WEBVTT

NOTE duration: ”01:01:13.984”

NOTE Confidence: 0.9941406

00:00:03.679 --> 00:00:04.180 Okay.

NOTE Confidence: 0.97111905

00:00:05.120 --> 00:00:07.759 Welcome, everyone. It's, my great

NOTE Confidence: 0.97111905

00:00:07.759 --> 00:00:10.019 pleasure to introduce today,

NOTE Confidence: 0.9980469

00:00:10.719 --> 00:00:11.460 two speakers.

NOTE Confidence: 0.98413086

00:00:12.480 --> 00:00:12.980 First,

NOTE Confidence: 0.9258694

00:00:14.184 --> 00:00:15.945 doctor Rachel Rabien. She's an

NOTE Confidence: 0.9258694

00:00:15.945 --> 00:00:17.385 assistant professor in the department

NOTE Confidence: 0.9258694

00:00:17.385 --> 00:00:18.204 of psychiatry

NOTE Confidence: 0.99104816

00:00:18.744 --> 00:00:19.965 at McGill University

NOTE Confidence: 0.96691895

00:00:20.425 --> 00:00:22.125 and researcher at the Douglas

NOTE Confidence: 0.96691895

00:00:22.265 --> 00:00:24.204 Research Institute where I work.

NOTE Confidence: 0.99194336

00:00:24.744 --> 00:00:26.585 And then, we'll be hearing

NOTE Confidence: 0.99194336

00:00:26.585 --> 00:00:28.125 about doctor Renato

NOTE Confidence: 0.82592773

00:00:28.560 --> 00:00:29.060 Polimanti,

NOTE Confidence: 0.9965007

00:00:29.760 --> 00:00:31.360 who's an associate professor of

NOTE Confidence: 0.9965007

00:00:31.360 --> 00:00:31.860 psychiatry

NOTE Confidence: 0.9528198

00:00:32.479 --> 00:00:34.320 in the biomedical informatics and

NOTE Confidence: 0.9528198

00:00:34.320 --> 00:00:36.079 data science and chronic disease

NOTE Confidence: 0.9528198

00:00:36.079 --> 00:00:37.680 epidemiology at Yale School of

NOTE Confidence: 0.9528198

00:00:37.680 --> 00:00:38.180 Medicine.

NOTE Confidence: 0.9716797

00:00:38.960 --> 00:00:39.460 So,

NOTE Confidence: 0.95125324

00:00:39.840 --> 00:00:41.114 first, I'll introduce,

NOTE Confidence: 0.9875488

00:00:41.675 --> 00:00:42.175 Rachel.

NOTE Confidence: 0.9734158

00:00:42.795 --> 00:00:44.714 She leads the Addiction Imaging

NOTE Confidence: 0.9734158

00:00:44.714 --> 00:00:46.015 and Mental Health Laboratory

NOTE Confidence: 0.97076416

00:00:46.394 --> 00:00:48.155 where her work focuses on

NOTE Confidence: 0.97076416

00:00:48.155 --> 00:00:49.454 understanding the clinical,

NOTE Confidence: 0.99443907

00:00:50.155 --> 00:00:51.695 cognitive, and neurobiological

NOTE Confidence: 0.9894409

00:00:52.394 --> 00:00:54.795 mechanisms underlying substance use and

NOTE Confidence: 0.9894409

00:00:54.795 --> 00:00:55.854 mental health disorders.

NOTE Confidence: 0.9976129

00:00:56.690 --> 00:00:59.110 Her research integrates advanced neuroimaging

NOTE Confidence: 0.9976129

00:00:59.330 --> 00:00:59.830 techniques,

NOTE Confidence: 0.9135742

00:01:00.290 --> 00:01:01.350 clinical assessments,

NOTE Confidence: 0.945638

00:01:01.650 --> 00:01:03.110 and translational neuroscience

NOTE Confidence: 0.9756917

00:01:03.490 --> 00:01:05.670 approaches to better understand addiction,

NOTE Confidence: 0.9756917

00:01:05.810 --> 00:01:08.150 psychosis risks, and recovery trajectories.

NOTE Confidence: 0.9720233

00:01:09.944 --> 00:01:11.705 Doctor Ravin's lecture will explore

NOTE Confidence: 0.9720233

00:01:11.705 --> 00:01:13.165 the clinical and neurobiological

NOTE Confidence: 0.996875

00:01:13.784 --> 00:01:15.884 factors that influence the severity

NOTE Confidence: 0.9385579

00:01:16.185 --> 00:01:18.125 and progression of cannabis withdrawal

NOTE Confidence: 0.9385579

00:01:18.265 --> 00:01:19.965 during periods of abstinence.

NOTE Confidence: 0.99591064

00:01:20.744 --> 00:01:22.744 Using findings from laboratory based

NOTE Confidence: 0.99591064

00:01:22.744 --> 00:01:24.330 cannabis abstinence models,

NOTE Confidence: 0.9820709

00:01:24.810 --> 00:01:26.730 the presentation will examine how

NOTE Confidence: 0.9820709

00:01:26.730 --> 00:01:29.870 individual differences, including biological sex

NOTE Confidence: 0.9820709

00:01:29.930 --> 00:01:31.230 and co use of other

NOTE Confidence: 0.9820709

00:01:31.450 --> 00:01:31.950 substances,

NOTE Confidence: 0.9610596

00:01:32.330 --> 00:01:34.030 may shape withdrawal experiences.

NOTE Confidence: 0.9973823

00:01:34.650 --> 00:01:36.650 The talk will also highlight

NOTE Confidence: 0.9973823

00:01:36.650 --> 00:01:37.550 the role of endocannabinoid

NOTE Confidence: 0.9892578

00:01:37.930 --> 00:01:40.095 system in driving variability in

NOTE Confidence: 0.9892578

00:01:40.255 --> 00:01:41.235 withdrawal trajectories,

NOTE Confidence: 0.9968262

00:01:41.855 --> 00:01:44.334 providing insights into mechanisms that

NOTE Confidence: 0.9968262

00:01:44.334 --> 00:01:46.334 may inform future treatment and

NOTE Confidence: 0.9968262

00:01:46.334 --> 00:01:47.475 intervention strategies

NOTE Confidence: 0.91174316

00:01:47.935 --> 00:01:49.315 for cannabis use disorder.

