WEBVTT

NOTE duration: "00:56:40.021"

NOTE Confidence: 0.822162

00:00:11.840 --> 00:00:12.960 Okay we should probably get

NOTE Confidence: 0.822162

00:00:12.960 --> 00:00:13.440 started,

NOTE Confidence: 0.9160914

00:00:13.955 --> 00:00:14.775 It's my

NOTE Confidence: 0.92310286

00:00:15.075 --> 00:00:16.295 pleasure to

NOTE Confidence: 0.68780005

00:00:17.395 --> 00:00:18.055 to have,

NOTE Confidence: 0.7136724

00:00:18.835 --> 00:00:19.815 Leena Palmiapin

NOTE Confidence: 0.7540302

00:00:20.915 --> 00:00:22.935 and Jessica Arins to,

NOTE Confidence: 0.94569385

00:00:23.635 --> 00:00:24.135 to

NOTE Confidence: 0.9602786

00:00:24.994 --> 00:00:27.154 our webinar series, hosted by

NOTE Confidence: 0.9602786

00:00:27.154 --> 00:00:28.435 the Yale Center for the

NOTE Confidence: 0.9602786

00:00:28.435 --> 00:00:29.970 Science of Cannabis and Cannabinoids.

NOTE Confidence: 0.9648402

00:00:31.736 --> 00:00:32.903 You know,

NOTE Confidence: 0.9779575

00:00:33.470 --> 00:00:35.470 we are really delighted to

NOTE Confidence: 0.9779575

00:00:35.470 --> 00:00:36.510 have the two of them

NOTE Confidence: 0.9779575

1

00:00:36.510 --> 00:00:38.510 present on something that we

NOTE Confidence: 0.9779575

00:00:38.510 --> 00:00:40.030 haven't really heard about very

NOTE Confidence: 0.9779575

00:00:40.030 --> 00:00:41.955 much before. As you know,

NOTE Confidence: 0.9656492

00:00:42.335 --> 00:00:43.935 this seminar series, this webinar

NOTE Confidence: 0.9656492

00:00:43.935 --> 00:00:45.155 series is really about,

NOTE Confidence: 0.96653414

00:00:45.775 --> 00:00:47.135 the science of cannabis and

NOTE Confidence: 0.96653414

00:00:47.135 --> 00:00:48.815 cannabinoids, and I couldn't think

NOTE Confidence: 0.96653414

00:00:48.815 --> 00:00:49.555 of a,

NOTE Confidence: 0.94301766

00:00:50.735 --> 00:00:52.015 of of a better person

NOTE Confidence: 0.94301766

00:00:52.015 --> 00:00:53.855 to tell us one some

NOTE Confidence: 0.94301766

00:00:53.855 --> 00:00:56.200 aspects of the relationship between,

NOTE Confidence: 0.94301766

00:00:56.520 --> 00:00:59.020 cannabis and dopamine and, and

NOTE Confidence: 0.94632256

00:00:59.400 --> 00:01:00.520 and and so I'm I'm

NOTE Confidence: 0.94632256

00:01:00.520 --> 00:01:02.600 really delighted to to have

NOTE Confidence: 0.94632256

00:01:02.600 --> 00:01:04.040 the two of them. I'm

NOTE Confidence: 0.94632256

00:01:04.040 --> 00:01:05.000 not going to,

NOTE Confidence: 0.9798988

00:01:05.880 --> 00:01:07.080 tell you about the many

NOTE Confidence: 0.9798988

00:01:07.080 --> 00:01:08.280 accomplishments of,

NOTE Confidence: 0.96874934

00:01:08.985 --> 00:01:11.145 of of, my colleagues here,

NOTE Confidence: 0.96874934

00:01:11.145 --> 00:01:12.665 but I'll let you read

NOTE Confidence: 0.96874934

00:01:12.665 --> 00:01:14.125 that. We, I think, communicated

NOTE Confidence: 0.96874934

00:01:14.265 --> 00:01:15.865 that in our in our

NOTE Confidence: 0.96874934

00:01:15.865 --> 00:01:17.865 announcement, but we are really

NOTE Confidence: 0.96874934

00:01:17.865 --> 00:01:18.765 happy. And

NOTE Confidence: 0.876509

00:01:19.065 --> 00:01:19.725 who knows?

NOTE Confidence: 0.9508355

00:01:20.345 --> 00:01:21.245 You may become,

NOTE Confidence: 0.9716361

00:01:22.130 --> 00:01:23.410 the fifty first state and

NOTE Confidence: 0.9716361

00:01:23.410 --> 00:01:24.370 we'll be working with you

NOTE Confidence: 0.9716361

00:01:24.370 --> 00:01:25.270 a little closer,

NOTE Confidence: 0.9934576

00:01:26.050 --> 00:01:27.170 over the next few years.

NOTE Confidence: 0.9934576

00:01:27.170 --> 00:01:29.090 So without further ado, I'm

NOTE Confidence: 0.9934576

00:01:29.090 --> 00:01:30.130 gonna hand it over to

NOTE Confidence: 0.9934576

00:01:30.130 --> 00:01:31.110 the two of you.

NOTE Confidence: 0.9849685

00:01:33.970 --> 00:01:35.330 Thank you. Thank you very

NOTE Confidence: 0.9849685

00:01:35.330 --> 00:01:35.830 much.

NOTE Confidence: 0.630291

00:01:36.315 --> 00:01:36.815 So

NOTE Confidence: 0.9760435

00:01:37.275 --> 00:01:38.155 can you all see my

NOTE Confidence: 0.9760435

00:01:38.155 --> 00:01:38.655 screen?

NOTE Confidence: 0.8174001

00:01:40.875 --> 00:01:41.775 Okay, excellent.

NOTE Confidence: 0.9308545

00:01:42.235 --> 00:01:43.775 Well, I will start with

NOTE Confidence: 0.91997147

00:01:44.875 --> 00:01:46.235 a declaration and then an

NOTE Confidence: 0.91997147

00:01:46.235 --> 00:01:46.735 apology.

NOTE Confidence: 0.89960384

00:01:47.675 --> 00:01:49.035 The declaration is we're not

NOTE Confidence: 0.89960384

00:01:49.035 --> 00:01:50.575 becoming fifty first state.

NOTE Confidence: 0.9494153

00:01:51.920 --> 00:01:52.800 You know, this is this

NOTE Confidence: 0.9494153

00:01:52.800 --> 00:01:53.540 is an interesting

NOTE Confidence: 0.91607714

00:01:54.080 --> 00:01:55.200 time to speak about,

NOTE Confidence: 0.91914886

00:01:55.520 --> 00:01:56.720 but anyway, I'll just start

NOTE Confidence: 0.91914886

00:01:56.720 --> 00:01:57.920 with that. And then second

NOTE Confidence: 0.91914886

00:01:57.920 --> 00:01:59.840 thing is the the apology

NOTE Confidence: 0.91914886

00:01:59.840 --> 00:02:01.200 is I'm sorry I have

NOTE Confidence: 0.91914886

00:02:01.200 --> 00:02:01.700 this

NOTE Confidence: 0.99673235

00:02:02.320 --> 00:02:02.820 peculiar

NOTE Confidence: 0.7566302

00:02:03.280 --> 00:02:03.780 eccentric,

NOTE Confidence: 0.98539615

00:02:04.640 --> 00:02:05.540 liking to

NOTE Confidence: 0.8625535

00:02:06.185 --> 00:02:08.025 titles that rhyme, titles that

NOTE Confidence: 0.8625535

00:02:08.025 --> 00:02:09.325 have a clang on them.

NOTE Confidence: 0.8625535

00:02:09.385 --> 00:02:11.165 So don't for dopamine delusions,

NOTE Confidence: 0.932031

00:02:11.705 --> 00:02:12.584 we all have d, but

NOTE Confidence: 0.932031

00:02:12.584 --> 00:02:13.705 we're not gonna talk about

NOTE Confidence: 0.932031

00:02:13.705 --> 00:02:15.065 delusions very much today. I'm

NOTE Confidence: 0.932031

00:02:15.065 --> 00:02:16.185 actually going to talk more

NOTE Confidence: 0.932031

00:02:16.185 --> 00:02:16.685 about,

NOTE Confidence: 0.99918145

00:02:17.224 --> 00:02:17.724 psychosis

NOTE Confidence: 0.9667029

00:02:18.370 --> 00:02:19.570 as a as a general

NOTE Confidence: 0.9667029

00:02:19.570 --> 00:02:21.090 syndrome and not about any

NOTE Confidence: 0.9667029

00:02:21.090 --> 00:02:22.389 specific, symptoms.

NOTE Confidence: 0.93179536

00:02:22.770 --> 00:02:24.130 And, sir, you're you're right.

NOTE Confidence: 0.93179536

00:02:24.130 --> 00:02:25.010 I you know,

NOTE Confidence: 0.9198937

00:02:25.889 --> 00:02:26.389 the,

NOTE Confidence: 0.9810426

00:02:28.290 --> 00:02:29.650 the place to really learn

NOTE Confidence: 0.9810426

00:02:29.650 --> 00:02:30.690 a lot about the effects

NOTE Confidence: 0.9810426

00:02:30.690 --> 00:02:32.014 of cannabis is, of course,

NOTE Confidence: 0.9810426

00:02:32.014 --> 00:02:33.615 the psychosis clinic. And I

NOTE Confidence: 0.9810426

00:02:33.615 --> 00:02:34.815 would say I'm not a

NOTE Confidence: 0.9810426

00:02:34.815 --> 00:02:36.095 I'm not a cannabis researcher

NOTE Confidence: 0.9810426

00:02:36.095 --> 00:02:37.135 myself. I haven't done many

NOTE Confidence: 0.9810426

00:02:37.135 --> 00:02:38.335 studies on cannabis, so I'm

NOTE Confidence: 0.9810426

00:02:38.335 --> 00:02:39.695 really learning a lot from,

NOTE Confidence: 0.9810426

00:02:39.935 --> 00:02:40.975 from your group and from

NOTE Confidence: 0.9810426

00:02:40.975 --> 00:02:42.415 others. My work is,

NOTE Confidence: 0.9732828

00:02:43.055 --> 00:02:44.655 in psychosis. I'm a clinician.

NOTE Confidence: 0.9732828

00:02:44.655 --> 00:02:45.395 I'm a psychiatrist.

NOTE Confidence: 0.9763918

00:02:47.110 --> 00:02:47.830 And I have to say

NOTE Confidence: 0.9763918

00:02:47.830 --> 00:02:49.190 I've used almost every tool

NOTE Confidence: 0.9763918

00:02:49.190 --> 00:02:50.470 that we can use to

NOTE Confidence: 0.9763918

00:02:50.470 --> 00:02:52.889 understand what is behind psychosis,

NOTE Confidence: 0.9763918

00:02:52.950 --> 00:02:53.990 and I continue to learn

NOTE Confidence: 0.9763918

00:02:53.990 --> 00:02:55.110 these tools and and use

NOTE Confidence: 0.9763918

00:02:55.110 --> 00:02:55.850 them as

NOTE Confidence: 0.71367794

00:02:56.230 --> 00:02:57.669 a natural and introduction about

NOTE Confidence: 0.71367794

00:02:57.669 --> 00:02:58.169 myself.

NOTE Confidence: 0.9657691

00:02:58.575 --> 00:02:59.535 And you see me using

NOTE Confidence: 0.9657691

00:02:59.535 --> 00:03:00.975 the word we very often,

NOTE Confidence: 0.9657691

00:03:00.975 --> 00:03:02.095 the royal we. When I

NOTE Confidence: 0.9657691

00:03:02.095 --> 00:03:03.695 say we, it's actually Jess

NOTE Confidence: 0.9657691

00:03:03.695 --> 00:03:04.755 who did all the work.

NOTE Confidence: 0.9657691

00:03:04.815 --> 00:03:05.935 So Jess is a PhD

NOTE Confidence: 0.9657691

00:03:05.935 --> 00:03:07.135 student in our group, and

NOTE Confidence: 0.9657691

00:03:07.135 --> 00:03:08.495 she did the the work

NOTE Confidence: 0.9657691

00:03:08.495 --> 00:03:09.955 that we're gonna present today.

NOTE Confidence: 0.9366049

00:03:11.160 --> 00:03:12.280 And my plan is really

NOTE Confidence: 0.9366049

00:03:12.280 --> 00:03:13.800 to start with some introduction

NOTE Confidence: 0.9366049

00:03:13.800 --> 00:03:14.620 to the problem,

NOTE Confidence: 0.972031

00:03:15.240 --> 00:03:16.760 and then, let Jess talk

NOTE Confidence: 0.972031

00:03:16.760 --> 00:03:17.800 about the methods that we

NOTE Confidence: 0.972031

00:03:17.800 --> 00:03:19.100 use to address the problem.

NOTE Confidence: 0.972031

00:03:19.240 --> 00:03:20.200 And then I'll come back

NOTE Confidence: 0.972031

00:03:20.200 --> 00:03:21.160 and, say a few words

NOTE Confidence: 0.972031

00:03:21.160 --> 00:03:22.520 about the implications and what

NOTE Confidence: 0.972031

00:03:22.520 --> 00:03:23.740 can be the take home

NOTE Confidence: 0.972031

00:03:23.975 --> 00:03:25.175 from, one of the studies

NOTE Confidence: 0.972031

00:03:25.175 --> 00:03:26.075 that we did recently.

NOTE Confidence: 0.90437466

00:03:28.455 --> 00:03:29.575 So this is my conflicts

NOTE Confidence: 0.90437466

00:03:29.575 --> 00:03:30.794 of interest, my declarations.

NOTE Confidence: 0.93701154

00:03:31.095 --> 00:03:32.215 In a nutshell, I don't

NOTE Confidence: 0.93701154

00:03:32.215 --> 00:03:33.895 have any affiliations whatsoever with

NOTE Confidence: 0.93701154

00:03:33.895 --> 00:03:35.415 anything, to do with cannabis

NOTE Confidence: 0.93701154

00:03:35.415 --> 00:03:37.575 related industry, lobbyists, or policy

NOTE Confidence: 0.93701154

00:03:37.575 --> 00:03:39.330 makers. We've given some talks

NOTE Confidence: 0.93701154

00:03:39.330 --> 00:03:40.870 and got paid for them

NOTE Confidence: 0.93701154

00:03:41.090 --> 00:03:42.850 through Artsukka and Janssen Canada

NOTE Confidence: 0.93701154

00:03:42.850 --> 00:03:44.390 who make antipsychotic drugs.

NOTE Confidence: 0.92792445

00:03:45.250 --> 00:03:47.010 And Jess also reports no

NOTE Confidence: 0.92792445

9

00:03:47.010 --> 00:03:48.370 no conflicts of interest for

NOTE Confidence: 0.92792445

00:03:48.370 --> 00:03:49.590 the talk relevant today.

NOTE Confidence: 0.9721677

00:03:50.450 --> 00:03:51.555 So this is our agenda.

NOTE Confidence: 0.9721677

00:03:51.555 --> 00:03:53.095 We're gonna introduce the problem

NOTE Confidence: 0.9721677

00:03:53.235 --> 00:03:55.155 of interface between psychosis and

NOTE Confidence: 0.9721677

00:03:55.155 --> 00:03:56.515 cannabis. Not a new problem.

NOTE Confidence: 0.9721677

00:03:56.515 --> 00:03:57.715 I think your group, all

NOTE Confidence: 0.9721677

00:03:57.715 --> 00:03:58.435 of you have heard a

NOTE Confidence: 0.9721677

00:03:58.435 --> 00:03:59.795 lot about it. But I'm

NOTE Confidence: 0.9721677

00:03:59.795 --> 00:04:01.315 gonna present an issue that

NOTE Confidence: 0.9721677

00:04:01.315 --> 00:04:02.995 comes comes often in a

NOTE Confidence: 0.9721677

00:04:02.995 --> 00:04:04.835 clinical conversation when we talk

NOTE Confidence: 0.9721677

00:04:04.835 --> 00:04:05.415 to patients

NOTE Confidence: 0.73283476

00:04:05.800 --> 00:04:06.540 in pharmaceutical clinic

NOTE Confidence: 0.97790015

00:04:07.160 --> 00:04:08.300 about these two issues,

NOTE Confidence: 0.9466805

00:04:08.680 --> 00:04:09.819 cannabis and psychosis.

NOTE Confidence: 0.97533655

00:04:10.520 --> 00:04:11.560 We get into a bit

NOTE Confidence: 0.97533655

00:04:11.560 --> 00:04:12.300 of a,

NOTE Confidence: 0.9432977

00:04:13.240 --> 00:04:15.800 impasse, a junction where patients

NOTE Confidence: 0.9432977

00:04:15.800 --> 00:04:17.080 have a different view and

NOTE Confidence: 0.9432977

00:04:17.080 --> 00:04:18.279 clinicians, we have a different

NOTE Confidence: 0.9432977

00:04:18.279 --> 00:04:19.400 view. And I wanna present

NOTE Confidence: 0.9432977

00:04:19.400 --> 00:04:20.520 that impasse a little bit

NOTE Confidence: 0.9432977

00:04:20.520 --> 00:04:21.180 in detail.

NOTE Confidence: 0.96745026

00:04:21.735 --> 00:04:23.095 And then I will, let,

NOTE Confidence: 0.96745026

00:04:23.415 --> 00:04:24.615 just talk about methods and

NOTE Confidence: 0.96745026

00:04:24.615 --> 00:04:25.975 results. And, you know, we

NOTE Confidence: 0.96745026

00:04:25.975 --> 00:04:27.275 are people from the future.

NOTE Confidence: 0.9689877

00:04:28.214 --> 00:04:29.815 We are going to tell

NOTE Confidence: 0.9689877

00:04:29.815 --> 00:04:31.255 you about a paper that's

NOTE Confidence: 0.9689877

00:04:31.255 --> 00:04:32.455 going to be published on

NOTE Confidence: 0.9689877

00:04:32.455 --> 00:04:33.895 April the ninth. It's not

NOTE Confidence: 0.9689877

00:04:33.895 --> 00:04:35.014 out there yet. But if

NOTE Confidence: 0.9689877

00:04:35.014 --> 00:04:36.635 any of you are interested,

NOTE Confidence: 0.97125137

00:04:37.069 --> 00:04:37.949 we're happy to share a

NOTE Confidence: 0.97125137

00:04:37.949 --> 00:04:39.229 preprint link that you can

NOTE Confidence: 0.97125137

00:04:39.229 --> 00:04:40.430 look at this paper. It's

NOTE Confidence: 0.97125137

00:04:40.430 --> 00:04:40.930 posted

NOTE Confidence: 0.85942996

00:04:41.389 --> 00:04:42.449 in the bio archives.

NOTE Confidence: 0.9128925

00:04:43.069 --> 00:04:43.949 And this paper is called

NOTE Confidence: 0.9128925

00:04:43.949 --> 00:04:45.550 convergence of cannabis and psychosis

NOTE Confidence: 0.9128925

00:04:45.550 --> 00:04:46.690 on the document system.

NOTE Confidence: 0.93405116

00:04:47.229 --> 00:04:48.509 And you'll see many other

NOTE Confidence: 0.93405116

00:04:48.509 --> 00:04:50.145 co authors and Jess will

NOTE Confidence: 0.51732826

00:04:50.845 --> 00:04:51.325 clarify,

NOTE Confidence: 0.99799883

00:04:51.725 --> 00:04:53.005 the contribution from other people

NOTE Confidence: 0.99799883

00:04:53.005 --> 00:04:53.885 that you don't see here

NOTE Confidence: 0.99799883

00:04:53.885 --> 00:04:54.625 on the screen

NOTE Confidence: 0.9092534

00:04:54.925 --> 00:04:56.625 who made this work possible.

NOTE Confidence: 0.9692339

00:04:56.925 --> 00:04:57.885 So let me start with

NOTE Confidence: 0.9692339

00:04:57.885 --> 00:04:58.545 the problem.

NOTE Confidence: 0.98096514

00:04:59.165 --> 00:05:00.305 The problem is,

NOTE Confidence: 0.85689867

00:05:01.245 --> 00:05:01.985 we know,

NOTE Confidence: 0.9585882

00:05:02.830 --> 00:05:03.870 for for for a while

NOTE Confidence: 0.9585882

00:05:03.870 --> 00:05:05.550 now, from, I would say,

NOTE Confidence: 0.9585882

00:05:05.550 --> 00:05:06.449 from eighteen

NOTE Confidence: 0.68151426

00:05:06.910 --> 00:05:07.410 eighteen

NOTE Confidence: 0.95549834

00:05:08.190 --> 00:05:09.550 forty five, if I'm not

NOTE Confidence: 0.95549834

00:05:09.550 --> 00:05:11.410 wrong, from Moro's initial description

NOTE Confidence: 0.94019586

00:05:11.789 --> 00:05:13.070 that cannabis has something to

NOTE Confidence: 0.94019586

00:05:13.070 --> 00:05:13.810 do with psychosis.

NOTE Confidence: 0.9812725

00:05:14.945 --> 00:05:16.225 And one of the very

NOTE Confidence: 0.9812725

13

00:05:16.225 --> 00:05:17.045 nice demonstrations

NOTE Confidence: 0.88037336

00:05:17.665 --> 00:05:18.165 experimentally

NOTE Confidence: 0.9927341

00:05:19.025 --> 00:05:20.305 of the effect of cannabis

NOTE Confidence: 0.9927341

00:05:20.305 --> 00:05:21.605 on on psychotic symptoms,

NOTE Confidence: 0.9768203

00:05:22.305 --> 00:05:23.505 was given by none other

NOTE Confidence: 0.9768203

00:05:23.505 --> 00:05:25.025 than Cyril here. A very

NOTE Confidence: 0.9768203

00:05:25.025 --> 00:05:26.805 nice experimental study where

NOTE Confidence: 0.9870039

00:05:27.529 --> 00:05:29.529 injection of the active ingredient

NOTE Confidence: 0.9870039

00:05:29.529 --> 00:05:31.150 of cannabis, which is tetrahydrocannabinol

NOTE Confidence: 0.5202417

00:05:32.330 --> 00:05:33.390 nine case c,

NOTE Confidence: 0.98250294

00:05:34.250 --> 00:05:34.650 really,

NOTE Confidence: 0.9496645

00:05:35.130 --> 00:05:36.270 produced transiently,

NOTE Confidence: 0.99304086

00:05:36.890 --> 00:05:38.410 symptoms of, positive symptoms of

NOTE Confidence: 0.99304086

00:05:38.410 --> 00:05:40.485 psychosis in healthy people who

NOTE Confidence: 0.99304086

00:05:40.485 --> 00:05:42.324 had no previous history of

NOTE Confidence: 0.99304086

00:05:42.324 --> 00:05:44.085 schizophrenia and no previous history

NOTE Confidence: 0.99304086

00:05:44.085 --> 00:05:46.025 of established cannabis use disorder.

NOTE Confidence: 0.90215194

00:05:46.725 --> 00:05:47.925 And this is important because

NOTE Confidence: 0.90215194

00:05:47.925 --> 00:05:49.925 this is experimental evidence, double

NOTE Confidence: 0.90215194

00:05:49.925 --> 00:05:52.324 blind randomized trial, where, you

NOTE Confidence: 0.90215194

00:05:52.324 --> 00:05:53.225 give some people,

NOTE Confidence: 0.8866912

00:05:54.139 --> 00:05:55.740 you know, no THC and

NOTE Confidence: 0.8866912

00:05:55.740 --> 00:05:57.040 and others in different doses

NOTE Confidence: 0.8866912

00:05:57.339 --> 00:05:58.639 and you really see

NOTE Confidence: 0.8425737

00:05:58.940 --> 00:05:59.600 a strong,

NOTE Confidence: 0.97152674

00:06:00.220 --> 00:06:02.220 experimental pharmacological effect. So it's

NOTE Confidence: 0.97152674

00:06:02.220 --> 00:06:03.260 a very key finding and

NOTE Confidence: 0.97152674

00:06:03.260 --> 00:06:04.540 it's been replicated in by

NOTE Confidence: 0.97152674

00:06:04.540 --> 00:06:06.139 other groups as well. So

NOTE Confidence: 0.97152674

00:06:06.139 --> 00:06:06.639 clearly,

NOTE Confidence: 0.935631

00:06:07.085 --> 00:06:08.605 we know that injecting the

NOTE Confidence: 0.935631

00:06:08.605 --> 00:06:11.085 active ingredient of cannabis induces

NOTE Confidence: 0.935631

00:06:11.085 --> 00:06:12.945 psychotic symptoms. It's undisputable.

NOTE Confidence: 0.96553534

00:06:14.765 --> 00:06:15.645 We also know a lot

NOTE Confidence: 0.96553534

00:06:15.645 --> 00:06:17.505 about the epidemiology in population

NOTE Confidence: 0.96553534

00:06:17.565 --> 00:06:19.404 level, what does cannabis do

NOTE Confidence: 0.96553534

00:06:19.404 --> 00:06:21.450 to psychosis risk And we

NOTE Confidence: 0.96553534

00:06:21.450 --> 00:06:22.410 know a lot in in

NOTE Confidence: 0.96553534

00:06:22.410 --> 00:06:23.310 Canada now

NOTE Confidence: 0.92821276

00:06:23.610 --> 00:06:24.330 given that,

NOTE Confidence: 0.9980791

00:06:25.050 --> 00:06:26.029 you know, we

NOTE Confidence: 0.97922873

00:06:27.210 --> 00:06:27.710 liberalized

NOTE Confidence: 0.9664492

00:06:28.330 --> 00:06:30.410 cannabis use, in twenty fifteen,

NOTE Confidence: 0.9664492

00:06:30.410 --> 00:06:31.610 and we legalized it in

NOTE Confidence: 0.9664492

00:06:31.610 --> 00:06:32.430 twenty eighteen.

NOTE Confidence: 0.9796163

00:06:32.970 --> 00:06:34.190 You know, we had this

NOTE Confidence: 0.9603592

00:06:34.544 --> 00:06:37.104 population wide laboratory set up

16

NOTE Confidence: 0.9603592

00:06:37.104 --> 00:06:38.805 in twenty fifteen and twenty

NOTE Confidence: 0.9603592

00:06:39.025 --> 00:06:40.065 eighteen, and we now know

NOTE Confidence: 0.9603592

00:06:40.225 --> 00:06:41.425 now have the observations from

NOTE Confidence: 0.9603592

00:06:41.425 --> 00:06:42.625 this laboratory. And this is

NOTE Confidence: 0.9603592

00:06:42.625 --> 00:06:43.904 an interesting study that came

NOTE Confidence: 0.9603592

00:06:43.904 --> 00:06:44.384 from,

NOTE Confidence: 0.77103513

00:06:44.865 --> 00:06:46.464 the CAMH Daniel Meiren and

NOTE Confidence: 0.77103513

00:06:46.464 --> 00:06:47.125 and colleagues

NOTE Confidence: 0.90636426

00:06:47.820 --> 00:06:49.180 not long ago, only two

NOTE Confidence: 0.90636426

00:06:49.180 --> 00:06:50.699 months ago in JAMA network,

NOTE Confidence: 0.90636426

00:06:50.860 --> 00:06:51.760 JAMA Open.

NOTE Confidence: 0.98000115

00:06:52.699 --> 00:06:54.460 It's a very, interesting evidence

NOTE Confidence: 0.98000115

00:06:54.460 --> 00:06:56.000 that, you know, this experimentation

NOTE Confidence: 0.9952063

00:06:56.540 --> 00:06:58.380 of liberalization and legalization has

NOTE Confidence: 0.9952063

00:06:58.380 --> 00:06:59.279 actually increased

NOTE Confidence: 0.97584414

17

00:06:59.915 --> 00:07:01.675 the risk attributable the risk

NOTE Confidence: 0.97584414

00:07:01.675 --> 00:07:03.535 of psychosis attributable to cannabis.

NOTE Confidence: 0.97584414

00:07:03.675 --> 00:07:04.875 It's a very large study.

NOTE Confidence: 0.97584414

00:07:05.035 --> 00:07:06.235 You know, it's a population

NOTE Confidence: 0.97584414

00:07:06.235 --> 00:07:08.654 wide administrative database based study.

