479432

00:45:14.180 --> 00:45:15.734 As you can see from the scale,

NOTE Confidence: 0.26479432

00:45:15.740 --> 00:45:18.512 when people have a fear of pain

NOTE Confidence: 0.26479432

00:45:18.512 --> 00:45:19.700 and catastrophizing thoughts,

NOTE Confidence: 0.26479432

00:45:19.700 --> 00:45:22.604 they tended to be higher when

NOTE Confidence: 0.26479432

00:45:22.604 --> 00:45:25.690 people have open mind and empathy

NOTE Confidence: 0.26479432

00:45:25.690 --> 00:45:28.366 in terms of ability to learn.

NOTE Confidence: 0.26479432

00:45:28.370 --> 00:45:29.636 Trial by trial,

NOTE Confidence: 0.26479432

00:45:29.636 --> 00:45:31.746 emotional distress impaired the ability

NOTE Confidence: 0.26479432

00:45:31.746 --> 00:45:34.631 to learn and the personal to know in

NOTE Confidence: 0.26479432

00:45:34.631 --> 00:45:37.009 the literature and for Placib effects,

NOTE Confidence: 0.26479432

00:45:37.010 --> 00:45:39.074 fear of the pain.

NOTE Confidence: 0.26479432

00:45:39.074 --> 00:45:41.138 Catastrophizing was associated with

NOTE Confidence: 0.26479432

00:45:41.138 --> 00:45:43.754 smaller Placib effects in terms

NOTE Confidence: 0.26479432

00:45:43.754 --> 00:45:46.259 of magnitude and proportion of

NOTE Confidence: 0.26479432

00:45:46.259 --> 00:45:48.402 responsiveness and also emotional

NOTE Confidence: 0.26479432

00:45:48.402 --> 00:45:51.048 distress is associated with higher

NOTE Confidence: 0.26479432

00:45:51.048 --> 00:45:54.100 extension rate or Placib effects and

NOTE Confidence: 0.26479432

00:45:54.100 --> 00:45:56.860 lower money to the end responsivity

NOTE Confidence: 0.26479432

00:45:56.860 --> 00:45:57.320 proportion.

NOTE Confidence: 0.33421454

00:46:01.280 --> 00:46:03.904 And the last part of this talk is

NOTE Confidence: 0.33421454

00:46:03.904 --> 00:46:06.870 focus on more you know the topics that

NOTE Confidence: 0.33421454

00:46:06.870 --> 00:46:10.960 you study in here, you know at CL.

NOTE Confidence: 0.33421454

00:46:10.960 --> 00:46:13.154 So we've Todd Gordo,

NOTE Confidence: 0.33421454

00:46:13.154 --> 00:46:15.896 we decided to start doing some

NOTE Confidence: 0.33421454

00:46:15.896 --> 00:46:18.592 conditioning in mice for ketamine.

NOTE Confidence: 0.33421454

00:46:18.592 --> 00:46:20.824 So what we did,

NOTE Confidence: 0.33421454

00:46:20.830 --> 00:46:24.855 we know that ketamine is this rapid

NOTE Confidence: 0.33421454

00:46:24.855 --> 00:46:26.580 antidepressant slash anaesthetic

NOTE Confidence: 0.33421454

00:46:26.665 --> 00:46:29.710 drug and we study Anaidonia in mice.

NOTE Confidence: 0.33421454

00:46:29.710 --> 00:46:31.114 This is quite complex.

NOTE Confidence: 0.33421454

00:46:31.114 --> 00:46:33.659 All the controls so that we need

NOTE Confidence: 0.33421454

00:46:33.659 --> 00:46:35.464 the conditioning was done for

NOTE Confidence: 0.33421454

00:46:35.464 --> 00:46:39.346 3 * 2 weeks apart to somehow

NOTE Confidence: 0.33421454

00:46:39.350 --> 00:46:41.110 eliminate the carryover effects.

NOTE Confidence: 0.33421454

00:46:41.110 --> 00:46:44.163 And our goal was to understand if

NOTE Confidence: 0.33421454

00:46:44.163 --> 00:46:46.749 we expose mice to the ketamine,

NOTE Confidence: 0.33421454

00:46:46.750 --> 00:46:48.775 can we create a ketamine

NOTE Confidence: 0.33421454

00:46:48.775 --> 00:46:50.800 like effects when we replace

NOTE Confidence: 0.33421454

00:46:50.877 --> 00:46:55.308 ketamine with placebo in mice.

NOTE Confidence: 0.33421454

00:46:55.310 --> 00:46:56.870 So the results show

NOTE Confidence: 0.7107004

00:47:00.310 --> 00:47:03.698 the morphic effects in the sense that

NOTE Confidence: 0.7107004

00:47:03.698 --> 00:47:09.000 in males we had some responses that

NOTE Confidence: 0.7107004

00:47:09.000 --> 00:47:13.425 were you know here you can see that

NOTE Confidence: 0.7107004

00:47:13.425 --> 00:47:15.700 we produce a ketamine like effects

NOTE Confidence: 0.7107004

00:47:15.700 --> 00:47:18.479 when we use saline solution and these

NOTE Confidence: 0.7107004

00:47:18.479 --> 00:47:21.221 are all the comparisons at one hour

NOTE Confidence: 0.7107004

00:47:21.221 --> 00:47:24.590 and 24 hours in females we didn't

NOTE Confidence: 0.7107004

00:47:24.590 --> 00:47:27.036 observe A ketamine like effects.

NOTE Confidence: 0.7107004

00:47:27.036 --> 00:47:31.141 So we were not able to create a sort

NOTE Confidence: 0.7107004

00:47:31.141 --> 00:47:33.895 of dose extension effects of the

NOTE Confidence: 0.7107004

00:47:33.895 --> 00:47:36.946 ketamine given for anedonia in in mice.

NOTE Confidence: 0.7107004

00:47:36.950 --> 00:47:37.750 Hey guys, goodnight to mine.

NOTE Confidence: 0.32759595

00:47:45.280 --> 00:47:50.388 So it is something that we publish here

NOTE Confidence: 0.32759595

00:47:50.388 --> 00:47:53.171 in collaboration with Professor Sinacora.

NOTE Confidence: 0.32759595

00:47:53.171 --> 00:47:56.633 So we start thinking more about

NOTE Confidence: 0.32759595

00:47:56.633 --> 00:47:58.639 expectations and therapeutic

NOTE Confidence: 0.32759595

00:47:58.639 --> 00:48:01.315 outcome in psychedelic surgeons.

NOTE Confidence: 0.32759595

00:48:01.320 --> 00:48:04.040 The idea is that this is a viewpoint,

NOTE Confidence: 0.32759595

00:48:04.040 --> 00:48:05.960 paper is still to be tested,

NOTE Confidence: 0.32759595

00:48:05.960 --> 00:48:08.966 but the idea is that when we use psychedelics

NOTE Confidence: 0.32759595

00:48:08.966 --> 00:48:11.820 we can change the mindset of patients.

NOTE Confidence: 0.32759595

00:48:11.820 --> 00:48:14.262 So we suggest that it's very

NOTE Confidence: 0.32759595

00:48:14.262 --> 00:48:16.831 critical to assess expectation in a

NOTE Confidence: 0.32759595

00:48:16.831 --> 00:48:18.575 patient who received psychedelics

NOTE Confidence: 0.32759595

00:48:18.580 --> 00:48:21.576 at the time Zero before we start,

NOTE Confidence: 0.32759595

00:48:21.580 --> 00:48:25.172 you know the procedure and also later on

NOTE Confidence: 0.32759595

00:48:25.172 --> 00:48:27.841 expecting that psychedelics somehow can

NOTE Confidence: 0.32759595

00:48:27.841 --> 00:48:31.213 change the mindset to the perception.

NOTE Confidence: 0.32759595

00:48:31.220 --> 00:48:33.940 And I show to you that we can

00:48:33.940 --> 00:48:35.330 manipulate expectation by exposing

00:48:35.330 --> 00:48:37.890 the people to a reduction of the pain

00:48:37.963 --> 00:48:40.222 that is a manipulation of experience.

00:48:40.222 --> 00:48:43.954 The psychedelics can create a strong,

00:48:43.960 --> 00:48:45.800 you know, different perception of

00:48:45.800 --> 00:48:48.000 the world around the patient from,

00:48:48.000 --> 00:48:50.450 you know, a mystical experience

00:48:50.450 --> 00:48:52.875 to improvement of the mood.

00:48:52.880 --> 00:48:55.305 And so this can somehow

00:48:55.305 --> 00:48:56.760 create new expectation.

00:48:56.760 --> 00:49:00.008 And the goal is when every time we

00:49:00.008 --> 00:49:02.256 study psychedelics to somehow keep in

00:49:02.256 --> 00:49:04.501 mind that we can have neurobiological

00:49:04.501 --> 00:49:08.248 phenomenon that we can call you know

00:49:08.248 --> 00:49:10.843 molecular effects and effects on

NOTE Confidence: 0.32759595

00:49:10.843 --> 00:49:13.722 expectation we can change through

NOTE Confidence: 0.32759595

00:49:13.722 --> 00:49:16.570 the biological effect expectancy.

NOTE Confidence: 0.32759595

00:49:16.570 --> 00:49:19.890 And of course this needed to be reflect

NOTE Confidence: 0.32759595

00:49:19.890 --> 00:49:23.467 at the level of recommendation so that

NOTE Confidence: 0.32759595

00:49:23.467 --> 00:49:26.674 expectation become a multiple assessment of,

NOTE Confidence: 0.32759595

00:49:26.674 --> 00:49:27.766 you know,

NOTE Confidence: 0.32759595

00:49:27.770 --> 00:49:30.610 the benefits induced by psycho,

NOTE Confidence: 0.32759595

00:49:30.610 --> 00:49:33.086 psychedelic and other psychotherapy,

NOTE Confidence: 0.32759595

00:49:33.086 --> 00:49:35.562 especially when we use

NOTE Confidence: 0.32759595

00:49:35.562 --> 00:49:38.010 psychedelics with psychotherapy.

NOTE Confidence: 0.32759595

00:49:38.010 --> 00:49:40.201 So then if we continue to think

NOTE Confidence: 0.32759595

00:49:40.201 --> 00:49:43.412 about what we learn from pain to be

NOTE Confidence: 0.32759595

00:49:43.412 --> 00:49:45.607 translated into the psychedelic medicine,

NOTE Confidence: 0.32759595

00:49:45.610 --> 00:49:47.810 one big question is what is the control,

NOTE Confidence: 0.32759595

00:49:47.810 --> 00:49:50.026 what is the design?

NOTE Confidence: 0.32759595

00:49:50.026 --> 00:49:53.725 And as long I read in the literature

NOTE Confidence: 0.32759595

00:49:53.725 --> 00:49:55.760 there are no placebo balanced

NOTE Confidence: 0.32759595

00:49:55.837 --> 00:49:58.249 placebo design for psychedelics,

NOTE Confidence: 0.32759595

00:49:58.250 --> 00:50:00.488 but it's a balanced placebo design.

NOTE Confidence: 0.32759595

00:50:00.490 --> 00:50:02.690 Essentially we wrote a very,

NOTE Confidence: 0.32759595

00:50:02.690 --> 00:50:03.950 you know,

NOTE Confidence: 0.32759595

00:50:03.950 --> 00:50:06.470 methodological focus review on

NOTE Confidence: 0.32759595

00:50:06.470 --> 00:50:07.100 osteoarthritis.

NOTE Confidence: 0.32759595

00:50:07.100 --> 00:50:10.620 And in preparing this talk I was thinking

NOTE Confidence: 0.32759595

00:50:10.620 --> 00:50:14.860 of paying us a lot to teach to psychiatry.

NOTE Confidence: 0.32759595

00:50:14.860 --> 00:50:17.158 So the balanced placebo design is

NOTE Confidence: 0.32759595

00:50:17.158 --> 00:50:20.096 a design where we have forearms and

NOTE Confidence: 0.32759595

00:50:20.096 --> 00:50:22.754 patient received the active drug and

NOTE Confidence: 0.32759595

00:50:22.754 --> 00:50:25.584 they are told this is not the active

NOTE Confidence: 0.32759595

00:50:25.584 --> 00:50:28.040 drug or they receive the active drug

NOTE Confidence: 0.32759595

00:50:28.040 --> 00:50:30.650 and they are told you receive the

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NOTE Confidence: 0.32759595

00:50:30.650 --> 00:50:32.780 active drug and the same for placebo.