NOTE Confidence: 0.9980469

00:01:50.415 --> 00:01:51.475 So with that,

NOTE Confidence: 0.96425086

00:01:51.775 --> 00:01:53.970 Rachel, you, have the floor,

NOTE Confidence: 0.96425086

00:01:53.970 --> 00:01:54.610 and I'll,

NOTE Confidence: 0.99658203

00:01:55.250 --> 00:01:56.790 introduce Renato after.

NOTE Confidence: 0.99765486

00:01:59.490 --> 00:02:00.690 Okay. Great. Thank you so

NOTE Confidence: 0.99765486

00:02:00.690 --> 00:02:01.970 much, Romina, for that nice

NOTE Confidence: 0.99765486

00:02:01.970 --> 00:02:02.470 introduction.

NOTE Confidence: 0.94892037

00:02:03.090 --> 00:02:04.370 Can everyone see my slides

NOTE Confidence: 0.94892037

00:02:04.370 --> 00:02:06.345 okay? Maybe just, great.

NOTE Confidence: 0.97624654

00:02:06.884 --> 00:02:07.924 Okay. So, yeah, so I'm

NOTE Confidence: 0.97624654

00:02:07.924 --> 00:02:09.364 really excited to share some

NOTE Confidence: 0.97624654

00:02:09.364 --> 00:02:10.645 of my lab's work on

NOTE Confidence: 0.97624654

00:02:10.645 --> 00:02:11.705 cannabis use

NOTE Confidence: 0.98738235

00:02:12.165 --> 00:02:13.925 and cannabis withdrawal and talk

NOTE Confidence: 0.98738235

00:02:13.925 --> 00:02:15.525 about some of the factors

NOTE Confidence: 0.98738235

00:02:15.525 --> 00:02:17.044 that we've identified that may

NOTE Confidence: 0.98738235

00:02:17.044 --> 00:02:19.044 moderate withdrawal severity as well

NOTE Confidence: 0.98738235

00:02:19.044 --> 00:02:19.785 as duration.

NOTE Confidence: 0.994812

00:02:20.419 --> 00:02:21.800 And I'll also discuss,

NOTE Confidence: 0.9992488

00:02:22.260 --> 00:02:24.040 several of the underlying mechanisms

NOTE Confidence: 0.9992488

00:02:24.099 --> 00:02:25.459 that we think may contribute

NOTE Confidence: 0.9992488

00:02:25.459 --> 00:02:26.440 to these effects.

NOTE Confidence: 0.9326579

00:02:29.860 --> 00:02:30.900 So I have nothing to

NOTE Confidence: 0.9326579

00:02:30.900 --> 00:02:31.400 disclose.

NOTE Confidence: 0.9988511

00:02:32.419 --> 00:02:33.780 So I think everybody here

NOTE Confidence: 0.9988511

00:02:33.780 --> 00:02:34.980 is well aware that rates

NOTE Confidence: 0.9988511

00:02:34.980 --> 00:02:36.534 of cannabis use are high

NOTE Confidence: 0.9988511

00:02:36.534 --> 00:02:37.275 and increasing

NOTE Confidence: 0.9897461

00:02:37.814 --> 00:02:39.915 alongside the relaxation of cannabis

NOTE Confidence: 0.9897461

00:02:39.974 --> 00:02:40.474 laws.

NOTE Confidence: 0.9918213

00:02:41.735 --> 00:02:43.334 About seven percent of both

NOTE Confidence: 0.9918213

00:02:43.334 --> 00:02:45.575 Canadians and Americans report daily

NOTE Confidence: 0.9918213

00:02:45.575 --> 00:02:47.014 or near daily use of

NOTE Confidence: 0.9918213

00:02:47.014 --> 00:02:47.514 cannabis.

NOTE Confidence: 0.99038553

00:02:47.974 --> 00:02:49.355 And this is really concerning

NOTE Confidence: 0.99038553

00:02:49.495 --> 00:02:50.580 because we know that this

NOTE Confidence: 0.99038553

00:02:50.740 --> 00:02:52.260 pattern of cannabis use is

NOTE Confidence: 0.99038553

00:02:52.260 --> 00:02:53.940 associated with a host of

NOTE Confidence: 0.99038553

00:02:53.940 --> 00:02:54.440 consequences,

NOTE Confidence: 0.99798584

00:02:55.220 --> 00:02:56.740 including the development of a

NOTE Confidence: 0.99798584

00:02:56.740 --> 00:02:57.960 cannabis use disorder.

NOTE Confidence: 0.9649658

00:02:59.540 --> 00:03:00.440 Yet, unfortunately,

NOTE Confidence: 0.9952741

00:03:00.740 --> 00:03:02.260 there remains to be no

NOTE Confidence: 0.9952741

00:03:02.260 --> 00:03:03.240 approved pharmacotherapies

NOTE Confidence: 0.96118164

00:03:04.020 --> 00:03:05.880 to treat cannabis use disorder,

NOTE Confidence: 0.9550781

00:03:06.275 --> 00:03:07.715 and this is despite many

NOTE Confidence: 0.9550781

00:03:07.715 --> 00:03:08.615 candidate medications

NOTE Confidence: 0.99820966

00:03:09.395 --> 00:03:10.535 having been tested.

NOTE Confidence: 0.97545624

00:03:12.435 --> 00:03:13.875 So clearly, there's an urgent

NOTE Confidence: 0.97545624

00:03:13.875 --> 00:03:15.155 need to develop novel and

NOTE Confidence: 0.97545624

00:03:15.155 --> 00:03:16.995 effective treatments for cannabis use

NOTE Confidence: 0.97545624

00:03:16.995 --> 00:03:18.675 disorder, and today I'll talk

NOTE Confidence: 0.97545624

00:03:18.675 --> 00:03:20.310 about couple of ingredients that

NOTE Confidence: 0.97545624

00:03:20.310 --> 00:03:22.070 I think are essential for

NOTE Confidence: 0.97545624

00:03:22.070 --> 00:03:22.810 this process.