NOTE Confidence: 0.932025

00:07:09.435 --> 00:07:11.195 Everybody fourteen to sixty five

NOTE Confidence: 0.932025

00:07:11.195 --> 00:07:12.340 who presented to one of

NOTE Confidence: 0.932025

00:07:12.340 --> 00:07:14.260 the hospitals in Ontario emergency

NOTE Confidence: 0.932025

00:07:14.420 --> 00:07:15.300 one of the hospitals with

NOTE Confidence: 0.932025

00:07:15.300 --> 00:07:16.760 emergency units in Ontario,

NOTE Confidence: 0.9537188

00:07:17.380 --> 00:07:18.980 were included in this. And

NOTE Confidence: 0.9537188

00:07:18.980 --> 00:07:20.280 the question was very simple.

NOTE Confidence: 0.9537188

00:07:20.340 --> 00:07:22.040 What happened to this presentation

NOTE Confidence: 0.9537188

00:07:22.180 --> 00:07:22.680 rates?

NOTE Confidence: 0.9985592

00:07:23.140 --> 00:07:24.180 And what happened to the

NOTE Confidence: 0.9985592

00:07:24.180 --> 00:07:25.000 number called

18

NOTE Confidence: 0.96724117

00:07:25.515 --> 00:07:28.015 PAF, population attributable fraction

NOTE Confidence: 0.9656124

00:07:28.875 --> 00:07:31.355 of, psychosis and cannabis after

NOTE Confidence: 0.9656124

00:07:31.355 --> 00:07:33.115 legalization. So this number PAF,

NOTE Confidence: 0.9656124

00:07:33.115 --> 00:07:33.995 that's what you see in

NOTE Confidence: 0.9656124

00:07:33.995 --> 00:07:35.115 this y axis. It's a

NOTE Confidence: 0.9656124

00:07:35.115 --> 00:07:35.855 very interesting,

NOTE Confidence: 0.8092299

00:07:36.395 --> 00:07:37.535 fraction. It's epidemiologists

NOTE Confidence: 0.9951341

00:07:38.155 --> 00:07:38.955 know this very well, but

NOTE Confidence: 0.9951341

00:07:38.955 --> 00:07:39.755 I'll take a minute to

NOTE Confidence: 0.9951341

00:07:39.755 --> 00:07:40.655 explain this.

NOTE Confidence: 0.99719524

00:07:41.069 --> 00:07:43.150 Population attributable fraction is a

NOTE Confidence: 0.99719524

00:07:43.150 --> 00:07:43.650 number

NOTE Confidence: 0.9997866

00:07:44.030 --> 00:07:45.009 that tells you

NOTE Confidence: 0.97071755

00:07:45.389 --> 00:07:46.509 if you have hundred people

NOTE Confidence: 0.97071755

00:07:46.509 --> 00:07:48.530 in your population with, psychosis,

NOTE Confidence: 0.9976632

00:07:49.150 --> 00:07:50.530 how many of those hundred,

NOTE Confidence: 0.9985224

00:07:51.310 --> 00:07:53.169 have psychosis that's attributable

NOTE Confidence: 0.9004903

00:07:53.505 --> 00:07:54.485 to cannabis.

NOTE Confidence: 0.9648149

00:07:55.025 --> 00:07:56.065 That in other words, if

NOTE Confidence: 0.9648149

00:07:56.065 --> 00:07:57.825 you eliminate cannabis completely from

NOTE Confidence: 0.9648149

00:07:57.825 --> 00:07:58.485 the population,

NOTE Confidence: 0.9448863

00:07:59.105 --> 00:07:59.985 well, whether you can do

NOTE Confidence: 0.9448863

00:07:59.985 --> 00:08:00.945 it is a question. But

NOTE Confidence: 0.9448863

00:08:00.945 --> 00:08:01.845 if you do it,

NOTE Confidence: 0.91015285

00:08:02.145 --> 00:08:03.585 how many cases will be

NOTE Confidence: 0.91015285

00:08:03.585 --> 00:08:06.145 gone from, annual presentations that

NOTE Confidence: 0.91015285

00:08:06.145 --> 00:08:07.250 we see in the c

NOTE Confidence: 0.91015285

00:08:07.250 --> 00:08:07.910 vid psychosis.

NOTE Confidence: 0.9980104

00:08:08.289 --> 00:08:09.270 So that number is

NOTE Confidence: 0.94991124

00:08:09.729 --> 00:08:11.570 and, traditionally, conventionally, you know,

NOTE Confidence: 0.94991124

00:08:11.570 --> 00:08:12.690 it's been quite low. It's

NOTE Confidence: 0.94991124

00:08:12.690 --> 00:08:14.210 around five percent. Five percent

NOTE Confidence: 0.94991124

00:08:14.210 --> 00:08:14.870 of cases,

NOTE Confidence: 0.9924859

00:08:15.250 --> 00:08:16.610 we expect those cases will

NOTE Confidence: 0.9924859

00:08:16.610 --> 00:08:17.270 be eliminated.

NOTE Confidence: 0.953768

00:08:18.289 --> 00:08:19.570 Will still exist. Ninety five

NOTE Confidence: 0.953768

00:08:19.570 --> 00:08:20.610 percent of cases will still

NOTE Confidence: 0.953768

00:08:20.610 --> 00:08:22.210 exist, but five percent may

NOTE Confidence: 0.953768

00:08:22.210 --> 00:08:23.865 not exist if cannabis is

NOTE Confidence: 0.953768

00:08:23.865 --> 00:08:24.905 completely gone from the face

NOTE Confidence: 0.953768

00:08:24.905 --> 00:08:26.345 of this earth. But see

NOTE Confidence: 0.953768

00:08:26.345 --> 00:08:27.465 what happens to the number

NOTE Confidence: 0.953768

00:08:27.465 --> 00:08:29.065 is around point zero five,

NOTE Confidence: 0.953768

00:08:29.305 --> 00:08:30.605 before twenty fifteen.

NOTE Confidence: 0.992578

00:08:30.985 --> 00:08:31.785 The first one is on

NOTE Confidence: 0.992578

00:08:31.785 --> 00:08:32.285 schizophrenia,

NOTE Confidence: 0.9648409

21

00:08:32.585 --> 00:08:33.725 which is a narrow diagnosis,

NOTE Confidence: 0.9948981

00:08:34.184 --> 00:08:35.145 and the second one is

NOTE Confidence: 0.9948981

00:08:35.145 --> 00:08:36.905 on psychosis not otherwise specified,

NOTE Confidence: 0.9948981

00:08:36.905 --> 00:08:38.105 which includes every kind of

NOTE Confidence: 0.9948981

00:08:38.105 --> 00:08:38.605 psychosis.

NOTE Confidence: 0.9610716

00:08:39.220 --> 00:08:40.020 And you see it's always

NOTE Confidence: 0.9610716

00:08:40.020 --> 00:08:41.700 around point zero five, in

NOTE Confidence: 0.9610716

00:08:41.700 --> 00:08:43.640 the decade before twenty fifteen,

NOTE Confidence: 0.96330166

00:08:45.059 --> 00:08:46.580 rising over time, but not

NOTE Confidence: 0.96330166

00:08:46.580 --> 00:08:47.080 massive.

NOTE Confidence: 0.9747594

00:08:47.460 --> 00:08:49.080 And then with legal liberalization,

NOTE Confidence: 0.9764843

00:08:49.700 --> 00:08:51.160 it goes up the acceleration

NOTE Confidence: 0.9764843

00:08:51.300 --> 00:08:52.179 of the slab. You can

NOTE Confidence: 0.9764843

00:08:52.179 --> 00:08:53.235 see the step up there.

NOTE Confidence: 0.9764843

00:08:53.554 --> 00:08:54.995 It it is nearing point

NOTE Confidence: 0.9764843

00:08:54.995 --> 00:08:56.195 one, which is ten percent

NOTE Confidence: 0.9764843

00:08:56.195 --> 00:08:56.934 of the population's

NOTE Confidence: 0.9786924

00:08:57.635 --> 00:08:58.774 risk. And after legalization,

NOTE Confidence: 0.9720543

00:08:59.075 --> 00:09:00.115 the risk is now around

NOTE Confidence: 0.9720543

00:09:00.115 --> 00:09:01.975 ten percent, both for schizophrenia

NOTE Confidence: 0.9517762

00:09:02.355 --> 00:09:03.894 and for psychosis NOS.

NOTE Confidence: 0.98304176

00:09:04.355 --> 00:09:05.795 So the key finding too

NOTE Confidence: 0.98304176

00:09:05.795 --> 00:09:07.654 is we have very convincing

NOTE Confidence: 0.9659349

00:09:08.429 --> 00:09:10.929 population wide laboratory evidence, epidemiological

NOTE Confidence: 0.9659349

00:09:11.150 --> 00:09:12.750 evidence to say that,

NOTE Confidence: 0.999224

00:09:13.390 --> 00:09:15.390 cannabis is related to presentations

NOTE Confidence: 0.999224

00:09:15.390 --> 00:09:16.050 of psychosis

NOTE Confidence: 0.9274921

00:09:16.590 --> 00:09:17.710 and this is very very

NOTE Confidence: 0.9274921

00:09:17.710 --> 00:09:19.390 compelling as well, equally compelling,

NOTE Confidence: 0.9274921

00:09:19.710 --> 00:09:21.150 to the experimental evidence we

NOTE Confidence: 0.9274921

00:09:21.150 --> 00:09:21.650 have.

23

NOTE Confidence: 0.9513496

00:09:23.045 --> 00:09:24.165 And we also have a

NOTE Confidence: 0.9513496

00:09:24.165 --> 00:09:25.365 third line of evidence that

NOTE Confidence: 0.9513496

00:09:25.365 --> 00:09:26.885 comes from clinical practice. I

NOTE Confidence: 0.9513496

00:09:26.885 --> 00:09:28.965 would say clinical wisdom really.

NOTE Confidence: 0.9513496

00:09:28.965 --> 00:09:29.845 You know, when you see

NOTE Confidence: 0.9513496

00:09:29.845 --> 00:09:30.985 people with schizophrenia,

NOTE Confidence: 0.97942656

00:09:31.525 --> 00:09:33.065 established psychotic disorders,

NOTE Confidence: 0.95395654

00:09:33.525 --> 00:09:34.670 you know that if,

NOTE Confidence: 0.9899802

00:09:35.230 --> 00:09:36.929 if those people with schizophrenia

NOTE Confidence: 0.876302

00:09:37.309 --> 00:09:38.829 smoke cannabis continue to use

NOTE Confidence: 0.876302

00:09:38.829 --> 00:09:39.329 cannabis,

NOTE Confidence: 0.94966984

00:09:39.709 --> 00:09:40.829 they could develop poor outcome.

NOTE Confidence: 0.94966984

00:09:40.829 --> 00:09:41.950 And you see them relapsing

NOTE Confidence: 0.94966984

00:09:41.950 --> 00:09:43.329 very often. You see them

NOTE Confidence: 0.9902077

00:09:43.630 --> 00:09:44.990 coming off the medications. You

NOTE Confidence: 0.9902077

00:09:44.990 --> 00:09:45.950 see all the kind of

NOTE Confidence: 0.9902077

00:09:45.950 --> 00:09:46.450 factors

NOTE Confidence: 0.99520195

00:09:46.855 --> 00:09:48.535 related to negative outcomes being

NOTE Confidence: 0.99520195

00:09:48.535 --> 00:09:49.895 higher in people who have

NOTE Confidence: 0.99520195

00:09:49.895 --> 00:09:51.195 ongoing cannabis use.

NOTE Confidence: 0.9720184

00:09:51.815 --> 00:09:53.575 And if those same patients,

NOTE Confidence: 0.9720184

00:09:53.575 --> 00:09:55.255 if they stop using cannabis,

NOTE Confidence: 0.9720184

00:09:55.255 --> 00:09:56.295 you see them having better

NOTE Confidence: 0.9720184

00:09:56.295 --> 00:09:58.054 outcomes. And this clinical wisdom

NOTE Confidence: 0.9720184

00:09:58.054 --> 00:09:59.895 is also well replicated and

NOTE Confidence: 0.9720184

00:09:59.895 --> 00:10:01.175 and published in in different

NOTE Confidence: 0.9720184

00:10:01.175 --> 00:10:02.395 format in different places

NOTE Confidence: 0.9973952

00:10:03.000 --> 00:10:03.740 across the world.

NOTE Confidence: 0.98485607

00:10:04.360 --> 00:10:05.240 So those are all, you

NOTE Confidence: 0.98485607

00:10:05.240 --> 00:10:06.440 know, very strong lines of

NOTE Confidence: 0.98485607

00:10:06.440 --> 00:10:08.520 evidence, but how useful those

NOTE Confidence: 0.98485607

00:10:08.520 --> 00:10:09.800 evidences are when you have

NOTE Confidence: 0.98485607

00:10:09.800 --> 00:10:10.840 a patient like this sitting

NOTE Confidence: 0.98485607

00:10:10.840 --> 00:10:11.480 in front of you in

NOTE Confidence: 0.98485607

00:10:11.480 --> 00:10:12.140 the clinic.

NOTE Confidence: 0.9763387

00:10:12.679 --> 00:10:13.880 In my clinic, I generally

NOTE Confidence: 0.9763387

00:10:13.880 --> 00:10:15.080 see people around twenty years

NOTE Confidence: 0.9763387

00:10:15.080 --> 00:10:16.975 of age, generally young men.

NOTE Confidence: 0.9763387

00:10:17.115 --> 00:10:18.075 Usually, they come with their

NOTE Confidence: 0.9763387

00:10:18.075 --> 00:10:18.575 parents.

NOTE Confidence: 0.86557776

00:10:19.515 --> 00:10:20.714 Not always a dad. Just

NOTE Confidence: 0.86557776

00:10:20.714 --> 00:10:21.595 like in this picture is

NOTE Confidence: 0.86557776

00:10:21.595 --> 00:10:22.975 usually the mom who comes.

NOTE Confidence: 0.96906996

00:10:23.434 --> 00:10:25.274 And the initial assessment conversation

NOTE Confidence: 0.96906996

00:10:25.274 --> 00:10:26.334 is usually about,

NOTE Confidence: 0.98531085

00:10:27.035 --> 00:10:28.154 the nature of the condition

NOTE Confidence: 0.98531085

26

00:10:28.154 --> 00:10:29.355 and what can the person

NOTE Confidence: 0.98531085

00:10:29.355 --> 00:10:30.394 and the family do to

NOTE Confidence: 0.98531085

00:10:30.394 --> 00:10:32.160 get better. So the conversation

NOTE Confidence: 0.98531085

00:10:32.220 --> 00:10:33.920 goes, something like this.

NOTE Confidence: 0.9497529

00:10:34.300 --> 00:10:35.260 I would say, you know,

NOTE Confidence: 0.9497529

00:10:35.260 --> 00:10:36.400 what you have is psychosis,

NOTE Confidence: 0.9778027

00:10:36.780 --> 00:10:38.300 and the patient would tend

NOTE Confidence: 0.9778027

00:10:38.300 --> 00:10:39.020 to agree with it and

NOTE Confidence: 0.9778027

00:10:39.020 --> 00:10:40.220 say, okay. Mind is playing

NOTE Confidence: 0.9778027

00:10:40.220 --> 00:10:41.100 tricks. What can I do

NOTE Confidence: 0.9778027

00:10:41.100 --> 00:10:41.840 about it?

NOTE Confidence: 0.9748041

00:10:42.380 --> 00:10:43.420 Well, they'll use their own

NOTE Confidence: 0.9748041

00:10:43.420 --> 00:10:45.340 slangs and, words to understand

NOTE Confidence: 0.9748041

00:10:45.340 --> 00:10:46.640 their their their experience.

NOTE Confidence: 0.96925867

00:10:47.554 --> 00:10:48.595 And generally, I say something

NOTE Confidence: 0.96925867

00:10:48.595 --> 00:10:49.635 like, I don't know exactly

NOTE Confidence: 0.96925867

00:10:49.635 --> 00:10:51.075 what causes it, but we

NOTE Confidence: 0.96925867

00:10:51.075 --> 00:10:51.875 know we can trace it

NOTE Confidence: 0.96925867

00:10:51.875 --> 00:10:52.995 back to high levels of

NOTE Confidence: 0.96925867

00:10:52.995 --> 00:10:54.434 dopamine in the brain. And

NOTE Confidence: 0.96925867

00:10:54.434 --> 00:10:55.154 then I'll go on to

NOTE Confidence: 0.96925867

00:10:55.154 --> 00:10:56.115 explain a little bit about

NOTE Confidence: 0.96925867

00:10:56.115 --> 00:10:56.615 dopamine.

NOTE Confidence: 0.9712669

00:10:56.995 --> 00:10:58.195 Generally, at this point, the

NOTE Confidence: 0.9712669

00:10:58.195 --> 00:10:59.315 dad or mom will will

NOTE Confidence: 0.9712669

00:10:59.315 --> 00:11:00.110 come in and say, okay.

NOTE Confidence: 0.9712669

00:11:00.110 --> 00:11:01.230 So there is something chemical

NOTE Confidence: 0.9712669

00:11:01.230 --> 00:11:02.269 here. What can we do

NOTE Confidence: 0.9712669

00:11:02.269 --> 00:11:03.230 about it? How can we

NOTE Confidence: 0.9712669

00:11:03.230 --> 00:11:03.730 fix

NOTE Confidence: 0.9811433

00:11:04.110 --> 00:11:05.389 it? That really opens up

NOTE Confidence: 0.9811433

28

00:11:05.389 --> 00:11:06.910 the discussion for medications and

NOTE Confidence: 0.9811433

00:11:06.910 --> 00:11:08.449 antipsychotics and so on.

NOTE Confidence: 0.97039014

00:11:08.910 --> 00:11:10.110 And one thing that we

NOTE Confidence: 0.97039014

00:11:10.110 --> 00:11:11.389 all say in practice is

NOTE Confidence: 0.97039014

00:11:11.389 --> 00:11:12.130 we say,

NOTE Confidence: 0.93850183

00:11:12.670 --> 00:11:14.290 managing psychosis involves,

NOTE Confidence: 0.97342414

00:11:15.085 --> 00:11:16.525 also steps we take to

NOTE Confidence: 0.97342414

00:11:16.525 --> 00:11:17.665 not to make it worse.

NOTE Confidence: 0.97342414

00:11:17.885 --> 00:11:19.665 So, you know, stopping cannabis,

NOTE Confidence: 0.97342414

00:11:19.804 --> 00:11:21.105 decreasing the use of cannabis

NOTE Confidence: 0.97342414

00:11:21.165 --> 00:11:21.965 is one thing that I

NOTE Confidence: 0.97342414

00:11:21.965 --> 00:11:22.945 would strongly recommend.

NOTE Confidence: 0.9400108

00:11:23.404 --> 00:11:25.005 Now that's the place where

NOTE Confidence: 0.9400108

00:11:25.005 --> 00:11:26.445 that's the point where the

NOTE Confidence: 0.9400108

00:11:26.445 --> 00:11:27.425 clinical conversation,

NOTE Confidence: 0.9025998

00:11:28.779 --> 00:11:29.520 starts running,

NOTE Confidence: 0.94032294

00:11:30.220 --> 00:11:31.660 parallel stream to what the

NOTE Confidence: 0.94032294

00:11:31.660 --> 00:11:33.260 patient has been saying so

NOTE Confidence: 0.94032294

00:11:33.260 --> 00:11:34.140 far. So they will say

NOTE Confidence: 0.94032294

00:11:34.140 --> 00:11:35.820 something like, blame the cannabis

NOTE Confidence: 0.94032294

00:11:35.820 --> 00:11:37.520 now, doc. Nice twist.

NOTE Confidence: 0.9777057

00:11:37.980 --> 00:11:39.420 For me, cannabis helps. It

NOTE Confidence: 0.9777057

00:11:39.420 --> 00:11:40.620 helps me to sleep, helps

NOTE Confidence: 0.9777057

00:11:40.620 --> 00:11:41.355 me to relax,

NOTE Confidence: 0.9686046

00:11:41.915 --> 00:11:43.115 and I've been smoking it

NOTE Confidence: 0.9686046

00:11:43.115 --> 00:11:44.635 for God knows, you know,

NOTE Confidence: 0.9686046

00:11:44.635 --> 00:11:45.675 how long, and I've been

NOTE Confidence: 0.9686046

00:11:45.675 --> 00:11:46.875 having psychosis only for the

NOTE Confidence: 0.9686046

00:11:46.875 --> 00:11:47.995 last three weeks or four

NOTE Confidence: 0.9686046

00:11:47.995 --> 00:11:49.434 weeks. So they would just

NOTE Confidence: 0.9686046

00:11:49.434 --> 00:11:51.035 start diverging from me and

NOTE Confidence: 0.9686046

00:11:51.035 --> 00:11:52.635 start not accepting the fact

NOTE Confidence: 0.9686046

00:11:52.635 --> 00:11:54.394 that cannabis may be contributing

NOTE Confidence: 0.9686046

00:11:54.394 --> 00:11:55.660 to their problems. Now at

NOTE Confidence: 0.9686046

00:11:55.660 --> 00:11:57.420 this stage, generally, I start

NOTE Confidence: 0.9686046

00:11:57.420 --> 00:11:58.460 saying things like, you know,

NOTE Confidence: 0.9686046

00:11:58.460 --> 00:11:59.660 I've been treating patients for

NOTE Confidence: 0.9686046

00:11:59.660 --> 00:12:00.620 so many years and, you

NOTE Confidence: 0.9686046

00:12:00.620 --> 00:12:02.000 know, we've seen people getting

NOTE Confidence: 0.9686046

00:12:02.059 --> 00:12:03.100 better when they stop it

NOTE Confidence: 0.9686046

00:12:03.100 --> 00:12:04.140 or getting worse when they

NOTE Confidence: 0.9686046

00:12:04.140 --> 00:12:06.059 don't. And then, the patient

NOTE Confidence: 0.9686046

00:12:06.059 --> 00:12:07.020 says, well, that may be

NOTE Confidence: 0.9686046

00:12:07.020 --> 00:12:08.140 true for your other patients,

NOTE Confidence: 0.9686046

00:12:08.140 --> 00:12:09.179 but I'm different. You know?

NOTE Confidence: 0.9686046

00:12:09.179 --> 00:12:10.525 For me, it helps. I'm

NOTE Confidence: 0.9686046

00:12:10.525 --> 00:12:11.325 not going to stop it,

NOTE Confidence: 0.9686046

00:12:11.325 --> 00:12:12.205 or they might not say

NOTE Confidence: 0.9686046

00:12:12.205 --> 00:12:13.005 I'm not going to stop

NOTE Confidence: 0.9686046

00:12:13.005 --> 00:12:14.285 it. They will just give

NOTE Confidence: 0.9686046

00:12:14.285 --> 00:12:15.665 me enough hints to say,

NOTE Confidence: 0.95543885

00:12:16.205 --> 00:12:17.085 it's a hard thing to

NOTE Confidence: 0.95543885

00:12:17.085 --> 00:12:17.965 swallow, a hard thing to

NOTE Confidence: 0.95543885

00:12:17.965 --> 00:12:19.325 swallow to to stop using

NOTE Confidence: 0.95543885

00:12:19.325 --> 00:12:19.825 weed.

NOTE Confidence: 0.90060955

00:12:20.445 --> 00:12:21.265 And, unfortunately,

NOTE Confidence: 0.9362636

00:12:21.645 --> 00:12:23.005 these days, increasingly, I see

NOTE Confidence: 0.9362636

00:12:23.005 --> 00:12:24.145 this. The parents

NOTE Confidence: 0.9802541

00:12:24.639 --> 00:12:26.160 would go and find some

NOTE Confidence: 0.9802541

00:12:26.160 --> 00:12:27.540 evidence that supports

NOTE Confidence: 0.9997375

00:12:27.920 --> 00:12:28.980 the use of cannabis

NOTE Confidence: 0.9905695

00:12:29.360 --> 00:12:30.019 to help.

NOTE Confidence: 0.96852005

00:12:30.559 --> 00:12:31.839 You know, they'll come either

00:12:31.839 --> 00:12:33.120 they will find nice trials

00:12:33.120 --> 00:12:34.559 published in big journals about

00:12:34.559 --> 00:12:35.059 cannabidiol,

00:12:35.600 --> 00:12:36.899 helping psychotic symptoms,

00:12:37.555 --> 00:12:38.675 and they will bring that

00:12:38.675 --> 00:12:39.795 up. I will bring some

00:12:39.795 --> 00:12:41.635 other, well, not so scientific

00:12:41.635 --> 00:12:42.615 evidence to,

00:12:43.075 --> 00:12:44.035 to argue the case to

00:12:44.035 --> 00:12:45.815 really reduce the cognitive dissonance

00:12:46.035 --> 00:12:47.155 that you see, in the

00:12:47.155 --> 00:12:48.055 family here.

00:12:48.515 --> 00:12:49.255 And eventually,

00:12:50.830 --> 00:12:52.030 the progress that we make

00:12:52.030 --> 00:12:53.230 in getting the person to

NOTE Confidence: 0.9850681

00:12:53.230 --> 00:12:54.830 stop smoking weed is very

NOTE Confidence: 0.9850681

00:12:54.830 --> 00:12:55.710 little in the first year

NOTE Confidence: 0.9850681

00:12:55.710 --> 00:12:56.370 of psychosis.

NOTE Confidence: 0.9830797

00:12:56.830 --> 00:12:57.790 They may reduce a little

NOTE Confidence: 0.9830797

00:12:57.790 --> 00:12:58.510 bit or they may just

NOTE Confidence: 0.9830797

00:12:58.510 --> 00:12:59.550 continue to use it in

NOTE Confidence: 0.9830797

00:12:59.550 --> 00:13:01.070 most cases and keep getting

NOTE Confidence: 0.9830797

00:13:01.070 --> 00:13:02.590 relapses and admissions in the

NOTE Confidence: 0.9830797

00:13:02.590 --> 00:13:03.090 hospital.

NOTE Confidence: 0.95776385

00:13:04.074 --> 00:13:05.755 The the whole discussion about

NOTE Confidence: 0.95776385

00:13:05.755 --> 00:13:07.995 complexity of psychosis, especially the

NOTE Confidence: 0.95776385

00:13:07.995 --> 00:13:09.755 causal complexity, there are many

NOTE Confidence: 0.95776385

00:13:09.755 --> 00:13:11.035 causes and cannabis is one

NOTE Confidence: 0.95776385

00:13:11.035 --> 00:13:12.714 of them, doesn't really sell

NOTE Confidence: 0.95776385

00:13:12.714 --> 00:13:13.995 well. I mean, complexity is

NOTE Confidence: 0.95776385

00:13:13.995 --> 00:13:15.454 good for us doing science.

NOTE Confidence: 0.95776385

00:13:15.675 --> 00:13:17.274 We embrace complexity. We know

NOTE Confidence: 0.95776385

00:13:17.274 --> 00:13:18.815 this complex. It's not simple.

NOTE Confidence: 0.95776385

00:13:18.950 --> 00:13:20.330 But clinical conversations,

NOTE Confidence: 0.9729294

00:13:20.870 --> 00:13:22.230 complexity is not a friend

NOTE Confidence: 0.9729294

00:13:22.230 --> 00:13:23.350 of clinicians, you know, in

NOTE Confidence: 0.9729294

00:13:23.350 --> 00:13:24.550 many ways. It doesn't really

NOTE Confidence: 0.9729294

00:13:24.550 --> 00:13:25.910 help us to to draw

NOTE Confidence: 0.9729294

00:13:25.910 --> 00:13:27.190 one to one line between

NOTE Confidence: 0.9729294

00:13:27.190 --> 00:13:29.270 problems and effects, between causes

NOTE Confidence: 0.9729294

00:13:29.270 --> 00:13:30.170 and and outcomes,

NOTE Confidence: 0.97952545

00:13:30.710 --> 00:13:31.830 which means, you know, patients

NOTE Confidence: 0.97952545

00:13:31.830 --> 00:13:33.029 start forming their own line

NOTE Confidence: 0.97952545

00:13:33.029 --> 00:13:34.965 of thinking, and therapeutic alliance

NOTE Confidence: 0.97952545

00:13:34.965 --> 00:13:36.505 really fails at this point.