NOTE Confidence: 0.32759595

00:50:32.780 --> 00:50:35.460 They are then administration where

NOTE Confidence: 0.32759595

00:50:35.460 --> 00:50:39.382 they say this is a placebo deceptively

NOTE Confidence: 0.32759595

00:50:39.382 --> 00:50:42.406 or this is a placebo and actually

NOTE Confidence: 0.32759595

00:50:42.406 --> 00:50:43.950 the receiver placebo.

NOTE Confidence: 0.32759595

00:50:43.950 --> 00:50:45.294 Probably by manipulating

NOTE Confidence: 0.32759595

00:50:45.294 --> 00:50:47.982 expectation and what they are told,

NOTE Confidence: 0.32759595

00:50:47.990 --> 00:50:51.615 we can disentangle the psychedelics

NOTE Confidence: 0.32759595

00:50:51.615 --> 00:50:54.910 component versus the expectancy action

NOTE Confidence: 0.32759595

00:50:54.910 --> 00:50:59.390 in that play a role in this case.

NOTE Confidence: 0.32759595

00:50:59.390 --> 00:51:03.572 And so the hypothetical balance that

NOTE Confidence: 0.32759595

00:51:03.572 --> 00:51:07.240 can be a crossover or parallel design

NOTE Confidence: 0.32759595

00:51:07.240 --> 00:51:10.327 can help us to understand what is

NOTE Confidence: 0.32759595

00:51:10.327 --> 00:51:13.263 the placebo minus the interactive

NOTE Confidence: 0.32759595

00:51:13.263 --> 00:51:16.315 effects of psychedelic unexpectation.

NOTE Confidence: 0.32759595

00:51:16.320 --> 00:51:16.922 The guard.

NOTE Confidence: 0.32759595

00:51:16.922 --> 00:51:18.427 The standard of additivity may

NOTE Confidence: 0.32759595

00:51:18.427 --> 00:51:20.120 not work for psychedelics,

NOTE Confidence: 0.32759595

00:51:20.120 --> 00:51:22.570 especially if we believe that

NOTE Confidence: 0.32759595

00:51:22.570 --> 00:51:24.040 we change expectations.

NOTE Confidence: 0.32759595

00:51:24.040 --> 00:51:24.547 Therefore,

NOTE Confidence: 0.32759595

00:51:24.547 --> 00:51:28.096 we needed to talk about synergic effects,

NOTE Confidence: 0.32759595

00:51:28.100 --> 00:51:30.552 interaction effects between expectation

NOTE Confidence: 0.32759595

00:51:30.552 --> 00:51:33.792 and drugs and thinking outside the

NOTE Confidence: 0.32759595

00:51:33.792 --> 00:51:36.810 box with new design for clinical

NOTE Confidence: 0.32759595

00:51:36.905 --> 00:51:39.960 trials or psychedelics can help us

NOTE Confidence: 0.32759595

00:51:39.960 --> 00:51:43.350 to understand the drug versus the

NOTE Confidence: 0.78663087

00:51:43.455 --> 00:51:45.753 placebo interactive effects

NOTE Confidence: 0.78663087

00:51:45.753 --> 00:51:48.817 and action and expectations

NOTE Confidence: 0.78663087

00:51:53.700 --> 00:51:56.060 in concluding.

NOTE Confidence: 0.78663087

00:51:56.060 --> 00:51:59.140 So when we aim to understand more

NOTE Confidence: 0.78663087

00:51:59.140 --> 00:52:02.080 placebo must be first the design,

NOTE Confidence: 0.78663087

00:52:02.080 --> 00:52:05.195 the control group are the critical component.

NOTE Confidence: 0.78663087

00:52:05.200 --> 00:52:07.120 If we start a placebo effects,

NOTE Confidence: 0.78663087

00:52:07.120 --> 00:52:10.039 we do need a no interventional group

NOTE Confidence: 0.78663087

00:52:10.040 --> 00:52:14.036 and also an assessment of expectations.

NOTE Confidence: 0.78663087

00:52:14.040 --> 00:52:15.968 This is a call for all the people

NOTE Confidence: 0.78663087

00:52:15.968 --> 00:52:17.598 who work with animal models,

NOTE Confidence: 0.78663087

00:52:17.600 --> 00:52:20.280 the more the better, so that we can,

NOTE Confidence: 0.78663087

00:52:20.280 --> 00:52:21.798 understanding the molecular

NOTE Confidence: 0.78663087

00:52:21.798 --> 00:52:23.316 and genetic mechanism,

NOTE Confidence: 0.78663087

00:52:23.320 --> 00:52:25.308 underline psychedelic effects but

NOTE Confidence: 0.78663087

00:52:25.308 --> 00:52:28.290 also antidepressant where there is a

NOTE Confidence: 0.78663087

00:52:28.366 --> 00:52:30.584 need for more studies, larger study.

NOTE Confidence: 0.78663087

00:52:30.584 --> 00:52:32.873 We wanted to share our data because

NOTE Confidence: 0.78663087

00:52:32.873 --> 00:52:35.418 the modelling I do is different than

NOTE Confidence: 0.78663087

00:52:35.418 --> 00:52:37.967 modelling other people in this room can do.

NOTE Confidence: 0.78663087

00:52:37.970 --> 00:52:40.634 And by interacting with one another

NOTE Confidence: 0.78663087

00:52:40.634 --> 00:52:43.554 we can discover new mechanism and

NOTE Confidence: 0.78663087

00:52:43.554 --> 00:52:46.204 way to tackle impulsive effects.

NOTE Confidence: 0.78663087

00:52:46.210 --> 00:52:47.735 And of course, replication when

NOTE Confidence: 0.78663087

00:52:47.735 --> 00:52:49.969 it starts from a lab as we know,

NOTE Confidence: 0.78663087

00:52:49.970 --> 00:52:51.012 means nothing.

NOTE Confidence: 0.78663087

00:52:51.012 --> 00:52:53.617 So in doing clinical trials,

NOTE Confidence: 0.78663087

00:52:53.620 --> 00:52:56.700 then let's try to learn how to

NOTE Confidence: 0.78663087

00:52:56.700 --> 00:52:59.100 measure expectation of improvement,

NOTE Confidence: 0.78663087

00:52:59.100 --> 00:53:00.148 allocation, assessment,

NOTE Confidence: 0.78663087

00:53:00.148 --> 00:53:03.816 but also standardise the words you use.

NOTE Confidence: 0.78663087

00:53:03.820 --> 00:53:05.362 The longer the time you spend

NOTE Confidence: 0.78663087

00:53:05.362 --> 00:53:06.133 with your patients,

NOTE Confidence: 0.78663087

00:53:06.140 --> 00:53:08.685 the larger the PLACIP effects the

NOTE Confidence: 0.78663087

00:53:08.685 --> 00:53:10.515 larger the number of visits the

NOTE Confidence: 0.78663087

00:53:10.515 --> 00:53:12.201 larger the PLACIP effects more

NOTE Confidence: 0.78663087

00:53:12.201 --> 00:53:14.313 marketing like in this country where

NOTE Confidence: 0.78663087

00:53:14.313 --> 00:53:16.057 the largest placip effects over

NOTE Confidence: 0.78663087

00:53:16.057 --> 00:53:18.019 any other country in the world.

NOTE Confidence: 0.78663087

00:53:18.020 --> 00:53:20.460 Because I'm going to be I'm not we

NOTE Confidence: 0.78663087

00:53:20.460 --> 00:53:22.460 have a beautiful marketing strategy.

NOTE Confidence: 0.78663087

00:53:22.460 --> 00:53:24.896 So this increase placi be fast.

NOTE Confidence: 0.78663087

00:53:24.900 --> 00:53:27.154 So the number of sites more sites

NOTE Confidence: 0.78663087

00:53:27.154 --> 00:53:28.540 more placi be fast.

NOTE Confidence: 0.78663087

00:53:28.540 --> 00:53:31.372 So the checklist how to collect

NOTE Confidence: 0.78663087

00:53:31.372 --> 00:53:34.047 adverse events and preming it best

NOTE Confidence: 0.78663087

00:53:34.047 --> 00:53:36.792 can be so relevant and I'm glad to

NOTE Confidence: 0.78663087

00:53:36.792 --> 00:53:39.294 discuss more on these things I oppose.

NOTE Confidence: 0.78663087

00:53:39.294 --> 00:53:42.213 Just a talk where you can think

NOTE Confidence: 0.78663087

00:53:42.213 --> 00:53:44.140 about this is my team,

NOTE Confidence: 0.78663087

00:53:44.140 --> 00:53:46.924 so a bigger thank you to all of

NOTE Confidence: 0.78663087

00:53:46.924 --> 00:53:49.588 them that do an amazing job in

NOTE Confidence: 0.78663087

00:53:49.588 --> 00:53:52.662 that come with new ideas but also

NOTE Confidence: 0.78663087

00:53:52.662 --> 00:53:55.678 work hard to get all this done.

NOTE Confidence: 0.78663087

00:53:55.680 --> 00:53:57.450 And in about 2-3 weeks this

NOTE Confidence: 0.78663087

00:53:57.450 --> 00:53:59.639 book will be out and it's free.

NOTE Confidence: 0.78663087

00:53:59.640 --> 00:54:02.468 So if you wish to learn more

NOTE Confidence: 0.78663087

00:54:02.468 --> 00:54:03.680 about Placid effects,

NOTE Confidence: 0.78663087

00:54:03.680 --> 00:54:06.638 Oxford University Press are more from

NOTE Confidence: 0.78663087

00:54:06.640 --> 00:54:09.680 N7 to read this book for free online.

NOTE Confidence: 0.78663087

00:54:09.680 --> 00:54:11.412 So feel free to,

NOTE Confidence: 0.78663087

00:54:11.412 --> 00:54:12.278 you know,

NOTE Confidence: 0.78663087

00:54:12.280 --> 00:54:15.266 Google and a big thank you to

NOTE Confidence: 0.78663087

00:54:15.266 --> 00:54:15.959 the Funding Agency.

NOTE Confidence: 0.78663087

00:54:15.960 --> 00:54:17.790 But more important to all of

NOTE Confidence: 0.78663087

00:54:17.790 --> 00:54:19.820 you who are interested in this

NOTE Confidence: 0.78663087

00:54:19.820 --> 00:54:22.032 topic that can help us learn

NOTE Confidence: 0.78663087

00:54:22.032 --> 00:54:24.192 more about not just psychedelics

NOTE Confidence: 0.78663087

00:54:24.192 --> 00:54:25.920 but psychiatry in general.

NOTE Confidence: 0.78663087

00:54:25.920 --> 00:54:26.360 Thank you.

NOTE Confidence: 0.42521125

00:54:33.380 --> 00:54:34.712 Thanks. So I this,

NOTE Confidence: 0.42521125

00:54:34.712 --> 00:54:36.562 I mean from somebody who's

NOTE Confidence: 0.42521125

00:54:36.562 --> 00:54:38.138 actually doing psychedelic work,

NOTE Confidence: 0.42521125

00:54:38.140 --> 00:54:41.580 I mean it's hard to disambiguate.

NOTE Confidence: 0.42521125

00:54:41.580 --> 00:54:44.118 I mean they're so tied together,

NOTE Confidence: 0.42521125

00:54:44.118 --> 00:54:46.270 you know it's really hard to separate and

NOTE Confidence: 0.42521125

00:54:46.321 --> 00:54:48.337 then look at people doing animal research.

NOTE Confidence: 0.42521125

00:54:48.340 --> 00:54:50.740 If you're getting these results,

NOTE Confidence: 0.42521125

00:54:50.740 --> 00:54:52.540 how do you, you know,

NOTE Confidence: 0.42521125

00:54:52.540 --> 00:54:54.876 how do you make sense of the fact

NOTE Confidence: 0.42521125

00:54:54.876 --> 00:54:56.641 that you're able to get this without

NOTE Confidence: 0.42521125

00:54:56.641 --> 00:54:59.568 any objective or or you would

NOTE Confidence: 0.42521125

00:54:59.568 --> 00:55:01.108 assume any expectations on part

NOTE Confidence: 0.42521125

00:55:01.108 --> 00:55:03.099 of the animals said they're good.

NOTE Confidence: 0.42521125

00:55:03.100 --> 00:55:04.604 I mean I think these are the big

NOTE Confidence: 0.42521125

00:55:04.604 --> 00:55:05.940 questions like how do you get these

NOTE Confidence: 0.42521125

00:55:05.940 --> 00:55:07.420 results if you don't have expectations.