NOTE Confidence: 0.9943034

00:03:23.669 --> 00:03:24.490 So the first,

NOTE Confidence: 0.99763995

00:03:24.870 --> 00:03:26.470 we need to identify variables

NOTE Confidence: 0.99763995

00:03:26.470 --> 00:03:28.169 that predict cannabis relapse.

NOTE Confidence: 0.9822022

00:03:28.870 --> 00:03:30.310 We also need to determine

NOTE Confidence: 0.9822022

00:03:30.310 --> 00:03:32.250 factors that moderate this variable.

NOTE Confidence: 0.9935128

00:03:32.845 --> 00:03:33.724 And then we need to

NOTE Confidence: 0.9935128

00:03:33.724 --> 00:03:35.245 map the mechanisms that are

NOTE Confidence: 0.9935128

00:03:35.245 --> 00:03:37.025 driving these moderating effects.

NOTE Confidence: 0.9879303

00:03:38.205 --> 00:03:39.405 So it's already pretty well

NOTE Confidence: 0.9879303

00:03:39.405 --> 00:03:41.165 established that cannabis withdrawal is

NOTE Confidence: 0.9879303

00:03:41.165 --> 00:03:42.864 a robust predictor of cannabis

NOTE Confidence: 0.9879303

00:03:42.925 --> 00:03:43.425 relapse.

NOTE Confidence: 0.99310595

00:03:44.205 --> 00:03:45.245 And just to go over

NOTE Confidence: 0.99310595

00:03:45.245 --> 00:03:47.084 what cannabis withdrawal is, it

NOTE Confidence: 0.99310595

00:03:47.084 --> 00:03:49.110 refers to a constellation of

NOTE Confidence: 0.99310595

00:03:49.110 --> 00:03:50.870 symptoms that emerge following the

NOTE Confidence: 0.99310595

00:03:50.870 --> 00:03:51.370 cessation

NOTE Confidence: 0.9742526

00:03:52.069 --> 00:03:53.590 or the reduction of heavy

NOTE Confidence: 0.9742526

00:03:53.590 --> 00:03:55.590 cannabis use. And it's pretty

NOTE Confidence: 0.9742526

00:03:55.590 --> 00:03:57.190 common up to about ninety

NOTE Confidence: 0.9742526

00:03:57.190 --> 00:03:58.870 percent of people with regular

NOTE Confidence: 0.9742526

00:03:58.870 --> 00:04:01.050 cannabis use will experience withdrawal

NOTE Confidence: 0.9742526

00:04:01.110 --> 00:04:01.610 symptoms.

NOTE Confidence: 0.95649064

00:04:03.095 --> 00:04:04.555 So, these symptoms are clinically

NOTE Confidence: 0.95649064

00:04:04.615 --> 00:04:06.375 significant because we know they

NOTE Confidence: 0.95649064

00:04:06.375 --> 00:04:07.835 interfere with daily functioning.

NOTE Confidence: 0.9634564

00:04:08.855 --> 00:04:10.135 The most common symptoms that

NOTE Confidence: 0.9634564

00:04:10.135 --> 00:04:11.435 we see in our lab

NOTE Confidence: 0.9634564

00:04:11.655 --> 00:04:13.095 tend to be effective symptoms

NOTE Confidence: 0.9634564

00:04:13.095 --> 00:04:15.015 like depression and anxiety or

NOTE Confidence: 0.9634564

00:04:15.015 --> 00:04:15.515 irritability,

NOTE Confidence: 0.9995117

00:04:16.630 --> 00:04:17.450 sleep disturbances

NOTE Confidence: 0.86689454

00:04:18.150 --> 00:04:20.410 as well as appetite disturbances,

NOTE Confidence: 0.9838867

00:04:21.110 --> 00:04:23.110 and also physical symptoms are

NOTE Confidence: 0.9838867

00:04:23.110 --> 00:04:24.010 pretty prevalent.

NOTE Confidence: 0.97016054

00:04:25.510 --> 00:04:26.870 Now these symptoms are pretty

NOTE Confidence: 0.97016054

00:04:26.870 --> 00:04:27.370 distressing,

NOTE Confidence: 0.99921876

00:04:27.990 --> 00:04:29.850 and they often cause people

NOTE Confidence: 0.992334

00:04:30.325 --> 00:04:31.765 to relapse. And even just

NOTE Confidence: 0.992334

00:04:31.765 --> 00:04:32.985 the thought of these symptoms

NOTE Confidence: 0.98291016

00:04:33.765 --> 00:04:34.745 can make people

NOTE Confidence: 0.9916992

00:04:35.125 --> 00:04:37.065 relapse during a quit attempt.

NOTE Confidence: 0.9885254

00:04:38.485 --> 00:04:39.685 So, it's important to note

NOTE Confidence: 0.9885254

00:04:39.685 --> 00:04:41.925 that, cannabis withdrawal follows a

NOTE Confidence: 0.9885254

00:04:41.925 --> 00:04:43.785 very distinct and elongated

NOTE Confidence: 0.9951172

00:04:44.085 --> 00:04:44.585 trajectory.

NOTE Confidence: 0.9795179

00:04:45.310 --> 00:04:47.310 So, symptoms typically begin about

NOTE Confidence: 0.9795179

00:04:47.310 --> 00:04:49.070 twenty four hours after someone

NOTE Confidence: 0.9795179

00:04:49.070 --> 00:04:51.070 quits. They usually peak within

NOTE Confidence: 0.9795179

00:04:51.070 --> 00:04:52.210 one week of quitting.

NOTE Confidence: 0.99518377

00:04:52.510 --> 00:04:53.790 And then after about twenty

NOTE Confidence: 0.99518377

00:04:53.790 --> 00:04:55.150 eight days, they pretty much

NOTE Confidence: 0.99518377

00:04:55.150 --> 00:04:55.650 dissipate.

NOTE Confidence: 0.98370767

00:04:56.190 --> 00:04:57.570 And this was first established

NOTE Confidence: 0.98370767

00:04:57.710 --> 00:04:58.910 back in two thousand and

NOTE Confidence: 0.98370767

00:04:58.910 --> 00:05:00.529 three by Budney and colleagues.