NOTE Confidence: 0.9793859

00:13:36.885 --> 00:13:37.845 So one of the questions

NOTE Confidence: 0.9793859

00:13:37.845 --> 00:13:39.125 is, can we actually draw

NOTE Confidence: 0.9793859

00:13:39.125 --> 00:13:41.465 a straight line between psychosis,

NOTE Confidence: 0.97874916

00:13:42.005 --> 00:13:43.765 dopamine, and cannabis? If we

NOTE Confidence: 0.97874916

00:13:43.765 --> 00:13:44.645 can draw a straight line

NOTE Confidence: 0.97874916

00:13:44.645 --> 00:13:46.265 like that, we may have,

NOTE Confidence: 0.97874916

00:13:46.405 --> 00:13:47.845 some better evidence to to

NOTE Confidence: 0.97874916

00:13:47.845 --> 00:13:49.050 present and and make a

NOTE Confidence: 0.97874916

00:13:49.050 --> 00:13:50.030 case in clinics.

NOTE Confidence: 0.9753564

00:13:51.210 --> 00:13:52.330 So what I want is

NOTE Confidence: 0.9753564

00:13:52.330 --> 00:13:53.929 clinically applicable evidence. Really, the

NOTE Confidence: 0.9753564

00:13:53.929 --> 00:13:55.610 evidence that comes from patients

NOTE Confidence: 0.9753564

00:13:55.610 --> 00:13:56.410 like this one that I

NOTE Confidence: 0.9753564

00:13:56.410 --> 00:13:57.309 see in the clinic.

NOTE Confidence: 0.94933975

00:13:57.610 --> 00:13:59.530 Young man using cannabis for

NOTE Confidence: 0.94933975

00:13:59.530 --> 00:14:01.065 a period of time, qualifying

NOTE Confidence: 0.94933975

00:14:01.065 --> 00:14:02.425 for cannabis use disorder in

NOTE Confidence: 0.94933975

00:14:02.425 --> 00:14:03.785 many cases, not a new

NOTE Confidence: 0.94933975

00:14:03.785 --> 00:14:05.465 user, chronic user, but now

NOTE Confidence: 0.94933975

00:14:05.465 --> 00:14:07.304 proceeding with psychotic symptoms. Can

NOTE Confidence: 0.94933975

00:14:07.304 --> 00:14:08.425 I say something about the

NOTE Confidence: 0.94933975

00:14:08.425 --> 00:14:10.105 dopamine to them that convinces

NOTE Confidence: 0.94933975

00:14:10.105 --> 00:14:11.485 them to to take action?

NOTE Confidence: 0.9387317

00:14:12.759 --> 00:14:13.639 So in other words, the

NOTE Confidence: 0.9387317

00:14:13.639 --> 00:14:14.839 research question is, is there

NOTE Confidence: 0.9387317

00:14:14.839 --> 00:14:16.040 a common alteration in the

NOTE Confidence: 0.9387317

00:14:16.040 --> 00:14:17.899 dopamine system in cannabis users

NOTE Confidence: 0.9387317

00:14:18.040 --> 00:14:19.579 and people with psychotic disorder?

NOTE Confidence: 0.9996778

00:14:19.959 --> 00:14:21.180 Can I tell my patients

NOTE Confidence: 0.93340987

00:14:21.880 --> 00:14:23.180 the weed that you smoke

NOTE Confidence: 0.9918661

00:14:23.720 --> 00:14:25.480 increases the same chemical in

NOTE Confidence: 0.9918661

00:14:25.480 --> 00:14:26.620 the same brine region

NOTE Confidence: 0.9869793

00:14:27.045 --> 00:14:28.245 where we don't want it

NOTE Confidence: 0.9869793

00:14:28.245 --> 00:14:29.685 to go up? That's really

NOTE Confidence: 0.9869793

00:14:29.685 --> 00:14:30.485 what I wanna do with

NOTE Confidence: 0.9869793

00:14:30.485 --> 00:14:30.985 this,

NOTE Confidence: 0.99370784

00:14:31.445 --> 00:14:32.425 research here.

NOTE Confidence: 0.94793165

00:14:32.885 --> 00:14:34.525 So, just before we go

NOTE Confidence: 0.94793165

00:14:34.525 --> 00:14:35.845 to the methods and results

NOTE Confidence: 0.94793165

00:14:35.845 --> 00:14:36.805 of how we approach that

NOTE Confidence: 0.94793165

00:14:36.805 --> 00:14:38.325 question, it's important to realize

NOTE Confidence: 0.94793165

00:14:38.325 --> 00:14:40.580 that the evidence of dopamine

NOTE Confidence: 0.94793165

00:14:40.580 --> 00:14:42.340 access in psychosis is merely

NOTE Confidence: 0.94793165

00:14:42.340 --> 00:14:43.940 an, irrefutable. There's a lot

NOTE Confidence: 0.94793165

00:14:43.940 --> 00:14:45.140 of evidence for that. This

NOTE Confidence: 0.94793165

00:14:45.140 --> 00:14:46.500 is a meta analysis by

NOTE Confidence: 0.94793165

00:14:46.500 --> 00:14:47.480 Oliver House

NOTE Confidence: 0.8875607

00:14:47.940 --> 00:14:49.060 published eleven years now, I

NOTE Confidence: 0.8875607

00:14:49.060 --> 00:14:50.900 think, twenty thirteen, twenty twelve,

NOTE Confidence: 0.8875607

00:14:50.900 --> 00:14:52.820 I think. Anyway, it's really,

NOTE Confidence: 0.8875607

00:14:52.980 --> 00:14:54.820 PET studies based on, fluoro

NOTE Confidence: 0.8875607

00:14:54.820 --> 00:14:56.895 dopa studies showing dopamine synthesis

NOTE Confidence: 0.8875607

00:14:56.955 --> 00:14:57.455 excess,

NOTE Confidence: 0.9779748

00:14:58.075 --> 00:14:59.615 in, in people with psychosis.

NOTE Confidence: 0.9620086

00:15:00.155 --> 00:15:01.595 And you see around point

NOTE Confidence: 0.9620086

00:15:01.595 --> 00:15:03.115 seven effect size, point seven

NOTE Confidence: 0.9620086

00:15:03.115 --> 00:15:04.495 to point eight, which is,

NOTE Confidence: 0.9821431

00:15:05.275 --> 00:15:07.035 nearly large effect size of

NOTE Confidence: 0.9821431

00:15:07.035 --> 00:15:08.895 dopamine excess in stratum.

NOTE Confidence: 0.91128

00:15:09.779 --> 00:15:11.380 As you may know, dopamine

NOTE Confidence: 0.91128

00:15:11.380 --> 00:15:13.300 is synthesized in, the neuron

NOTE Confidence: 0.91128

00:15:13.300 --> 00:15:14.820 start somewhere in midbrain in

NOTE Confidence: 0.91128

00:15:14.820 --> 00:15:16.820 substantia nigra and ventral tegmental

NOTE Confidence: 0.91128

00:15:16.820 --> 00:15:18.660 area, but they release hackers

NOTE Confidence: 0.91128

00:15:18.660 --> 00:15:20.100 in in stratum. That's where

NOTE Confidence: 0.91128

00:15:20.100 --> 00:15:22.120 the projections are, microstridal projections.

NOTE Confidence: 0.9871009

00:15:22.545 --> 00:15:23.985 So stratum is where you

NOTE Confidence: 0.9871009

00:15:23.985 --> 00:15:24.885 see excessive,

NOTE Confidence: 0.9440816

00:15:25.345 --> 00:15:27.605 big, vesicular storage of dopamine,

NOTE Confidence: 0.9440816

00:15:27.665 --> 00:15:28.964 which is increased in psychosis.

NOTE Confidence: 0.9456831

00:15:29.985 --> 00:15:31.185 And we we we actually

NOTE Confidence: 0.9456831

00:15:31.185 --> 00:15:32.964 see that with antipsychotic usage,

NOTE Confidence: 0.93944716

00:15:33.345 --> 00:15:34.545 in in people with resistance

NOTE Confidence: 0.93944716

00:15:34.545 --> 00:15:36.645 schizophrenia, the pathophysiology is different.

NOTE Confidence: 0.93944716

00:15:36.690 --> 00:15:38.210 But in people with acute

NOTE Confidence: 0.93944716

00:15:38.210 --> 00:15:39.650 psychotic symptoms and,

NOTE Confidence: 0.96233964

00:15:40.130 --> 00:15:42.470 schizophrenia itself, there is higher

NOTE Confidence: 0.96233964

00:15:42.530 --> 00:15:44.370 storage of, synthesis and storage

NOTE Confidence: 0.96233964

00:15:44.370 --> 00:15:45.250 of dopamine. So it's a

NOTE Confidence: 0.96233964

00:15:45.250 --> 00:15:46.630 it's a very well established

NOTE Confidence: 0.96233964

00:15:46.770 --> 00:15:48.630 line of evidence here. It's

NOTE Confidence: 0.96233964

00:15:48.690 --> 00:15:49.730 said to be the final

NOTE Confidence: 0.96233964

00:15:49.730 --> 00:15:51.490 common pathway for psychotic symptoms

NOTE Confidence: 0.96233964

00:15:51.490 --> 00:15:51.990 in

NOTE Confidence: 0.73610437

00:15:52.455 --> 00:15:52.955 schizophrenia.

NOTE Confidence: 0.91397613

00:15:54.295 --> 00:15:55.815 But the link between cannabis

NOTE Confidence: 0.91397613

00:15:55.815 --> 00:15:56.775 and dopamine is not that

NOTE Confidence: 0.91397613

00:15:56.775 --> 00:15:57.275 clear.

NOTE Confidence: 0.9603802

00:15:57.655 --> 00:15:58.855 In fact, the the early

NOTE Confidence: 0.9603802

00:15:58.855 --> 00:16:00.775 studies actually showed if you

NOTE Confidence: 0.9603802

00:16:00.775 --> 00:16:01.275 inject,

NOTE Confidence: 0.8694294

00:16:01.895 --> 00:16:03.335 THC just like the the

NOTE Confidence: 0.8694294

00:16:03.335 --> 00:16:04.535 study that I showed earlier,

NOTE Confidence: 0.8694294

00:16:04.535 --> 00:16:05.355 several study,

NOTE Confidence: 0.86273634

00:16:05.830 --> 00:16:07.670 Acute injection of THC, pet

NOTE Confidence: 0.86273634

00:16:07.670 --> 00:16:09.190 studies doing that actually showed

NOTE Confidence: 0.86273634

00:16:09.190 --> 00:16:11.529 increases triadal dopaminergic synthesis.

NOTE Confidence: 0.90803164

00:16:11.910 --> 00:16:13.110 So if you inject THC,

NOTE Confidence: 0.90803164

00:16:13.110 --> 00:16:14.810 you get increased triadal dopamine

NOTE Confidence: 0.90803164

00:16:15.110 --> 00:16:15.610 synthesis.

NOTE Confidence: 0.9787207

00:16:16.070 --> 00:16:17.430 But chronic users had a

NOTE Confidence: 0.9787207

00:16:17.430 --> 00:16:19.270 very different picture. Chronic cannabis

NOTE Confidence: 0.9787207

00:16:19.270 --> 00:16:21.545 use leads to blunted dopamine

NOTE Confidence: 0.9787207

00:16:21.545 --> 00:16:22.045 synthesis

NOTE Confidence: 0.9685573

00:16:22.504 --> 00:16:24.264 and less release. So really

NOTE Confidence: 0.9685573

00:16:24.264 --> 00:16:26.745 opposing effects between acute, injections

NOTE Confidence: 0.9685573

00:16:26.745 --> 00:16:28.345 and chronic use. And as

NOTE Confidence: 0.9685573

00:16:28.345 --> 00:16:29.625 you know, chronic use in,

NOTE Confidence: 0.9685573

00:16:29.865 --> 00:16:30.904 in real life, in real

NOTE Confidence: 0.9685573

00:16:30.904 --> 00:16:32.425 world, it's not just THC.

NOTE Confidence: 0.9685573

00:16:32.425 --> 00:16:34.300 It's cannabidiol as well. And

NOTE Confidence: 0.9685573

00:16:34.300 --> 00:16:36.300 cannabidiol itself has opposing effects

NOTE Confidence: 0.9685573

00:16:36.300 --> 00:16:37.820 pharmacologically. It's a partial d

NOTE Confidence: 0.9685573

00:16:37.820 --> 00:16:40.000 two agonist, has antipsychotic effects.

NOTE Confidence: 0.9685573

00:16:40.140 --> 00:16:41.100 So the question is in

NOTE Confidence: 0.9685573

00:16:41.100 --> 00:16:42.320 long term cannabis users,

NOTE Confidence: 0.96327055

00:16:43.100 --> 00:16:44.300 the users that we generally

NOTE Confidence: 0.96327055

00:16:44.300 --> 00:16:45.920 see in psychosis clinics, pharmaceutical

NOTE Confidence: 0.96327055

00:16:45.980 --> 00:16:47.745 clinics, what is cannabis doing

NOTE Confidence: 0.96327055

00:16:47.745 --> 00:16:49.105 to the physiology, the final

NOTE Confidence: 0.96327055

00:16:49.105 --> 00:16:50.964 common pathway of their symptoms?

NOTE Confidence: 0.96327055

00:16:51.185 --> 00:16:51.985 The best way to answer

NOTE Confidence: 0.96327055

00:16:51.985 --> 00:16:52.865 this question is to doing

NOTE Confidence: 0.96327055

00:16:52.865 --> 00:16:53.825 pet studies on a large

NOTE Confidence: 0.96327055

00:16:53.825 --> 00:16:55.185 number of first episode psychotic

NOTE Confidence: 0.96327055

00:16:55.185 --> 00:16:56.464 patients when they are acutely

NOTE Confidence: 0.96327055

00:16:56.464 --> 00:16:56.964 psychotic,

NOTE Confidence: 0.91202265

00:16:57.584 --> 00:16:58.865 and and see how much,

NOTE Confidence: 0.91202265

00:16:59.185 --> 00:17:00.785 weed they're smoking and relate

NOTE Confidence: 0.91202265

00:17:00.785 --> 00:17:02.560 these two. But, you know,

NOTE Confidence: 0.91202265

00:17:02.560 --> 00:17:03.600 your group has done a

NOTE Confidence: 0.91202265

00:17:03.600 --> 00:17:04.559 lot of pet studies. You'll

NOTE Confidence: 0.91202265

00:17:04.559 --> 00:17:05.600 know how difficult they are,

NOTE Confidence: 0.91202265

00:17:05.600 --> 00:17:07.299 how technically challenging they are,

NOTE Confidence: 0.91202265

00:17:07.520 --> 00:17:08.640 and also there's a issue

NOTE Confidence: 0.91202265

00:17:08.640 --> 00:17:10.419 of radiation extra for longitudinal

NOTE Confidence: 0.91202265

00:17:10.559 --> 00:17:12.240 studies. And the high cost

NOTE Confidence: 0.91202265

00:17:12.240 --> 00:17:13.840 that, that is associated with

NOTE Confidence: 0.91202265

00:17:13.840 --> 00:17:15.674 the pet really precludes us

NOTE Confidence: 0.91202265

00:17:15.674 --> 00:17:17.035 to do a a big,

NOTE Confidence: 0.91202265

00:17:17.275 --> 00:17:18.734 large scale clinical study,

NOTE Confidence: 0.9765237

00:17:19.275 --> 00:17:20.234 with with PET as an

NOTE Confidence: 0.9765237

00:17:20.234 --> 00:17:21.835 instrument. So I'm gonna stop

NOTE Confidence: 0.9765237

00:17:21.835 --> 00:17:23.755 here and invite just to

NOTE Confidence: 0.9765237

00:17:23.755 --> 00:17:25.455 to carry on talking about

NOTE Confidence: 0.9583192

00:17:25.755 --> 00:17:27.674 the methods and results. Jess.

NOTE Confidence: 0.9583192

00:17:27.674 --> 00:17:28.655 Thank you, Anna.

NOTE Confidence: 0.9022753

00:17:29.640 --> 00:17:30.680 So before I can get

NOTE Confidence: 0.9022753

00:17:30.680 --> 00:17:31.580 into our methods,

NOTE Confidence: 0.99688685

00:17:31.960 --> 00:17:33.800 I'm gonna switch gears and

NOTE Confidence: 0.99688685

00:17:33.800 --> 00:17:35.660 talk about something called neuromelanin.

NOTE Confidence: 0.96676165

00:17:36.680 --> 00:17:38.040 Next slide. Thank you. I'm

NOTE Confidence: 0.96676165

00:17:38.040 --> 00:17:39.240 gonna trust you to to

NOTE Confidence: 0.96676165

00:17:39.240 --> 00:17:40.060 do the cursive.

NOTE Confidence: 0.9771898

00:17:41.174 --> 00:17:43.674 So this neuromelanin synthesis pathway

NOTE Confidence: 0.9771898

00:17:43.815 --> 00:17:45.195 occurs with cytosolic

NOTE Confidence: 0.8994409

00:17:45.494 --> 00:17:45.994 catecholamines,

NOTE Confidence: 0.9916685

00:17:46.455 --> 00:17:47.914 so dopamine and norepinephrine

NOTE Confidence: 0.94897705

00:17:48.774 --> 00:17:50.715 that aren't transported into vesicles

NOTE Confidence: 0.94897705

00:17:50.855 --> 00:17:51.595 or degraded.

NOTE Confidence: 0.98417044

00:17:52.215 --> 00:17:53.414 So due to the presence

NOTE Confidence: 0.98417044

00:17:53.414 --> 00:17:54.075 of catecholamines,

NOTE Confidence: 0.9921766

00:17:54.910 --> 00:17:57.230 neuromelanin concentration is highest in

NOTE Confidence: 0.9921766

00:17:57.230 --> 00:17:58.590 the dopamine cells of the

NOTE Confidence: 0.9921766

00:17:58.590 --> 00:18:00.530 substantia nigra and ventral tegmental

NOTE Confidence: 0.9921766

00:18:00.590 --> 00:18:01.090 area

NOTE Confidence: 0.9597677

00:18:01.390 --> 00:18:02.690 and in certain norepinephrine

NOTE Confidence: 0.9948163

00:18:02.990 --> 00:18:04.530 cells in the locus coeruleus.

NOTE Confidence: 0.9913004

00:18:05.869 --> 00:18:07.310 A twenty twenty study that

NOTE Confidence: 0.9913004

00:18:07.310 --> 00:18:09.330 used PET imaging and neuromelanin

NOTE Confidence: 0.9913004

00:18:09.550 --> 00:18:10.050 imaging

NOTE Confidence: 0.9658424

00:18:11.005 --> 00:18:12.945 within the substantia nigra and

NOTE Confidence: 0.9658424

00:18:13.085 --> 00:18:14.925 ventral tegmental area did find

NOTE Confidence: 0.9658424

00:18:14.925 --> 00:18:16.285 that neuromelanin can be a

NOTE Confidence: 0.9658424

00:18:16.285 --> 00:18:18.225 proxy measure of dopamine function.

NOTE Confidence: 0.95692825

00:18:18.684 --> 00:18:19.885 So in our study, we

NOTE Confidence: 0.95692825

00:18:19.885 --> 00:18:21.585 are looking at the substantia

NOTE Confidence: 0.95692825

00:18:21.645 --> 00:18:23.405 nigra and ventral tegmental area

NOTE Confidence: 0.95692825

00:18:23.405 --> 00:18:24.465 or the SNVTA,

NOTE Confidence: 0.9754764

00:18:25.670 --> 00:18:27.350 And we analyzed both of

NOTE Confidence: 0.9754764

00:18:27.350 --> 00:18:28.630 these together due to some

NOTE Confidence: 0.9754764

00:18:28.630 --> 00:18:31.130 challenges in distinguishing the regions

NOTE Confidence: 0.9754764

00:18:31.350 --> 00:18:33.210 based on MRI signal intensity.

NOTE Confidence: 0.92227614

00:18:33.990 --> 00:18:34.490 Oh,

NOTE Confidence: 0.9832707

00:18:35.109 --> 00:18:36.170 can you hear me?

NOTE Confidence: 0.8957164

00:18:37.575 --> 00:18:38.315 Yeah? Okay.

NOTE Confidence: 0.9803934

00:18:40.054 --> 00:18:41.335 So this is because both

NOTE Confidence: 0.9803934

00:18:41.335 --> 00:18:43.034 regions contain neuromelanin

NOTE Confidence: 0.9184747

00:18:43.414 --> 00:18:44.554 producing dopaminergic

NOTE Confidence: 0.94598216

00:18:44.855 --> 00:18:47.115 neurons leading to similar imaging

NOTE Confidence: 0.94598216

00:18:47.335 --> 00:18:47.835 characteristics.

NOTE Confidence: 0.9775619

00:18:48.294 --> 00:18:49.575 So we also use this

NOTE Confidence: 0.9775619

00:18:49.575 --> 00:18:51.255 common approach where we're referring

NOTE Confidence: 0.9775619

00:18:51.255 --> 00:18:52.475 to this combined region.

NOTE Confidence: 0.9854779

00:18:53.690 --> 00:18:54.650 So the take home message

NOTE Confidence: 0.9854779

00:18:54.650 --> 00:18:55.630 from this slide

NOTE Confidence: 0.97642165

00:18:56.010 --> 00:18:57.470 is that in catecholamine

NOTE Confidence: 0.9431164

00:18:57.770 --> 00:18:59.210 producing areas of the brain,

NOTE Confidence: 0.9431164

00:18:59.210 --> 00:19:00.190 so the SNVTA

NOTE Confidence: 0.9935769

00:19:00.650 --> 00:19:01.390 for dopamine

NOTE Confidence: 0.95340556

00:19:01.690 --> 00:19:03.290 and the locus coeruleus for

NOTE Confidence: 0.95340556

00:19:03.290 --> 00:19:03.790 norepinephrine,

NOTE Confidence: 0.99147904

00:19:04.490 --> 00:19:05.390 excess catecholamines

NOTE Confidence: 0.97077125

00:19:05.770 --> 00:19:07.385 in the cytosol undergo this

NOTE Confidence: 0.97077125

00:19:07.385 --> 00:19:08.905 pathway where they are degraded

NOTE Confidence: 0.97077125

00:19:08.905 --> 00:19:09.804 down to neuromelanin,

NOTE Confidence: 0.9940086

00:19:10.345 --> 00:19:11.465 which may be a marker

NOTE Confidence: 0.9940086

00:19:11.465 --> 00:19:12.205 for catecholamine

NOTE Confidence: 0.9961924

00:19:12.505 --> 00:19:14.125 function in these areas.

NOTE Confidence: 0.9954551

00:19:15.304 --> 00:19:16.125 Next slide.

NOTE Confidence: 0.886627

00:19:18.799 --> 00:19:20.340 So, neuromelanin granules

NOTE Confidence: 0.97227997

00:19:20.960 --> 00:19:22.720 accumulate gradually in the soma

NOTE Confidence: 0.97227997

00:19:22.720 --> 00:19:23.840 of these cells and are

NOTE Confidence: 0.97227997

00:19:23.840 --> 00:19:26.080 only cleared from tissue following

NOTE Confidence: 0.97227997

00:19:26.080 --> 00:19:26.820 cell death.

NOTE Confidence: 0.9771151

00:19:27.359 --> 00:19:29.760 Therefore, neuromelanin content within the

NOTE Confidence: 0.9771151

00:19:29.760 --> 00:19:31.955 substantia nigra and ventral tegmental

NOTE Confidence: 0.9771151

00:19:32.095 --> 00:19:34.335 area increases steadily throughout life

NOTE Confidence: 0.9771151

00:19:34.335 --> 00:19:36.174 and similar effects are seen

NOTE Confidence: 0.9771151

00:19:36.174 --> 00:19:37.395 in the locus coeruleus.

NOTE Confidence: 0.98109955

00:19:38.655 --> 00:19:40.895 When neuromelanin content crosses a

NOTE Confidence: 0.98109955

00:19:40.895 --> 00:19:42.755 specific threshold of stimulation,

NOTE Confidence: 0.9695157

00:19:43.215 --> 00:19:44.994 neuronal dysfunction and neurodegeneration

NOTE Confidence: 0.9207075

00:19:45.535 --> 00:19:46.355 can occur.

NOTE Confidence: 0.9831316

00:19:46.859 --> 00:19:48.320 And while neuromelanin

NOTE Confidence: 0.9957151

00:19:48.619 --> 00:19:49.119 accumulation

NOTE Confidence: 0.9335713

00:19:49.420 --> 00:19:50.960 seems to have a predominantly

NOTE Confidence: 0.9335713

00:19:51.180 --> 00:19:52.720 protective function and health,

NOTE Confidence: 0.98246145

00:19:53.180 --> 00:19:54.240 in these neurodegenerative

NOTE Confidence: 0.79095805

00:19:54.619 --> 00:19:55.119 conditions,

NOTE Confidence: 0.9791929

00:19:55.500 --> 00:19:56.400 having extracellular

NOTE Confidence: 0.9973144

00:19:56.780 --> 00:19:57.840 release of neuromelanin

NOTE Confidence: 0.994094

00:19:58.300 --> 00:19:59.740 following cell death is thought

NOTE Confidence: 0.994094

00:19:59.740 --> 00:20:00.400 to trigger

NOTE Confidence: 0.99186736

00:20:00.925 --> 00:20:01.984 inflammatory processes

NOTE Confidence: 0.98559535

00:20:02.285 --> 00:20:02.945 that can,

NOTE Confidence: 0.99701834

00:20:03.484 --> 00:20:05.265 compound the pathological process.

NOTE Confidence: 0.98890555

00:20:06.125 --> 00:20:07.484 So from this side, what

NOTE Confidence: 0.98890555

00:20:07.484 --> 00:20:08.365 I want you to know

NOTE Confidence: 0.98890555

00:20:08.365 --> 00:20:09.345 is that neuromelanin

NOTE Confidence: 0.96604776

00:20:09.645 --> 00:20:11.105 increases with age in everyone,

NOTE Confidence: 0.9990385

00:20:11.565 --> 00:20:13.405 but it's difficult to infer

NOTE Confidence: 0.9990385

00:20:13.405 --> 00:20:15.165 if higher or lower levels

NOTE Confidence: 0.9990385

00:20:15.165 --> 00:20:15.825 of neuromelanin

NOTE Confidence: 0.98404765

00:20:16.369 --> 00:20:18.070 are representing ill or beneficial

NOTE Confidence: 0.98404765

00:20:18.130 --> 00:20:19.650 effects, so it's important to

NOTE Confidence: 0.98404765

00:20:19.650 --> 00:20:21.330 be cautious when we're making

NOTE Confidence: 0.98404765

00:20:21.330 --> 00:20:22.930 any inferences from higher or

NOTE Confidence: 0.98404765

00:20:22.930 --> 00:20:24.230 lower neuromelanin,

NOTE Confidence: 0.98506635

00:20:24.850 --> 00:20:27.109 especially in relation to clinical

NOTE Confidence: 0.98506635

00:20:27.170 --> 00:20:27.670 populations.

NOTE Confidence: 0.93561095

00:20:28.934 --> 00:20:29.674 Next slide.

NOTE Confidence: 0.94105774

00:20:30.615 --> 00:20:32.695 So historically, as Juana said,

NOTE Confidence: 0.94105774

00:20:32.695 --> 00:20:34.075 research on catecholamines

NOTE Confidence: 0.9696266

00:20:34.375 --> 00:20:35.994 has focused on pet research.