NOTE Confidence: 0.42521125

00:55:07.420 --> 00:55:11.835 But I think the the real question is

NOTE Confidence: 0.42521125

00:55:11.835 --> 00:55:14.966 how do you do these studies when there

NOTE Confidence: 0.42521125

00:55:14.966 --> 00:55:17.110 is such an acute effect of the drug

NOTE Confidence: 0.42521125

00:55:17.110 --> 00:55:20.456 that it unmasked every single time.

NOTE Confidence: 0.42521125

00:55:20.456 --> 00:55:22.748 So you can't really do a

NOTE Confidence: 0.42521125

00:55:22.750 --> 00:55:24.043 placebo-controlled study unless

NOTE Confidence: 0.42521125

00:55:24.043 --> 00:55:26.629 you have something else that can

NOTE Confidence: 0.42521125

00:55:26.629 --> 00:55:29.270 generate a similar effect acutely.

NOTE Confidence: 0.42521125

00:55:29.270 --> 00:55:31.020 But it I do have an idea

NOTE Confidence: 0.42521125

00:55:31.020 --> 00:55:32.070 how do you get around that

NOTE Confidence: 0.38415885

00:55:33.070 --> 00:55:34.590 This is a big equation. You know

NOTE Confidence: 0.38415885

00:55:34.590 --> 00:55:36.030 what is the control for secondary,

NOTE Confidence: 0.38415885

00:55:36.190 --> 00:55:37.590 I mean it's if you talk to

NOTE Confidence: 0.38415885

00:55:37.590 --> 00:55:38.734 the FDA, you talk to anybody.

NOTE Confidence: 0.38415885

00:55:38.734 --> 00:55:39.664 This is the big question

NOTE Confidence: 0.38415885

00:55:39.830 --> 00:55:43.440 how do you so and I I thought

NOTE Confidence: 0.38415885

00:55:43.440 --> 00:55:45.240 a lot before coming here.

NOTE Confidence: 0.38415885

00:55:45.240 --> 00:55:48.030 There are you know different studies

NOTE Confidence: 0.38415885

00:55:48.030 --> 00:55:51.633 where they try to change the dose so

NOTE Confidence: 0.38415885

00:55:51.633 --> 00:55:54.104 sub clinical doses but still you know

NOTE Confidence: 0.38415885

00:55:54.104 --> 00:55:56.629 the sub clinical doses people don't

NOTE Confidence: 0.38415885

00:55:56.629 --> 00:56:01.508 have the same mystical or you know wow

NOTE Confidence: 0.38415885

00:56:01.508 --> 00:56:04.076 reaction that the psychedelics can cause.

NOTE Confidence: 0.38415885

00:56:04.080 --> 00:56:09.204 So sub the therapeutic dose does the

NOTE Confidence: 0.38415885

00:56:09.204 --> 00:56:12.495 classical approach of you know know

NOTE Confidence: 0.38415885

00:56:12.495 --> 00:56:14.865 those has not been the solution.

NOTE Confidence: 0.38415885

00:56:14.870 --> 00:56:17.198 Some other people have tried placebo

NOTE Confidence: 0.38415885

00:56:17.198 --> 00:56:20.022 and of course you you know somehow

NOTE Confidence: 0.38415885

00:56:20.022 --> 00:56:22.142 destroying all the blinding because

NOTE Confidence: 0.38415885

00:56:22.142 --> 00:56:24.840 it's so clear that a placebo versus

NOTE Confidence: 0.38415885

00:56:24.840 --> 00:56:28.095 psychedelics is easy to guess what here

NOTE Confidence: 0.38415885

00:56:28.095 --> 00:56:31.666 is there so the allocation doesn't work.

NOTE Confidence: 0.38415885

00:56:31.670 --> 00:56:34.628 Other people try Tamizo or other

NOTE Confidence: 0.38415885

00:56:34.628 --> 00:56:37.562 drugs to have some sides effects and

NOTE Confidence: 0.38415885

00:56:37.562 --> 00:56:40.926 we do know that when we produce sides

NOTE Confidence: 0.38415885

00:56:40.926 --> 00:56:44.024 effects we increase the chance to have

NOTE Confidence: 0.38415885

00:56:44.024 --> 00:56:46.712 a placebo response because a patient

NOTE Confidence: 0.38415885

00:56:46.712 --> 00:56:50.702 say OK I'm feeling and as I feel sick

NOTE Confidence: 0.38415885

00:56:50.702 --> 00:56:53.151 probably I receive the active drug.

NOTE Confidence: 0.38415885

00:56:53.151 --> 00:56:55.930 So the question first I would suggest

NOTE Confidence: 0.38415885

00:56:56.006 --> 00:56:58.958 for any person who does psychedelic

NOTE Confidence: 0.38415885

00:56:58.958 --> 00:57:01.644 treatment to assess expectation and to

NOTE Confidence: 0.38415885

00:57:01.644 --> 00:57:04.423 tackle this kind of you know question,

NOTE Confidence: 0.38415885

00:57:04.423 --> 00:57:07.429 none with the gold standard of

NOTE Confidence: 0.38415885

00:57:07.429 --> 00:57:11.420 additivity that clearly this kind of

NOTE Confidence: 0.38415885

00:57:11.420 --> 00:57:14.456 you know urgent go beyond additivity.

NOTE Confidence: 0.38415885

00:57:14.460 --> 00:57:16.965 You can't merely compare PLACIP

NOTE Confidence: 0.38415885

00:57:16.965 --> 00:57:20.140 versus you know psychedelics or active

NOTE Confidence: 0.38415885

00:57:20.140 --> 00:57:23.060 comparators or sub therapeutic doses.

NOTE Confidence: 0.38415885

00:57:23.060 --> 00:57:26.580 Then it's time to think about other approach.

NOTE Confidence: 0.38415885

00:57:26.580 --> 00:57:30.827 Other approach can be you know challen

NOTE Confidence: 0.38415885

00:57:30.827 --> 00:57:32.863 challenging because of regulatory

NOTE Confidence: 0.38415885

00:57:32.863 --> 00:57:35.020 requirements that they may not,

NOTE Confidence: 0.38415885

00:57:35.020 --> 00:57:37.114 but also you know the balance

NOTE Confidence: 0.38415885

00:57:37.114 --> 00:57:38.980 plus simple design that can be

NOTE Confidence: 0.6122345

00:57:41.160 --> 00:57:42.684 double-blind plus simple

NOTE Confidence: 0.6122345

00:57:42.684 --> 00:57:45.732 design where we blind both the

NOTE Confidence: 0.6122345

00:57:45.732 --> 00:57:47.959 therapist and the patient with,

NOTE Confidence: 0.6122345

00:57:47.960 --> 00:57:50.136 you know, misleading information

NOTE Confidence: 0.6122345

00:57:50.136 --> 00:57:52.880 with that has not been tested.

NOTE Confidence: 0.6122345

00:57:52.880 --> 00:57:56.732 Maybe that can help somehow to

NOTE Confidence: 0.6122345

00:57:56.732 --> 00:58:00.312 see how you know, using balance

NOTE Confidence: 0.6122345

00:58:00.312 --> 00:58:03.280 plus simple design help, although

NOTE Confidence: 0.6122345

00:58:03.400 --> 00:58:05.224 that doesn't necessarily address

NOTE Confidence: 0.6122345

00:58:05.224 --> 00:58:06.760 the question about acute,

NOTE Confidence: 0.6122345

00:58:06.760 --> 00:58:08.120 you know, acute blind.

NOTE Confidence: 0.3747367

00:58:09.470 --> 00:58:12.350 I have I have a suggestion

NOTE Confidence: 0.3747367

00:58:12.350 --> 00:58:15.150 Cyril D'souza. One possibility

NOTE Confidence: 0.3747367

00:58:15.150 --> 00:58:16.350 is for example to use

NOTE Confidence: 0.3747367

00:58:17.550 --> 00:58:18.870 a drug that does produce

NOTE Confidence: 0.3747367

00:58:18.870 --> 00:58:21.108 hallucinogenic effects that is not

NOTE Confidence: 0.3747367

00:58:21.510 --> 00:58:24.135 predicted to, for example produce

NOTE Confidence: 0.3747367

00:58:24.135 --> 00:58:26.190 anti depression depressant effects.

NOTE Confidence: 0.3747367

00:58:26.190 --> 00:58:28.830 So that would be for example,

NOTE Confidence: 0.3747367

00:58:28.830 --> 00:58:30.390 a drug like Salman RNA

NOTE Confidence: 0.3747367

00:58:30.390 --> 00:58:32.790 which is, which produces

NOTE Confidence: 0.3747367

00:58:32.790 --> 00:58:35.950 potent hallucinogenic effects

NOTE Confidence: 0.3747367

00:58:35.950 --> 00:58:39.320 but is generally perceived as being,

NOTE Confidence: 0.83140635

00:58:39.320 --> 00:58:41.480 you know, unpleasant,

NOTE Confidence: 0.83140635

00:58:41.480 --> 00:58:44.360 at least for the moment. So that would be

NOTE Confidence: 0.83140635

00:58:45.640 --> 00:58:48.280 111 possibility. And the other possibility

NOTE Confidence: 0.83140635

00:58:48.280 --> 00:58:50.360 would be, for example,

NOTE Confidence: 0.83140635

00:58:50.360 --> 00:58:51.980 since in the case of depression,

NOTE Confidence: 0.83140635

00:58:51.980 --> 00:58:55.130 there may be patients who who go through

NOTE Confidence: 0.83140635

00:58:55.130 --> 00:58:58.000 ECT and receive anaesthesia for ECT,

NOTE Confidence: 0.83140635

00:58:58.320 --> 00:58:59.040 what if you,

NOTE Confidence: 0.83140635

00:59:00.520 --> 00:59:02.012 you know, give them an anaesthetic

NOTE Confidence: 0.83140635

00:59:02.012 --> 00:59:04.600 agent so they don't experience

NOTE Confidence: 0.83140635

00:59:04.600 --> 00:59:06.200 the acute psychedelic effects?

NOTE Confidence: 0.83140635

00:59:07.360 --> 00:59:07.680 And

NOTE Confidence: 0.29364285

00:59:10.240 --> 00:59:11.520 I can't comment on that.

NOTE Confidence: 0.29364285

00:59:11.520 --> 00:59:13.005 Let's comment on both points

NOTE Confidence: 0.29364285

00:59:13.005 --> 00:59:14.193 that are very stimulating.

NOTE Confidence: 0.29364285

00:59:14.200 --> 00:59:16.510 Of course, a positive comparator

NOTE Confidence: 0.29364285

00:59:16.510 --> 00:59:19.720 where we can create the experience

NOTE Confidence: 0.29364285

00:59:19.720 --> 00:59:22.440 somehow without having antidepressant

NOTE Confidence: 0.29364285

00:59:22.440 --> 00:59:25.340 effects can be a strategy.

NOTE Confidence: 0.29364285

00:59:25.340 --> 00:59:28.780 The idea to have this drug while people

NOTE Confidence: 0.29364285

00:59:28.866 --> 00:59:31.976 are anesthetized has been shown recently

NOTE Confidence: 0.29364285

00:59:31.976 --> 00:59:35.448 by Boris and this team from Stanford.

NOTE Confidence: 0.29364285

00:59:35.450 --> 00:59:38.250 And what do they have with ketamine?

NOTE Confidence: 0.29364285

00:59:38.250 --> 00:59:40.010 What do they did?

NOTE Confidence: 0.29364285

00:59:40.010 --> 00:59:43.930 They give ketamine to people who were,

00:59:43.930 --> 00:59:46.810 you know, prepared for their

00:59:46.810 --> 00:59:49.210 surgical procedure and the idea

00:59:49.210 --> 00:59:52.409 was and they had major depression.

00:59:52.410 --> 00:59:54.450 So if we inject ketamine,

00:59:54.450 --> 00:59:57.740 they should have long lasting effects of

00:59:57.740 --> 01:00:00.850 ketamine on their depression post surgery.

01:00:00.850 --> 01:00:03.664 And I suggest I little did this.

01:00:03.670 --> 01:00:05.788 The manuscript that is very intriguing,

01:00:05.790 --> 01:00:06.742 but probably,

01:00:06.742 --> 01:00:10.550 I mean this is something like self marketing.