NOTE Confidence: 0.98105466

00:05:01.175 --> 00:05:03.035 And about fifteen years later,

NOTE Confidence: 0.9939453

00:05:03.735 --> 00:05:05.115 I was able to replicate,

NOTE Confidence: 0.83414716

00:05:05.654 --> 00:05:07.255 with my lab that as

NOTE Confidence: 0.83414716

00:05:07.255 --> 00:05:08.714 a very similar trajectory.

NOTE Confidence: 0.9606291

00:05:11.975 --> 00:05:14.375 So alongside increasing cannabis use,

NOTE Confidence: 0.9606291

00:05:14.375 --> 00:05:15.690 we're also seeing a rise

NOTE Confidence: 0.9606291

00:05:15.690 --> 00:05:17.529 in tobacco co use in

NOTE Confidence: 0.9606291

00:05:17.529 --> 00:05:18.830 people who use cannabis.

NOTE Confidence: 0.9974162

00:05:19.450 --> 00:05:20.490 And you can see here

NOTE Confidence: 0.9974162

00:05:20.490 --> 00:05:21.770 from this recent study that

NOTE Confidence: 0.9974162

00:05:21.770 --> 00:05:22.590 was published,

NOTE Confidence: 0.99853516

00:05:23.370 --> 00:05:25.230 the blue line here denotes,

NOTE Confidence: 0.9886569

00:05:25.690 --> 00:05:27.290 cannabis and tobacco co use,

NOTE Confidence: 0.9886569

00:05:27.290 --> 00:05:28.170 and you can see that

NOTE Confidence: 0.9886569

00:05:28.170 --> 00:05:29.230 rates are rising.

NOTE Confidence: 0.99902344

00:05:29.974 --> 00:05:30.875 The green line,

NOTE Confidence: 0.9553667

00:05:31.574 --> 00:05:33.895 depicts cannabis exclusive use, so

NOTE Confidence: 0.9553667

00:05:33.895 --> 00:05:35.275 people who just use cannabis

NOTE Confidence: 0.9553667

00:05:35.335 --> 00:05:35.835 alone.

NOTE Confidence: 0.99899775

00:05:36.214 --> 00:05:37.974 And this orange line is

NOTE Confidence: 0.99899775

00:05:37.974 --> 00:05:39.495 the rates of tobacco use,

NOTE Confidence: 0.99899775

00:05:39.495 --> 00:05:40.615 which you can see over

NOTE Confidence: 0.99899775

00:05:40.615 --> 00:05:41.835 the last several decades

NOTE Confidence: 0.9931543

00:05:42.615 --> 00:05:45.014 have immensely declined. But what

NOTE Confidence: 0.9931543

00:05:45.014 --> 00:05:46.830 we're seeing is that in

NOTE Confidence: 0.9931543

00:05:46.830 --> 00:05:48.830 people who use cannabis, we're

NOTE Confidence: 0.9931543

00:05:48.830 --> 00:05:50.290 not seeing that same decline

NOTE Confidence: 0.9931543

00:05:50.430 --> 00:05:52.210 of tobacco use. In fact,

NOTE Confidence: 1

00:05:52.669 --> 00:05:53.169 people

NOTE Confidence: 0.98786926

00:05:53.550 --> 00:05:55.310 who use cannabis, we're seeing

NOTE Confidence: 0.98786926

00:05:55.310 --> 00:05:56.669 that their rates of tobacco

NOTE Confidence: 0.98786926

00:05:56.669 --> 00:05:58.350 use are actually remaining quite

NOTE Confidence: 0.98786926

00:05:58.350 --> 00:05:58.850 stagnant.

NOTE Confidence: 0.93218994

00:05:59.535 --> 00:06:01.055 And most people who used

NOTE Confidence: 0.93218994

00:06:01.055 --> 00:06:02.755 cannabis actually also

NOTE Confidence: 0.9709961

00:06:03.375 --> 00:06:05.475 co use a tobacco product.

NOTE Confidence: 0.98583984

00:06:07.535 --> 00:06:09.695 So accumulating evidence suggests that

NOTE Confidence: 0.98583984

00:06:09.695 --> 00:06:11.375 tobacco co use is associated

NOTE Confidence: 0.98583984

00:06:11.375 --> 00:06:13.075 with poor treatment outcomes

NOTE Confidence: 0.9652778

00:06:13.510 --> 00:06:14.790 compared to those people who

NOTE Confidence: 0.9652778

00:06:14.790 --> 00:06:16.170 just use cannabis alone.

NOTE Confidence: 0.971026

00:06:16.630 --> 00:06:17.850 And this has been demonstrated

NOTE Confidence: 0.971026

00:06:17.990 --> 00:06:20.310 across various studies. So Gray

NOTE Confidence: 0.971026

00:06:20.310 --> 00:06:21.350 et al showed that people

NOTE Confidence: 0.971026

00:06:21.350 --> 00:06:23.270 with tobacco co use were

NOTE Confidence: 0.971026

00:06:23.270 --> 00:06:24.710 fifty percent more likely to

NOTE Confidence: 0.971026

00:06:24.710 --> 00:06:26.550 relapse during a cannabis treatment

NOTE Confidence: 0.971026

00:06:26.550 --> 00:06:27.050 trial

NOTE Confidence: 0.99421036

00:06:27.854 --> 00:06:29.235 compared to people with cannabis

NOTE Confidence: 0.99421036

00:06:29.375 --> 00:06:30.194 only use.

NOTE Confidence: 0.9098063

00:06:30.495 --> 00:06:31.935 Moore and Bugney showed that

NOTE Confidence: 0.9098063

00:06:31.935 --> 00:06:33.535 people with current tobacco co

NOTE Confidence: 0.9098063

00:06:33.535 --> 00:06:35.395 use relapsed to cannabis faster

NOTE Confidence: 0.95011395

00:06:35.935 --> 00:06:37.455 than those who previously used

NOTE Confidence: 0.95011395

00:06:37.455 --> 00:06:37.955 tobacco.

NOTE Confidence: 0.925076

00:06:38.654 --> 00:06:40.014 And Meg Haney's lab at

NOTE Confidence: 0.925076

00:06:40.014 --> 00:06:40.514 Columbia

NOTE Confidence: 0.9982422

00:06:40.895 --> 00:06:42.255 showed that people with co

NOTE Confidence: 0.9982422

00:06:42.255 --> 00:06:44.080 use were twenty times more

NOTE Confidence: 0.9982422

00:06:44.080 --> 00:06:45.700 likely to relapse to cannabis

NOTE Confidence: 0.99593097

00:06:46.080 --> 00:06:47.839 than people with cannabis only

NOTE Confidence: 0.99593097

00:06:47.839 --> 00:06:48.339 use.