NOTE Confidence: 0.9940362

00:20:36.375 --> 00:20:37.514 However, limitations

NOTE Confidence: 0.9809658

00:20:37.815 --> 00:20:39.734 associated with this method, including

NOTE Confidence: 0.9809658

00:20:39.734 --> 00:20:40.875 cost and invasiveness,

NOTE Confidence: 0.99174815

00:20:41.659 --> 00:20:43.500 have motivated the development of

NOTE Confidence: 0.99174815

00:20:43.500 --> 00:20:46.240 alternative neuroimaging methods for catecholamine

NOTE Confidence: 0.9747282

00:20:46.619 --> 00:20:48.539 function, which can be more

NOTE Confidence: 0.9747282

00:20:48.539 --> 00:20:50.539 safely and readily applied, which

NOTE Confidence: 0.9747282

00:20:50.539 --> 00:20:51.679 is where neuromelanin

NOTE Confidence: 0.98237085

00:20:51.980 --> 00:20:54.159 sensitive MRI comes into play.

NOTE Confidence: 0.9914608

00:20:54.815 --> 00:20:56.195 So neuromelanin complexes

NOTE Confidence: 0.97360957

00:20:56.895 --> 00:20:57.715 are paramagnetic,

NOTE Confidence: 0.95482147

00:20:58.415 --> 00:20:59.955 making it possible to capture

NOTE Confidence: 0.95482147

00:21:00.015 --> 00:21:02.275 the magnetic signature of neuromelanin

NOTE Confidence: 0.95482147

00:21:02.575 --> 00:21:03.455 so they're able to be

NOTE Confidence: 0.95482147

00:21:03.455 --> 00:21:04.674 captured non invasively

NOTE Confidence: 0.9473299

00:21:05.135 --> 00:21:06.195 due to this paramagnetic

NOTE Confidence: 0.96762055

00:21:06.494 --> 00:21:07.695 property, and this is what

NOTE Confidence: 0.96762055

00:21:07.695 --> 00:21:08.674 we call neuromelanin

NOTE Confidence: 0.9960612

00:21:08.975 --> 00:21:10.035 sensitive MRI.

NOTE Confidence: 0.9179238

00:21:11.580 --> 00:21:13.660 Several MRI full sequences have

NOTE Confidence: 0.9179238

00:21:13.660 --> 00:21:15.680 been used for neuromelanin MRI

NOTE Confidence: 0.8529844

00:21:16.220 --> 00:21:17.200 and in conjunction

NOTE Confidence: 0.9788838

00:21:17.500 --> 00:21:19.580 with the paramagnetic nature of

NOTE Confidence: 0.9788838

00:21:19.580 --> 00:21:20.320 these complexes,

NOTE Confidence: 0.99626535

00:21:21.100 --> 00:21:21.600 magnetization

NOTE Confidence: 0.9992222

00:21:21.980 --> 00:21:23.415 transfer is believed

NOTE Confidence: 0.8238023

00:21:23.815 --> 00:21:25.175 to drive the contrast in

NOTE Confidence: 0.8238023

00:21:25.175 --> 00:21:26.875 the new pheromelanin rich region.

NOTE Confidence: 0.931252

00:21:27.734 --> 00:21:28.795 And in short,

NOTE Confidence: 0.9794421

00:21:29.655 --> 00:21:31.355 MT works by

NOTE Confidence: 0.9986337

00:21:31.734 --> 00:21:33.275 using the exchange

NOTE Confidence: 0.99915755

00:21:34.055 --> 00:21:34.795 of magnetization

NOTE Confidence: 0.99897873

00:21:35.255 --> 00:21:35.755 between

NOTE Confidence: 0.9565675

00:21:36.055 --> 00:21:37.355 free water protons

NOTE Confidence: 0.99598134

00:21:38.070 --> 00:21:38.809 and macromolecule

NOTE Confidence: 0.9868146

00:21:39.350 --> 00:21:41.289 bound protons, which is neuromelanin

NOTE Confidence: 0.94476

00:21:41.590 --> 00:21:42.409 in these regions,

NOTE Confidence: 0.9934971

00:21:42.869 --> 00:21:44.950 leading to increased sensitivity in

NOTE Confidence: 0.9934971

00:21:44.950 --> 00:21:45.450 neuromelanin

NOTE Confidence: 0.97762764

00:21:45.909 --> 00:21:46.809 rich regions.

NOTE Confidence: 0.98188734

00:21:48.390 --> 00:21:49.510 But now that we know

NOTE Confidence: 0.98188734

00:21:49.510 --> 00:21:51.590 that neuromelanin sensitive MRI is

NOTE Confidence: 0.98188734

00:21:51.590 --> 00:21:52.250 a noninvasive

NOTE Confidence: 0.99884576

00:21:52.615 --> 00:21:53.674 proxy of dopamine

NOTE Confidence: 0.7985359

00:21:54.294 --> 00:21:56.394 function in the SNP BTA,

NOTE Confidence: 0.99879247

00:21:57.095 --> 00:21:58.375 why do we care about

NOTE Confidence: 0.99879247

00:21:58.375 --> 00:21:59.034 this region?

NOTE Confidence: 0.94164693

00:21:59.894 --> 00:22:01.255 As we saw earlier, acute

NOTE Confidence: 0.94164693

00:22:01.255 --> 00:22:03.095 THC results in increased striatal

NOTE Confidence: 0.94164693

00:22:03.095 --> 00:22:05.674 dopaminergic synthesis, whereas chronic cannabis

NOTE Confidence: 0.94164693

00:22:05.734 --> 00:22:07.815 use blunt dopamine synthesis and

NOTE Confidence: 0.94164693

00:22:07.815 --> 00:22:08.315 release.

NOTE Confidence: 0.976776

00:22:08.670 --> 00:22:09.630 And we also saw that

NOTE Confidence: 0.976776

00:22:09.630 --> 00:22:11.390 dopamine in the striatum is

NOTE Confidence: 0.976776

00:22:11.390 --> 00:22:12.690 implicated in psychosis.

NOTE Confidence: 0.9529042

00:22:14.030 --> 00:22:15.810 The striatum doesn't contain neuromelanin,

NOTE Confidence: 0.9529042

00:22:15.950 --> 00:22:17.710 so striatal's opening functioning needs

NOTE Confidence: 0.9529042

00:22:17.710 --> 00:22:19.230 to be examined with PET

NOTE Confidence: 0.9529042

00:22:19.230 --> 00:22:19.730 scans.

NOTE Confidence: 0.8912693

00:22:20.110 --> 00:22:21.810 However, as Lano said before,

NOTE Confidence: 0.99500203

00:22:22.595 --> 00:22:23.494 via the nigrostriatal

NOTE Confidence: 0.96835333

00:22:23.875 --> 00:22:25.175 pathway, the striatum,

NOTE Confidence: 0.91946924

00:22:26.275 --> 00:22:28.295 receives projections from the substantia

NOTE Confidence: 0.91946924

00:22:28.355 --> 00:22:29.655 nigra. So presumably,

NOTE Confidence: 0.9995167

00:22:30.195 --> 00:22:30.695 any

NOTE Confidence: 0.95049447

00:22:31.155 --> 00:22:33.655 decreases in neuromelanin MRI signal

NOTE Confidence: 0.95049447

00:22:33.715 --> 00:22:35.555 within the SNVTA would mean

NOTE Confidence: 0.95049447

00:22:35.555 --> 00:22:37.415 decreased dopamine within the striatum.

NOTE Confidence: 0.9765642

00:22:37.960 --> 00:22:39.400 And, in fact, a twenty

NOTE Confidence: 0.9765642

00:22:39.400 --> 00:22:40.220 twenty study,

NOTE Confidence: 0.9560571

00:22:41.240 --> 00:22:42.940 used PET imaging and neuromelanin

NOTE Confidence: 0.9560571

00:22:43.080 --> 00:22:45.240 imaging within the substantia nigra

NOTE Confidence: 0.9560571

00:22:45.240 --> 00:22:46.940 and ventral tegmental area,

NOTE Confidence: 0.99238515

00:22:47.560 --> 00:22:49.580 found that individuals with higher

NOTE Confidence: 0.99238515

00:22:49.640 --> 00:22:50.140 neuromelanin

NOTE Confidence: 0.85226387

00:22:50.440 --> 00:22:52.680 MRI signal had greater triatal

NOTE Confidence: 0.85226387

00:22:52.680 --> 00:22:54.135 dopamine release capacity,

NOTE Confidence: 0.9861537

00:22:54.675 --> 00:22:56.535 so this suggests that examining

NOTE Confidence: 0.9861537

00:22:56.675 --> 00:22:58.355 neuromelanin in this area may

NOTE Confidence: 0.9861537

00:22:58.355 --> 00:22:59.655 be a marker of dopamine

NOTE Confidence: 0.9861537

00:22:59.715 --> 00:23:00.215 function

NOTE Confidence: 0.93165016

00:23:00.515 --> 00:23:01.975 of the nigricidal pathway.

NOTE Confidence: 0.9771255

00:23:03.555 --> 00:23:04.595 So that brings me to

NOTE Confidence: 0.9771255

00:23:04.595 --> 00:23:05.795 why we're actually using this

NOTE Confidence: 0.9771255

00:23:05.795 --> 00:23:06.600 to our study.

NOTE Confidence: 0.9109251

00:23:07.559 --> 00:23:08.520 Our data was from a

NOTE Confidence: 0.9109251

00:23:08.520 --> 00:23:10.520 study called Weed Outcomes and

NOTE Confidence: 0.9109251

00:23:10.520 --> 00:23:12.359 White Matter funded by the

NOTE Confidence: 0.9109251

00:23:12.359 --> 00:23:14.460 Canadian Institutes of Health Research.

NOTE Confidence: 0.92742866

00:23:14.760 --> 00:23:15.720 We were lucky to have

NOTE Confidence: 0.92742866

00:23:15.720 --> 00:23:17.240 some really great collaborators on

NOTE Confidence: 0.92742866

00:23:17.240 --> 00:23:18.919 this including Phil Tibble, Aly

NOTE Confidence: 0.92742866

00:23:18.919 --> 00:23:20.600 Khan, Rachel Rabban, and Clifford

NOTE Confidence: 0.92742866

00:23:20.600 --> 00:23:21.100 Cassidy.

NOTE Confidence: 0.9817404

00:23:22.484 --> 00:23:24.085 At baseline, we had sixty

NOTE Confidence: 0.9817404

00:23:24.085 --> 00:23:26.484 four participants completing clinical and

NOTE Confidence: 0.9817404

00:23:26.484 --> 00:23:27.465 cognitive questionnaires,

NOTE Confidence: 0.9769928

00:23:27.765 --> 00:23:29.625 a saliva sample to quantify

NOTE Confidence: 0.9769928

00:23:29.765 --> 00:23:30.825 THC content,

NOTE Confidence: 0.98378056

00:23:31.365 --> 00:23:32.805 and an MRI scan that

NOTE Confidence: 0.98378056

00:23:32.805 --> 00:23:34.825 included a two d GRE,

NOTE Confidence: 0.9250965

00:23:35.845 --> 00:23:36.345 neuromelanin

NOTE Confidence: 0.99746794

00:23:36.645 --> 00:23:37.145 sequence.

NOTE Confidence: 0.9542154

00:23:38.460 --> 00:23:40.000 Of these sixty four participants,

NOTE Confidence: 0.9542154

00:23:40.140 --> 00:23:41.119 twenty six

NOTE Confidence: 0.97686857

00:23:41.500 --> 00:23:43.260 had a cannabis use disorder

NOTE Confidence: 0.97686857

00:23:43.260 --> 00:23:44.640 and thirty eight did not

NOTE Confidence: 0.97686857

00:23:44.859 --> 00:23:46.940 with some participants in both

NOTE Confidence: 0.97686857

00:23:46.940 --> 00:23:48.240 groups having a DSM-five

NOTE Confidence: 0.99874467

00:23:48.540 --> 00:23:50.000 diagnosis of schizophrenia

NOTE Confidence: 0.9983098

00:23:50.300 --> 00:23:51.760 from a research psychiatrist

NOTE Confidence: 0.99491256

00:23:52.465 --> 00:23:53.904 and the cannabis use disorder

NOTE Confidence: 0.99491256

00:23:53.904 --> 00:23:55.365 was diagnosed by the psychiatrist

NOTE Confidence: 0.99491256

00:23:55.504 --> 00:23:56.164 as well.

NOTE Confidence: 0.9079157

00:23:57.424 --> 00:23:58.965 The first episode of schizophrenia

NOTE Confidence: 0.9618782

00:23:59.664 --> 00:24:01.664 participants with and without cannabis

NOTE Confidence: 0.9618782

00:24:01.664 --> 00:24:03.585 use disorder were recruited from

NOTE Confidence: 0.9618782

00:24:03.585 --> 00:24:05.605 the prevention and early intervention

NOTE Confidence: 0.9678585

00:24:05.984 --> 00:24:07.365 for psychosis program

NOTE Confidence: 0.9107786

00:24:07.759 --> 00:24:09.119 or PEP clinic in London,

NOTE Confidence: 0.9107786

00:24:09.119 --> 00:24:09.619 Ontario,

NOTE Confidence: 0.90149814

00:24:10.080 --> 00:24:11.440 and were within six months

NOTE Confidence: 0.90149814

00:24:11.440 --> 00:24:12.559 of entry to the program,

NOTE Confidence: 0.90149814

00:24:12.559 --> 00:24:13.600 so that's why we refer

NOTE Confidence: 0.90149814

00:24:13.600 --> 00:24:14.899 to them as first episode.

NOTE Confidence: 0.92336446

00:24:16.080 --> 00:24:17.919 Controls with and without cannabis

NOTE Confidence: 0.92336446

00:24:17.919 --> 00:24:19.600 use disorder were recruited from

NOTE Confidence: 0.92336446

00:24:19.600 --> 00:24:20.960 the community, and at one

NOTE Confidence: 0.92336446

00:24:20.960 --> 00:24:22.399 year we had thirty seven

NOTE Confidence: 0.92336446

00:24:22.399 --> 00:24:22.725 participants

NOTE Confidence: 0.7639057

00:24:23.845 --> 00:24:24.965 come back to redo all

NOTE Confidence: 0.7639057

00:24:24.965 --> 00:24:26.744 questionnaires, saliva, THC,

NOTE Confidence: 0.8843449

00:24:27.285 --> 00:24:28.277 and the MRI. And everyone

NOTE Confidence: 0.8843449

00:24:28.277 --> 00:24:29.924 who completed the follow-up did

NOTE Confidence: 0.8843449

00:24:30.164 --> 00:24:31.765 indeed have the same diagnosis

NOTE Confidence: 0.8843449

00:24:31.765 --> 00:24:33.145 that they had at baseline.

NOTE Confidence: 0.89418447

00:24:35.125 --> 00:24:36.184 Next slide.

NOTE Confidence: 0.7091786

00:24:36.885 --> 00:24:37.544 Next slide.

NOTE Confidence: 0.7652837

00:24:38.290 --> 00:24:39.030 Next slide.

NOTE Confidence: 0.7777555

00:24:39.970 --> 00:24:41.590 As they're excluding three participants

NOTE Confidence: 0.9184884

00:24:41.970 --> 00:24:43.750 due to MRI artifacts,

NOTE Confidence: 0.94353324

00:24:44.130 --> 00:24:45.330 we were left with thirty

NOTE Confidence: 0.94353324

00:24:45.330 --> 00:24:47.490 six individuals without a cannabis

NOTE Confidence: 0.94353324

00:24:47.490 --> 00:24:49.010 use disorder and twenty five

NOTE Confidence: 0.94353324

00:24:49.010 --> 00:24:50.550 with the cannabis use disorder.

NOTE Confidence: 0.90490067

00:24:51.725 --> 00:24:52.925 Here, I wanna highlight that

NOTE Confidence: 0.90490067

00:24:52.925 --> 00:24:54.625 the sample was mostly men

NOTE Confidence: 0.9581642

00:24:55.005 --> 00:24:56.465 and that there were numerically

NOTE Confidence: 0.9581642

00:24:56.685 --> 00:24:58.785 more first episode schizophrenia

NOTE Confidence: 0.94395125

00:24:59.165 --> 00:25:01.265 participants in the COD group.

NOTE Confidence: 0.99087536

00:25:01.725 --> 00:25:02.225 Additionally,

NOTE Confidence: 0.95915794

00:25:03.359 --> 00:25:05.280 CUD severity was collected based

NOTE Confidence: 0.95915794

00:25:05.280 --> 00:25:06.420 on the number of DSM

NOTE Confidence: 0.95915794

00:25:06.559 --> 00:25:08.480 symptoms for for CUD that

NOTE Confidence: 0.95915794

00:25:08.480 --> 00:25:10.320 participants met. So if they

NOTE Confidence: 0.95915794

00:25:10.320 --> 00:25:12.179 had two to three symptoms,

NOTE Confidence: 0.95915794

00:25:12.400 --> 00:25:14.320 they were classified as having

NOTE Confidence: 0.95915794

00:25:14.320 --> 00:25:15.299 a mild CUD,

NOTE Confidence: 0.9241884

00:25:16.145 --> 00:25:17.345 Four to five was moderate

NOTE Confidence: 0.9241884

00:25:17.345 --> 00:25:19.024 and more than six was

NOTE Confidence: 0.9241884

00:25:19.024 --> 00:25:19.524 severe.

NOTE Confidence: 0.9849625

00:25:19.904 --> 00:25:21.365 And just as a refresher,

NOTE Confidence: 0.9849625

00:25:21.664 --> 00:25:24.225 the DSM five defines cannabis

NOTE Confidence: 0.9849625

00:25:24.225 --> 00:25:25.765 use disorder as the presence

NOTE Confidence: 0.96484584

00:25:26.304 --> 00:25:28.465 of clinically significant impairment or

NOTE Confidence: 0.96484584

00:25:28.465 --> 00:25:30.320 distress in twelve months. So

NOTE Confidence: 0.96484584

00:25:30.320 --> 00:25:31.440 they have at least two

NOTE Confidence: 0.96484584

00:25:31.440 --> 00:25:33.440 of eleven symptoms including stuff

NOTE Confidence: 0.96484584

00:25:33.440 --> 00:25:34.820 like tolerance, withdrawal,

NOTE Confidence: 0.9542088

00:25:35.440 --> 00:25:36.480 trying to cut down but

NOTE Confidence: 0.9542088

00:25:36.480 --> 00:25:37.380 being unsuccessful,

NOTE Confidence: 0.9605492

00:25:38.560 --> 00:25:39.060 etcetera.

NOTE Confidence: 0.9957352

00:25:40.320 --> 00:25:41.140 Next slide.

NOTE Confidence: 0.9804761

00:25:43.415 --> 00:25:44.855 Here, I want to highlight

NOTE Confidence: 0.9804761

00:25:44.855 --> 00:25:46.475 that we're looking at participants

NOTE Confidence: 0.9804761

00:25:46.615 --> 00:25:47.835 in their early 20s.

NOTE Confidence: 0.9531843

00:25:49.015 --> 00:25:50.794 There was no significant differences

NOTE Confidence: 0.9531843

00:25:50.855 --> 00:25:52.135 found between the group with

NOTE Confidence: 0.9531843

00:25:52.135 --> 00:25:53.335 CUD and the group without

NOTE Confidence: 0.9531843

00:25:53.335 --> 00:25:55.174 CUD regarding sex, age, or

NOTE Confidence: 0.9531843

00:25:55.174 --> 00:25:56.155 years of education.

NOTE Confidence: 0.948279

00:25:56.920 --> 00:25:58.700 The COD group had significantly

NOTE Confidence: 0.948279

00:25:58.840 --> 00:26:01.180 lower premorbid IQ and category

NOTE Confidence: 0.948279

00:26:01.240 --> 00:26:03.420 fluency scores but higher nicotine

NOTE Confidence: 0.948279

00:26:03.480 --> 00:26:05.580 use and saliva THC levels.

NOTE Confidence: 0.9892228

00:26:06.760 --> 00:26:08.200 Those with COD scored a

NOTE Confidence: 0.9892228

00:26:08.200 --> 00:26:09.180 mean of

NOTE Confidence: 0.9669777

00:26:09.544 --> 00:26:10.825 ten point six of the

NOTE Confidence: 0.9669777

00:26:10.825 --> 00:26:12.105 possible twenty four on the

NOTE Confidence: 0.9669777

00:26:12.105 --> 00:26:12.605 cannabis

NOTE Confidence: 0.98903275

00:26:12.984 --> 00:26:14.125 substance use questionnaire

NOTE Confidence: 0.962128

00:26:15.145 --> 00:26:16.825 with a mean onset age

NOTE Confidence: 0.962128

00:26:16.825 --> 00:26:18.025 of around eighteen years, so

NOTE Confidence: 0.962128

00:26:18.025 --> 00:26:19.565 this suggests that most individuals

NOTE Confidence: 0.962128

00:26:19.705 --> 00:26:21.005 had a moderate dependence

NOTE Confidence: 0.94945174

00:26:21.544 --> 00:26:22.744 with less than ten years

NOTE Confidence: 0.94945174

00:26:22.744 --> 00:26:23.885 duration of use.

NOTE Confidence: 0.9883581

00:26:25.350 --> 00:26:26.090 Next slide.

NOTE Confidence: 0.9942918

00:26:27.750 --> 00:26:29.270 These are the results from

NOTE Confidence: 0.9942918

00:26:29.270 --> 00:26:30.950 just three specific questions on

NOTE Confidence: 0.9942918

00:26:30.950 --> 00:26:32.410 the substance use questionnaire.

NOTE Confidence: 0.94575614

00:26:33.030 --> 00:26:35.030 We feel this encapsulates the

NOTE Confidence: 0.94575614

00:26:35.030 --> 00:26:36.390 spread of cannabis use over

NOTE Confidence: 0.94575614

00:26:36.390 --> 00:26:37.770 the two groups quite nicely,

NOTE Confidence: 0.94575614

00:26:37.910 --> 00:26:39.450 so you can see that,

NOTE Confidence: 0.97649

00:26:40.125 --> 00:26:41.965 the participants without COD were

NOTE Confidence: 0.97649

00:26:41.965 --> 00:26:44.125 not cannabis naive and, therefore,

NOTE Confidence: 0.97649

00:26:44.125 --> 00:26:45.484 they're more representative of the

NOTE Confidence: 0.97649

00:26:45.484 --> 00:26:47.645 general population that shared many

NOTE Confidence: 0.97649

00:26:47.645 --> 00:26:48.145 characteristics

NOTE Confidence: 0.92750317

00:26:48.925 --> 00:26:50.045 of the with the group

NOTE Confidence: 0.92750317

00:26:50.045 --> 00:26:52.125 of participants with COD except

NOTE Confidence: 0.92750317

00:26:52.125 --> 00:26:53.565 they didn't have the COD

NOTE Confidence: 0.92750317

00:26:53.565 --> 00:26:54.065 status.

NOTE Confidence: 0.9880791

00:26:54.790 --> 00:26:56.010 And I want to specifically

NOTE Confidence: 0.9880791

00:26:56.230 --> 00:26:57.270 highlight that not a lot

NOTE Confidence: 0.9880791

00:26:57.270 --> 00:26:59.030 of COD participants believe that

NOTE Confidence: 0.9880791

00:26:59.030 --> 00:27:00.310 they ever had a problem

NOTE Confidence: 0.9880791

00:27:00.310 --> 00:27:01.690 due to their cannabis use,

NOTE Confidence: 0.9880791

00:27:01.910 --> 00:27:03.510 and this really suggests that

NOTE Confidence: 0.9880791

00:27:03.510 --> 00:27:04.950 there is quite a big

NOTE Confidence: 0.9880791

00:27:04.950 --> 00:27:07.430 disconnect between clinical diagnosis and

NOTE Confidence: 0.9880791

00:27:07.430 --> 00:27:09.290 subjective perception of harm.

NOTE Confidence: 0.78401005

00:27:10.994 --> 00:27:11.494 Okay.

NOTE Confidence: 0.9707011

00:27:12.435 --> 00:27:13.395 So before we look at

NOTE Confidence: 0.9707011

00:27:13.395 --> 00:27:14.915 our main results, I want

NOTE Confidence: 0.9707011

00:27:14.915 --> 00:27:16.855 to highlight two important,

NOTE Confidence: 0.9965778

00:27:17.635 --> 00:27:18.135 methodological

NOTE Confidence: 0.99434054

00:27:18.675 --> 00:27:19.795 choices that we made in

NOTE Confidence: 0.99434054

00:27:19.795 --> 00:27:20.455 this work.

NOTE Confidence: 0.9195819

00:27:21.155 --> 00:27:23.010 So first, we searched for

NOTE Confidence: 0.9195819

00:27:23.010 --> 00:27:24.930 voxels that were significantly related

NOTE Confidence: 0.9195819

00:27:24.930 --> 00:27:26.690 to cannabis use disorders in

NOTE Confidence: 0.9195819

00:27:26.690 --> 00:27:28.230 our sample of participants,

NOTE Confidence: 0.96726394

00:27:28.850 --> 00:27:30.630 and we did indeed find

NOTE Confidence: 0.96726394

00:27:30.850 --> 00:27:32.930 voxels that were significantly higher

NOTE Confidence: 0.96726394

00:27:32.930 --> 00:27:34.450 in those with COD compared

NOTE Confidence: 0.96726394

00:27:34.450 --> 00:27:35.350 to those without.

NOTE Confidence: 0.8150138

00:27:35.655 --> 00:27:36.855 So post talks, we called

NOTE Confidence: 0.8150138

00:27:36.855 --> 00:27:38.315 those COD voxels.

NOTE Confidence: 0.94489557

00:27:39.575 --> 00:27:41.195 Second, we chose to analyze

NOTE Confidence: 0.94489557

00:27:41.335 --> 00:27:43.255 a subset of voxels based

NOTE Confidence: 0.94489557

00:27:43.255 --> 00:27:45.355 on a previous neuromelanin study

NOTE Confidence: 0.94489557

00:27:45.575 --> 00:27:47.595 and examine the mean neuromelanin

NOTE Confidence: 0.94489557

00:27:47.815 --> 00:27:50.155 MRI signal for those specific

NOTE Confidence: 0.94489557

00:27:50.375 --> 00:27:51.390 SNVTA subsets.

NOTE Confidence: 0.8757568

00:27:52.670 --> 00:27:54.109 And here we chose an

NOTE Confidence: 0.8757568

00:27:54.109 --> 00:27:55.090 external source

NOTE Confidence: 0.9363138

00:27:55.630 --> 00:27:57.710 to determine the psychosis possible

NOTE Confidence: 0.9363138

00:27:57.710 --> 00:27:59.710 subset to prevent any, like,

NOTE Confidence: 0.9363138

00:27:59.710 --> 00:28:01.630 circular reasoning so that any

NOTE Confidence: 0.9363138

00:28:01.630 --> 00:28:04.045 evidence for convergence with psychosis

NOTE Confidence: 0.9363138

00:28:04.045 --> 00:28:05.565 is independent of our data

NOTE Confidence: 0.9363138

00:28:05.565 --> 00:28:07.425 set and comes from observations

NOTE Confidence: 0.95363724

00:28:08.045 --> 00:28:09.325 in individuals who have not

NOTE Confidence: 0.95363724

00:28:09.325 --> 00:28:10.145 taken medication.

NOTE Confidence: 0.99100095

00:28:10.605 --> 00:28:11.405 So you can see in

NOTE Confidence: 0.99100095

00:28:11.405 --> 00:28:12.145 this paper

NOTE Confidence: 0.952351

00:28:12.445 --> 00:28:13.244 here that,

NOTE Confidence: 0.9620497

00:28:14.285 --> 00:28:15.645 the subset of voxels was

NOTE Confidence: 0.9620497

00:28:15.645 --> 00:28:17.725 correlated with positive psychosis symptoms

NOTE Confidence: 0.9620497

00:28:17.725 --> 00:28:18.890 and unmedicated

NOTE Confidence: 0.98031527

00:28:19.830 --> 00:28:21.369 schizophrenia in the top

NOTE Confidence: 0.95371604

00:28:21.670 --> 00:28:23.590 and with positive symptoms and

NOTE Confidence: 0.95371604

00:28:23.590 --> 00:28:25.270 clinical high risk in the

NOTE Confidence: 0.95371604

00:28:25.270 --> 00:28:25.770 bottom.