01:00:10.550 --> 01:00:14.502 There is an accord and I comment on

01:00:14.502 --> 01:00:17.020 this manuscript and the article that

01:00:17.020 --> 01:00:19.270 came out today where we described

01:00:19.270 --> 01:00:21.590 by the challenging pitfalls,

01:00:21.590 --> 01:00:24.383 but also how somehow when we create

01:00:24.383 --> 01:00:26.940 a sort of silencing expectation

NOTE Confidence: 0.29364285

01:00:26.940 --> 01:00:30.110 like the Open Eden Paradigm,

NOTE Confidence: 0.29364285

01:00:30.110 --> 01:00:32.476 we may also destroy all the effects

NOTE Confidence: 0.29364285

01:00:32.476 --> 01:00:34.768 of the antidepressant like ketamine.

NOTE Confidence: 0.29364285

01:00:34.768 --> 01:00:35.840 In fact,

NOTE Confidence: 0.29364285

01:00:35.840 --> 01:00:38.320 patients who receive ketamine

NOTE Confidence: 0.29364285

01:00:38.320 --> 01:00:40.800 or placebo improve equally.

NOTE Confidence: 0.29364285

01:00:40.800 --> 01:00:42.712 Over 50% responded, Yeah,

NOTE Confidence: 0.29364285

01:00:42.712 --> 01:00:44.280 and they both improve.

NOTE Confidence: 0.29364285

01:00:44.280 --> 01:00:45.640 So that is the challenge.

NOTE Confidence: 0.29364285

01:00:45.640 --> 01:00:47.185 If 50 percentage improve and

NOTE Confidence: 0.29364285

01:00:47.185 --> 01:00:49.130 this is the same 53 percentage

NOTE Confidence: 0.29364285

01:00:49.130 --> 01:00:51.116 that I saw in my patient,

NOTE Confidence: 0.29364285

01:00:51.120 --> 01:00:53.731 no matter if they receive a placebo

NOTE Confidence: 0.29364285

01:00:53.731 --> 01:00:55.839 ketamine before beginning anesthetize it,

NOTE Confidence: 0.29364285

01:00:55.840 --> 01:00:58.270 then the medicine that we practice

NOTE Confidence: 0.29364285

01:00:58.270 --> 01:01:01.343 may need to be scrutinized because

NOTE Confidence: 0.29364285

01:01:01.343 --> 01:01:03.608 expectation needed to be studied.

NOTE Confidence: 0.29364285

01:01:03.610 --> 01:01:07.906 Because maybe that is a concept that some

NOTE Confidence: 0.29364285

01:01:07.906 --> 01:01:11.930 while some hours in 2003 very popular

NOTE Confidence: 0.29364285

01:01:11.930 --> 01:01:14.658 in the literature for antidepressant

NOTE Confidence: 0.29364285

01:01:14.658 --> 01:01:17.106 it's that you need the expectation

NOTE Confidence: 0.29364285

01:01:17.106 --> 01:01:19.930 to see an antidepressant effect.

NOTE Confidence: 0.29364285

01:01:19.930 --> 01:01:23.101 When we did the Adziban with an

NOTE Confidence: 0.29364285

01:01:23.101 --> 01:01:24.460 Indian administration especially

NOTE Confidence: 0.29364285

01:01:24.538 --> 01:01:25.957 didn't improve Boris.

NOTE Confidence: 0.29364285

01:01:25.957 --> 01:01:28.092 Today you have ketamine and

NOTE Confidence: 0.29364285

01:01:28.092 --> 01:01:30.380 placebo and they improve equally

NOTE Confidence: 0.29364285

01:01:30.380 --> 01:01:32.512 not despite begin anesthetized.

NOTE Confidence: 0.29364285

01:01:32.512 --> 01:01:35.177 So then let's tackle expectation.

NOTE Confidence: 0.29364285

01:01:35.180 --> 01:01:37.791 We truly needed to understand our wine

NOTE Confidence: 0.29364285

01:01:37.791 --> 01:01:40.186 desert that I molecular changes and

NOTE Confidence: 0.29364285

01:01:40.186 --> 01:01:43.467 merely rely on the concept that we can

NOTE Confidence: 0.29364285

01:01:43.467 --> 01:01:45.831 use the world standard of comparing

NOTE Confidence: 0.29364285

01:01:45.831 --> 01:01:50.512 A placebo armor with a ketamine or

NOTE Confidence: 0.29364285

01:01:50.512 --> 01:01:54.604 psychedelic are may not help us.

NOTE Confidence: 0.29364285

01:01:54.604 --> 01:01:57.070 And also Chris asked about

NOTE Confidence: 0.29364285

01:01:57.070 --> 01:01:59.220 the duration of this effects.

NOTE Confidence: 0.29364285

01:01:59.220 --> 01:02:02.324 There are a paper in the literature show

NOTE Confidence: 0.29364285

01:02:02.324 --> 01:02:05.475 that patients who had placebo responses 10

NOTE Confidence: 0.29364285

01:02:05.475 --> 01:02:08.940 years before they continue to be respondents.

NOTE Confidence: 0.29364285

01:02:08.940 --> 01:02:09.836 And anecdotally,

NOTE Confidence: 0.29364285

01:02:09.836 --> 01:02:12.076 when we were serious Parkinson

NOTE Confidence: 0.29364285

01:02:12.076 --> 01:02:14.100 patients that they received,

NOTE Confidence: 0.29364285

01:02:14.100 --> 01:02:14.940 you know,

NOTE Confidence: 0.29364285

01:02:14.940 --> 01:02:16.620 treatment with a battery,

NOTE Confidence: 0.29364285

01:02:16.620 --> 01:02:18.996 we had the patients who came to the

NOTE Confidence: 0.29364285

01:02:18.996 --> 01:02:21.372 lab were being reassessed clinically.

NOTE Confidence: 0.29364285

01:02:21.372 --> 01:02:24.480 They didn't know that the battery

NOTE Confidence: 0.29364285

01:02:24.561 --> 01:02:26.966 was off because they travel from

NOTE Confidence: 0.29364285

01:02:26.966 --> 01:02:28.862 the metal detector and they were

NOTE Confidence: 0.29364285

01:02:28.862 --> 01:02:30.850 continued to have huge improvement.

NOTE Confidence: 0.29364285

01:02:30.850 --> 01:02:32.716 They didn't realize.

NOTE Confidence: 0.29364285

01:02:32.716 --> 01:02:38.550 So what can we call this a long lasting plus

NOTE Confidence: 0.29364285

01:02:38.550 --> 01:02:41.234 CB effects expectation that makes them,

NOTE Confidence: 0.29364285

01:02:41.234 --> 01:02:41.970 you know,

NOTE Confidence: 0.29364285

01:02:41.970 --> 01:02:45.530 not realizing that that resolve

NOTE Confidence: 0.29364285

01:02:45.530 --> 01:02:47.330 and they continue to improve

NOTE Confidence: 0.29364285

01:02:47.330 --> 01:02:48.770 and conducting their life.

NOTE Confidence: 0.29364285

01:02:48.770 --> 01:02:49.050 I think,

NOTE Confidence: 0.36872393

01:02:51.570 --> 01:02:53.250 Luana, Luana, I have a question

NOTE Confidence: 0.36872393

01:02:53.250 --> 01:02:56.953 about how you would recommend we

NOTE Confidence: 0.36872393

01:02:56.953 --> 01:02:58.868 measure expectancy, because as yet

NOTE Confidence: 0.36872393

01:02:58.868 --> 01:03:00.760 I'm unaware of any standardized

NOTE Confidence: 0.36872393

01:03:00.760 --> 01:03:04.058 way of measuring expectancy,

NOTE Confidence: 0.36872393

01:03:04.060 --> 01:03:07.180 especially for psychedelic studies

NOTE Confidence: 0.35384247

01:03:09.580 --> 01:03:10.979 about expectations and expectancy,

NOTE Confidence: 0.35384247

01:03:10.979 --> 01:03:12.737 just so it's clear to everybody.

NOTE Confidence: 0.35384247

01:03:14.340 --> 01:03:16.720 So we define operationally

NOTE Confidence: 0.35384247

01:03:16.720 --> 01:03:19.695 expectations when we measure it.

NOTE Confidence: 0.35384247

01:03:19.700 --> 01:03:21.900 And there are several scales,

NOTE Confidence: 0.35384247

01:03:21.900 --> 01:03:25.130 like the Stanford Expectation Scale,

NOTE Confidence: 0.35384247

01:03:25.130 --> 01:03:28.070 the Credibility scale or

NOTE Confidence: 0.35384247

01:03:28.070 --> 01:03:31.010 merely visual analogue scale.

NOTE Confidence: 0.35384247

01:03:31.010 --> 01:03:33.728 We compare in the lab two

NOTE Confidence: 0.35384247

01:03:33.728 --> 01:03:35.087 different assessments and

NOTE Confidence: 0.6303803

01:03:37.330 --> 01:03:40.410 we see that the visual analogue scale,

NOTE Confidence: 0.6303803

01:03:40.410 --> 01:03:44.250 it's easy to understand and somehow

NOTE Confidence: 0.6303803

01:03:44.250 --> 01:03:48.300 helpful to understand the expectations.

NOTE Confidence: 0.6303803

01:03:48.300 --> 01:03:51.682 In the paper that we publish with the

NOTE Confidence: 0.6303803

01:03:51.682 --> 01:03:53.974 distribution of Placib effects in chronic

NOTE Confidence: 0.6303803

01:03:53.974 --> 01:03:56.099 pain patients and earth controls,

NOTE Confidence: 0.6303803

01:03:56.100 --> 01:03:58.740 the NMT and so on,

NOTE Confidence: 0.6303803

01:03:58.740 --> 01:04:02.250 there was an association between

NOTE Confidence: 0.6303803

01:04:02.250 --> 01:04:04.814 expectations versus Placib effects.

NOTE Confidence: 0.6303803

01:04:04.814 --> 01:04:07.122 But expectation didn't mediate

NOTE Confidence: 0.6303803

01:04:07.122 --> 01:04:08.853 the Placib effects.

NOTE Confidence: 0.6303803

01:04:08.860 --> 01:04:11.905 So if we want a simple tool,

NOTE Confidence: 0.6303803

01:04:11.910 --> 01:04:14.310 I suggest visual Analogue Scale where

NOTE Confidence: 0.6303803

01:04:14.310 --> 01:04:17.837 they just have a cursor and we can

NOTE Confidence: 0.6303803

01:04:17.837 --> 01:04:20.142 measure without any numerical anchors.

NOTE Confidence: 0.6303803

01:04:20.150 --> 01:04:22.985 But the expectancy to me is even

NOTE Confidence: 0.6303803

01:04:22.985 --> 01:04:25.370 more intriguing and important in

NOTE Confidence: 0.6303803

01:04:25.370 --> 01:04:28.030 a ideal world like us that are

NOTE Confidence: 0.6303803

01:04:28.030 --> 01:04:31.317 well funded and we have brain and

NOTE Confidence: 0.6303803

01:04:31.317 --> 01:04:33.269 resources to tackle questions.

NOTE Confidence: 0.6303803

01:04:33.270 --> 01:04:36.189 I suggest not to study middle expectation,

NOTE Confidence: 0.6303803

01:04:36.190 --> 01:04:39.627 measuring how much people expect to improve,

NOTE Confidence: 0.6303803

01:04:39.630 --> 01:04:42.710 rather measuring expectancy with modelling,

NOTE Confidence: 0.6303803

01:04:42.710 --> 01:04:43.764 brain imaging.

NOTE Confidence: 0.6303803

01:04:43.764 --> 01:04:47.453 And try to see how the interplay

NOTE Confidence: 0.6303803

01:04:47.453 --> 01:04:51.257 of beliefs and mindset at the level

NOTE Confidence: 0.6303803

01:04:51.257 --> 01:04:53.840 of neuronal change can help us

NOTE Confidence: 0.6303803

01:04:53.840 --> 01:04:55.480 to understand the responsibility

NOTE Confidence: 0.6303803

01:04:55.480 --> 01:04:56.550 to treatment

NOTE Confidence: 0.5378341

01:04:59.070 --> 01:05:01.090 about measuring expectation and

NOTE Confidence: 0.5378341

01:05:01.090 --> 01:05:03.110 studying the brain correlates

NOTE Confidence: 0.5378341

01:05:03.110 --> 01:05:05.390 of beliefs and expectancies.

NOTE Confidence: 0.5378341

01:05:05.390 --> 01:05:09.166 Thank you. Sure. OK.

NOTE Confidence: 0.5378341

01:05:09.166 --> 01:05:10.296 Mr. I got two questions.