NOTE Confidence: 0.9784465

00:06:49.920 --> 00:06:51.279 So this raises the question,

NOTE Confidence: 0.9784465

00:06:51.279 --> 00:06:53.200 what's responsible for this higher

NOTE Confidence: 0.9784465

00:06:53.200 --> 00:06:55.300 or faster cannabis relapse rates

NOTE Confidence: 0.9784465

00:06:55.520 --> 00:06:57.380 in people with tobacco couse?

NOTE Confidence: 0.9692383

00:06:57.784 --> 00:06:58.764 Could it be withdrawal?

NOTE Confidence: 0.9698079

00:06:59.544 --> 00:07:01.404 So we sought to investigate

NOTE Confidence: 0.9698079

00:07:01.544 --> 00:07:03.464 this relationship looking to see

NOTE Confidence: 0.9698079

00:07:03.464 --> 00:07:05.324 if tobacco co use influences

NOTE Confidence: 0.9698079

00:07:05.544 --> 00:07:07.085 cannabis withdrawal severity

NOTE Confidence: 0.9926758

00:07:07.464 --> 00:07:08.664 in people with a current

NOTE Confidence: 0.9926758

00:07:08.664 --> 00:07:09.884 cannabis use disorder

NOTE Confidence: 0.9001465

00:07:10.264 --> 00:07:10.764 during,

NOTE Confidence: 0.94685245

00:07:11.509 --> 00:07:13.110 an abstinence paradigm where we

NOTE Confidence: 0.94685245

00:07:13.110 --> 00:07:14.389 ask people to quit for

NOTE Confidence: 0.94685245

00:07:14.389 --> 00:07:15.370 twenty eight days.

NOTE Confidence: 0.9449426

00:07:15.990 --> 00:07:17.110 And we chose the twenty

NOTE Confidence: 0.9449426

00:07:17.110 --> 00:07:18.710 eight day period so to

NOTE Confidence: 0.9449426

00:07:18.710 --> 00:07:21.030 coincide with withdrawal trajectory, which

NOTE Confidence: 0.9449426

00:07:21.030 --> 00:07:22.310 we know to be twenty

NOTE Confidence: 0.9449426

00:07:22.310 --> 00:07:24.465 eight days and also with

NOTE Confidence: 0.9449426

00:07:24.544 --> 00:07:26.465 the urinary elimination of THC

NOTE Confidence: 0.9449426

00:07:26.465 --> 00:07:27.365 from the body.

NOTE Confidence: 0.994751

00:07:28.705 --> 00:07:30.245 So we conducted a secondary

NOTE Confidence: 0.994751

00:07:30.385 --> 00:07:31.665 analysis. We had,

NOTE Confidence: 0.9995117

00:07:32.544 --> 00:07:33.365 twenty participants

NOTE Confidence: 0.9848938

00:07:33.665 --> 00:07:34.865 who met criteria for a

NOTE Confidence: 0.9848938

00:07:34.865 --> 00:07:36.085 cannabis use disorder,

NOTE Confidence: 0.9536621

00:07:36.385 --> 00:07:37.665 and we parsed them according

NOTE Confidence: 0.9536621

00:07:37.665 --> 00:07:39.604 to their current tobacco use.

NOTE Confidence: 0.9517985

00:07:40.960 --> 00:07:41.919 So we had a group,

NOTE Confidence: 0.9517985

00:07:41.919 --> 00:07:42.960 which we called our co

NOTE Confidence: 0.9517985

00:07:42.960 --> 00:07:44.240 users, and we denoted them

NOTE Confidence: 0.9517985

00:07:44.240 --> 00:07:45.919 by c t plus. So

NOTE Confidence: 0.9517985

00:07:45.919 --> 00:07:47.039 these are people who met

NOTE Confidence: 0.9517985

00:07:47.039 --> 00:07:48.580 for a cannabis use disorder

NOTE Confidence: 0.99449325

00:07:49.039 --> 00:07:50.719 and smoked either ten or

NOTE Confidence: 0.99449325

00:07:50.719 --> 00:07:52.419 more cigarettes per day.

NOTE Confidence: 0.9987522

00:07:52.884 --> 00:07:53.685 And then we had a

NOTE Confidence: 0.9987522

00:07:53.685 --> 00:07:55.384 cannabis only user group,

NOTE Confidence: 0.9963379

00:07:56.004 --> 00:07:56.985 which also,

NOTE Confidence: 0.9996745

00:07:57.604 --> 00:07:59.044 had to include people with

NOTE Confidence: 0.9996745

00:07:59.044 --> 00:08:00.745 very light tobacco use

NOTE Confidence: 0.9543186

00:08:01.205 --> 00:08:02.724 because we actually didn't have

NOTE Confidence: 0.9543186

00:08:02.724 --> 00:08:04.405 enough people who just used

NOTE Confidence: 0.9543186

00:08:04.405 --> 00:08:06.004 cannabis alone. So the CT

NOTE Confidence: 0.9543186

00:08:06.004 --> 00:08:07.410 minus group is a group

NOTE Confidence: 0.9543186

00:08:07.410 --> 00:08:09.090 of individuals who used either

NOTE Confidence: 0.9543186

00:08:09.090 --> 00:08:10.070 cannabis alone

NOTE Confidence: 0.9102539

00:08:10.530 --> 00:08:11.970 or co used but less

NOTE Confidence: 0.9102539

00:08:11.970 --> 00:08:13.669 than five cigarettes per day.

NOTE Confidence: 0.9988064

00:08:15.729 --> 00:08:17.090 And so we just recruited

NOTE Confidence: 0.9988064

00:08:17.090 --> 00:08:18.389 people from the community.

NOTE Confidence: 0.96715367

00:08:19.345 --> 00:08:20.465 Everybody in the sample was

NOTE Confidence: 0.96715367

00:08:20.465 --> 00:08:21.585 male just because it was

NOTE Confidence: 0.96715367

00:08:21.585 --> 00:08:22.885 a secondary analysis.