NOTE Confidence: 0.9972578

00:28:26.630 --> 00:28:27.450 Next slide.

NOTE Confidence: 0.98483896

00:28:29.990 --> 00:28:31.670 So here are our main

NOTE Confidence: 0.98483896

00:28:31.670 --> 00:28:32.170 results.

NOTE Confidence: 0.8699634

00:28:33.785 --> 00:28:34.905 First, I wanna draw your

NOTE Confidence: 0.8699634

00:28:34.905 --> 00:28:36.684 attention to figure b,

NOTE Confidence: 0.7622311

00:28:38.345 --> 00:28:39.304 the the red one. Thank

NOTE Confidence: 0.7622311

00:28:39.304 --> 00:28:39.804 you.

NOTE Confidence: 0.98091227

00:28:40.424 --> 00:28:41.804 So on the y axis

NOTE Confidence: 0.98091227

00:28:41.945 --> 00:28:44.105 is the neuromelanin MRI signal

NOTE Confidence: 0.98091227

00:28:44.105 --> 00:28:45.405 of the COD voxels.

NOTE Confidence: 0.97124535

00:28:45.840 --> 00:28:47.360 So, again, those are voxels

NOTE Confidence: 0.97124535

00:28:47.360 --> 00:28:48.179 that are significantly

NOTE Confidence: 0.94789696

00:28:48.480 --> 00:28:50.340 higher in our CUD participants,

NOTE Confidence: 0.9690001

00:28:50.960 --> 00:28:51.919 and you can see that

NOTE Confidence: 0.9690001

00:28:51.919 --> 00:28:53.679 the signal is higher compared

NOTE Confidence: 0.9690001

00:28:53.679 --> 00:28:55.220 to the no CUD, control,

NOTE Confidence: 0.9690001

00:28:55.279 --> 00:28:57.200 and FES group, but that

NOTE Confidence: 0.9690001

00:28:57.200 --> 00:28:59.395 CUD and FES is numerically

NOTE Confidence: 0.9690001

00:28:59.535 --> 00:29:00.895 higher than just FES, so

NOTE Confidence: 0.9690001

00:29:00.895 --> 00:29:02.355 there's an additive effect.

NOTE Confidence: 0.9909787

00:29:04.174 --> 00:29:05.294 And this is likely due

NOTE Confidence: 0.9909787

00:29:05.294 --> 00:29:06.915 to our participants being medicated,

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NOTE Confidence: 0.9909787

00:29:07.135 --> 00:29:08.255 so they have low symptom

NOTE Confidence: 0.9909787

00:29:08.255 --> 00:29:08.755 burden.

NOTE Confidence: 0.93375194

00:29:10.430 --> 00:29:11.950 In B, we're looking at

NOTE Confidence: 0.93375194

00:29:11.950 --> 00:29:13.710 the neuromelanin MRI signal of

NOTE Confidence: 0.93375194

00:29:13.710 --> 00:29:15.710 the psychosis voxels, so this

NOTE Confidence: 0.93375194

00:29:15.710 --> 00:29:17.250 is from that external source,

NOTE Confidence: 0.98245543

00:29:17.630 --> 00:29:18.670 and we can see here

NOTE Confidence: 0.98245543

00:29:18.670 --> 00:29:20.290 that it is indeed higher,

NOTE Confidence: 0.9251782

00:29:21.150 --> 00:29:22.670 in the CZ group, but

NOTE Confidence: 0.9251782

00:29:22.670 --> 00:29:24.130 not in the FES group,

NOTE Confidence: 0.9251782

00:29:24.195 --> 00:29:25.554 And, again, this is because

NOTE Confidence: 0.9251782

00:29:25.554 --> 00:29:27.715 our participants were medicated, so

NOTE Confidence: 0.9251782

00:29:27.715 --> 00:29:29.255 they had low symptom burden.

NOTE Confidence: 0.934233

00:29:29.875 --> 00:29:30.995 There was also a small

NOTE Confidence: 0.934233

00:29:30.995 --> 00:29:32.355 number of voxels in each

NOTE Confidence: 0.934233

00:29:32.355 --> 00:29:34.215 group that had lower pneumonia

NOTE Confidence: 0.934233

00:29:34.274 --> 00:29:35.554 and MRI signal, but they

NOTE Confidence: 0.934233

00:29:35.554 --> 00:29:37.634 were not statistically significant, and

NOTE Confidence: 0.934233

00:29:37.634 --> 00:29:38.595 they're not shown in this

NOTE Confidence: 0.934233

00:29:38.595 --> 00:29:39.095 figure.

NOTE Confidence: 0.9664196

00:29:41.929 --> 00:29:42.429 Next.

NOTE Confidence: 0.8729337

00:29:43.690 --> 00:29:45.289 Similarly, if we look not

NOTE Confidence: 0.8729337

00:29:45.289 --> 00:29:46.889 just at the psychosis boxes

NOTE Confidence: 0.8729337

00:29:46.889 --> 00:29:48.909 but at the entire SNVTA,

NOTE Confidence: 0.96743417

00:29:49.850 --> 00:29:50.730 we do see a trend

NOTE Confidence: 0.96743417

00:29:50.730 --> 00:29:52.889 towards higher neuromelanin signal in

NOTE Confidence: 0.96743417

00:29:52.889 --> 00:29:54.669 the FES group after adjusting

NOTE Confidence: 0.96743417

00:29:54.705 --> 00:29:56.044 for COD. Likely,

NOTE Confidence: 0.9988332

00:29:57.424 --> 00:29:58.705 this is due to the

NOTE Confidence: 0.9988332

00:29:58.705 --> 00:29:59.205 blunting

NOTE Confidence: 0.9358658

00:29:59.745 --> 00:30:00.945 that the patients are on

NOTE Confidence: 0.9358658

00:30:00.945 --> 00:30:01.445 antipsychotics

NOTE Confidence: 0.76121217

00:30:02.144 --> 00:30:03.284 reducing their symptoms.

NOTE Confidence: 0.9924729

00:30:04.945 --> 00:30:05.765 Next slide.

NOTE Confidence: 0.9922354

00:30:07.820 --> 00:30:10.380 In the psychosis voxels, we

NOTE Confidence: 0.9922354

00:30:10.380 --> 00:30:12.240 found a significant association

NOTE Confidence: 0.85963374

00:30:12.700 --> 00:30:15.100 between normelanin MRI signal and

NOTE Confidence: 0.85963374

00:30:15.100 --> 00:30:16.080 COD severity

NOTE Confidence: 0.9282856

00:30:16.540 --> 00:30:18.700 with participants grouped as no

NOTE Confidence: 0.9282856

00:30:18.700 --> 00:30:20.460 COD, mild and moderate or

NOTE Confidence: 0.9282856

00:30:20.460 --> 00:30:20.960 severe.

NOTE Confidence: 0.9655973

00:30:21.394 --> 00:30:22.755 We chose these groupings to

NOTE Confidence: 0.9655973

00:30:22.755 --> 00:30:25.075 balance sample size across groups

NOTE Confidence: 0.9655973

00:30:25.075 --> 00:30:26.355 while still trying to preserve

NOTE Confidence: 0.9655973

00:30:26.355 --> 00:30:28.755 any meaningful distinctions between CUD

NOTE Confidence: 0.9655973

00:30:28.755 --> 00:30:29.255 severities.

NOTE Confidence: 0.99093807

00:30:29.635 --> 00:30:30.674 And we did find that

NOTE Confidence: 0.99093807

00:30:30.674 --> 00:30:32.514 most people who satisfy cannabis

NOTE Confidence: 0.99093807

00:30:32.514 --> 00:30:33.575 use disorder criteria

NOTE Confidence: 0.96047825

00:30:33.875 --> 00:30:35.154 appear to fall in the

NOTE Confidence: 0.96047825

00:30:35.154 --> 00:30:36.054 mild category.

NOTE Confidence: 0.9422863

00:30:36.910 --> 00:30:38.130 So previous research

NOTE Confidence: 0.82769924

00:30:38.510 --> 00:30:40.510 shows such as necessitate this

NOTE Confidence: 0.82769924

00:30:40.510 --> 00:30:41.870 majority to be considered as

NOTE Confidence: 0.82769924

00:30:41.870 --> 00:30:43.090 a separate group. Additionally,

NOTE Confidence: 0.96020055

00:30:44.350 --> 00:30:45.550 surveys have found that group

NOTE Confidence: 0.96020055

00:30:45.550 --> 00:30:46.910 being moderate and severe makes

NOTE Confidence: 0.96020055

00:30:46.910 --> 00:30:48.510 a subgroup with comparable size

NOTE Confidence: 0.96020055

00:30:48.510 --> 00:30:49.790 to mild CUD at the

NOTE Confidence: 0.96020055

00:30:49.790 --> 00:30:50.850 population level.

NOTE Confidence: 0.9903311

00:30:51.885 --> 00:30:53.345 And based on these results,

NOTE Confidence: 0.9903311

00:30:53.405 --> 00:30:55.325 the higher CUD severity is

NOTE Confidence: 0.9903311

00:30:55.325 --> 00:30:56.545 associated with

NOTE Confidence: 0.9187038

00:30:57.005 --> 00:30:58.865 higher psychosis blood flow signal.

NOTE Confidence: 0.9187038

00:30:59.085 --> 00:31:01.085 So, this indicates that an

NOTE Confidence: 0.9187038

00:31:01.085 --> 00:31:03.405 escalating severity of CUD may

NOTE Confidence: 0.9187038

00:31:03.405 --> 00:31:05.005 be associated with an increased

NOTE Confidence: 0.9187038

00:31:05.005 --> 00:31:06.180 neuromelanin signal

NOTE Confidence: 0.9922073

00:31:06.660 --> 00:31:08.180 in midbrain regions that are

NOTE Confidence: 0.9922073

00:31:08.180 --> 00:31:10.180 most sensitive to psychotic symptom

NOTE Confidence: 0.9922073

00:31:10.180 --> 00:31:10.680 burden.

NOTE Confidence: 0.9536005

00:31:14.100 --> 00:31:15.700 We also ran a mixed

NOTE Confidence: 0.9536005

00:31:15.700 --> 00:31:17.960 model analysis between voxel subsets

NOTE Confidence: 0.9536005

00:31:18.100 --> 00:31:19.780 and symptom scores and found

NOTE Confidence: 0.9536005

00:31:19.780 --> 00:31:22.044 a trend between mean neuromelanin

NOTE Confidence: 0.9536005

00:31:22.184 --> 00:31:24.365 MRI signals from COD voxels

NOTE Confidence: 0.8988539

00:31:24.745 --> 00:31:26.445 and PAM's negative scores,

NOTE Confidence: 0.9721764

00:31:26.904 --> 00:31:28.745 suggesting that even in treated

NOTE Confidence: 0.9721764

00:31:28.745 --> 00:31:30.924 individuals with schizophrenia, higher neurome-
lanin

NOTE Confidence: 0.9721764

00:31:31.145 --> 00:31:33.225 and cannabis related voxels may

NOTE Confidence: 0.9721764

00:31:33.225 --> 00:31:35.085 indicate higher negative symptoms.

NOTE Confidence: 0.93314517

00:31:36.090 --> 00:31:37.370 But here we didn't find

NOTE Confidence: 0.93314517

00:31:37.370 --> 00:31:38.750 any relationship between

NOTE Confidence: 0.97522664

00:31:39.370 --> 00:31:40.970 signal of the COD voxels

NOTE Confidence: 0.97522664

00:31:40.970 --> 00:31:42.490 and PANS positive or general

NOTE Confidence: 0.97522664

00:31:42.490 --> 00:31:42.990 symptoms

NOTE Confidence: 0.9239533

00:31:43.370 --> 00:31:45.370 nor psychosis voxels and any

NOTE Confidence: 0.9239533

00:31:45.370 --> 00:31:46.670 of the PANS subsets.

NOTE Confidence: 0.99311095

00:31:50.695 --> 00:31:52.955 Of course, certain limitations exist.

NOTE Confidence: 0.9924876

00:31:53.655 --> 00:31:55.515 As I explained earlier, neuromelanin

NOTE Confidence: 0.9648131

00:31:55.895 --> 00:31:57.495 increases with age, but our

NOTE Confidence: 0.9648131

00:31:57.495 --> 00:31:59.515 sample is relatively young,

NOTE Confidence: 0.96946824

00:31:59.815 --> 00:32:00.935 and we did look at

NOTE Confidence: 0.96946824

00:32:00.935 --> 00:32:02.535 change in neuromelanin over a

NOTE Confidence: 0.96946824

00:32:02.535 --> 00:32:03.895 one year period. Although we

NOTE Confidence: 0.96946824

00:32:03.895 --> 00:32:06.060 found nothing significant. This is

NOTE Confidence: 0.96946824

00:32:06.060 --> 00:32:07.180 likely due to the length

NOTE Confidence: 0.96946824

00:32:07.180 --> 00:32:08.000 of the follow-up.

NOTE Confidence: 0.93318796

00:32:09.020 --> 00:32:10.460 Our sample was small and

NOTE Confidence: 0.93318796

00:32:10.460 --> 00:32:12.060 were powered only to detect

NOTE Confidence: 0.93318796

00:32:12.060 --> 00:32:13.600 large effects over time.

NOTE Confidence: 0.99434894

00:32:14.700 --> 00:32:16.060 Participants did have a history

NOTE Confidence: 0.99434894

00:32:16.060 --> 00:32:18.060 of using other substances, although

NOTE Confidence: 0.99434894

00:32:18.060 --> 00:32:19.200 they did not have

NOTE Confidence: 0.916509

00:32:19.534 --> 00:32:21.075 current substance use disorders,

NOTE Confidence: 0.9560501

00:32:21.615 --> 00:32:23.554 and patients were taking antipsychotics,

NOTE Confidence: 0.9929306

00:32:23.855 --> 00:32:24.815 which we know act on

NOTE Confidence: 0.9929306

00:32:24.815 --> 00:32:25.955 the dopamine system.

NOTE Confidence: 0.9934679

00:32:26.894 --> 00:32:27.394 Additionally,

NOTE Confidence: 0.99433935

00:32:27.855 --> 00:32:28.735 we don't know if any

NOTE Confidence: 0.99433935

00:32:28.735 --> 00:32:29.715 changes in neuromelanin

NOTE Confidence: 0.9837069

00:32:30.015 --> 00:32:31.375 signal between groups are due

NOTE Confidence: 0.9837069

00:32:31.375 --> 00:32:32.335 to the CUD or if

NOTE Confidence: 0.9837069

00:32:32.335 --> 00:32:33.635 it's the other way around,

NOTE Confidence: 0.9837069

00:32:33.910 --> 00:32:35.270 but our study wasn't set

NOTE Confidence: 0.9837069

00:32:35.270 --> 00:32:35.990 up to be able to

NOTE Confidence: 0.9837069

00:32:35.990 --> 00:32:37.350 address that question. So these

NOTE Confidence: 0.9837069

00:32:37.350 --> 00:32:38.950 are all factors that need

NOTE Confidence: 0.9837069

00:32:38.950 --> 00:32:40.330 to be taken into consideration

NOTE Confidence: 0.9837069

00:32:40.470 --> 00:32:41.770 when looking at our findings.

NOTE Confidence: 0.97619855

00:32:42.230 --> 00:32:43.930 Oh, and this is from

NOTE Confidence: 0.97255284

00:32:44.390 --> 00:32:45.830 just ahead of this. This

NOTE Confidence: 0.97255284

00:32:45.830 --> 00:32:47.350 is from, a meta analysis

NOTE Confidence: 0.97255284

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00:32:47.350 --> 00:32:48.730 that we did last year

NOTE Confidence: 0.97255284

00:32:48.904 --> 00:32:50.284 looking at different substances,

NOTE Confidence: 0.9530705

00:32:51.304 --> 00:32:52.825 different substance use disorders in

NOTE Confidence: 0.9530705

00:32:52.825 --> 00:32:53.945 neuromyelanin, and you can see

NOTE Confidence: 0.9530705

00:32:53.945 --> 00:32:55.565 that it's very it differs,

NOTE Confidence: 0.9530705

00:32:55.625 --> 00:32:56.125 like,

NOTE Confidence: 0.9505528

00:32:56.825 --> 00:32:58.345 very much depending on the

NOTE Confidence: 0.9505528

00:32:58.345 --> 00:33:00.105 the substance. So that's another

NOTE Confidence: 0.9505528

00:33:00.105 --> 00:33:01.304 limit that adds to the

NOTE Confidence: 0.9505528

00:33:01.304 --> 00:33:03.304 limitations that participants use other

NOTE Confidence: 0.9505528

00:33:03.304 --> 00:33:03.804 substances.

NOTE Confidence: 0.9691787

00:33:05.030 --> 00:33:06.309 And with that, I'll pass

NOTE Confidence: 0.9691787

00:33:06.309 --> 00:33:07.830 it back to Lena for

NOTE Confidence: 0.9691787

00:33:07.830 --> 00:33:08.570 the conclusion.

NOTE Confidence: 0.4091209

00:33:17.025 --> 00:33:17.525 Can

NOTE Confidence: 0.98243666

00:33:19.345 --> 00:33:19.845 you

NOTE Confidence: 0.99729407

00:33:20.865 --> 00:33:21.525 hear me

NOTE Confidence: 0.94262815

00:33:21.905 --> 00:33:23.025 now? Thank you. Thank you,

NOTE Confidence: 0.94262815

00:33:23.025 --> 00:33:23.525 Jess.

NOTE Confidence: 0.9783016

00:33:24.145 --> 00:33:24.945 I have a couple of

NOTE Confidence: 0.9783016

00:33:24.945 --> 00:33:26.225 slides to reflect a little

NOTE Confidence: 0.9783016

00:33:26.225 --> 00:33:27.585 bit on the results that

NOTE Confidence: 0.9783016

00:33:27.585 --> 00:33:29.185 Jess showed us now.

NOTE Confidence: 0.91586864

00:33:29.585 --> 00:33:30.625 And after that, we'll take

NOTE Confidence: 0.91586864

00:33:30.625 --> 00:33:32.245 some questions if that's okay.

NOTE Confidence: 0.9814336

00:33:32.760 --> 00:33:34.280 So, what are the implications

NOTE Confidence: 0.9814336

00:33:34.280 --> 00:33:35.080 of this? You know, in

NOTE Confidence: 0.9814336

00:33:35.080 --> 00:33:37.240 this individual study, we did

NOTE Confidence: 0.9814336

00:33:37.240 --> 00:33:38.620 observe higher neuromelanin

NOTE Confidence: 0.91676885

00:33:39.000 --> 00:33:40.360 in people who use cannabis

NOTE Confidence: 0.91676885

00:33:40.360 --> 00:33:41.240 for a longer period of

NOTE Confidence: 0.91676885

00:33:41.240 --> 00:33:43.180 time. And the effect of

NOTE Confidence: 0.91676885

00:33:43.480 --> 00:33:45.420 cannabis on neuromelanin is particularly

NOTE Confidence: 0.91676885

00:33:45.480 --> 00:33:46.760 pronounced in people with first

NOTE Confidence: 0.91676885

00:33:46.760 --> 00:33:48.875 episode schizophrenia. The effect size

NOTE Confidence: 0.91676885

00:33:48.875 --> 00:33:50.635 is double. And this increase

NOTE Confidence: 0.91676885

00:33:50.635 --> 00:33:51.294 is happening

NOTE Confidence: 0.9879146

00:33:51.995 --> 00:33:53.054 in the same area

NOTE Confidence: 0.9830865

00:33:53.515 --> 00:33:55.695 where, if increase is present,

NOTE Confidence: 0.9830865

00:33:55.835 --> 00:33:57.595 it reflects higher severity of

NOTE Confidence: 0.9830865

00:33:57.595 --> 00:33:59.215 psychosis psychotic symptoms.

NOTE Confidence: 0.948046

00:33:59.515 --> 00:34:00.794 So this doesn't work well

NOTE Confidence: 0.948046

00:34:00.794 --> 00:34:01.695 for our patients.

NOTE Confidence: 0.9475947

00:34:02.110 --> 00:34:03.230 Clearly, one of the implication

NOTE Confidence: 0.9475947

00:34:03.230 --> 00:34:04.429 is people with the cannabis

NOTE Confidence: 0.9475947

00:34:04.429 --> 00:34:05.169 use disorder

NOTE Confidence: 0.7424167

00:34:05.470 --> 00:34:07.070 but with higher neuromelanin MRI

NOTE Confidence: 0.7424167

00:34:07.070 --> 00:34:07.570 signal,

NOTE Confidence: 0.98830426

00:34:08.190 --> 00:34:09.630 are having a problem that

NOTE Confidence: 0.98830426

00:34:09.630 --> 00:34:11.170 relates to expression of psychosis.

NOTE Confidence: 0.8150844

00:34:12.510 --> 00:34:13.170 So cannabis

NOTE Confidence: 0.9542893

00:34:13.469 --> 00:34:14.770 may affect the hypothesized

NOTE Confidence: 0.9641237

00:34:15.070 --> 00:34:16.985 final common pathway, which is

NOTE Confidence: 0.9641237

00:34:16.985 --> 00:34:19.225 dopaminergic pathway here for clinical

NOTE Confidence: 0.9641237

00:34:19.225 --> 00:34:20.285 expression of psychosis.

NOTE Confidence: 0.9179347

00:34:21.545 --> 00:34:22.745 You might have also seen

NOTE Confidence: 0.9179347

00:34:22.745 --> 00:34:24.025 that, there are, you know,

NOTE Confidence: 0.9179347

00:34:24.025 --> 00:34:24.925 in the larger

NOTE Confidence: 0.95266277

00:34:25.225 --> 00:34:26.265 mask where we did a

NOTE Confidence: 0.95266277

00:34:26.265 --> 00:34:28.445 search for neuromelaninib signal changes,

NOTE Confidence: 0.9992736

00:34:28.850 --> 00:34:29.750 we did see

NOTE Confidence: 0.9632617

00:34:30.050 --> 00:34:31.250 some some spots in the

NOTE Confidence: 0.9632617

00:34:31.250 --> 00:34:32.790 brain within the midbrain

NOTE Confidence: 0.9439479

00:34:33.410 --> 00:34:35.430 where CUD use was associated

NOTE Confidence: 0.9439479

00:34:35.570 --> 00:34:37.670 with lower neuromelanin signal.

NOTE Confidence: 0.98545367

00:34:38.050 --> 00:34:39.590 It wasn't statistically significant,

NOTE Confidence: 0.91344136

00:34:39.890 --> 00:34:41.410 but nevertheless, it is present

NOTE Confidence: 0.91344136

00:34:41.410 --> 00:34:42.690 in the CD users. There

NOTE Confidence: 0.91344136

00:34:42.690 --> 00:34:43.510 are some areas

NOTE Confidence: 0.9647764

00:34:43.985 --> 00:34:44.864 areas that are not so

NOTE Confidence: 0.9647764

00:34:44.864 --> 00:34:46.805 relevant for positive psychotic symptoms

NOTE Confidence: 0.9647764

00:34:46.945 --> 00:34:48.405 that are showing lower neuromelanin.

NOTE Confidence: 0.94405407

00:34:48.864 --> 00:34:49.905 What does it mean? Does

NOTE Confidence: 0.94405407

00:34:49.905 --> 00:34:50.565 it mean

NOTE Confidence: 0.92564857

00:34:50.864 --> 00:34:51.844 there is some neurodegeneration?

NOTE Confidence: 0.98112565

00:34:52.465 --> 00:34:53.344 This is a very young

NOTE Confidence: 0.98112565

00:34:53.344 --> 00:34:54.305 group. I would like to

NOTE Confidence: 0.98112565

00:34:54.305 --> 00:34:55.045 think not.

NOTE Confidence: 0.87344235

00:34:55.745 --> 00:34:57.025 But there is clearly a

NOTE Confidence: 0.87344235

00:34:57.025 --> 00:34:59.420 a mixed picture here. Increases

NOTE Confidence: 0.87344235

00:34:59.480 --> 00:35:01.640 happening where psychosis is where

NOTE Confidence: 0.87344235

00:35:01.640 --> 00:35:02.940 it is relevant for psychosis

NOTE Confidence: 0.8545388

00:35:03.239 --> 00:35:04.540 and there is some insignificant

NOTE Confidence: 0.9845033

00:35:05.079 --> 00:35:06.760 but notable drop happening in

NOTE Confidence: 0.9845033

00:35:06.760 --> 00:35:07.960 other places. We need to

NOTE Confidence: 0.9845033

00:35:07.960 --> 00:35:09.319 further examine this before we

NOTE Confidence: 0.9845033

00:35:09.319 --> 00:35:10.520 can be confident what this

NOTE Confidence: 0.9845033

00:35:10.520 --> 00:35:11.020 means.

NOTE Confidence: 0.9755842

00:35:12.984 --> 00:35:13.945 But I think what we

NOTE Confidence: 0.9755842

00:35:13.945 --> 00:35:14.744 have so far,

NOTE Confidence: 0.9679681

00:35:15.145 --> 00:35:16.585 helps us to come back

NOTE Confidence: 0.9679681

00:35:16.585 --> 00:35:17.964 to the question that I

NOTE Confidence: 0.9655801

00:35:18.265 --> 00:35:20.445 raised earlier, a clinical question.

NOTE Confidence: 0.9655801

84

00:35:20.665 --> 00:35:21.704 I think we have at

NOTE Confidence: 0.9655801

00:35:21.704 --> 00:35:23.484 least one study that can

NOTE Confidence: 0.9655801

00:35:23.545 --> 00:35:25.065 support you if you want

NOTE Confidence: 0.9655801

00:35:25.065 --> 00:35:26.719 to say there is likely

NOTE Confidence: 0.9655801

00:35:26.719 --> 00:35:27.859 a common alteration

NOTE Confidence: 0.96369475

00:35:28.239 --> 00:35:29.920 in the dopamine system in

NOTE Confidence: 0.96369475

00:35:29.920 --> 00:35:31.359 both cannabis users and people

NOTE Confidence: 0.96369475

00:35:31.359 --> 00:35:32.020 with psychosis.

NOTE Confidence: 0.96698284

00:35:32.799 --> 00:35:34.079 So the the line can

NOTE Confidence: 0.96698284

00:35:34.079 --> 00:35:35.140 be drawn between,

NOTE Confidence: 0.8815277

00:35:35.839 --> 00:35:36.339 dopamine,

NOTE Confidence: 0.8855602

00:35:38.094 --> 00:35:39.695 dope and dilutions, so to

NOTE Confidence: 0.8855602

00:35:39.695 --> 00:35:40.195 speak.

NOTE Confidence: 0.9284307

00:35:41.055 --> 00:35:41.935 Line may not be very

NOTE Confidence: 0.9284307

00:35:41.935 --> 00:35:43.135 thick as a single study.

NOTE Confidence: 0.9284307

00:35:43.135 --> 00:35:44.114 It has its limitations,

NOTE Confidence: 0.885851

00:35:44.415 --> 00:35:45.855 but nevertheless, a line can

NOTE Confidence: 0.885851

00:35:45.855 --> 00:35:46.515 be drawn.

NOTE Confidence: 0.9839417

00:35:46.895 --> 00:35:47.855 And, you know, I'll be

NOTE Confidence: 0.9839417

00:35:47.855 --> 00:35:49.535 more confident now to to

NOTE Confidence: 0.9839417

00:35:49.535 --> 00:35:50.495 talk to my patients and

NOTE Confidence: 0.9839417

00:35:50.495 --> 00:35:51.535 tell them if you're smoking

NOTE Confidence: 0.9839417

00:35:51.535 --> 00:35:53.070 weed for a while, which

NOTE Confidence: 0.9839417

00:35:53.070 --> 00:35:54.610 most of my patients are,

NOTE Confidence: 0.9393391

00:35:55.230 --> 00:35:56.430 then they're likely to have

NOTE Confidence: 0.9393391

00:35:56.430 --> 00:35:57.630 higher amount of dopamine in

NOTE Confidence: 0.9393391

00:35:57.630 --> 00:35:59.390 the same brine region where

NOTE Confidence: 0.9393391

00:35:59.390 --> 00:36:00.190 we don't want it to

NOTE Confidence: 0.9393391

00:36:00.190 --> 00:36:01.310 go up because if it

NOTE Confidence: 0.9393391

00:36:01.310 --> 00:36:02.989 goes up there, that relates

NOTE Confidence: 0.9393391

00:36:02.989 --> 00:36:03.969 to risk of psychosis,

NOTE Confidence: 0.93068844

00:36:04.350 --> 00:36:05.870 in particular symptoms of severity

NOTE Confidence: 0.93068844

00:36:05.870 --> 00:36:06.450 of psychosis.