NOTE Confidence: 0.5378341

01:05:10.300 --> 01:05:12.804 Yes, one is in that slide that you

NOTE Confidence: 0.5378341

01:05:12.804 --> 01:05:15.210 showed all of the components of

NOTE Confidence: 0.5378341

01:05:15.210 --> 01:05:18.012 expectancy and the placebo effect, all that.

NOTE Confidence: 0.5378341

01:05:18.012 --> 01:05:19.692 And then you mentioned certain

NOTE Confidence: 0.5378341

01:05:19.692 --> 01:05:21.084 components of expectancy, right.

NOTE Confidence: 0.5378341

01:05:21.084 --> 01:05:22.620 So the patient's priors,

NOTE Confidence: 0.5378341

01:05:22.620 --> 01:05:23.772 experiences or beliefs,

NOTE Confidence: 0.5378341

01:05:23.772 --> 01:05:26.460 how did you get to those elements?

NOTE Confidence: 0.5378341

01:05:26.460 --> 01:05:28.020 Like did you assess that?

NOTE Confidence: 0.5378341

01:05:28.020 --> 01:05:30.500 Did you openly ask them,

NOTE Confidence: 0.5378341

01:05:30.500 --> 01:05:35.180 so they're referring to this,

NOTE Confidence: 0.5378341

01:05:35.180 --> 01:05:37.210 correct.

NOTE Confidence: 0.5378341

01:05:37.210 --> 01:05:37.664 No, no,

NOTE Confidence: 0.5378341

01:05:37.664 --> 01:05:39.026 no way before like in the

NOTE Confidence: 0.5378341

01:05:39.026 --> 01:05:40.130 beginning of the present.

NOTE Confidence: 0.43637162

01:05:40.130 --> 01:05:41.528 Yeah, I think in your overview

NOTE Confidence: 0.43637162

01:05:41.528 --> 01:05:43.050 slide you were saying all the

NOTE Confidence: 0.43637162

01:05:43.050 --> 01:05:44.126 things that could influence.

NOTE Confidence: 0.43637162

01:05:44.130 --> 01:05:48.006 Yes, that, so that expectancy there.

NOTE Confidence: 0.43637162

01:05:48.010 --> 01:05:50.593 So this is a summary of what we have

NOTE Confidence: 0.43637162

01:05:50.593 --> 01:05:53.409 been studying over the last 1-2 decades.

NOTE Confidence: 0.43637162

01:05:53.410 --> 01:05:55.295 So the concept is that

NOTE Confidence: 0.43637162

01:05:55.295 --> 01:05:56.803 expectations can be measured.

NOTE Confidence: 0.43637162

01:05:56.810 --> 01:05:59.912 Expectancy is something more related to

NOTE Confidence: 0.43637162

01:05:59.912 --> 01:06:03.431 the brain changes when we don't measure

NOTE Confidence: 0.43637162

01:06:03.431 --> 01:06:06.793 expectations and so we know that we

NOTE Confidence: 0.43637162

01:06:06.793 --> 01:06:09.958 can study anticipation of treatment.

NOTE Confidence: 0.43637162

01:06:09.960 --> 01:06:12.276 So at least with brain imaging,

NOTE Confidence: 0.43637162

01:06:12.280 --> 01:06:15.112 we have been looking at anticipatory

NOTE Confidence: 0.43637162

01:06:15.112 --> 01:06:18.773 phase when you expect something acute a

98

NOTE Confidence: 0.43637162

01:06:18.773 --> 01:06:21.583 treatment and somehow this anticipation

NOTE Confidence: 0.43637162

01:06:21.583 --> 01:06:24.743 can trigger brain changes and it's

NOTE Confidence: 0.43637162

01:06:24.743 --> 01:06:27.671 our ability to predict future events.

NOTE Confidence: 0.43637162

01:06:27.680 --> 01:06:30.470 So another way to think about

NOTE Confidence: 0.43637162

01:06:30.470 --> 01:06:33.359 this is real ability to predict

NOTE Confidence: 0.43637162

01:06:33.360 --> 01:06:35.332 and anticipate future events.

NOTE Confidence: 0.43637162

01:06:35.332 --> 01:06:39.240 So we call this expectancy and in terms

NOTE Confidence: 0.43637162

01:06:39.240 --> 01:06:42.120 of expectation is more a measurement

NOTE Confidence: 0.43637162

01:06:42.120 --> 01:06:45.700 of patient believe and outcome.

NOTE Confidence: 0.43637162

01:06:45.700 --> 01:06:48.800 This is their ability.

NOTE Confidence: 0.43637162

01:06:48.800 --> 01:06:52.279 If your questions is about this part,

NOTE Confidence: 0.43637162

01:06:52.280 --> 01:06:54.872 this is just a summer of all the studies

NOTE Confidence: 0.43637162

01:06:54.872 --> 01:06:57.614 that we have been conducting where we

NOTE Confidence: 0.43637162

01:06:57.614 --> 01:06:59.782 can manipulate the suggestion therapeutic

NOTE Confidence: 0.43637162

01:06:59.782 --> 01:07:03.214 experience by asking patients about how

NOTE Confidence: 0.43637162

01:07:03.214 --> 01:07:06.256 many good clinical experience you had.

NOTE Confidence: 0.43637162

01:07:06.256 --> 01:07:08.466 There are studies show observation

NOTE Confidence: 0.43637162

01:07:08.466 --> 01:07:11.066 in other people and contestual

NOTE Confidence: 0.43637162

01:07:11.066 --> 01:07:12.890 and interpersonal interaction.

NOTE Confidence: 0.43637162

01:07:12.890 --> 01:07:15.272 It's made last summer over 20

NOTE Confidence: 0.43637162

01:07:15.272 --> 01:07:17.570 years studies that we conduct,

NOTE Confidence: 0.43637162

01:07:17.570 --> 01:07:21.370 other people conduct, yes, yes.

NOTE Confidence: 0.43637162

01:07:21.370 --> 01:07:23.610 And the second question.

NOTE Confidence: 0.43637162

01:07:23.610 --> 01:07:25.902 So second question was with regards

NOTE Confidence: 0.43637162

01:07:25.902 --> 01:07:29.512 to the question physician aspects

NOTE Confidence: 0.43637162

01:07:29.512 --> 01:07:32.576 that might influence patients.

NOTE Confidence: 0.43637162

01:07:32.580 --> 01:07:32.793 Yeah.

NOTE Confidence: 0.43637162

01:07:32.793 --> 01:07:34.497 And you said that you tested the warmth,

NOTE Confidence: 0.43637162

01:07:34.500 --> 01:07:38.256 encompass empathy that that was negative.

NOTE Confidence: 0.43637162

01:07:38.260 --> 01:07:41.298 But I was wondering if you investigated

NOTE Confidence: 0.43637162

01:07:41.298 --> 01:07:43.785 whether you can group physicians

NOTE Confidence: 0.43637162

01:07:43.785 --> 01:07:46.545 by their patients response because

NOTE Confidence: 0.43637162

01:07:46.545 --> 01:07:49.602 there's this paper on antidepressant

NOTE Confidence: 0.43637162

01:07:49.602 --> 01:07:52.493 effects that does that well.

NOTE Confidence: 0.43637162

01:07:52.493 --> 01:07:54.358 We did in our experiments.

NOTE Confidence: 0.43637162

01:07:54.360 --> 01:07:57.414 So I would refrain from generalizing

NOTE Confidence: 0.43637162

01:07:57.414 --> 01:08:00.428 because there are other studies show

NOTE Confidence: 0.43637162

01:08:00.428 --> 01:08:02.828 that the physicians the study you

NOTE Confidence: 0.43637162

01:08:02.828 --> 01:08:05.488 mentioned and to other study warmer

NOTE Confidence: 0.43637162

01:08:05.488 --> 01:08:08.560 and competency influence outcome.

NOTE Confidence: 0.43637162

01:08:08.560 --> 01:08:11.680 We are not observing that implicit

NOTE Confidence: 0.43637162

01:08:11.680 --> 01:08:13.760 effects through our paradigm.

NOTE Confidence: 0.43637162

01:08:13.760 --> 01:08:17.926 But of course there are you know

NOTE Confidence: 0.43637162

01:08:17.930 --> 01:08:20.750 this are elements that are part

NOTE Confidence: 0.43637162

01:08:20.750 --> 01:08:22.630 of the interpersonal interaction

NOTE Confidence: 0.43637162

01:08:22.710 --> 01:08:25.210 that may affect clinical outcomes.

NOTE Confidence: 0.43637162

01:08:25.210 --> 01:08:26.810 But even without sorry, sorry,

NOTE Confidence: 0.43637162

01:08:26.810 --> 01:08:28.832 I'm sorry but even without knowing

NOTE Confidence: 0.43637162

01:08:28.832 --> 01:08:30.939 the specific component did you observe

NOTE Confidence: 0.43637162

01:08:30.939 --> 01:08:33.117 like a grouping among physicians like

NOTE Confidence: 0.43637162

01:08:33.117 --> 01:08:36.171 a certain physicians have we see an

NOTE Confidence: 0.43637162

01:08:36.171 --> 01:08:38.114 experimental effect we know that in

NOTE Confidence: 0.43637162

01:08:38.114 --> 01:08:40.118 the lab there are some people that

NOTE Confidence: 0.43637162

01:08:40.118 --> 01:08:42.176 trigger larger plus if effects we

NOTE Confidence: 0.43637162

01:08:42.176 --> 01:08:43.980 should publish that the experimental

NOTE Confidence: 0.43637162

01:08:43.980 --> 01:08:47.060 effect and I bet that you see that

NOTE Confidence: 0.43637162

01:08:47.136 --> 01:08:49.926 with your experiment or your patient.

NOTE Confidence: 0.43637162

01:08:49.930 --> 01:08:52.776 It's something that we don't know if

NOTE Confidence: 0.43637162

01:08:52.776 --> 01:08:55.406 it's the verbal nonverbal communication,

NOTE Confidence: 0.43637162

01:08:55.410 --> 01:08:57.516 the attitude the way to connect

NOTE Confidence: 0.43637162

01:08:57.516 --> 01:08:58.569 with your patient,

NOTE Confidence: 0.43637162

01:08:58.570 --> 01:09:01.209 but we do see an experimental effect.

NOTE Confidence: 0.43637162

01:09:01.210 --> 01:09:03.340 Thanks for asking. Anything.

NOTE Confidence: 0.2554846

01:09:03.860 --> 01:09:04.442 So, I'm sorry.

NOTE Confidence: 0.2554846

01:09:04.442 --> 01:09:06.220 I have to run off and catch a train,

NOTE Confidence: 0.2554846

01:09:06.220 --> 01:09:08.140 which means I have to take my computer.

NOTE Confidence: 0.2554846

01:09:08.140 --> 01:09:10.100 So I'm going to take my computer in.

NOTE Confidence: 0.2554846

01:09:10.100 --> 01:09:11.216 But that doesn't mean that this.

NOTE Confidence: 0.2554846

01:09:11.220 --> 01:09:13.318 I think you have anyone enough. No, no, no.

NOTE Confidence: 0.2554846

01:09:13.318 --> 01:09:14.820 They'll stay on. Oh, they stay on.

NOTE Confidence: 0.2554846

01:09:15.780 --> 01:09:16.780 Your slides will go away.

NOTE Confidence: 0.2554846

01:09:20.620 --> 01:09:21.333 All right, that's me.

NOTE Confidence: 0.2554846

01:09:21.333 --> 01:09:23.180 Let me make sure. Oh, watch

NOTE Confidence: 0.2554846

01:09:23.220 --> 01:09:25.100 this. I'm not going to kill the meeting.

NOTE Confidence: 0.2554846

01:09:25.100 --> 01:09:26.646 I've done this anytime where

NOTE Confidence: 0.2554846

01:09:26.646 --> 01:09:27.686 I've accidentally killed

NOTE Confidence: 0.2554846

01:09:27.686 --> 01:09:28.860 the meeting conditioned to

NOTE Confidence: 0.37161314

01:09:32.880 --> 01:09:34.518 OK, Jessica, you're the you're the boss.

NOTE Confidence: 0.37161314

01:09:36.120 --> 01:09:39.839 Thank you. All right. OK,

NOTE Confidence: 0.37161314

01:09:39.840 --> 01:09:40.800 Chris, while you're doing it,

NOTE Confidence: 0.37161314

01:09:40.800 --> 01:09:42.644 I can say maybe address this too.