NOTE Confidence: 0.97559756

00:08:23.905 --> 00:08:24.785 Like I said, they all

NOTE Confidence: 0.97559756

00:08:24.785 --> 00:08:25.905 met for a cannabis use

NOTE Confidence: 0.97559756

00:08:25.905 --> 00:08:27.345 disorder and came up positive

NOTE Confidence: 0.97559756

00:08:27.345 --> 00:08:29.125 for THC at the screening

NOTE Confidence: 0.97559756

00:08:29.185 --> 00:08:29.685 day.

NOTE Confidence: 0.99595016

00:08:29.985 --> 00:08:31.185 They were willing to abstain

NOTE Confidence: 0.99595016

00:08:31.185 --> 00:08:32.705 for cannabis for twenty eight

NOTE Confidence: 0.99595016

00:08:32.705 --> 00:08:33.745 days, but they were not

NOTE Confidence: 0.99595016

00:08:33.745 --> 00:08:34.645 treatment seeking.

NOTE Confidence: 0.95706177

00:08:35.320 --> 00:08:36.760 We excluded anyone with a

NOTE Confidence: 0.95706177

00:08:36.760 --> 00:08:38.300 current psychiatric disorder,

NOTE Confidence: 0.9904175

00:08:39.320 --> 00:08:40.600 if they came up positive

NOTE Confidence: 0.9904175

00:08:40.600 --> 00:08:42.360 for a psychoactive substance other

NOTE Confidence: 0.9904175

00:08:42.360 --> 00:08:43.179 than THC,

NOTE Confidence: 0.99502563

00:08:43.639 --> 00:08:44.760 if they were using any

NOTE Confidence: 0.99502563

00:08:44.760 --> 00:08:46.679 medications that were psychotropic in

NOTE Confidence: 0.99502563

00:08:46.679 --> 00:08:47.880 nature in the last six

NOTE Confidence: 0.99502563

00:08:47.880 --> 00:08:48.380 months,

NOTE Confidence: 0.9984809

00:08:48.865 --> 00:08:49.745 And if they had any

NOTE Confidence: 0.9984809

00:08:49.745 --> 00:08:51.125 serious medical or neurological

NOTE Confidence: 0.9989258

00:08:51.585 --> 00:08:54.005 conditions, we also excluded them.

NOTE Confidence: 0.98909503

00:08:55.184 --> 00:08:56.465 So this was our study

NOTE Confidence: 0.98909503

00:08:56.465 --> 00:08:56.965 design.

NOTE Confidence: 0.9796001

00:08:57.665 --> 00:08:59.745 Once eligibility was confirmed, we

NOTE Confidence: 0.9796001

00:08:59.745 --> 00:09:01.860 asked participants to quit the

NOTE Confidence: 0.9796001

00:09:01.860 --> 00:09:03.300 night before, about twelve hours

NOTE Confidence: 0.9796001

00:09:03.300 --> 00:09:04.500 before coming in for the

NOTE Confidence: 0.9796001

00:09:04.500 --> 00:09:06.420 baseline visit. And this was

NOTE Confidence: 0.9796001

00:09:06.420 --> 00:09:07.800 to try to capture them

NOTE Confidence: 0.9796001

00:09:08.020 --> 00:09:09.540 between the window of acute

NOTE Confidence: 0.9796001

00:09:09.540 --> 00:09:11.940 intoxication, but also before the

NOTE Confidence: 0.9796001

00:09:11.940 --> 00:09:13.080 onset of withdrawal.

NOTE Confidence: 0.9720917

00:09:13.985 --> 00:09:15.025 So then we then got

NOTE Confidence: 0.9720917

00:09:15.025 --> 00:09:16.065 people to come in for

NOTE Confidence: 0.9720917

00:09:16.065 --> 00:09:18.305 weekly study visits where we

NOTE Confidence: 0.9720917

00:09:18.305 --> 00:09:19.665 assess withdrawal. So we use

NOTE Confidence: 0.9720917

00:09:19.665 --> 00:09:21.985 the marijuana withdrawal checklist, which

NOTE Confidence: 0.9720917

00:09:21.985 --> 00:09:23.525 is a self report questionnaire

NOTE Confidence: 0.9720917

00:09:23.825 --> 00:09:24.565 where people

NOTE Confidence: 0.9830892

00:09:24.945 --> 00:09:26.885 rated the severity of fifteen

NOTE Confidence: 0.9830892

00:09:27.025 --> 00:09:28.760 of the most commonly reported

NOTE Confidence: 0.9830892

00:09:28.820 --> 00:09:30.580 withdrawal symptoms, and they were

NOTE Confidence: 0.9830892

00:09:30.580 --> 00:09:31.940 rated on a scale from

NOTE Confidence: 0.9830892

00:09:31.940 --> 00:09:33.860 zero being not present at

NOTE Confidence: 0.9830892

00:09:33.860 --> 00:09:36.200 all to three very severe.

NOTE Confidence: 0.9970703

00:09:38.900 --> 00:09:39.720 And so

NOTE Confidence: 0.9322151

00:09:40.145 --> 00:09:41.505 we also use the timeline

NOTE Confidence: 0.9322151

00:09:41.505 --> 00:09:42.465 follow back just to get

NOTE Confidence: 0.9322151

00:09:42.465 --> 00:09:43.825 a self report measure of

NOTE Confidence: 0.9322151

00:09:43.825 --> 00:09:44.804 substance use.

NOTE Confidence: 0.9597168

00:09:45.425 --> 00:09:46.865 And to get people to

NOTE Confidence: 0.9597168

00:09:46.865 --> 00:09:48.545 achieve absence, we offer them

NOTE Confidence: 0.9597168

00:09:48.545 --> 00:09:50.005 weekly behavioral therapy

NOTE Confidence: 0.8409424

00:09:50.385 --> 00:09:51.205 very briefly.

NOTE Confidence: 0.955003

00:09:51.745 --> 00:09:53.105 But what really got people

NOTE Confidence: 0.955003

00:09:53.105 --> 00:09:54.304 to quit is we offered

NOTE Confidence: 0.955003

00:09:54.304 --> 00:09:55.980 them contingency management.