NOTE Confidence: 0.9703914

00:36:07.295 --> 00:36:08.415 So this question can be

NOTE Confidence: 0.9703914

00:36:08.415 --> 00:36:09.795 answered with with some conviction

NOTE Confidence: 0.9703914

00:36:09.855 --> 00:36:10.835 now with our patients.

NOTE Confidence: 0.9556625

00:36:12.335 --> 00:36:13.055 But why don't we go

NOTE Confidence: 0.9556625

00:36:13.055 --> 00:36:14.175 next, when you, you know,

NOTE Confidence: 0.9556625

00:36:14.175 --> 00:36:15.135 when you have studies like

NOTE Confidence: 0.9556625

00:36:15.135 --> 00:36:16.895 this? I think, it's important

NOTE Confidence: 0.9556625

00:36:16.895 --> 00:36:18.175 to realize the limitations of

NOTE Confidence: 0.9556625

00:36:18.175 --> 00:36:19.375 every measurement that we do,

NOTE Confidence: 0.9556625

00:36:19.375 --> 00:36:21.315 clinical measurements as well as

NOTE Confidence: 0.9556625

00:36:21.579 --> 00:36:22.880 imaging measurements, and,

NOTE Confidence: 0.9746419

00:36:23.339 --> 00:36:24.619 just highlighted some of the

NOTE Confidence: 0.9746419

00:36:24.619 --> 00:36:26.299 technical challenges with it. So

NOTE Confidence: 0.9746419

00:36:26.299 --> 00:36:26.940 one of the things we're

NOTE Confidence: 0.9746419

00:36:26.940 --> 00:36:27.900 trying to do now is

NOTE Confidence: 0.9746419

00:36:27.900 --> 00:36:28.780 to see if we can

NOTE Confidence: 0.9746419

00:36:28.780 --> 00:36:30.140 have more sensitive measures of

NOTE Confidence: 0.9746419

00:36:30.140 --> 00:36:30.640 neuromelanin,

NOTE Confidence: 0.91059273

00:36:31.180 --> 00:36:32.380 especially can we use an

NOTE Confidence: 0.91059273

00:36:32.380 --> 00:36:35.020 external extrinsic magnetization transfer, MT

NOTE Confidence: 0.91059273

00:36:35.020 --> 00:36:36.505 pulse to to improve the

NOTE Confidence: 0.91059273

00:36:36.505 --> 00:36:38.205 definition of the area, SMBDA

NOTE Confidence: 0.91059273

00:36:38.265 --> 00:36:38.765 area,

NOTE Confidence: 0.94162494

00:36:39.465 --> 00:36:40.665 and really, like, pass them

NOTE Confidence: 0.94162494

00:36:40.665 --> 00:36:42.344 apart better so that our

NOTE Confidence: 0.94162494

00:36:42.344 --> 00:36:44.505 confidence in spatial precision can

NOTE Confidence: 0.94162494

00:36:44.505 --> 00:36:45.165 be improved.

NOTE Confidence: 0.9689479

00:36:45.785 --> 00:36:47.225 Secondly, we're also trying to,

NOTE Confidence: 0.9689479

00:36:47.465 --> 00:36:48.660 see if we can increase

NOTE Confidence: 0.9689479

00:36:48.719 --> 00:36:49.920 the the the amount of

NOTE Confidence: 0.9689479

00:36:49.920 --> 00:36:51.360 people that we follow-up over

NOTE Confidence: 0.9689479

00:36:51.360 --> 00:36:52.719 a period of time. As

NOTE Confidence: 0.9689479

00:36:52.719 --> 00:36:53.600 you might have seen in

NOTE Confidence: 0.9689479

00:36:53.600 --> 00:36:54.180 the flowchart,

NOTE Confidence: 0.8811113

00:36:54.560 --> 00:36:56.500 we were not blindly successful

NOTE Confidence: 0.8811113

00:36:56.640 --> 00:36:58.000 in following everybody up, and

NOTE Confidence: 0.8811113

00:36:58.000 --> 00:36:59.200 that's nature of the population

NOTE Confidence: 0.8811113

00:36:59.200 --> 00:37:00.739 we study first episode psychosis

NOTE Confidence: 0.8452508

00:37:01.280 --> 00:37:02.640 in a naturalistic study like

NOTE Confidence: 0.8452508

00:37:02.640 --> 00:37:04.415 this, especially with kambosine disease,

NOTE Confidence: 0.98904866

00:37:04.955 --> 00:37:06.155 tracking them back within a

NOTE Confidence: 0.98904866

00:37:06.155 --> 00:37:07.355 specific period of time is

NOTE Confidence: 0.98904866

00:37:07.355 --> 00:37:08.094 very hard.

NOTE Confidence: 0.98243886

00:37:08.555 --> 00:37:09.594 And we would also like

NOTE Confidence: 0.98243886

00:37:09.594 --> 00:37:10.875 to study older age groups

NOTE Confidence: 0.98243886

00:37:10.875 --> 00:37:11.695 because neuromelanin

NOTE Confidence: 0.9758964

00:37:12.795 --> 00:37:14.235 is an interesting signal, but

NOTE Confidence: 0.9758964

00:37:14.235 --> 00:37:16.250 it is sensitive to age

NOTE Confidence: 0.9758964

00:37:16.250 --> 00:37:17.930 in older cohorts, not in

NOTE Confidence: 0.9758964

00:37:17.930 --> 00:37:19.450 younger cohorts. In fact, if

NOTE Confidence: 0.9758964

00:37:19.450 --> 00:37:20.570 you wanna put a seventeen

NOTE Confidence: 0.9758964

00:37:20.570 --> 00:37:21.450 year old or a sixteen

NOTE Confidence: 0.9758964

00:37:21.450 --> 00:37:22.670 year old in the scanner,

NOTE Confidence: 0.9758964

00:37:22.890 --> 00:37:24.090 you cannot really get good

NOTE Confidence: 0.9758964

00:37:24.090 --> 00:37:25.530 neuromelanin signal at all because

NOTE Confidence: 0.9758964

00:37:25.530 --> 00:37:26.570 it takes some time for

NOTE Confidence: 0.9758964

00:37:26.570 --> 00:37:27.770 neuromelanin to build up in

NOTE Confidence: 0.9758964

00:37:27.770 --> 00:37:28.349 the brain,

NOTE Confidence: 0.9928879

00:37:28.650 --> 00:37:29.690 for us to define the

NOTE Confidence: 0.9928879

00:37:29.690 --> 00:37:30.190 signal.

NOTE Confidence: 0.979605

00:37:31.535 --> 00:37:32.575 So that's something we wanna

NOTE Confidence: 0.979605

00:37:32.575 --> 00:37:33.695 do, you know, later on,

NOTE Confidence: 0.979605

00:37:33.855 --> 00:37:34.895 older age groups to be

NOTE Confidence: 0.979605

00:37:34.895 --> 00:37:35.935 included in a study like

NOTE Confidence: 0.979605

00:37:35.935 --> 00:37:36.435 this.

NOTE Confidence: 0.9828543

00:37:37.055 --> 00:37:38.175 Third, we are quite interested

NOTE Confidence: 0.9828543

00:37:38.175 --> 00:37:39.215 in seeing what happens if

NOTE Confidence: 0.9828543

00:37:39.215 --> 00:37:40.655 people stop smoking weed for

NOTE Confidence: 0.9828543

00:37:40.655 --> 00:37:41.775 a period of time. If

NOTE Confidence: 0.9828543

00:37:41.775 --> 00:37:43.295 they stop for, let's say,

NOTE Confidence: 0.9828543

00:37:43.295 --> 00:37:44.035 six months,

NOTE Confidence: 0.95440215

00:37:44.710 --> 00:37:45.910 would that slow down the

NOTE Confidence: 0.95440215

00:37:45.910 --> 00:37:47.130 neuromelanin accumulation,

NOTE Confidence: 0.9684374

00:37:47.590 --> 00:37:48.870 if they already have psychotic

NOTE Confidence: 0.9684374

00:37:48.870 --> 00:37:50.310 symptoms? We know it helps

NOTE Confidence: 0.9684374

00:37:50.310 --> 00:37:51.430 with cognition. We know it

NOTE Confidence: 0.9684374

00:37:51.430 --> 00:37:52.950 helps with relapse risk, but

NOTE Confidence: 0.9684374

00:37:52.950 --> 00:37:53.910 can we show that it

NOTE Confidence: 0.9684374

00:37:53.910 --> 00:37:55.210 also helps with neuromelanin

NOTE Confidence: 0.9888659

00:37:55.510 --> 00:37:56.010 signal

NOTE Confidence: 0.9688475

00:37:56.469 --> 00:37:58.555 plateauing, not increasing further? It

NOTE Confidence: 0.9688475

00:37:58.555 --> 00:37:59.675 will increase in everyone, but

NOTE Confidence: 0.9688475

00:37:59.675 --> 00:38:00.555 we wanna show that people

NOTE Confidence: 0.9688475

00:38:00.555 --> 00:38:01.215 with abstinence

NOTE Confidence: 0.9947812

00:38:01.755 --> 00:38:03.435 have slower increase or flatter

NOTE Confidence: 0.9947812

00:38:03.435 --> 00:38:03.935 increase,

NOTE Confidence: 0.9637066

00:38:04.475 --> 00:38:05.695 which will help us to

NOTE Confidence: 0.9637066

00:38:05.835 --> 00:38:07.435 make causal claims with more

NOTE Confidence: 0.9637066

00:38:07.435 --> 00:38:07.935 confidence.

NOTE Confidence: 0.96483344

00:38:08.795 --> 00:38:09.675 And we also have this

NOTE Confidence: 0.96483344

00:38:09.675 --> 00:38:11.275 little pet peeve. Somehow, we

NOTE Confidence: 0.96483344

00:38:11.275 --> 00:38:11.850 want to

NOTE Confidence: 0.98523927

00:38:12.489 --> 00:38:12.989 record,

NOTE Confidence: 0.9469555

00:38:13.530 --> 00:38:15.450 locus coeruleus signals as well

NOTE Confidence: 0.9469555

00:38:15.450 --> 00:38:17.150 because the signal of neuromelanin

NOTE Confidence: 0.9469555

00:38:17.370 --> 00:38:18.970 in locus coeruleus reflects more

NOTE Confidence: 0.9469555

00:38:18.970 --> 00:38:19.550 of norepinephrine

NOTE Confidence: 0.94638175

00:38:19.850 --> 00:38:21.530 levels than dopamine levels. So

NOTE Confidence: 0.94638175

00:38:21.530 --> 00:38:22.170 we would like to be

NOTE Confidence: 0.94638175

00:38:22.170 --> 00:38:23.690 doubly sure that what we

NOTE Confidence: 0.94638175

00:38:23.690 --> 00:38:24.810 see is not simply an

NOTE Confidence: 0.94638175

00:38:24.810 --> 00:38:26.510 artifact of our imaging technology.

NOTE Confidence: 0.94638175

00:38:26.650 --> 00:38:28.224 It's really document. So we

NOTE Confidence: 0.94638175

00:38:28.224 --> 00:38:30.224 wanna separate the, cannabis effect

NOTE Confidence: 0.94638175

00:38:30.224 --> 00:38:31.445 between locus and

NOTE Confidence: 0.92597926

00:38:33.425 --> 00:38:34.964 substantia nigra in the future.

NOTE Confidence: 0.95956266

00:38:36.305 --> 00:38:38.145 Well, that's that's probably it.

NOTE Confidence: 0.95956266

00:38:38.385 --> 00:38:39.025 This is all we have

NOTE Confidence: 0.95956266

00:38:39.025 --> 00:38:39.825 to say, and I wanna

NOTE Confidence: 0.95956266

00:38:39.825 --> 00:38:41.470 thank, all the patients as

NOTE Confidence: 0.95956266

00:38:41.470 --> 00:38:42.670 well, who took part on

NOTE Confidence: 0.95956266

00:38:42.670 --> 00:38:43.470 the study and all these

NOTE Confidence: 0.95956266

00:38:43.470 --> 00:38:44.290 funding agencies,

NOTE Confidence: 0.9330727

00:38:45.070 --> 00:38:45.950 and all the partners that

NOTE Confidence: 0.9330727

00:38:45.950 --> 00:38:47.710 you saw, our collaborators, especially

NOTE Confidence: 0.9330727

00:38:47.710 --> 00:38:49.970 Cliff Cassidy. His technology was

NOTE Confidence: 0.9330727

00:38:50.190 --> 00:38:51.470 very helpful for us to

NOTE Confidence: 0.9330727

00:38:51.470 --> 00:38:52.190 to do what we did,

NOTE Confidence: 0.9330727

00:38:52.190 --> 00:38:53.730 and and Phil Tibogo, who

NOTE Confidence: 0.9360035

00:38:54.414 --> 00:38:55.454 is a co partner in

NOTE Confidence: 0.9360035

00:38:55.535 --> 00:38:57.214 partner in crime for getting

NOTE Confidence: 0.9360035

00:38:57.214 --> 00:38:58.335 this funding and getting this

NOTE Confidence: 0.9360035

94

00:38:58.335 --> 00:38:58.815 question,

NOTE Confidence: 0.93842965

00:38:59.135 --> 00:39:00.575 asked in this study. So

NOTE Confidence: 0.93842965

00:39:00.575 --> 00:39:01.454 thank you very much. We

NOTE Confidence: 0.93842965

00:39:01.454 --> 00:39:02.734 are here to take questions

NOTE Confidence: 0.93842965

00:39:02.734 --> 00:39:04.275 and discuss this further.

NOTE Confidence: 0.81556576

00:39:08.690 --> 00:39:10.869 Thanks, Jess and Lina, for,

NOTE Confidence: 0.7888752

00:39:12.049 --> 00:39:13.190 wonderful presentation.

NOTE Confidence: 0.9563907

00:39:13.569 --> 00:39:14.230 You know,

NOTE Confidence: 0.99915785

00:39:14.690 --> 00:39:16.450 this is the first study

NOTE Confidence: 0.99915785

00:39:16.450 --> 00:39:17.190 looking at

NOTE Confidence: 0.88974935

00:39:17.650 --> 00:39:18.150 neuromelanin,

NOTE Confidence: 0.871216

00:39:18.930 --> 00:39:20.549 in cannabis use in psychosis.

NOTE Confidence: 0.93649215

00:39:20.849 --> 00:39:21.349 So,

NOTE Confidence: 0.9912911

00:39:22.015 --> 00:39:23.135 I wanna open it up

NOTE Confidence: 0.9912911

00:39:23.135 --> 00:39:23.855 to the floor.

NOTE Confidence: 0.97512746

00:39:24.175 --> 00:39:25.855 Anyone has questions, feel free

NOTE Confidence: 0.97512746

00:39:25.855 --> 00:39:27.155 to unmute and

NOTE Confidence: 0.9446817

00:39:27.614 --> 00:39:29.215 ask a question. Or if

NOTE Confidence: 0.9446817

00:39:29.215 --> 00:39:30.415 you'd like to, you can

NOTE Confidence: 0.9446817

00:39:30.415 --> 00:39:32.255 type your question in the

NOTE Confidence: 0.9446817

00:39:32.255 --> 00:39:33.455 chat and I can repeat

NOTE Confidence: 0.9446817

00:39:33.455 --> 00:39:33.955 it.

NOTE Confidence: 0.87507707

00:39:34.950 --> 00:39:35.670 Can I ask you a

NOTE Confidence: 0.87507707

00:39:35.670 --> 00:39:36.170 question?

NOTE Confidence: 0.7669227

00:39:36.630 --> 00:39:38.570 Sure. Hi. I'm Nikkole,

NOTE Confidence: 0.8899993

00:39:39.349 --> 00:39:41.050 Rakesh Lab, Yale University.

NOTE Confidence: 0.96548253

00:39:41.430 --> 00:39:42.890 I'm just curious to know,

NOTE Confidence: 0.9865355

00:39:43.270 --> 00:39:44.570 if we have data,

NOTE Confidence: 0.6560228

00:39:46.710 --> 00:39:47.190 with,

NOTE Confidence: 0.92499834

00:39:48.565 --> 00:39:49.864 patients with Parkinson's

NOTE Confidence: 0.9170128

00:39:50.165 --> 00:39:52.165 disease treated with HCC. I

NOTE Confidence: 0.9170128

00:39:52.165 --> 00:39:53.364 mean, I assume that, you

NOTE Confidence: 0.9170128

00:39:53.364 --> 00:39:54.585 know, if you have Parkinson's

NOTE Confidence: 0.9170128

00:39:54.645 --> 00:39:56.665 problem, you don't develop psychosis,

NOTE Confidence: 0.8838841

00:39:57.125 --> 00:39:58.985 but even after, you know,

NOTE Confidence: 0.8838841

00:39:59.045 --> 00:39:59.525 a lot of,

NOTE Confidence: 0.873005

00:40:00.165 --> 00:40:00.825 you know,

NOTE Confidence: 0.8986762

00:40:02.500 --> 00:40:04.420 after exposure to high dose

NOTE Confidence: 0.8986762

00:40:04.420 --> 00:40:05.000 of THC?

NOTE Confidence: 0.89691013

00:40:06.500 --> 00:40:07.720 I mean, you know,

NOTE Confidence: 0.7154869

00:40:08.260 --> 00:40:09.720 the the immune system is

NOTE Confidence: 0.8358669

00:40:10.500 --> 00:40:12.500 is affected in Parkinson's disease.

NOTE Confidence: 0.8358669

00:40:12.500 --> 00:40:13.700 So so what happened to

NOTE Confidence: 0.8358669

00:40:13.700 --> 00:40:14.440 those people?

NOTE Confidence: 0.94263196

00:40:16.935 --> 00:40:18.135 Thank you for that question,

NOTE Confidence: 0.94263196

00:40:18.135 --> 00:40:19.094 Nicola. I think it's very

NOTE Confidence: 0.94263196

00:40:19.094 --> 00:40:20.715 interesting. What happens to Parkinson's

NOTE Confidence: 0.94263196

00:40:20.935 --> 00:40:22.295 people in terms of the

NOTE Confidence: 0.94263196

00:40:22.295 --> 00:40:23.915 relationship between dopamine and psychosis?

NOTE Confidence: 0.94263196

00:40:24.055 --> 00:40:25.655 Right. I'll let Jessica tell

NOTE Confidence: 0.94263196

00:40:25.655 --> 00:40:26.795 a little bit about neuromalin

NOTE Confidence: 0.94263196

00:40:26.855 --> 00:40:28.375 studies in in Parkinson's, but

NOTE Confidence: 0.94263196

00:40:28.375 --> 00:40:29.495 I would just make two

NOTE Confidence: 0.94263196

00:40:29.495 --> 00:40:31.094 very quick comments on psychosis

NOTE Confidence: 0.94263196

00:40:31.094 --> 00:40:31.755 and Parkinson's.

NOTE Confidence: 0.92657524

00:40:32.750 --> 00:40:33.950 Parkinson's increases the risk of

NOTE Confidence: 0.92657524

00:40:33.950 --> 00:40:36.130 psychosis, actually. People with Parkinson's

NOTE Confidence: 0.92657524

00:40:36.190 --> 00:40:37.950 disease develop psychotic symptoms, but

NOTE Confidence: 0.92657524

00:40:37.950 --> 00:40:39.309 generally at a later stage

NOTE Confidence: 0.92657524

00:40:39.309 --> 00:40:40.589 of the illness, after much

NOTE Confidence: 0.92657524

00:40:40.589 --> 00:40:41.089 neurodegeneration

NOTE Confidence: 0.9186573

00:40:41.469 --> 00:40:42.989 has happened, not as first

NOTE Confidence: 0.9186573

00:40:42.989 --> 00:40:43.489 presentation,

NOTE Confidence: 0.88144004

00:40:43.790 --> 00:40:45.170 usually as later presentation.

NOTE Confidence: 0.9470986

00:40:45.765 --> 00:40:47.145 And also due to iatrogenic

NOTE Confidence: 0.9470986

00:40:47.364 --> 00:40:48.484 effects, the drugs that we

NOTE Confidence: 0.9470986

00:40:48.484 --> 00:40:49.924 use to treat Parkinson's like

NOTE Confidence: 0.9470986

00:40:49.924 --> 00:40:50.424 levodopa

NOTE Confidence: 0.9277048

00:40:51.045 --> 00:40:52.325 itself can increase the risk

NOTE Confidence: 0.9277048

00:40:52.325 --> 00:40:52.984 of hallucinations

NOTE Confidence: 0.9026425

00:40:53.285 --> 00:40:54.645 and and even delusions in

NOTE Confidence: 0.9026425

00:40:54.645 --> 00:40:55.625 in in some patients.

NOTE Confidence: 0.9117826

00:40:56.085 --> 00:40:57.684 So, yeah, definitely there is

NOTE Confidence: 0.9117826

00:40:57.684 --> 00:40:58.579 a link. But what do

NOTE Confidence: 0.9117826

00:40:58.579 --> 00:40:59.900 we know about dopamine in

NOTE Confidence: 0.9117826

00:40:59.900 --> 00:41:01.599 in Parkinson's may not match

NOTE Confidence: 0.9117826

00:41:01.739 --> 00:41:03.180 clearly with what we've just

NOTE Confidence: 0.9117826

00:41:03.180 --> 00:41:04.559 shown in nonorganic

NOTE Confidence: 0.9614875

00:41:05.260 --> 00:41:07.440 functional psychotic patients here? And

NOTE Confidence: 0.9614875

00:41:07.500 --> 00:41:08.219 Jess will tell you a

NOTE Confidence: 0.9614875

00:41:08.219 --> 00:41:09.660 little bit about neuromelanin studies

NOTE Confidence: 0.9614875

00:41:09.660 --> 00:41:10.400 in Parkinson's.

NOTE Confidence: 0.9911521

00:41:11.165 --> 00:41:11.484 Yep.

NOTE Confidence: 0.98312175

00:41:12.205 --> 00:41:14.785 Most neuromelanin studies actually are,

NOTE Confidence: 0.9611238

00:41:15.484 --> 00:41:17.244 done in the Parkinson's population,

NOTE Confidence: 0.9611238

00:41:17.244 --> 00:41:18.605 so there's a lot of,

NOTE Confidence: 0.9611238

00:41:18.925 --> 00:41:20.224 research on that.

NOTE Confidence: 0.99091464

00:41:21.165 --> 00:41:22.685 There is a decrease in

NOTE Confidence: 0.99091464

00:41:22.685 --> 00:41:23.185 neuromelanin,

NOTE Confidence: 0.9802831

00:41:23.565 --> 00:41:24.844 but it's actually thought to

NOTE Confidence: 0.9802831

00:41:24.844 --> 00:41:25.469 be that

NOTE Confidence: 0.9526881

00:41:26.030 --> 00:41:27.710 neuromelanin accumulates too much and

NOTE Confidence: 0.9526881

00:41:27.710 --> 00:41:28.989 then the cells die and

NOTE Confidence: 0.9526881

100

00:41:28.989 --> 00:41:30.030 that's why we're seeing the

NOTE Confidence: 0.9526881

00:41:30.030 --> 00:41:30.530 decrease.

NOTE Confidence: 0.87048286

00:41:33.230 --> 00:41:34.030 I I don't know if

NOTE Confidence: 0.87048286

00:41:34.030 --> 00:41:35.390 there's anything you wanna add,

NOTE Confidence: 0.87048286

00:41:35.390 --> 00:41:35.890 Lana.

NOTE Confidence: 0.93041253

00:41:36.430 --> 00:41:37.890 Yeah. That's that's probably true.

NOTE Confidence: 0.93041253

00:41:38.030 --> 00:41:38.530 So

NOTE Confidence: 0.92531025

00:41:39.550 --> 00:41:40.930 there's a reduction in neuromelanin

NOTE Confidence: 0.92531025

00:41:41.150 --> 00:41:42.844 that been shown in Parkinson's

NOTE Confidence: 0.92531025

00:41:42.905 --> 00:41:44.205 patients. In fact, there's no

NOTE Confidence: 0.95722365

00:41:44.585 --> 00:41:46.445 no MRI study has documented

NOTE Confidence: 0.95722365

00:41:46.505 --> 00:41:47.645 any increase in the neuromelanin

NOTE Confidence: 0.95722365

00:41:47.864 --> 00:41:49.065 at all in Parkinson's. There's

NOTE Confidence: 0.95722365

00:41:49.065 --> 00:41:51.065 postmortem studies where early stage

NOTE Confidence: 0.95722365

00:41:51.065 --> 00:41:53.400 Parkinson's have shown signals of,

NOTE Confidence: 0.95722365

00:41:53.640 --> 00:41:54.680 in in some neurons, there

NOTE Confidence: 0.95722365

00:41:54.680 --> 00:41:55.719 is a signal of increased

NOTE Confidence: 0.95722365

00:41:55.719 --> 00:41:57.640 neuromelanin, but larger effect is

NOTE Confidence: 0.95722365

00:41:57.640 --> 00:41:58.839 a reduction of neuromelanin in

NOTE Confidence: 0.95722365

00:41:58.839 --> 00:42:00.359 Parkinson's. And every MRI study

NOTE Confidence: 0.95722365

00:42:00.359 --> 00:42:01.799 has shown the same reduction

NOTE Confidence: 0.95722365

00:42:01.799 --> 00:42:02.460 of neuromelanin.

NOTE Confidence: 0.93423295

00:42:03.480 --> 00:42:05.000 So Parkinson's psychosis may not

NOTE Confidence: 0.93423295

00:42:05.000 --> 00:42:06.200 be explained by increase in

NOTE Confidence: 0.93423295

00:42:06.200 --> 00:42:06.700 neuromelanin,

NOTE Confidence: 0.8708228

00:42:07.160 --> 00:42:08.299 so to speak. I see.

NOTE Confidence: 0.9875016

00:42:09.525 --> 00:42:10.964 There's a question by Marjorie.

NOTE Confidence: 0.9875016

00:42:10.964 --> 00:42:12.085 Marjorie, do you wanna ask

NOTE Confidence: 0.9875016

00:42:12.085 --> 00:42:13.364 your question, or do you

NOTE Confidence: 0.9875016

00:42:13.364 --> 00:42:14.325 want me to just read

NOTE Confidence: 0.9875016

00:42:14.325 --> 00:42:15.065 out your question

NOTE Confidence: 0.994723

00:42:15.765 --> 00:42:16.744 from the chat?

NOTE Confidence: 0.969796

00:42:17.605 --> 00:42:18.964 No. Sure. Hi. My name

NOTE Confidence: 0.969796

00:42:18.964 --> 00:42:19.704 is Marjorie.

NOTE Confidence: 0.9789757

00:42:20.085 --> 00:42:21.204 I'm a nurse. I'm from

NOTE Confidence: 0.9789757

00:42:21.204 --> 00:42:22.184 VCU Health.

NOTE Confidence: 0.9712484

00:42:23.339 --> 00:42:25.099 So, yes, as I'm listening

NOTE Confidence: 0.9712484

00:42:25.099 --> 00:42:26.000 to all this,

NOTE Confidence: 0.98098075

00:42:27.099 --> 00:42:28.619 it's really interesting. Thank you

NOTE Confidence: 0.98098075

00:42:28.619 --> 00:42:29.900 all for your time and

NOTE Confidence: 0.98098075

00:42:29.900 --> 00:42:31.339 for, you know, for,

NOTE Confidence: 0.95933396

00:42:31.660 --> 00:42:33.500 presenting, giving us this knowledge

NOTE Confidence: 0.95933396

00:42:33.500 --> 00:42:34.319 to consider.