NOTE Confidence: 0.37161314

01:09:42.644 --> 01:09:44.672 It gets more complex though, too,

NOTE Confidence: 0.37161314

01:09:44.672 --> 01:09:47.320 because then there's contextual factors,

NOTE Confidence: 0.37161314

01:09:47.320 --> 01:09:51.152 right? So what could be a a

NOTE Confidence: 0.37161314

01:09:51.152 --> 01:09:52.400 favorable placebo response?

NOTE Confidence: 0.37161314

01:09:52.400 --> 01:09:54.200 Or who may be a person who's more

NOTE Confidence: 0.37161314

01:09:54.200 --> 01:09:55.833 likely to have a placebo response

NOTE Confidence: 0.37161314

01:09:55.833 --> 01:09:57.525 in one situation could be very

NOTE Confidence: 0.37161314

01:09:57.586 --> 01:09:59.210 different in another situation.

NOTE Confidence: 0.37161314

01:09:59.210 --> 01:10:01.646 So that and that's culturally.

NOTE Confidence: 0.37161314

01:10:01.646 --> 01:10:05.370 But even from 11 endless to another,

NOTE Confidence: 0.37161314

01:10:05.370 --> 01:10:07.827 a physician that may engender a good

NOTE Confidence: 0.37161314

01:10:07.827 --> 01:10:09.489 political response to a surgery

NOTE Confidence: 0.37161314

01:10:09.490 --> 01:10:12.580 intervention may be a different thing

NOTE Confidence: 0.37161314

01:10:12.580 --> 01:10:14.774 that would engender a good political

NOTE Confidence: 0.37161314

01:10:14.774 --> 01:10:17.250 response to some other type of intervention.

NOTE Confidence: 0.37161314

01:10:17.250 --> 01:10:17.541 They.

NOTE Confidence: 0.37161314

01:10:17.541 --> 01:10:18.414 I think that's.

NOTE Confidence: 0.37161314

01:10:18.414 --> 01:10:21.514 It's fair to say some of the more recent

NOTE Confidence: 0.37161314

01:10:21.514 --> 01:10:24.088 research suggested that it's very contextual.

NOTE Confidence: 0.37161314

01:10:24.090 --> 01:10:25.094 It's not so simple.

NOTE Confidence: 0.37161314

01:10:25.094 --> 01:10:25.847 It's not like,

NOTE Confidence: 0.25623393

01:10:26.390 --> 01:10:27.308 which makes a lot of sense,

NOTE Confidence: 0.25623393

01:10:27.310 --> 01:10:28.846 like things that the things that make

NOTE Confidence: 0.25623393

01:10:28.846 --> 01:10:31.150 you confident in a plumber's skills

NOTE Confidence: 0.25623393

01:10:31.150 --> 01:10:33.322 are going to be very different in the

NOTE Confidence: 0.25623393

01:10:33.322 --> 01:10:35.950 person buying the plane, Right? Yeah.

NOTE Confidence: 0.25623393

01:10:35.950 --> 01:10:39.390 Plumbing I mean the Super response,

NOTE Confidence: 0.36159262

01:10:41.590 --> 01:10:44.602 yes can I also so about the our last

NOTE Confidence: 0.36159262

01:10:44.602 --> 01:10:47.009 how how can we know how much of the

NOTE Confidence: 0.36159262

01:10:47.009 --> 01:10:49.229 effect of the psychedelics of placebo.

NOTE Confidence: 0.36159262

01:10:49.230 --> 01:10:51.550 I know that in some studies to know

NOTE Confidence: 0.36159262

01:10:51.550 --> 01:10:53.230 how much of the effect is placebo.

NOTE Confidence: 0.36159262

01:10:53.230 --> 01:10:54.550 I mean it's mostly for pain.

NOTE Confidence: 0.36159262

01:10:54.550 --> 01:10:57.487 I think it's they use naloxone because

NOTE Confidence: 0.36159262

01:10:57.487 --> 01:10:59.846 you know one of the underlying mechanism

NOTE Confidence: 0.36159262

01:10:59.846 --> 01:11:03.150 of analysis in a placebo response

NOTE Confidence: 0.36159262

01:11:03.150 --> 01:11:06.648 in for pain is intrinsic opioid.

NOTE Confidence: 0.36159262

01:11:06.650 --> 01:11:09.390 So they use another song to mask that

NOTE Confidence: 0.36159262

01:11:09.390 --> 01:11:11.705 and to see how much of the effect is

NOTE Confidence: 0.36159262

01:11:11.705 --> 01:11:13.845 there like the real right for example

NOTE Confidence: 0.36159262

01:11:13.845 --> 01:11:15.929 keterolac for keterolac we can't do that

NOTE Confidence: 0.36159262

01:11:15.930 --> 01:11:19.376 but I mean we have been using monabant.

NOTE Confidence: 0.36159262

01:11:19.376 --> 01:11:25.346 So the idea I mean well placebo analgesia

NOTE Confidence: 0.36159262

01:11:25.346 --> 01:11:28.935 has been you know study mostly with

NOTE Confidence: 0.36159262

01:11:28.935 --> 01:11:31.100 pharmacological approach before we had

NOTE Confidence: 0.36159262

01:11:31.170 --> 01:11:35.443 the brain imaging and so on in 197374

NOTE Confidence: 0.36159262

01:11:35.443 --> 01:11:40.689 a teenage a patient with wisdom you

NOTE Confidence: 0.36159262

01:11:40.689 --> 01:11:43.284 know withdrawal and surgical procedure

NOTE Confidence: 0.36159262

01:11:43.284 --> 01:11:45.883 were somehow randomized to selling

NOTE Confidence: 0.36159262

01:11:45.883 --> 01:11:48.547 and or morphine and pre injecting

NOTE Confidence: 0.36159262

01:11:48.547 --> 01:11:51.602 idols of naloxone block completely the

NOTE Confidence: 0.36159262

01:11:51.602 --> 01:11:54.347 effects of placebo energies because

NOTE Confidence: 0.36159262

01:11:54.347 --> 01:11:56.464 patients respond also to selling.

NOTE Confidence: 0.36159262

01:11:56.464 --> 01:11:58.830 But this is also the bitcher story

NOTE Confidence: 0.36159262

01:11:58.903 --> 01:12:01.127 when he was in Sicily and the post

NOTE Confidence: 0.36159262

01:12:01.127 --> 01:12:03.418 war and somehow he is failing to

NOTE Confidence: 0.36159262

01:12:03.418 --> 01:12:05.705 treat good that the patient when

NOTE Confidence: 0.36159262

01:12:05.705 --> 01:12:08.430 he had finished you know the pain.

NOTE Confidence: 0.36159262

01:12:08.430 --> 01:12:10.214 So actually my question is that can we

NOTE Confidence: 0.36159262

01:12:10.214 --> 01:12:11.932 do that for psychologics I don't know

NOTE Confidence: 0.36159262

01:12:11.932 --> 01:12:14.110 how much of the like an antagonist does.

NOTE Confidence: 0.3292058

01:12:14.110 --> 01:12:16.364 So there's there is talk about using

NOTE Confidence: 0.3292058

01:12:16.364 --> 01:12:18.366 like tanzarin and some of the other

NOTE Confidence: 0.3292058

01:12:18.366 --> 01:12:20.550 5 HD two drugs to block the effect.

NOTE Confidence: 0.53082645

01:12:21.170 --> 01:12:23.969 But then what we can do like in the

NOTE Confidence: 0.53082645

01:12:23.969 --> 01:12:26.896 ketamine study with mice that use greater

NOTE Confidence: 0.53082645

01:12:26.896 --> 01:12:28.932 conditioning you know psychedelics 2

NOTE Confidence: 0.53082645

01:12:28.932 --> 01:12:31.599 weeks apart or one months apart and

NOTE Confidence: 0.53082645

01:12:31.599 --> 01:12:34.972 other psychedelics and then placebo by

NOTE Confidence: 0.53082645

01:12:34.972 --> 01:12:37.936 pre injecting psychedelic antagonist.

NOTE Confidence: 0.53082645

01:12:37.940 --> 01:12:41.420 Oh no no I'm actually not using about

NOTE Confidence: 0.53082645

01:12:41.420 --> 01:12:43.569 you're talking about not because I don't

NOTE Confidence: 0.53082645

01:12:43.569 --> 01:12:45.820 know the opioid you like the intro I'm

NOTE Confidence: 0.53082645

01:12:45.820 --> 01:12:47.796 talking about using something to block she's.

NOTE Confidence: 0.53082645

01:12:47.796 --> 01:12:50.180 Yes I know that intrinsic opioids are

NOTE Confidence: 0.53082645

01:12:50.180 --> 01:12:53.236 like one of the one of the main you

NOTE Confidence: 0.53082645

01:12:53.236 --> 01:12:55.166 know circuits in the brain that you

NOTE Confidence: 0.53082645

01:12:55.166 --> 01:12:57.133 know not that is an absolutely nice.

NOTE Confidence: 0.53082645

01:12:57.140 --> 01:12:57.860 Yeah ketamine

NOTE Confidence: 0.27070886

01:12:57.860 --> 01:13:01.820 also at Stanford using Nelloxon to

NOTE Confidence: 0.27070886

01:13:01.820 --> 01:13:03.700 reportedly block them the ketamine

NOTE Confidence: 0.27070886

01:13:03.700 --> 01:13:05.970 antidepressant response in a small number

NOTE Confidence: 0.36756226

01:13:06.690 --> 01:13:08.738 of people. So the idea is kind of

NOTE Confidence: 0.36756226

01:13:08.738 --> 01:13:10.284 we block the placebo components

NOTE Confidence: 0.36756226

01:13:10.284 --> 01:13:12.644 that are using in a given that

NOTE Confidence: 0.36756226

01:13:12.644 --> 01:13:15.402 the new opioid system is one of

NOTE Confidence: 0.36756226

01:13:15.402 --> 01:13:18.480 the most important system that has

NOTE Confidence: 0.36756226

01:13:18.480 --> 01:13:20.850 been done for ketamine for example.

NOTE Confidence: 0.36756226

01:13:20.850 --> 01:13:22.410 And that's a cool idea.

NOTE Confidence: 0.36756226

01:13:22.410 --> 01:13:26.494 The caveat is that OK,

NOTE Confidence: 0.36756226

01:13:26.494 --> 01:13:28.678 it's through the endogenous opioid

NOTE Confidence: 0.36756226

01:13:28.678 --> 01:13:31.366 system play a relevant role for placebo

NOTE Confidence: 0.36756226

01:13:31.366 --> 01:13:33.802 but it's not the only system we know

NOTE Confidence: 0.36756226

01:13:33.802 --> 01:13:36.110 that we have a release of dopamine,

NOTE Confidence: 0.36756226

01:13:36.110 --> 01:13:38.228 we have a release of endogenous

NOTE Confidence: 0.27090457

01:13:40.750 --> 01:13:43.654 but people try to block expectation

NOTE Confidence: 0.27090457

01:13:43.654 --> 01:13:46.630 with anesthetic drugs, you know. So

NOTE Confidence: 0.27090457

01:13:46.990 --> 01:13:49.942 I'm very curious about the nature of the

NOTE Confidence: 0.27090457

01:13:49.942 --> 01:13:52.256 stimulus that trigger the placebo response.

NOTE Confidence: 0.27090457

01:13:52.256 --> 01:13:54.712 Do we have any study that I don't

NOTE Confidence: 0.27090457

01:13:54.712 --> 01:13:57.220 know how an approach of more operant

NOTE Confidence: 0.27090457

01:13:57.220 --> 01:13:58.820 conditioning maybe engage people,

NOTE Confidence: 0.27090457

01:13:58.820 --> 01:14:01.228 maybe saying even a ritualistic behaviour

NOTE Confidence: 0.27090457

01:14:01.228 --> 01:14:05.473 and see if the behaviour is changed a

NOTE Confidence: 0.27090457

01:14:05.473 --> 01:14:07.804 magnitude of response and if there is

NOTE Confidence: 0.27090457

01:14:07.804 --> 01:14:10.900 a in some cases there is some effect of

NOTE Confidence: 0.27090457

01:14:10.900 --> 01:14:13.788 novelty and oddness of that stimulus.

NOTE Confidence: 0.27090457

01:14:13.788 --> 01:14:16.580 For example in case of psychedelics

NOTE Confidence: 0.27090457

01:14:16.580 --> 01:14:19.220 we have because they are odd,

NOTE Confidence: 0.27090457

01:14:19.220 --> 01:14:22.208 they are doing that and maybe if we use

NOTE Confidence: 0.27090457

01:14:22.208 --> 01:14:24.220 that multiple times it somehow has the

NOTE Confidence: 0.27090457

01:14:24.220 --> 01:14:26.940 effect wears off as it becomes more familiar.