NOTE Confidence: 0.8864746

00:10:03.420 --> 00:10:03.920 Bonus.

NOTE Confidence: 0.9547679

00:10:04.300 --> 00:10:05.420 And we didn't just rely

NOTE Confidence: 0.9547679

00:10:05.420 --> 00:10:07.339 on self report. We actually

NOTE Confidence: 0.9547679

00:10:07.339 --> 00:10:09.179 collected urine twice weekly. And

NOTE Confidence: 0.9547679

00:10:09.179 --> 00:10:10.220 so we were able to

NOTE Confidence: 0.9547679

00:10:10.220 --> 00:10:12.375 confirm abstinence by chemically.

NOTE Confidence: 0.8929036

00:10:14.115 --> 00:10:15.955 So twenty participants completed the

NOTE Confidence: 0.8929036

00:10:15.955 --> 00:10:16.455 study.

NOTE Confidence: 0.96533203

00:10:16.995 --> 00:10:18.195 We had eleven people in

NOTE Confidence: 0.96533203

00:10:18.195 --> 00:10:19.555 the co use group and

NOTE Confidence: 0.96533203

00:10:19.555 --> 00:10:20.295 nine in

NOTE Confidence: 0.83353096

00:10:20.675 --> 00:10:22.675 the cannabis only co use

NOTE Confidence: 0.83353096

00:10:22.675 --> 00:10:23.415 light group.

NOTE Confidence: 0.9498088

00:10:24.650 --> 00:10:25.850 Two people in the co

NOTE Confidence: 0.9498088

00:10:25.850 --> 00:10:27.230 use group relapsed,

NOTE Confidence: 0.99958146

00:10:27.770 --> 00:10:28.970 and none in the other

NOTE Confidence: 0.99958146

00:10:28.970 --> 00:10:29.870 group relapsed.

NOTE Confidence: 0.9975586

00:10:30.490 --> 00:10:31.690 What was really nice is

NOTE Confidence: 0.9975586

00:10:31.690 --> 00:10:32.809 that the groups were well

NOTE Confidence: 0.9975586

00:10:32.809 --> 00:10:33.950 matched on age,

NOTE Confidence: 0.95953774

00:10:34.809 --> 00:10:36.890 across all parameters of cannabis

NOTE Confidence: 0.95953774

00:10:36.890 --> 00:10:39.130 use, including lifetime years as

NOTE Confidence: 0.95953774

00:10:39.130 --> 00:10:41.065 well as frequency of use.

NOTE Confidence: 0.9530945

00:10:41.445 --> 00:10:42.805 And obviously, they differed on

NOTE Confidence: 0.9530945

00:10:42.805 --> 00:10:44.184 tobacco use. So

NOTE Confidence: 0.98813474

00:10:44.565 --> 00:10:46.325 our co users were smoking

NOTE Confidence: 0.98813474

00:10:46.325 --> 00:10:47.545 about a pack a day

NOTE Confidence: 0.9175415

00:10:48.085 --> 00:10:50.265 and, met for moderate nicotine

NOTE Confidence: 0.9175415

00:10:50.325 --> 00:10:51.865 dependence, while our

NOTE Confidence: 0.9300537

00:10:52.170 --> 00:10:53.690 CT minus group were just

NOTE Confidence: 0.9300537

00:10:53.690 --> 00:10:55.050 using on average about three

NOTE Confidence: 0.9300537

00:10:55.050 --> 00:10:56.170 and a half cigarettes per

NOTE Confidence: 0.9300537

00:10:56.170 --> 00:10:56.670 day

NOTE Confidence: 0.88449097

00:10:57.210 --> 00:10:59.470 and that met for minimal

NOTE Confidence: 0.88449097

00:10:59.610 --> 00:11:00.589 or very mild,

NOTE Confidence: 0.9987793

00:11:02.570 --> 00:11:03.710 nicotine dependence.

NOTE Confidence: 0.9930827

00:11:05.464 --> 00:11:06.824 So when we looked at

NOTE Confidence: 0.9930827

00:11:06.824 --> 00:11:07.324 participants

NOTE Confidence: 0.98739344

00:11:07.625 --> 00:11:09.625 with, cannabis use disorder with

NOTE Confidence: 0.98739344

00:11:09.625 --> 00:11:11.144 either no or low tobacco

NOTE Confidence: 0.98739344

00:11:11.144 --> 00:11:11.644 use,

NOTE Confidence: 0.9966395

00:11:12.024 --> 00:11:13.144 what we saw is this

NOTE Confidence: 0.9966395

00:11:13.144 --> 00:11:15.225 very typical or the classic

NOTE Confidence: 0.9966395

00:11:15.225 --> 00:11:17.404 withdrawal trajectory that we expected

NOTE Confidence: 0.9966395

00:11:17.545 --> 00:11:18.204 to see.

NOTE Confidence: 0.99348146

00:11:18.940 --> 00:11:20.300 However, when we looked at

NOTE Confidence: 0.99348146

00:11:20.300 --> 00:11:21.500 the co use group, we

NOTE Confidence: 0.99348146

00:11:21.500 --> 00:11:23.040 saw a very different pattern.

NOTE Confidence: 0.99348146

00:11:23.339 --> 00:11:24.300 So we saw that in

NOTE Confidence: 0.99348146

00:11:24.300 --> 00:11:26.320 this group, their their severity

NOTE Confidence: 0.99348146

00:11:26.459 --> 00:11:28.399 of cannabis withdrawal was elevated,

NOTE Confidence: 0.9988732

00:11:28.779 --> 00:11:30.699 and it remained elevated across

NOTE Confidence: 0.9988732

00:11:30.699 --> 00:11:31.660 all of the weeks that

NOTE Confidence: 0.9988732

00:11:31.660 --> 00:11:32.720 we assessed withdrawal.

NOTE Confidence: 0.9818374

00:11:34.705 --> 00:11:35.665 And so now that we

NOTE Confidence: 0.9818374

00:11:35.665 --> 00:11:37.025 had a behavior to explain

NOTE Confidence: 0.9818374

00:11:37.025 --> 00:11:38.465 high relapse rates in co

NOTE Confidence: 0.9818374

00:11:38.465 --> 00:11:40.225 users, we were now interested

NOTE Confidence: 0.9818374

00:11:40.225 --> 00:11:42.005 in determining what the molecular

NOTE Confidence: 0.9818374

00:11:42.225 --> 00:11:43.925 mechanisms were that were underlying

NOTE Confidence: 0.9818374

00:11:44.065 --> 00:11:45.525 these elevated rates.