NOTE Confidence: 0.9394087

00:42:35.545 --> 00:42:37.305 Just wondering when it comes

NOTE Confidence: 0.9394087

00:42:37.305 --> 00:42:39.305 to other substances, and we

NOTE Confidence: 0.9394087

00:42:39.305 --> 00:42:40.265 we work, of course, with

NOTE Confidence: 0.9394087

00:42:40.265 --> 00:42:41.625 lots of patients with opioid

NOTE Confidence: 0.9394087

00:42:41.625 --> 00:42:42.445 use disorder,

NOTE Confidence: 0.94782645

00:42:43.305 --> 00:42:44.825 some treated, some that aren't

NOTE Confidence: 0.94782645

00:42:44.825 --> 00:42:45.965 on treatment yet.

NOTE Confidence: 0.94351834

00:42:46.425 --> 00:42:47.885 So just wanted to know

NOTE Confidence: 0.94351834

00:42:48.140 --> 00:42:49.040 if the dopamine

NOTE Confidence: 0.9334648

00:42:49.739 --> 00:42:51.660 surge that people on other

NOTE Confidence: 0.9334648

00:42:51.660 --> 00:42:52.940 substances and, of course, I'm

NOTE Confidence: 0.9334648

00:42:52.940 --> 00:42:54.480 really thinking about opioids.

NOTE Confidence: 0.9342496

00:42:56.219 --> 00:42:57.200 Does that also,

NOTE Confidence: 0.9863168

00:42:59.180 --> 00:43:00.075 do the same thing as

NOTE Confidence: 0.9863168

00:43:00.234 --> 00:43:02.015 cannabis as far as increasing

NOTE Confidence: 0.97109973

00:43:02.315 --> 00:43:04.474 dopamine in that particular part

NOTE Confidence: 0.97109973

00:43:04.474 --> 00:43:05.375 of the brain?

NOTE Confidence: 0.91834956

00:43:07.114 --> 00:43:08.555 Because I think again, are

NOTE Confidence: 0.91834956

00:43:08.555 --> 00:43:10.094 are they also now preemptively

NOTE Confidence: 0.98879516

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00:43:10.875 --> 00:43:13.055 a precursor for psychosis development?

NOTE Confidence: 0.94172037

00:43:15.819 --> 00:43:17.020 Yeah. Thanks for the question,

NOTE Confidence: 0.94172037

00:43:17.579 --> 00:43:19.099 Marjorie. Just spent eighteen months

NOTE Confidence: 0.94172037

00:43:19.099 --> 00:43:19.900 of her life trying to

NOTE Confidence: 0.94172037

00:43:19.900 --> 00:43:21.099 answer this question, so I

NOTE Confidence: 0.94172037

00:43:21.099 --> 00:43:21.900 will let her tell you

NOTE Confidence: 0.94172037

00:43:21.900 --> 00:43:23.119 the findings she has.

NOTE Confidence: 0.997314

00:43:24.140 --> 00:43:24.960 Thank you.

NOTE Confidence: 0.88720024

00:43:26.859 --> 00:43:27.739 Yeah. So,

NOTE Confidence: 0.9408817

00:43:29.805 --> 00:43:31.484 from what I Lana can

NOTE Confidence: 0.9408817

00:43:31.484 --> 00:43:33.025 can totally correct me,

NOTE Confidence: 0.997595

00:43:33.645 --> 00:43:35.025 but I believe that opioids

NOTE Confidence: 0.997595

00:43:35.244 --> 00:43:35.744 inhibit

NOTE Confidence: 0.9479787

00:43:36.125 --> 00:43:38.045 the GABA neurons in the

NOTE Confidence: 0.9479787

00:43:38.045 --> 00:43:38.545 VTA.

NOTE Confidence: 0.9516775

00:43:39.085 --> 00:43:40.765 So then there's increased dopamine

105

NOTE Confidence: 0.9516775

00:43:40.765 --> 00:43:42.125 release in the striatum that

NOTE Confidence: 0.9516775

00:43:42.125 --> 00:43:42.625 way,

NOTE Confidence: 0.95753485

00:43:44.349 --> 00:43:45.710 which means that there would

NOTE Confidence: 0.95753485

00:43:45.710 --> 00:43:46.210 be,

NOTE Confidence: 0.9045367

00:43:47.230 --> 00:43:48.829 with chronic opioid use, there's

NOTE Confidence: 0.9045367

00:43:48.829 --> 00:43:50.450 increased dromelanin levels,

NOTE Confidence: 0.9558764

00:43:51.150 --> 00:43:52.609 so definitely a similar

NOTE Confidence: 0.9203121

00:43:53.150 --> 00:43:54.530 situation happening there.

NOTE Confidence: 0.93439233

00:43:57.265 --> 00:43:58.065 Yeah. Just to add to

NOTE Confidence: 0.93439233

00:43:58.065 --> 00:43:59.585 that, you know, but imaging

NOTE Confidence: 0.93439233

00:43:59.585 --> 00:44:01.105 studies, the meta analysis that,

NOTE Confidence: 0.93439233

00:44:01.344 --> 00:44:02.945 just showed, we looked at

NOTE Confidence: 0.93439233

00:44:02.945 --> 00:44:04.625 all the different substance uses

NOTE Confidence: 0.93439233

00:44:04.625 --> 00:44:06.385 like cocaine use, you know,

NOTE Confidence: 0.93439233

00:44:06.385 --> 00:44:07.984 cannabis, including cannabis and other

NOTE Confidence: 0.93439233

00:44:07.984 --> 00:44:09.205 substances as well.

NOTE Confidence: 0.97011495

00:44:09.719 --> 00:44:11.420 There is no convincing evidence

NOTE Confidence: 0.97011495

00:44:11.480 --> 00:44:13.480 demonstrated in clinical samples that

NOTE Confidence: 0.97011495

00:44:13.480 --> 00:44:13.980 neuromelanin

NOTE Confidence: 0.8332077

00:44:14.280 --> 00:44:16.200 goes up in any other

NOTE Confidence: 0.8332077

00:44:16.200 --> 00:44:17.800 substance users yet. So, you

NOTE Confidence: 0.8332077

00:44:17.800 --> 00:44:19.080 know, the the medicines we

NOTE Confidence: 0.8332077

00:44:19.080 --> 00:44:20.360 showed was really like null

NOTE Confidence: 0.8332077

00:44:20.360 --> 00:44:20.860 result.

NOTE Confidence: 0.97742283

00:44:21.800 --> 00:44:22.760 Part of the problem is

NOTE Confidence: 0.97742283

00:44:22.760 --> 00:44:24.300 studies are very insufficiently

NOTE Confidence: 0.7487593

00:44:24.600 --> 00:44:25.100 sampled.

NOTE Confidence: 0.92766947

00:44:26.175 --> 00:44:27.535 Power is very low to

NOTE Confidence: 0.92766947

00:44:27.535 --> 00:44:29.235 to demonstrate something like this.

NOTE Confidence: 0.92766947

00:44:29.455 --> 00:44:31.295 We need more evidence to

NOTE Confidence: 0.92766947

00:44:31.295 --> 00:44:32.255 to really like answer this

NOTE Confidence: 0.92766947

00:44:32.255 --> 00:44:33.395 question with any conviction.

NOTE Confidence: 0.97927284

00:44:34.015 --> 00:44:35.215 Mhmm. Okay. Thank you so

NOTE Confidence: 0.97927284

00:44:35.215 --> 00:44:35.715 much.

NOTE Confidence: 0.93955773

00:44:36.815 --> 00:44:38.094 And there's a question by

NOTE Confidence: 0.93955773

00:44:38.094 --> 00:44:39.935 Cameron Davidson. Cameron, do you

NOTE Confidence: 0.93955773

00:44:39.935 --> 00:44:41.500 wanna ask a question or

NOTE Confidence: 0.93955773

00:44:41.500 --> 00:44:42.880 would you like go ahead.

NOTE Confidence: 0.98298395

00:44:43.259 --> 00:44:44.239 Sure. Absolutely.

NOTE Confidence: 0.9846306

00:44:45.259 --> 00:44:46.940 First off, interesting presentation. Thank

NOTE Confidence: 0.9846306

00:44:46.940 --> 00:44:49.119 you. Good good presentation overall.

NOTE Confidence: 0.8837869

00:44:49.980 --> 00:44:51.119 My question is like,

NOTE Confidence: 0.9394105

00:44:51.420 --> 00:44:52.799 is more of a fundamental

NOTE Confidence: 0.9394105

00:44:52.859 --> 00:44:54.799 question about your perception of

NOTE Confidence: 0.97298163

00:44:55.224 --> 00:44:56.925 of this effect. Is this,

NOTE Confidence: 0.9726086

00:44:57.785 --> 00:44:58.744 do you believe that this

NOTE Confidence: 0.9726086

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00:44:58.744 --> 00:44:59.244 is,

NOTE Confidence: 0.9972545

00:45:01.785 --> 00:45:04.204 partially related to genetic predisposition

NOTE Confidence: 0.97117144

00:45:04.585 --> 00:45:06.185 and that those are those

NOTE Confidence: 0.97117144

00:45:06.185 --> 00:45:08.105 who are more predisposed are

NOTE Confidence: 0.97117144

00:45:08.105 --> 00:45:09.300 more likely to get it?

NOTE Confidence: 0.97117144

00:45:09.380 --> 00:45:10.340 Or do you think that

NOTE Confidence: 0.97117144

00:45:10.340 --> 00:45:12.420 eventually, even neurotypical people who

NOTE Confidence: 0.97117144

00:45:12.420 --> 00:45:13.800 have maybe some resistance

NOTE Confidence: 0.99279106

00:45:14.260 --> 00:45:15.380 to this interference with the

NOTE Confidence: 0.99279106

00:45:15.380 --> 00:45:16.900 dopaminergic system, do you think

NOTE Confidence: 0.99279106

00:45:16.900 --> 00:45:18.660 that they would eventually develop

NOTE Confidence: 0.99279106

00:45:18.660 --> 00:45:19.160 this,

NOTE Confidence: 0.99920577

00:45:20.020 --> 00:45:21.315 based upon enough

NOTE Confidence: 0.85217905

00:45:21.875 --> 00:45:23.875 extreme use and for the

NOTE Confidence: 0.85217905

00:45:23.875 --> 00:45:25.335 long enough duration. Is

NOTE Confidence: 0.91490436

00:45:25.714 --> 00:45:26.835 that sort of the argument

NOTE Confidence: 0.91490436

00:45:26.835 --> 00:45:27.635 that you're making or is

NOTE Confidence: 0.91490436

00:45:27.635 --> 00:45:28.135 it

NOTE Confidence: 0.98285

00:45:28.435 --> 00:45:29.734 we're capturing the predisposition

NOTE Confidence: 0.92742336

00:45:30.675 --> 00:45:31.954 at least in this study

NOTE Confidence: 0.92742336

00:45:31.954 --> 00:45:32.614 and then,

NOTE Confidence: 0.97917557

00:45:33.714 --> 00:45:34.675 looking at it in a

NOTE Confidence: 0.97917557

00:45:34.675 --> 00:45:35.494 different way?

NOTE Confidence: 0.98333627

00:45:37.230 --> 00:45:39.170 That's a very thoughtful question,

NOTE Confidence: 0.95132244

00:45:39.550 --> 00:45:40.590 Cameron. So if I if

NOTE Confidence: 0.95132244

00:45:40.590 --> 00:45:42.290 I understand correctly, you

NOTE Confidence: 0.9956254

00:45:42.830 --> 00:45:43.650 you're thinking

NOTE Confidence: 0.9750932

00:45:44.270 --> 00:45:45.469 there may be some people

NOTE Confidence: 0.9750932

00:45:45.469 --> 00:45:46.850 who are using cannabis

NOTE Confidence: 0.9635431

00:45:47.310 --> 00:45:48.190 for a long period of

NOTE Confidence: 0.9635431

00:45:48.190 --> 00:45:49.364 time. They may not show

NOTE Confidence: 0.9635431

110

00:45:49.364 --> 00:45:50.985 any dopamine excess, no neuromelan

NOTE Confidence: 0.9635431

00:45:51.045 --> 00:45:52.325 excess, but they may still

NOTE Confidence: 0.9635431

00:45:52.325 --> 00:45:53.945 develop psychosis because

NOTE Confidence: 0.98369086

00:45:54.485 --> 00:45:55.785 they, they have alternate

NOTE Confidence: 0.9540629

00:45:56.085 --> 00:45:57.765 mechanisms to develop psychosis. Is

NOTE Confidence: 0.9540629

00:45:57.765 --> 00:45:59.285 that right? Correct. That that's

NOTE Confidence: 0.9540629

00:45:59.285 --> 00:46:00.085 part of it as well.

NOTE Confidence: 0.9540629

00:46:00.085 --> 00:46:01.525 That's that's part of it

NOTE Confidence: 0.9540629

00:46:01.525 --> 00:46:02.619 as well as may it

NOTE Confidence: 0.9540629

00:46:02.619 --> 00:46:04.380 may not be dopamine related

NOTE Confidence: 0.9540629

00:46:04.380 --> 00:46:05.580 psychosis. It might be something

NOTE Confidence: 0.9540629

00:46:05.580 --> 00:46:06.400 else. But,

NOTE Confidence: 0.9252944

00:46:07.500 --> 00:46:08.780 my question is is is

NOTE Confidence: 0.9252944

00:46:08.780 --> 00:46:10.060 it just the interference with

NOTE Confidence: 0.9252944

00:46:10.060 --> 00:46:10.719 the system

NOTE Confidence: 0.9452217

00:46:11.340 --> 00:46:12.619 that eventually leads to this

NOTE Confidence: 0.9452217

00:46:12.619 --> 00:46:13.660 or are there do you

NOTE Confidence: 0.9452217

00:46:13.660 --> 00:46:14.540 believe that there might be

NOTE Confidence: 0.9452217

00:46:14.540 --> 00:46:15.894 individuals who might be maybe

NOTE Confidence: 0.9452217

00:46:15.894 --> 00:46:17.255 resistant or resilient to this

NOTE Confidence: 0.9452217

00:46:17.255 --> 00:46:17.994 type of

NOTE Confidence: 0.9922297

00:46:18.454 --> 00:46:19.194 dopaminergic interaction?

NOTE Confidence: 0.9731187

00:46:20.135 --> 00:46:21.255 Yeah. That's, you know, I

NOTE Confidence: 0.9731187

00:46:21.335 --> 00:46:22.535 I'm talking deeply about it,

NOTE Confidence: 0.9731187

00:46:22.535 --> 00:46:23.414 but that's that's really a

NOTE Confidence: 0.9731187

00:46:23.414 --> 00:46:24.375 good point. I mean, one

NOTE Confidence: 0.9731187

00:46:24.375 --> 00:46:25.494 thing to think about,

NOTE Confidence: 0.906059

00:46:26.214 --> 00:46:27.035 here is,

NOTE Confidence: 0.95410985

00:46:28.460 --> 00:46:30.219 is dopamine essential? Is dopamine

NOTE Confidence: 0.95410985

00:46:30.219 --> 00:46:31.519 excess essential for psychosis?

NOTE Confidence: 0.9925462

00:46:32.059 --> 00:46:32.779 I think if you look

NOTE Confidence: 0.9925462

00:46:32.779 --> 00:46:33.819 at all of these final

NOTE Confidence: 0.9925462

00:46:33.819 --> 00:46:35.119 common pathway arguments,

NOTE Confidence: 0.9606812

00:46:35.579 --> 00:46:36.940 the arguments take the tone

NOTE Confidence: 0.9606812

00:46:36.940 --> 00:46:37.980 that you need to have

NOTE Confidence: 0.9606812

00:46:37.980 --> 00:46:39.339 some level of dopamine excess

NOTE Confidence: 0.9606812

00:46:39.339 --> 00:46:40.779 to develop psychotic symptoms in

NOTE Confidence: 0.9606812

00:46:40.779 --> 00:46:42.545 the first place. But notwithstanding

NOTE Confidence: 0.9606812

00:46:42.684 --> 00:46:44.605 all that arguments, you actually

NOTE Confidence: 0.9606812

00:46:44.605 --> 00:46:45.805 see a substantial number of

NOTE Confidence: 0.9606812

00:46:45.805 --> 00:46:47.344 people not responding to antipsychotics,

NOTE Confidence: 0.9606812

00:46:47.484 --> 00:46:49.665 not responding to dopamine manipulation

NOTE Confidence: 0.9606812

00:46:49.724 --> 00:46:50.844 in any way and and

NOTE Confidence: 0.9606812

00:46:50.844 --> 00:46:52.684 not developing psychotic episodes after

NOTE Confidence: 0.9606812

00:46:52.684 --> 00:46:54.045 taking, you know, dopamine releasing

NOTE Confidence: 0.9606812

00:46:54.045 --> 00:46:56.180 substances like cocaine and whatnot.

NOTE Confidence: 0.9160079

00:46:56.480 --> 00:46:58.079 So there's clearly an alternate

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NOTE Confidence: 0.9160079

00:46:58.079 --> 00:46:59.520 pathway to psychosis that has

NOTE Confidence: 0.9160079

00:46:59.520 --> 00:47:00.640 nothing to do with dopamine,

NOTE Confidence: 0.9160079

00:47:00.640 --> 00:47:01.760 I would say, from from

NOTE Confidence: 0.9160079

00:47:01.760 --> 00:47:02.980 what we know so far.

NOTE Confidence: 0.9160079

00:47:03.040 --> 00:47:04.160 What the pathway is a

NOTE Confidence: 0.9160079

00:47:04.160 --> 00:47:05.440 million dollar question. I think,

NOTE Confidence: 0.9160079

00:47:05.440 --> 00:47:06.500 you know, part of us

NOTE Confidence: 0.9160079

00:47:06.560 --> 00:47:07.785 are trying to answer that.

NOTE Confidence: 0.9160079

00:47:08.025 --> 00:47:08.905 And what kind of is

NOTE Confidence: 0.9160079

00:47:08.905 --> 00:47:09.864 addressed to that pathway will

NOTE Confidence: 0.9160079

00:47:09.864 --> 00:47:10.744 only become clear if you

NOTE Confidence: 0.9160079

00:47:10.744 --> 00:47:11.944 know what pathway we're talking

NOTE Confidence: 0.9160079

00:47:11.944 --> 00:47:13.885 about other than the document.

NOTE Confidence: 0.91579163

00:47:14.344 --> 00:47:15.785 So I I completely agree

NOTE Confidence: 0.91579163

00:47:15.785 --> 00:47:17.224 with your it's sympathized with

NOTE Confidence: 0.91579163

114

00:47:17.224 --> 00:47:18.344 your sentiments, but I don't

NOTE Confidence: 0.91579163

00:47:18.344 --> 00:47:19.305 think any of us have

NOTE Confidence: 0.91579163

00:47:19.305 --> 00:47:20.585 good answer for for that

NOTE Confidence: 0.91579163

00:47:20.585 --> 00:47:21.244 at the moment.

NOTE Confidence: 0.9800264

00:47:21.680 --> 00:47:23.120 Sorry. I just wanted to

NOTE Confidence: 0.9800264

00:47:23.120 --> 00:47:24.580 ask the, of course, fundamental

NOTE Confidence: 0.9800264

00:47:24.640 --> 00:47:26.320 question or philosophical question. Thank

NOTE Confidence: 0.9800264

00:47:26.320 --> 00:47:27.220 you for your answer.

NOTE Confidence: 0.9792289

00:47:29.360 --> 00:47:30.720 Sydney, you have a question.

NOTE Confidence: 0.9792289

00:47:30.720 --> 00:47:31.920 Would you like to ask

NOTE Confidence: 0.9792289

00:47:31.920 --> 00:47:32.420 it?

NOTE Confidence: 0.8799472

00:47:37.025 --> 00:47:37.525 Oh,

NOTE Confidence: 0.9889523

00:47:38.224 --> 00:47:39.664 so the question that Sydney

NOTE Confidence: 0.9889523

00:47:39.664 --> 00:47:41.105 has is, is there any

NOTE Confidence: 0.9889523

00:47:41.105 --> 00:47:42.625 information regarding the effect of

NOTE Confidence: 0.9889523

00:47:42.625 --> 00:47:44.405 the method of cannabis use,

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NOTE Confidence: 0.9521734

00:47:46.305 --> 00:47:48.085 or the percentage of THC

NOTE Confidence: 0.9521734

00:47:48.145 --> 00:47:48.724 in products

NOTE Confidence: 0.89175546

00:47:49.680 --> 00:47:51.619 in relation to symptoms, diagnoses

NOTE Confidence: 0.90033484

00:47:52.000 --> 00:47:52.819 of psychosis?

NOTE Confidence: 0.8930506

00:47:54.239 --> 00:47:55.359 Cyril, you may be able

NOTE Confidence: 0.8930506

00:47:55.359 --> 00:47:56.319 to answer that question better

NOTE Confidence: 0.8930506

00:47:56.319 --> 00:47:57.680 than anyone else. I've already

NOTE Confidence: 0.8930506

00:47:57.680 --> 00:47:58.980 acknowledged your face.

NOTE Confidence: 0.96374714

00:47:59.680 --> 00:48:00.960 Sure. Sure. So I think

NOTE Confidence: 0.96374714

00:48:00.960 --> 00:48:02.880 there's pretty convincing evidence that,

NOTE Confidence: 0.9124136

00:48:04.235 --> 00:48:06.155 the THC content of of

NOTE Confidence: 0.9124136

00:48:06.155 --> 00:48:07.675 cannabis is what's really critical.

NOTE Confidence: 0.9124136

00:48:07.675 --> 00:48:08.575 There have been epidemiological

NOTE Confidence: 0.83916044

00:48:09.114 --> 00:48:10.635 studies shown by, you know,

NOTE Confidence: 0.83916044

00:48:10.635 --> 00:48:12.335 Marta De Forti et al.

NOTE Confidence: 0.77341247

00:48:12.715 --> 00:48:14.335 And publishing Lancet Psychiatry

NOTE Confidence: 0.8816896

00:48:14.875 --> 00:48:15.695 showing that

NOTE Confidence: 0.9884145

00:48:16.560 --> 00:48:17.520 if you use,

NOTE Confidence: 0.9654426

00:48:17.840 --> 00:48:19.600 high potency cannabis and by

NOTE Confidence: 0.9654426

00:48:19.600 --> 00:48:21.440 the way, high potency cannabis

NOTE Confidence: 0.9654426

00:48:21.440 --> 00:48:23.120 in that study was ten

NOTE Confidence: 0.9654426

00:48:23.120 --> 00:48:24.640 percent THC, which we now

NOTE Confidence: 0.9654426

00:48:24.640 --> 00:48:26.100 know is pretty weak cannabis

NOTE Confidence: 0.97612774

00:48:26.480 --> 00:48:27.780 in this day and age.

NOTE Confidence: 0.97612774

00:48:27.840 --> 00:48:28.880 But if you used high

NOTE Confidence: 0.97612774

00:48:28.880 --> 00:48:30.640 potency cannabis and you used

NOTE Confidence: 0.97612774

00:48:30.640 --> 00:48:31.300 it daily,

NOTE Confidence: 0.9970122

00:48:31.665 --> 00:48:33.425 your risk of schizophrenia was

NOTE Confidence: 0.9970122

00:48:33.425 --> 00:48:34.545 six times higher than if

NOTE Confidence: 0.9970122

00:48:34.545 --> 00:48:35.825 you didn't use cannabis at

NOTE Confidence: 0.9970122

00:48:35.825 --> 00:48:36.325 all.

NOTE Confidence: 0.9027128

00:48:36.785 --> 00:48:38.245 So there is an information

NOTE Confidence: 0.9027128

00:48:38.305 --> 00:48:39.665 about that. The,

NOTE Confidence: 0.9957247

00:48:40.545 --> 00:48:41.585 you know, the effect of

NOTE Confidence: 0.9957247

00:48:41.585 --> 00:48:43.364 CBD is an intriguing one.

NOTE Confidence: 0.95815516

00:48:43.839 --> 00:48:45.680 There's some studies suggesting that

NOTE Confidence: 0.95815516

00:48:45.680 --> 00:48:47.460 CBD may even have antipsychotic

NOTE Confidence: 0.92055357

00:48:47.760 --> 00:48:48.660 effects, but,

NOTE Confidence: 0.97025436

00:48:49.280 --> 00:48:50.480 I think the jury is

NOTE Confidence: 0.97025436

00:48:50.480 --> 00:48:51.780 still out there. Some studies

NOTE Confidence: 0.97025436

00:48:51.839 --> 00:48:53.520 suggesting that, but other studies

NOTE Confidence: 0.97025436

00:48:53.520 --> 00:48:54.180 not showing,

NOTE Confidence: 0.9579357

00:48:54.800 --> 00:48:56.099 not showing that. So,

NOTE Confidence: 0.97352695

00:48:57.215 --> 00:48:58.495 so, yeah, I hope I

NOTE Confidence: 0.97352695

00:48:58.495 --> 00:48:59.475 answered that question.

NOTE Confidence: 0.972795

00:49:00.655 --> 00:49:02.415 If you can indulge me,

NOTE Confidence: 0.95669305

00:49:02.975 --> 00:49:04.575 Lena and Jess, I have

NOTE Confidence: 0.95669305

00:49:04.575 --> 00:49:05.695 a few questions of my

NOTE Confidence: 0.95669305

00:49:05.695 --> 00:49:06.835 own. One would be

NOTE Confidence: 0.9685606

00:49:07.215 --> 00:49:08.415 one is more a suggestion

NOTE Confidence: 0.9685606

00:49:08.415 --> 00:49:09.455 than anything. I think it's

NOTE Confidence: 0.9685606

00:49:09.455 --> 00:49:10.655 really cool that you're thinking

NOTE Confidence: 0.9685606

00:49:10.655 --> 00:49:11.155 about,

NOTE Confidence: 0.9808245

00:49:12.270 --> 00:49:13.550 about looking at what happens

NOTE Confidence: 0.9808245

00:49:13.550 --> 00:49:15.230 when people abstain from using

NOTE Confidence: 0.9808245

00:49:15.230 --> 00:49:15.730 cannabis.

NOTE Confidence: 0.96815425

00:49:16.110 --> 00:49:17.550 What happens to neuromelan, and

NOTE Confidence: 0.96815425

00:49:17.550 --> 00:49:18.690 is it something reversible?

NOTE Confidence: 0.97029376

00:49:19.150 --> 00:49:20.830 I would also suggest that

NOTE Confidence: 0.97029376

00:49:20.830 --> 00:49:22.510 you consider the the opposite,

NOTE Confidence: 0.97029376

00:49:22.510 --> 00:49:23.870 which is some of the

NOTE Confidence: 0.97029376

00:49:23.870 --> 00:49:25.390 subjects who are not using

NOTE Confidence: 0.97029376

00:49:25.390 --> 00:49:25.890 cannabis

NOTE Confidence: 0.97008336

00:49:26.225 --> 00:49:27.665 are likely to start using

NOTE Confidence: 0.97008336

00:49:27.665 --> 00:49:28.885 cannabis in the future.

NOTE Confidence: 0.84317464

00:49:29.265 --> 00:49:30.385 And so that would be

NOTE Confidence: 0.84317464

00:49:30.385 --> 00:49:31.445 that if the mirror,

NOTE Confidence: 0.9207256

00:49:31.985 --> 00:49:33.765 image of an abstinence study,

NOTE Confidence: 0.9207256

00:49:33.985 --> 00:49:35.285 so what happens to

NOTE Confidence: 0.9070933

00:49:35.585 --> 00:49:36.945 someone who's not using, who

NOTE Confidence: 0.9070933

00:49:36.945 --> 00:49:38.305 starts using, what happens to

NOTE Confidence: 0.9070933

00:49:38.305 --> 00:49:40.245 neuromelanin in in those subjects.

NOTE Confidence: 0.9583713

00:49:40.640 --> 00:49:42.000 That's so that's a suggestion

NOTE Confidence: 0.9583713

00:49:42.000 --> 00:49:42.900 that I would consider.