NOTE Confidence: 0.39028335

01:14:28.340 --> 01:14:31.604 So the operant conditioning has been

NOTE Confidence: 0.39028335

01:14:31.604 --> 01:14:35.340 used both in humans and in animals.

NOTE Confidence: 0.39028335

01:14:35.340 --> 01:14:38.420 The number of studies is very limited.

NOTE Confidence: 0.39028335

01:14:38.420 --> 01:14:42.100 So we have not too much knowledge yet

NOTE Confidence: 0.39028335

01:14:42.100 --> 01:14:45.316 and the idea was that's the novelty and

NOTE Confidence: 0.39028335

01:14:45.316 --> 01:14:48.511 actually I quoted a paper and we designed

NOTE Confidence: 0.39028335

01:14:48.511 --> 01:14:50.670 a study with they grew up in Leuven.

NOTE Confidence: 0.39028335

01:14:50.670 --> 01:14:55.078 That study a lot of condition John named

NOTE Confidence: 0.39028335

01:14:55.078 --> 01:14:58.787 Lion and the results were not very appealing.

NOTE Confidence: 0.39028335

01:14:58.790 --> 01:15:02.304 I mean, we didn't find stronger PLACIP

NOTE Confidence: 0.39028335

01:15:02.304 --> 01:15:05.200 effects by using this operant conditioning,

NOTE Confidence: 0.39028335

01:15:05.200 --> 01:15:07.525 yes, but probably we thought

NOTE Confidence: 0.39028335

01:15:07.525 --> 01:15:09.590 that was too complex,

NOTE Confidence: 0.39028335

01:15:09.590 --> 01:15:11.828 too many stimulations that patients got,

NOTE Confidence: 0.39028335

01:15:11.830 --> 01:15:16.580 participants got lost in the paradigm.

NOTE Confidence: 0.39028335

01:15:16.580 --> 01:15:19.538 But I mean there are a few

NOTE Confidence: 0.39028335

01:15:19.538 --> 01:15:20.770 studies in animals as well,

NOTE Confidence: 0.39028335

01:15:20.770 --> 01:15:23.210 but there is also tend to be inconsistent.

NOTE Confidence: 0.39028335

01:15:23.210 --> 01:15:28.110 So yes and the novelty doesn't

NOTE Confidence: 0.39028335

01:15:28.110 --> 01:15:30.986 seems to be the critical component

NOTE Confidence: 0.39028335

01:15:30.986 --> 01:15:33.898 for placipic pets here.

NOTE Confidence: 0.39028335

01:15:33.900 --> 01:15:36.100 But probably this interesting in

NOTE Confidence: 0.39028335

01:15:36.100 --> 01:15:38.300 psychedelic trials to study naive

NOTE Confidence: 0.39028335

01:15:38.367 --> 01:15:40.443 versus non naive patient and see

NOTE Confidence: 0.39028335

01:15:40.443 --> 01:15:42.400 how this change and perspective

NOTE Confidence: 0.39028335

01:15:42.400 --> 01:15:44.900 longitudinal study can also help.

NOTE Confidence: 0.39028335

01:15:44.900 --> 01:15:47.681 You know if we go on with open label

NOTE Confidence: 0.39028335

01:15:47.681 --> 01:15:50.108 trials where they know that they

NOTE Confidence: 0.39028335

01:15:50.108 --> 01:15:52.356 receive the treatment and we follow

NOTE Confidence: 0.39028335

01:15:52.356 --> 01:15:54.512 this patient for 5-10 years then we

NOTE Confidence: 0.39028335

01:15:54.512 --> 01:15:56.276 can understand the more especially

NOTE Confidence: 0.39028335

01:15:56.276 --> 01:15:59.076 if we have a large court of patients

NOTE Confidence: 0.39028335

01:15:59.076 --> 01:16:01.038 when we can start phenotyping and

NOTE Confidence: 0.39028335

01:16:01.038 --> 01:16:03.428 try to study different aspects.

NOTE Confidence: 0.39028335

01:16:03.428 --> 01:16:04.580 I think

NOTE Confidence: 0.59606475

01:16:04.820 --> 01:16:08.420 one of the main concerns regarding

NOTE Confidence: 0.59606475

01:16:08.420 --> 01:16:12.410 sort of expectations is all the

NOTE Confidence: 0.59606475

01:16:12.410 --> 01:16:14.300 well most of the studies done,

NOTE Confidence: 0.59606475

01:16:14.300 --> 01:16:16.430 most of the patients and psychedelics

NOTE Confidence: 0.59606475

01:16:16.430 --> 01:16:18.994 have been highly educated people

NOTE Confidence: 0.59606475

01:16:18.994 --> 01:16:21.052 that are well aware of these effects

NOTE Confidence: 0.59606475

01:16:21.052 --> 01:16:23.356 and I know it's one of the real

NOTE Confidence: 0.59606475

01:16:23.356 --> 01:16:25.260 concerns the FDA has does this.

NOTE Confidence: 0.59606475

01:16:25.260 --> 01:16:28.460 If you look at many of these studies,

NOTE Confidence: 0.59606475

01:16:28.460 --> 01:16:30.380 98% college graduates,

NOTE Confidence: 0.59606475

01:16:30.380 --> 01:16:32.732 you know there there's a real

NOTE Confidence: 0.59606475

01:16:32.732 --> 01:16:34.436 need to make sure that you're not

NOTE Confidence: 0.59606475

01:16:34.436 --> 01:16:36.924 just selecting people that have

NOTE Confidence: 0.59606475

01:16:36.924 --> 01:16:39.140 very high expectations about,

NOTE Confidence: 0.51350194

01:16:39.380 --> 01:16:41.820 yeah, diverse people, larger studies

NOTE Confidence: 0.51350194

01:16:41.820 --> 01:16:45.140 also the number are very small. It's

NOTE Confidence: 0.51350194

01:16:45.140 --> 01:16:46.740 the same thing in

NOTE Confidence: 0.51350194

01:16:46.740 --> 01:16:47.499 psychodynamic psychotherapy.

NOTE Confidence: 0.51350194

01:16:47.499 --> 01:16:50.012 Going back 50 years ago if you

NOTE Confidence: 0.51350194

01:16:50.012 --> 01:16:51.155 weren't psychologically minded

114

NOTE Confidence: 0.51350194

01:16:51.155 --> 01:16:52.980 code word for intelligent and

NOTE Confidence: 0.51350194

01:16:52.980 --> 01:16:54.440 you've read about psychoanalysis,

NOTE Confidence: 0.51350194

01:16:54.440 --> 01:16:55.640 it wasn't positive in effect.

NOTE Confidence: 0.31495857

01:16:55.640 --> 01:16:58.237 So there is you just recruitment biases.

NOTE Confidence: 0.31495857

01:16:58.240 --> 01:17:00.040 This people wants to be

NOTE Confidence: 0.31495857

01:17:00.040 --> 01:17:01.840 in the trial you know.

NOTE Confidence: 0.31495857

01:17:01.840 --> 01:17:04.928 So I think once a week truly study

NOTE Confidence: 0.31495857

01:17:04.928 --> 01:17:07.942 beliefs and expectations probably change,

NOTE Confidence: 0.31495857

01:17:07.942 --> 01:17:10.998 you know the study design but also the

NOTE Confidence: 0.31495857

01:17:11.000 --> 01:17:14.439 change also I don't know if it's ethical.

NOTE Confidence: 0.31495857

01:17:14.440 --> 01:17:16.560 Maybe we can remove like

NOTE Confidence: 0.31495857

01:17:16.560 --> 01:17:18.450 eliminate non placebo responders,

NOTE Confidence: 0.31495857

01:17:18.450 --> 01:17:21.570 you know they're on a simple trial

NOTE Confidence: 0.31495857

01:17:21.570 --> 01:17:24.650 placebo responders and they can give you

NOTE Confidence: 0.31495857

01:17:24.650 --> 01:17:28.810 trial for the those who do not respond.

NOTE Confidence: 0.31495857

01:17:28.810 --> 01:17:30.730 But that's consistent though like

NOTE Confidence: 0.31495857

01:17:30.730 --> 01:17:32.266 are people consistently placebo

NOTE Confidence: 0.31495857

01:17:32.266 --> 01:17:33.580 responders regardless of their

NOTE Confidence: 0.31495857

01:17:33.580 --> 01:17:35.362 previous history with that specific

NOTE Confidence: 0.31495857

01:17:35.362 --> 01:17:37.202 treatment and that specific condition.

NOTE Confidence: 0.31495857

01:17:37.210 --> 01:17:40.222 There are studies we call this

NOTE Confidence: 0.31495857

01:17:40.222 --> 01:17:41.490 reproducibility classy effects.

NOTE Confidence: 0.31495857

01:17:41.490 --> 01:17:43.010 So that means a,

NOTE Confidence: 0.28924468

01:17:45.130 --> 01:17:47.407 he is a person who is a receiver responder,

NOTE Confidence: 0.28924468

01:17:47.410 --> 01:17:50.706 constantly a placebo responder.

NOTE Confidence: 0.28924468

01:17:50.706 --> 01:17:53.900 And our chronic pain patients came back

NOTE Confidence: 0.28924468

01:17:53.900 --> 01:17:58.610 to the lab and there is a good proportion

NOTE Confidence: 0.28924468

01:17:58.610 --> 01:18:00.991 of patients who continue to be a

NOTE Confidence: 0.28924468

01:18:00.991 --> 01:18:04.010 responder in terms of general disability.

NOTE Confidence: 0.28924468

01:18:04.010 --> 01:18:06.474 So someone who responded to a modality will

NOTE Confidence: 0.28924468

01:18:06.474 --> 01:18:09.090 be also a responder to another modality.

NOTE Confidence: 0.28924468

01:18:09.090 --> 01:18:11.304 There are some studies so that

NOTE Confidence: 0.28924468

01:18:11.304 --> 01:18:13.250 we can respond to pain.

NOTE Confidence: 0.28924468

01:18:13.250 --> 01:18:17.192 Also you know, a trigger to be a responder

NOTE Confidence: 0.28924468

01:18:17.200 --> 01:18:20.440 to emotional regulation and more resolvers.

NOTE Confidence: 0.28924468

01:18:20.440 --> 01:18:23.160 So if I,

NOTE Confidence: 0.28924468

01:18:23.160 --> 01:18:23.760 I, I

NOTE Confidence: 0.3543838

01:18:23.760 --> 01:18:25.080 know we're running well beyond,

NOTE Confidence: 0.3543838

01:18:25.080 --> 01:18:26.552 we can continue to go, but I don't

NOTE Confidence: 0.3543838

01:18:26.552 --> 01:18:28.280 know if I'm holding anybody up,

NOTE Confidence: 0.3543838

01:18:28.280 --> 01:18:30.000 but you can continue to go

NOTE Confidence: 0.3543838

01:18:31.040 --> 01:18:33.398 in terms of running the phase,

NOTE Confidence: 0.3543838

01:18:33.400 --> 01:18:34.996 that has been a big question.

NOTE Confidence: 0.3543838

01:18:35.000 --> 01:18:35.816 You know, kind of.

NOTE Confidence: 0.3543838

01:18:35.816 --> 01:18:37.040 We first to give a placebo.

NOTE Confidence: 0.3543838

01:18:37.040 --> 01:18:39.170 If they respond, we remove them.

NOTE Confidence: 0.3543838

01:18:39.170 --> 01:18:43.048 Ethically speaking is not the best practice.

NOTE Confidence: 0.3543838

01:18:43.050 --> 01:18:45.066 And also again, we select the

NOTE Confidence: 0.3543838

01:18:45.066 --> 01:18:47.290 pool of people who respond. Here,

NOTE Confidence: 0.48491967

01:18:48.890 --> 01:18:50.590 it it reminds me of one of the studies I

NOTE Confidence: 0.48491967

01:18:50.639 --> 01:18:52.535 was just reading going back to the 1930s.

NOTE Confidence: 0.48491967

01:18:52.535 --> 01:18:56.156 Harry Gold, who is one of the Harry Gold,

NOTE Confidence: 0.48491967

01:18:56.156 --> 01:18:57.168 one of the leaders,

NOTE Confidence: 0.48491967

01:18:57.170 --> 01:18:59.844 the reason we do placebo control trials.

NOTE Confidence: 0.48491967

01:18:59.850 --> 01:19:01.128 He was running a study with

NOTE Confidence: 0.48491967

01:19:01.130 --> 01:19:03.226 zantines for angina.

NOTE Confidence: 0.48491967

01:19:03.226 --> 01:19:06.060 You know cardiac pain and at the time

NOTE Confidence: 0.48491967

01:19:06.060 --> 01:19:07.908 it was about an 80% response rate.

NOTE Confidence: 0.48491967

01:19:07.908 --> 01:19:09.528 He takes his antenna and

NOTE Confidence: 0.48491967

01:19:09.528 --> 01:19:10.500 reduces cardiac pain.

NOTE Confidence: 0.48491967

01:19:10.500 --> 01:19:12.372 So he wanted to do a study in order.

NOTE Confidence: 0.48491967

01:19:12.380 --> 01:19:14.550 One of the early ideas of trying

NOTE Confidence: 0.48491967

01:19:14.550 --> 01:19:16.900 to rule out placebo responders,

NOTE Confidence: 0.48491967

01:19:16.900 --> 01:19:18.742 he was giving nitroglycerin to people

NOTE Confidence: 0.48491967

01:19:18.742 --> 01:19:20.899 who was having an engineer and the

NOTE Confidence: 0.48491967

01:19:20.899 --> 01:19:22.850 the goal was to exclude people that

NOTE Confidence: 0.48491967

01:19:22.850 --> 01:19:24.347 had a placebo response and only

NOTE Confidence: 0.48491967

01:19:24.347 --> 01:19:26.141 include the people that only had

NOTE Confidence: 0.48491967

01:19:26.141 --> 01:19:28.288 a real response to nitroglycerin.

NOTE Confidence: 0.48491967

01:19:28.290 --> 01:19:29.222 Do you know the results of this

NOTE Confidence: 0.48491967

01:19:29.222 --> 01:19:32.370 same exactly from everybody.

NOTE Confidence: 0.28692842

01:19:33.610 --> 01:19:34.765 So you couldn't you know

NOTE Confidence: 0.28692842

01:19:34.765 --> 01:19:35.689 it's really hard people

NOTE Confidence: 0.28692842

01:19:36.490 --> 01:19:39.770 new placebo responders emerged.

NOTE Confidence: 0.28692842

01:19:39.770 --> 01:19:43.770 Yeah. I was curious about about this

NOTE Confidence: 0.28692842

01:19:43.770 --> 01:19:45.584 effect at the very beginning across

NOTE Confidence: 0.28692842

01:19:45.584 --> 01:19:47.828 analgesic you have different level of

NOTE Confidence: 0.28692842

01:19:47.828 --> 01:19:49.928 placebo effect and I was wondering

NOTE Confidence: 0.28692842

01:19:49.928 --> 01:19:52.518 whether we know if some drugs will

NOTE Confidence: 0.28692842

01:19:52.518 --> 01:19:55.114 have like higher placebo effects and

NOTE Confidence: 0.28692842

01:19:55.114 --> 01:19:57.855 if there is any reason in the at the

NOTE Confidence: 0.28692842

01:19:57.855 --> 01:19:59.530 narrow biological level for this. Yes,

NOTE Confidence: 0.5034442

01:20:01.770 --> 01:20:05.467 our thought was that for drugs that work

NOTE Confidence: 0.5034442

01:20:05.467 --> 01:20:10.082 like opioids based as compared to some

NOTE Confidence: 0.5034442

01:20:10.082 --> 01:20:13.538 non opioids that stand to work less at

NOTE Confidence: 0.5034442

01:20:13.538 --> 01:20:17.940 least for the post operative pain the.

NOTE Confidence: 0.5034442

01:20:17.940 --> 01:20:21.812 You know money to the the placebo component

NOTE Confidence: 0.5034442

01:20:21.812 --> 01:20:24.960 may varies because that reflects how

NOTE Confidence: 0.5034442

01:20:24.960 --> 01:20:29.740 much if cautious or effective a drug is.

NOTE Confidence: 0.5034442

01:20:29.740 --> 01:20:33.808 We also think that there is an interaction if

NOTE Confidence: 0.5034442

01:20:33.808 --> 01:20:39.279 that like with metamazole that is non opioid,

NOTE Confidence: 0.5034442

01:20:39.280 --> 01:20:40.900 we saw that the interaction

NOTE Confidence: 0.5034442

01:20:40.900 --> 01:20:42.196 effect is very strong.

NOTE Confidence: 0.5034442

01:20:42.200 --> 01:20:45.890 I mean if you have also a placebo component

NOTE Confidence: 0.5034442

01:20:45.890 --> 01:20:48.631 through the expectation probably the

NOTE Confidence: 0.5034442

01:20:48.631 --> 01:20:51.119 money told of the same drug is larger.

NOTE Confidence: 0.5034442

01:20:51.120 --> 01:20:54.256 So in general drugs that per SE are

NOTE Confidence: 0.5034442

01:20:54.256 --> 01:20:57.397 very effective tended to have a smaller

NOTE Confidence: 0.5034442

01:20:57.397 --> 01:21:00.213 placebo component unless there is an

NOTE Confidence: 0.5034442

01:21:00.213 --> 01:21:02.979 interaction if that's like they trigger

NOTE Confidence: 0.5034442

01:21:02.979 --> 01:21:06.192 some molecular mechanism that can

NOTE Confidence: 0.5034442

01:21:06.192 --> 01:21:09.323 interact and we know how much the nuclear

NOTE Confidence: 0.5034442

01:21:09.323 --> 01:21:11.300 system interact with other system.

NOTE Confidence: 0.5034442

01:21:11.300 --> 01:21:14.338 And in that sense you don't see

NOTE Confidence: 0.5034442

01:21:14.340 --> 01:21:15.900 cumulative effects, you know

NOTE Confidence: 0.26831526

01:21:17.300 --> 01:21:18.340 but when isn't it fair,

NOTE Confidence: 0.26831526

01:21:18.340 --> 01:21:19.978 I mean to getting your point that

NOTE Confidence: 0.26831526

01:21:19.978 --> 01:21:21.842 some of the other points like a

NOTE Confidence: 0.26831526

01:21:21.842 --> 01:21:23.498 drug that has an immediate effect

NOTE Confidence: 0.26831526

01:21:23.500 --> 01:21:26.097 is more likely to have a placebo

NOTE Confidence: 0.26831526

01:21:26.100 --> 01:21:28.180 response than a drug that that you

NOTE Confidence: 0.26831526

01:21:28.180 --> 01:21:30.220 is blind is truly math correct.

NOTE Confidence: 0.26831526

01:21:30.700 --> 01:21:35.999 I don't know also well the question.

NOTE Confidence: 0.26831526

01:21:36.000 --> 01:21:38.140 The consciousness and self

NOTE Confidence: 0.26831526

01:21:38.140 --> 01:21:40.280 perception is very relevant.

NOTE Confidence: 0.26831526

01:21:40.280 --> 01:21:42.360 The I don't know actually.

NOTE Confidence: 0.26831526

01:21:42.360 --> 01:21:43.800 Now I understand the question,

NOTE Confidence: 0.26831526

01:21:43.800 --> 01:21:47.678 but so for example, if we give people a

NOTE Confidence: 0.30930802

01:21:49.760 --> 01:21:53.560 normal that can change the

NOTE Confidence: 0.30930802

01:21:53.560 --> 01:21:56.816 level of cortisol in the body,

NOTE Confidence: 0.30930802

01:21:56.816 --> 01:21:59.640 the Placib effect is not

NOTE Confidence: 0.30930802

01:21:59.640 --> 01:22:02.680 existing or an antibiotic,

NOTE Confidence: 0.30930802

01:22:02.680 --> 01:22:05.998 then the placebo component is not there.

NOTE Confidence: 0.30930802

01:22:06.000 --> 01:22:08.400 Somehow the placebo effects

NOTE Confidence: 0.30930802

01:22:08.400 --> 01:22:10.800 amplify the therapeutic benefit.

NOTE Confidence: 0.30930802

01:22:10.800 --> 01:22:13.236 When we have experience of that,

NOTE Confidence: 0.30930802

01:22:13.240 --> 01:22:15.856 I mean if you take a patient with

NOTE Confidence: 0.30930802

01:22:15.856 --> 01:22:17.503 genetic disorders and they don't

NOTE Confidence: 0.30930802

01:22:17.503 --> 01:22:20.445 feel pain and you tell them this

NOTE Confidence: 0.30930802

01:22:20.445 --> 01:22:22.576 treatment is analgesic for them,

NOTE Confidence: 0.30930802

01:22:22.576 --> 01:22:24.290 doesn't mean anything, you know.

NOTE Confidence: 0.30930802

01:22:24.290 --> 01:22:26.425 And so there will be not an

NOTE Confidence: 0.30930802

01:22:26.425 --> 01:22:27.840 analgesic plasibe effects.

NOTE Confidence: 0.30930802

01:22:27.840 --> 01:22:30.512 Or if we tell patients this drug is

NOTE Confidence: 0.30930802

01:22:30.512 --> 01:22:33.458 going to increase your cortisol level,

NOTE Confidence: 0.30930802

01:22:33.460 --> 01:22:36.660 they don't know what a cortisol level is

NOTE Confidence: 0.30930802

01:22:36.660 --> 01:22:40.188 or we use some Atriptan back in Turin,

NOTE Confidence: 0.30930802

01:22:40.188 --> 01:22:42.820 you know that it's used for migraine

NOTE Confidence: 0.30930802

01:22:42.903 --> 01:22:46.300 attacks if but also some side effects.

NOTE Confidence: 0.30930802

01:22:46.300 --> 01:22:49.812 So they can get an improvement at the

NOTE Confidence: 0.30930802

01:22:49.812 --> 01:22:53.699 level of migraine and pain related to

NOTE Confidence: 0.30930802

01:22:53.699 --> 01:22:57.379 the migraine but not necessarily the bio

NOTE Confidence: 0.30930802

01:22:57.380 --> 01:23:00.817 chemical change in markers in the blood.

NOTE Confidence: 0.30930802

01:23:00.820 --> 01:23:01.254 However,

NOTE Confidence: 0.30930802

01:23:01.254 --> 01:23:04.292 if we use air conditioning like that's

NOTE Confidence: 0.30930802

01:23:04.292 --> 01:23:06.851 been shown with you know cytokines,

NOTE Confidence: 0.30930802

01:23:06.851 --> 01:23:09.910 like if we use cyclosporine a several

NOTE Confidence: 0.30930802

01:23:09.991 --> 01:23:13.057 time and then we replace cyclosporine A,

NOTE Confidence: 0.30930802

01:23:13.060 --> 01:23:16.300 we see a modulation of Illinois 6 and

NOTE Confidence: 0.30930802

01:23:16.300 --> 01:23:18.691 interferon gamma in the blood because

NOTE Confidence: 0.30930802

01:23:18.691 --> 01:23:22.448 the body learn that kind of measurement.

NOTE Confidence: 0.30930802

01:23:22.450 --> 01:23:25.186 I am a big champion of framing plasy

NOTE Confidence: 0.30930802

01:23:25.186 --> 01:23:27.887 B effects as learning effects and so

NOTE Confidence: 0.32518166

01:23:29.930 --> 01:23:34.810 somehow we can either bypass our

NOTE Confidence: 0.32518166

01:23:34.810 --> 01:23:36.438 conscious perception of symptom.

NOTE Confidence: 0.32518166

01:23:36.438 --> 01:23:39.490 We can still act with conditioning paradigm,

NOTE Confidence: 0.32518166

01:23:39.490 --> 01:23:42.346 you know and train our body

NOTE Confidence: 0.32518166

01:23:42.346 --> 01:23:44.250 to produce a response.

NOTE Confidence: 0.32518166

01:23:44.250 --> 01:23:47.540 But this kind of effects can't be

NOTE Confidence: 0.32518166

01:23:47.540 --> 01:23:50.040 elicit with verbal suggestion.

NOTE Confidence: 0.32518166

01:23:50.040 --> 01:23:51.720 Yes, I think we, I mean,

NOTE Confidence: 0.32518166

01:23:51.720 --> 01:23:52.840 it's well beyond it.

NOTE Confidence: 0.32518166

01:23:52.840 --> 01:23:54.760 Thank you all. Thank

NOTE Confidence: 0.28611216

01:23:54.760 --> 01:23:56.840 you. Thank you. That was great, Lena. Thank

NOTE Confidence: 0.28611216

01:23:56.840 --> 01:23:58.560 you. It's very cool.