NOTE Confidence: 0.9421375

00:49:44.000 --> 00:49:44.719 My question,

NOTE Confidence: 0.9923264

00:49:45.200 --> 00:49:46.239 or my comment has to

NOTE Confidence: 0.9923264

00:49:46.239 --> 00:49:47.360 do with the role of

NOTE Confidence: 0.9923264

00:49:47.360 --> 00:49:47.860 dopamine,

NOTE Confidence: 0.96420234

00:49:48.560 --> 00:49:49.540 and in

NOTE Confidence: 0.9809648

00:49:49.840 --> 00:49:51.540 in cannabis related psychosis.

NOTE Confidence: 0.9980502

00:49:52.239 --> 00:49:52.739 So

NOTE Confidence: 0.87152094

00:49:53.335 --> 00:49:54.135 when you look at the

NOTE Confidence: 0.87152094

00:49:54.135 --> 00:49:54.875 PET studies,

NOTE Confidence: 0.95671225

00:49:55.895 --> 00:49:57.575 the PET studies have fairly

NOTE Confidence: 0.95671225

00:49:57.575 --> 00:49:58.075 mixed,

NOTE Confidence: 0.96805894

00:49:58.855 --> 00:50:00.375 results. There's some studies that

NOTE Confidence: 0.96805894

00:50:00.375 --> 00:50:01.035 have shown

NOTE Confidence: 0.98882324

00:50:01.495 --> 00:50:03.355 some small increase in dopamine

NOTE Confidence: 0.98882324

00:50:03.415 --> 00:50:04.715 release, other studies

NOTE Confidence: 0.95342237

00:50:05.270 --> 00:50:06.469 showing no change,

NOTE Confidence: 0.9718012

00:50:06.869 --> 00:50:07.530 at all,

NOTE Confidence: 0.9545748

00:50:08.469 --> 00:50:08.969 and,

NOTE Confidence: 0.9910022

00:50:09.910 --> 00:50:11.270 and clearly not anywhere in

NOTE Confidence: 0.9910022

00:50:11.270 --> 00:50:12.390 the range of what,

NOTE Confidence: 0.9261498

00:50:12.790 --> 00:50:13.910 what happens when you give

NOTE Confidence: 0.9261498

00:50:13.910 --> 00:50:15.849 someone say dopamine amphetamines

NOTE Confidence: 0.9620954

00:50:16.230 --> 00:50:17.450 or or a stimulant.

NOTE Confidence: 0.9762748

00:50:18.535 --> 00:50:19.815 And then in our hands,

NOTE Confidence: 0.9762748

00:50:19.815 --> 00:50:21.495 we found that in the

NOTE Confidence: 0.9762748

00:50:21.495 --> 00:50:23.035 experimental study that,

NOTE Confidence: 0.9964882

00:50:23.495 --> 00:50:24.155 the sister

NOTE Confidence: 0.9575096

00:50:24.614 --> 00:50:26.215 experimental study that you showed

NOTE Confidence: 0.9575096

00:50:26.215 --> 00:50:27.655 here where we gave,

NOTE Confidence: 0.96239895

00:50:28.055 --> 00:50:29.035 people with schizophrenia,

NOTE Confidence: 0.92763495

00:50:29.415 --> 00:50:30.535 invited them to take part

NOTE Confidence: 0.92763495

00:50:30.535 --> 00:50:31.415 in the study where they

NOTE Confidence: 0.92763495

00:50:31.415 --> 00:50:32.315 received THC.

NOTE Confidence: 0.99586487

00:50:32.775 --> 00:50:34.430 We found that treatment with

NOTE Confidence: 0.99586487

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00:50:34.430 --> 00:50:34.930 dopamine

NOTE Confidence: 0.994379

00:50:35.230 --> 00:50:35.730 antagonists

NOTE Confidence: 0.96611506

00:50:37.550 --> 00:50:38.610 did not blunt

NOTE Confidence: 0.9984036

00:50:39.070 --> 00:50:39.570 the

NOTE Confidence: 0.98138916

00:50:39.950 --> 00:50:41.470 effect of THC. So that

NOTE Confidence: 0.98138916

00:50:41.470 --> 00:50:42.930 was in people with schizophrenia.

NOTE Confidence: 0.99518746

00:50:43.470 --> 00:50:44.350 And then we did a

NOTE Confidence: 0.99518746

00:50:44.350 --> 00:50:46.370 follow-up study in healthy individuals

NOTE Confidence: 0.99518746

00:50:46.590 --> 00:50:47.730 where we gave them

NOTE Confidence: 0.9233211

00:50:48.114 --> 00:50:48.614 haloperidone,

NOTE Confidence: 0.9004634

00:50:48.915 --> 00:50:51.015 the prototypical tip, antipsychotic

NOTE Confidence: 0.9327867

00:50:51.875 --> 00:50:52.755 to see whether it would

NOTE Confidence: 0.9327867

00:50:52.755 --> 00:50:54.455 block the effects of THC.

NOTE Confidence: 0.9327867

00:50:54.515 --> 00:50:55.955 And we we really didn't

NOTE Confidence: 0.9327867

00:50:55.955 --> 00:50:56.855 find that convincing,

NOTE Confidence: 0.9713159

00:50:58.114 --> 00:50:59.715 you know, effect. So I'd

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NOTE Confidence: 0.9713159

00:50:59.715 --> 00:51:01.570 like you to, to comment

NOTE Confidence: 0.9713159

00:51:01.570 --> 00:51:02.930 a little more on on

NOTE Confidence: 0.9713159

00:51:02.930 --> 00:51:04.770 on dopamine as being central

NOTE Confidence: 0.9713159

00:51:04.770 --> 00:51:05.510 to the,

NOTE Confidence: 0.93852556

00:51:06.050 --> 00:51:07.890 to the psychosis like effects

NOTE Confidence: 0.93852556

00:51:07.890 --> 00:51:08.790 of of THC.

NOTE Confidence: 0.8746964

00:51:09.410 --> 00:51:11.250 Yeah. That's, that's great,

NOTE Confidence: 0.9157694

00:51:11.969 --> 00:51:13.010 points to rely. I have

NOTE Confidence: 0.9157694

00:51:13.010 --> 00:51:14.050 to look up those studies

NOTE Confidence: 0.9157694

00:51:14.050 --> 00:51:14.930 that you mentioned in more

NOTE Confidence: 0.9157694

00:51:14.930 --> 00:51:16.635 detail, but fascinating to see

NOTE Confidence: 0.9058501

00:51:17.175 --> 00:51:17.675 antipsychotics

NOTE Confidence: 0.9915457

00:51:17.975 --> 00:51:19.995 do not alleviate or nullify,

NOTE Confidence: 0.9412974

00:51:20.775 --> 00:51:22.535 the expected dopamine mediated effects

NOTE Confidence: 0.9412974

00:51:22.535 --> 00:51:23.195 of cannabis.

NOTE Confidence: 0.9399193

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00:51:23.895 --> 00:51:25.175 The, point that, you know,

NOTE Confidence: 0.9399193

00:51:25.175 --> 00:51:26.295 one point to take from

NOTE Confidence: 0.9399193

00:51:26.295 --> 00:51:27.735 the new imaging study that

NOTE Confidence: 0.9399193

00:51:27.735 --> 00:51:29.250 we just showed is that

NOTE Confidence: 0.9399193

00:51:29.250 --> 00:51:30.770 these effects, when did they

NOTE Confidence: 0.9399193

00:51:30.770 --> 00:51:32.310 happen cannot be answered.

NOTE Confidence: 0.9716658

00:51:32.770 --> 00:51:33.570 You know, these people have

NOTE Confidence: 0.9716658

00:51:33.570 --> 00:51:35.410 been using, cannabis for seven

NOTE Confidence: 0.9716658

00:51:35.410 --> 00:51:36.530 years on average, and most

NOTE Confidence: 0.9716658

00:51:36.530 --> 00:51:37.330 of them have been using

NOTE Confidence: 0.9716658

00:51:37.330 --> 00:51:38.950 for ten years, minimum,

NOTE Confidence: 0.9473447

00:51:39.969 --> 00:51:40.930 ten years at at at

NOTE Confidence: 0.9473447

00:51:40.930 --> 00:51:42.050 a stretch, you know, without

NOTE Confidence: 0.9473447

00:51:42.050 --> 00:51:42.870 any interruptions.

NOTE Confidence: 0.99921083

00:51:43.410 --> 00:51:43.910 So

NOTE Confidence: 0.950965

00:51:44.395 --> 00:51:45.595 the elevation might have happened

125

NOTE Confidence: 0.950965

00:51:45.595 --> 00:51:46.635 at a very early stage.

NOTE Confidence: 0.950965

00:51:46.635 --> 00:51:47.675 It's really hard to say

NOTE Confidence: 0.950965

00:51:47.675 --> 00:51:48.955 at what point the cycles

NOTE Confidence: 0.950965

00:51:48.955 --> 00:51:49.755 of this is related to

NOTE Confidence: 0.950965

00:51:49.755 --> 00:51:50.975 the the actual elevation.

NOTE Confidence: 0.9827221

00:51:52.235 --> 00:51:53.755 And the effects we see

NOTE Confidence: 0.9827221

00:51:53.755 --> 00:51:54.955 cannot be taken as acute

NOTE Confidence: 0.9827221

00:51:54.955 --> 00:51:55.995 effects at all. So, you

NOTE Confidence: 0.9827221

00:51:55.995 --> 00:51:57.755 know, whether antipsychotics will reverse

NOTE Confidence: 0.9827221

00:51:57.755 --> 00:51:58.715 any of them, I I

NOTE Confidence: 0.9827221

00:51:58.715 --> 00:51:59.615 would be very doubtful.

NOTE Confidence: 0.83993214

00:52:00.050 --> 00:52:01.430 Antisecondics will change

NOTE Confidence: 0.98192596

00:52:01.890 --> 00:52:02.770 them in any way. And

NOTE Confidence: 0.98192596

00:52:02.770 --> 00:52:04.450 and and what you what

NOTE Confidence: 0.98192596

00:52:04.450 --> 00:52:05.250 you just,

NOTE Confidence: 0.9732612

00:52:05.650 --> 00:52:07.090 discussed is all effects at

NOTE Confidence: 0.9732612

00:52:07.090 --> 00:52:08.849 the release level, the synthesis

NOTE Confidence: 0.9732612

00:52:08.849 --> 00:52:10.050 level, at the strata level,

NOTE Confidence: 0.9732612

00:52:10.050 --> 00:52:11.410 I guess, not really at

NOTE Confidence: 0.9732612

00:52:11.410 --> 00:52:13.349 the dopamine neuron count level,

NOTE Confidence: 0.9732612

00:52:13.570 --> 00:52:15.190 which takes longer time to

NOTE Confidence: 0.6957409

00:52:16.105 --> 00:52:17.965 present in the neuromyelomine signals.

NOTE Confidence: 0.9722287

00:52:18.825 --> 00:52:19.625 And, you know, I I

NOTE Confidence: 0.9722287

00:52:19.625 --> 00:52:20.425 do I'm going back to

NOTE Confidence: 0.9722287

00:52:20.425 --> 00:52:21.625 Cameron's question as well with

NOTE Confidence: 0.9722287

00:52:21.625 --> 00:52:22.505 with the point that you

NOTE Confidence: 0.9722287

00:52:22.505 --> 00:52:23.465 made. I I don't think

NOTE Confidence: 0.9722287

00:52:23.465 --> 00:52:24.905 we can say anything about

NOTE Confidence: 0.9722287

00:52:24.905 --> 00:52:26.364 the central or the primacy,

NOTE Confidence: 0.96439976

00:52:27.065 --> 00:52:29.005 the cardinal role that dopamine

NOTE Confidence: 0.96439976

00:52:29.145 --> 00:52:30.825 plays in in psychosis from

127

NOTE Confidence: 0.96439976

00:52:30.825 --> 00:52:31.920 studies like this in any

NOTE Confidence: 0.96439976

00:52:31.920 --> 00:52:33.119 way. And I think, you

NOTE Confidence: 0.96439976

00:52:33.119 --> 00:52:34.239 know, there is this clearly

NOTE Confidence: 0.96439976

00:52:34.239 --> 00:52:34.739 a

NOTE Confidence: 0.95671815

00:52:35.359 --> 00:52:37.680 large unknown, the unexplained variance

NOTE Confidence: 0.95671815

00:52:37.680 --> 00:52:39.140 of psychosis, so to speak,

NOTE Confidence: 0.96822375

00:52:39.920 --> 00:52:41.280 which overlaps a lot with

NOTE Confidence: 0.96822375

00:52:41.280 --> 00:52:42.480 the unexplained variance of the

NOTE Confidence: 0.96822375

00:52:42.480 --> 00:52:44.420 cannabis' effect on on psychosis

NOTE Confidence: 0.96822375

00:52:44.559 --> 00:52:46.079 risk as well. And unless

NOTE Confidence: 0.96822375

00:52:46.079 --> 00:52:46.739 we have

NOTE Confidence: 0.98987556

00:52:47.315 --> 00:52:48.114 some leads,

NOTE Confidence: 0.8565702

00:52:48.594 --> 00:52:50.614 to be investigated theoretical

NOTE Confidence: 0.950451

00:52:50.994 --> 00:52:52.515 basis investigated those links, I

NOTE Confidence: 0.950451

00:52:52.515 --> 00:52:53.974 think we'll continue to be

NOTE Confidence: 0.950451

00:52:54.114 --> 00:52:55.234 shooting in the dark for,

NOTE Confidence: 0.950451

00:52:55.555 --> 00:52:56.914 for what other mechanisms are

NOTE Confidence: 0.950451

00:52:56.914 --> 00:52:57.414 there.

NOTE Confidence: 0.91406995

00:52:58.434 --> 00:52:59.714 Thanks for the answer. Can

NOTE Confidence: 0.91406995

00:52:59.714 --> 00:53:01.350 you can you just repeat?

NOTE Confidence: 0.91406995

00:53:01.430 --> 00:53:02.390 And then I know you

NOTE Confidence: 0.91406995

00:53:02.390 --> 00:53:03.510 guys have already said this,

NOTE Confidence: 0.91406995

00:53:03.510 --> 00:53:05.130 and maybe I didn't understand

NOTE Confidence: 0.7513829

00:53:05.670 --> 00:53:06.730 it really well.

NOTE Confidence: 0.9782953

00:53:07.830 --> 00:53:10.090 So the the neuromelanin findings

NOTE Confidence: 0.9782953

00:53:10.150 --> 00:53:11.910 are not findings that would

NOTE Confidence: 0.9782953

00:53:11.910 --> 00:53:12.410 reflect

NOTE Confidence: 0.99474686

00:53:12.710 --> 00:53:14.170 some acute effect.

NOTE Confidence: 0.988581

00:53:14.790 --> 00:53:16.410 It's something that would reflect

NOTE Confidence: 0.9305145

00:53:17.255 --> 00:53:18.215 a much more,

NOTE Confidence: 0.9079914

00:53:19.815 --> 00:53:20.855 maybe you can just say

NOTE Confidence: 0.9079914

00:53:20.855 --> 00:53:22.215 it yourself. Yeah. So it's

NOTE Confidence: 0.9079914

00:53:22.215 --> 00:53:23.175 a it's a longer effect.

NOTE Confidence: 0.9079914

00:53:23.175 --> 00:53:24.614 So the the biggest difference

NOTE Confidence: 0.9079914

00:53:24.614 --> 00:53:25.895 between a PET study and

NOTE Confidence: 0.9079914

00:53:25.895 --> 00:53:27.415 a neuromyelins studies like this

NOTE Confidence: 0.9079914

00:53:27.415 --> 00:53:28.715 is the sensitivity

NOTE Confidence: 0.9988833

00:53:29.015 --> 00:53:29.755 of signal

NOTE Confidence: 0.99969935

00:53:30.270 --> 00:53:31.170 to change

NOTE Confidence: 0.83768827

00:53:31.710 --> 00:53:32.750 the time scale of the

NOTE Confidence: 0.83768827

00:53:32.750 --> 00:53:33.250 sensitivity

NOTE Confidence: 0.9918433

00:53:33.550 --> 00:53:34.989 is very different. So you

NOTE Confidence: 0.9918433

00:53:34.989 --> 00:53:36.350 can have a challenge that

NOTE Confidence: 0.9918433

00:53:36.350 --> 00:53:36.850 increases

NOTE Confidence: 0.9205709

00:53:37.550 --> 00:53:38.510 the pet signal, you can

NOTE Confidence: 0.9205709

00:53:38.510 --> 00:53:39.710 have an after treatment challenge

NOTE Confidence: 0.9205709

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00:53:39.710 --> 00:53:40.989 that changes pet signal, but

NOTE Confidence: 0.9205709

00:53:40.989 --> 00:53:42.030 you cannot do those things

NOTE Confidence: 0.9205709

00:53:42.030 --> 00:53:43.164 to show a a difference

NOTE Confidence: 0.9205709

00:53:43.164 --> 00:53:45.424 in neuromelanin signal because neuromelanin

NOTE Confidence: 0.9205709

00:53:45.565 --> 00:53:47.164 signal comes from dopamine auto

NOTE Confidence: 0.9205709

00:53:47.164 --> 00:53:48.525 oxidation, which is a longer

NOTE Confidence: 0.9205709

00:53:48.525 --> 00:53:50.045 process. It takes time to

NOTE Confidence: 0.9205709

00:53:50.045 --> 00:53:51.105 accumulate in the cytosol.

NOTE Confidence: 0.98453647

00:53:51.565 --> 00:53:52.924 By just giving a drug

NOTE Confidence: 0.98453647

00:53:52.924 --> 00:53:53.405 challenging,

NOTE Confidence: 0.9934733

00:53:53.964 --> 00:53:55.724 challenge paradigm, you cannot change

NOTE Confidence: 0.9934733

00:53:55.724 --> 00:53:56.690 that that signal.

NOTE Confidence: 0.9810941

00:53:56.989 --> 00:53:58.190 Now having said that, there

NOTE Confidence: 0.9810941

00:53:58.190 --> 00:53:59.250 are studies in Parkinson's

NOTE Confidence: 0.9868864

00:53:59.710 --> 00:54:00.829 showing people who are doing

NOTE Confidence: 0.9868864

00:54:00.829 --> 00:54:02.829 exercise programs for six months

NOTE Confidence: 0.9868864

00:54:02.829 --> 00:54:03.890 are showing some,

NOTE Confidence: 0.95814854

00:54:04.430 --> 00:54:06.270 changes in in neuromelative signal.

NOTE Confidence: 0.95814854

00:54:06.270 --> 00:54:07.890 But mind you, those changes

NOTE Confidence: 0.95814854

00:54:07.950 --> 00:54:09.885 are really slowing down of

NOTE Confidence: 0.95814854

00:54:10.045 --> 00:54:10.545 reduction

NOTE Confidence: 0.99501467

00:54:11.085 --> 00:54:13.025 rather than increase or decrease

NOTE Confidence: 0.8938116

00:54:13.325 --> 00:54:14.844 in the pet sense is

NOTE Confidence: 0.8938116

00:54:14.844 --> 00:54:15.885 really slowing down of the

NOTE Confidence: 0.8938116

00:54:15.885 --> 00:54:17.325 trajectory and that's over six

NOTE Confidence: 0.8938116

00:54:17.325 --> 00:54:18.065 months period.

NOTE Confidence: 0.9296123

00:54:18.364 --> 00:54:19.485 So the bottom line is

NOTE Confidence: 0.9296123

00:54:19.485 --> 00:54:20.605 you cannot do the same

NOTE Confidence: 0.9296123

00:54:20.605 --> 00:54:21.405 thing that you do with

NOTE Confidence: 0.9296123

00:54:21.405 --> 00:54:22.844 pet studies using your mammalian

NOTE Confidence: 0.9296123

00:54:22.844 --> 00:54:23.344 signals.

NOTE Confidence: 0.9634326

00:54:27.090 --> 00:54:28.469 Great. Other questions?

NOTE Confidence: 0.9736214

00:54:29.810 --> 00:54:30.849 If not, I have one

NOTE Confidence: 0.9736214

00:54:30.849 --> 00:54:32.050 other. And I noticed that

NOTE Confidence: 0.9736214

00:54:32.050 --> 00:54:32.950 in your sample,

NOTE Confidence: 0.9751182

00:54:33.410 --> 00:54:34.770 most of the cannabis use

NOTE Confidence: 0.9751182

00:54:34.770 --> 00:54:36.869 disorder subjects were also smokers,

NOTE Confidence: 0.9751182

00:54:37.090 --> 00:54:39.355 tobacco smokers. Yes. And can

NOTE Confidence: 0.9751182

00:54:39.355 --> 00:54:40.575 you speculate on

NOTE Confidence: 0.98617524

00:54:41.275 --> 00:54:43.215 the impact of tobacco smoking

NOTE Confidence: 0.98617524

00:54:43.355 --> 00:54:44.575 on neuromelanin?

NOTE Confidence: 0.996292

00:54:45.915 --> 00:54:46.415 Yes.

NOTE Confidence: 0.9966433

00:54:46.715 --> 00:54:48.315 Yeah. We we did control

NOTE Confidence: 0.9966433

00:54:48.315 --> 00:54:49.355 for that in all of

NOTE Confidence: 0.9966433

00:54:49.355 --> 00:54:49.855 our,

NOTE Confidence: 0.8198974

00:54:50.555 --> 00:54:51.055 analyses.

NOTE Confidence: 0.93310153

00:54:51.915 --> 00:54:53.195 There was no difference at

NOTE Confidence: 0.93310153

00:54:53.195 --> 00:54:54.255 all. So

NOTE Confidence: 0.9212098

00:54:54.900 --> 00:54:56.260 likely just because of it's

NOTE Confidence: 0.9212098

00:54:56.260 --> 00:54:57.780 the same participants where it

NOTE Confidence: 0.9212098

00:54:57.780 --> 00:54:58.819 could be that we're looking

NOTE Confidence: 0.9212098

00:54:58.819 --> 00:55:00.119 at the nicotine effect,

NOTE Confidence: 0.9561518

00:55:00.579 --> 00:55:02.599 and the cannabis effect together,

NOTE Confidence: 0.9789972

00:55:03.460 --> 00:55:04.660 but from the study, we

NOTE Confidence: 0.9789972

00:55:04.660 --> 00:55:06.420 we weren't able to to

NOTE Confidence: 0.9789972

00:55:06.420 --> 00:55:07.480 look at that exactly.

NOTE Confidence: 0.97128826

00:55:08.660 --> 00:55:09.160 Yeah.

NOTE Confidence: 0.9333932

00:55:09.515 --> 00:55:10.395 I have to also admit

NOTE Confidence: 0.9333932

00:55:10.395 --> 00:55:11.195 that we, you know, we

NOTE Confidence: 0.9333932

00:55:11.195 --> 00:55:12.555 don't have good quality nicotine

NOTE Confidence: 0.9333932

00:55:12.555 --> 00:55:14.795 data here, Cyril. We we

NOTE Confidence: 0.9333932

00:55:14.795 --> 00:55:15.515 we added a lot of

NOTE Confidence: 0.9333932

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00:55:15.515 --> 00:55:16.815 these, assessments,

NOTE Confidence: 0.8889709

00:55:18.155 --> 00:55:19.675 afterthought, really, you know, especially

NOTE Confidence: 0.8889709

00:55:19.675 --> 00:55:21.755 with Rachel Regan's involvement. We

NOTE Confidence: 0.8889709

00:55:21.755 --> 00:55:23.275 started thinking more about nicotine

NOTE Confidence: 0.8889709

00:55:23.275 --> 00:55:23.969 and its role,

NOTE Confidence: 0.9472993

00:55:24.609 --> 00:55:25.989 and did some follow back.

NOTE Confidence: 0.9472993

00:55:26.210 --> 00:55:27.650 For example, we didn't quantify

NOTE Confidence: 0.9472993

00:55:27.650 --> 00:55:28.770 nicotine in any other way.

NOTE Confidence: 0.9472993

00:55:28.770 --> 00:55:30.130 For cannabis, we had saliva,

NOTE Confidence: 0.9472993

00:55:30.130 --> 00:55:31.330 THC, and all that kind

NOTE Confidence: 0.9472993

00:55:31.330 --> 00:55:32.690 of stuff. But for nicotine,

NOTE Confidence: 0.9472993

00:55:32.690 --> 00:55:34.630 it's really a self rated

NOTE Confidence: 0.9755815

00:55:35.010 --> 00:55:36.550 admission that people said.

NOTE Confidence: 0.96984893

00:55:40.105 --> 00:55:41.085 Great. Other questions?

NOTE Confidence: 0.945619

00:55:46.344 --> 00:55:47.484 I wanna be respectful

NOTE Confidence: 0.97887516

00:55:47.864 --> 00:55:49.785 of everyone's time, but thank

NOTE Confidence: 0.97887516

00:55:49.785 --> 00:55:52.000 you so much, Jess and

NOTE Confidence: 0.97887516

00:55:52.000 --> 00:55:54.180 Lena, for this wonderful presentation.

NOTE Confidence: 0.978557

00:55:55.120 --> 00:55:56.340 Thank you for the opportunity.

NOTE Confidence: 0.9466036

00:55:57.120 --> 00:55:58.320 No. And and and,

NOTE Confidence: 0.9798168

00:55:58.720 --> 00:56:00.080 hopefully, we'll have you back

NOTE Confidence: 0.9798168

00:56:00.080 --> 00:56:01.120 in some in, you know,

NOTE Confidence: 0.9798168

00:56:01.120 --> 00:56:02.400 in the following years with

NOTE Confidence: 0.9798168

00:56:02.400 --> 00:56:03.060 new data.

NOTE Confidence: 0.976152

00:56:03.840 --> 00:56:04.720 Just for the rest of

NOTE Confidence: 0.976152

00:56:04.720 --> 00:56:05.680 the group, I wanted to

NOTE Confidence: 0.976152

00:56:05.680 --> 00:56:07.220 mention that next month,

NOTE Confidence: 0.883406

00:56:08.454 --> 00:56:10.295 webinar, we have Ryan Bogdan

NOTE Confidence: 0.883406

00:56:10.295 --> 00:56:11.515 who's gonna be presenting

NOTE Confidence: 0.96158737

00:56:12.135 --> 00:56:13.815 data on cannabis effects from

NOTE Confidence: 0.96158737

00:56:13.815 --> 00:56:15.594 the group, the big ABCD

NOTE Confidence: 0.96158737

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00:56:15.734 --> 00:56:16.234 study.

NOTE Confidence: 0.9092203

00:56:17.094 --> 00:56:18.375 Please see if you can

NOTE Confidence: 0.9092203

00:56:18.375 --> 00:56:19.734 join and, of course, Lena

NOTE Confidence: 0.9092203

00:56:19.734 --> 00:56:21.015 and Jess, you're welcome to

NOTE Confidence: 0.9092203

00:56:21.015 --> 00:56:21.974 join if you'd if you'd

NOTE Confidence: 0.9092203

00:56:21.974 --> 00:56:22.560 like to.

NOTE Confidence: 0.8270731

00:56:23.040 --> 00:56:24.400 So thank you again, and,

NOTE Confidence: 0.93288153

00:56:25.840 --> 00:56:27.600 and we we really appreciate

NOTE Confidence: 0.93288153

00:56:27.600 --> 00:56:28.100 it.

NOTE Confidence: 0.9128335

00:56:28.480 --> 00:56:29.600 Thank you, Suru. Thank you,

NOTE Confidence: 0.9128335

00:56:29.600 --> 00:56:30.480 Wendy as well for all

NOTE Confidence: 0.9128335

00:56:30.480 --> 00:56:32.100 your help. See you all.

NOTE Confidence: 0.9935013

00:56:32.800 --> 00:56:33.300 Great.

NOTE Confidence: 0.83678424

00:56:34.560 --> 00:56:35.060 Thanks.

NOTE Confidence: 0.9952199

00:56:35.600 --> 00:56:36.900 Bye bye. Bye.