NOTE Confidence: 0.9972769

00:11:46.600 --> 00:11:47.800 And so what we know

NOTE Confidence: 0.9972769

00:11:47.800 --> 00:11:49.660 is that chronic cannabis use

NOTE Confidence: 0.9972769

00:11:49.800 --> 00:11:50.860 alters the endocannabinoid

NOTE Confidence: 0.86865234

00:11:51.400 --> 00:11:51.900 system.

NOTE Confidence: 0.98173386

00:11:52.760 --> 00:11:54.120 Lots of studies showing that

NOTE Confidence: 0.98173386

00:11:54.120 --> 00:11:55.960 chronic use of cannabis causes

NOTE Confidence: 0.98173386

00:11:55.960 --> 00:11:56.460 downregulation

NOTE Confidence: 0.9956299

00:11:56.840 --> 00:11:58.520 of cannabinoid one receptors in

NOTE Confidence: 0.9956299

00:11:58.520 --> 00:12:00.285 the brain. We also see

NOTE Confidence: 0.9956299

00:12:00.285 --> 00:12:01.645 this in the periphery. We

NOTE Confidence: 0.9956299

00:12:01.645 --> 00:12:03.585 see a decrease in endocannabinoid

NOTE Confidence: 0.99316406

00:12:03.965 --> 00:12:05.005 levels that have been measured

NOTE Confidence: 0.99316406

00:12:05.005 --> 00:12:05.745 in blood.

NOTE Confidence: 0.9935547

00:12:06.445 --> 00:12:08.705 And very interestingly, cannabis withdrawal

NOTE Confidence: 0.9935547

00:12:08.845 --> 00:12:10.385 has been linked to endocannabinoid

NOTE Confidence: 0.9685872

00:12:11.005 --> 00:12:11.505 dysregulation,

NOTE Confidence: 0.9557989

00:12:12.285 --> 00:12:13.325 which has been shown by

NOTE Confidence: 0.9557989

00:12:13.325 --> 00:12:14.225 doctor D'Souza,

NOTE Confidence: 0.9841872

00:12:14.880 --> 00:12:16.559 And higher withdrawal severity is

NOTE Confidence: 0.9841872

00:12:16.559 --> 00:12:19.140 actually associated with greater cannabinoid

NOTE Confidence: 0.9841872

00:12:19.280 --> 00:12:20.660 one receptor downregulation.

NOTE Confidence: 0.95955986

00:12:22.400 --> 00:12:24.400 Similar relationships have been shown

NOTE Confidence: 0.95955986

00:12:24.400 --> 00:12:25.840 in the periphery where withdrawal

NOTE Confidence: 0.95955986

00:12:25.840 --> 00:12:27.460 symptoms like depression, anxiety

NOTE Confidence: 0.94248044

00:12:27.840 --> 00:12:29.059 have been linked to endocannabinoid

NOTE Confidence: 0.9277344

00:12:29.520 --> 00:12:30.020 levels.

NOTE Confidence: 0.9427562

00:12:30.774 --> 00:12:32.295 And also studies in both

NOTE Confidence: 0.9427562

00:12:32.295 --> 00:12:33.895 humans and animals have shown

NOTE Confidence: 0.9427562

00:12:33.895 --> 00:12:35.095 that if we use a

NOTE Confidence: 0.9427562

00:12:35.095 --> 00:12:35.915 THA inhibitor,

NOTE Confidence: 0.9845715

00:12:37.735 --> 00:12:39.975 we can increase anandamide levels.

NOTE Confidence: 0.9845715

00:12:39.975 --> 00:12:41.334 So anandamide is one of

NOTE Confidence: 0.9845715

00:12:41.334 --> 00:12:42.635 the prominent endocannabinoids,

NOTE Confidence: 0.96007866

00:12:43.910 --> 00:12:45.510 and thaw is the enzyme

NOTE Confidence: 0.96007866

00:12:45.510 --> 00:12:46.950 that degrades anandmine. So if

NOTE Confidence: 0.96007866

00:12:46.950 --> 00:12:48.090 we block the breakdown

NOTE Confidence: 0.974775

00:12:48.710 --> 00:12:50.790 of anandamide, we're gonna see

NOTE Confidence: 0.974775

00:12:50.790 --> 00:12:52.870 increasing levels, and this actually

NOTE Confidence: 0.974775

00:12:52.870 --> 00:12:54.010 leads to a reduction

NOTE Confidence: 0.9974365

00:12:54.470 --> 00:12:56.170 of cannabis withdrawal symptoms.

NOTE Confidence: 0.9879536

00:12:57.885 --> 00:12:59.165 So what this suggests in

NOTE Confidence: 0.9879536

00:12:59.165 --> 00:13:00.525 the context of our data

NOTE Confidence: 0.9879536

00:13:00.525 --> 00:13:02.125 is that perhaps tobacco co

NOTE Confidence: 0.9879536

00:13:02.125 --> 00:13:04.385 use may exacerbate endocannabinoid

NOTE Confidence: 0.9960124

00:13:05.565 --> 00:13:07.905 dysfunction in people with cannabis

NOTE Confidence: 0.9960124

00:13:07.965 --> 00:13:08.465 use.

NOTE Confidence: 0.99924046

00:13:09.809 --> 00:13:11.090 And so we were able

NOTE Confidence: 0.99924046

00:13:11.090 --> 00:13:12.230 to test this hypothesis

NOTE Confidence: 0.9935303

00:13:12.530 --> 00:13:14.710 in another secondary analysis

NOTE Confidence: 0.9897461

00:13:15.490 --> 00:13:17.110 using data from Romina's,

NOTE Confidence: 0.9925198

00:13:18.210 --> 00:13:20.210 Romina's cohort. So she collected

NOTE Confidence: 0.9925198

00:13:20.210 --> 00:13:22.070 data in people with cannabis

NOTE Confidence: 0.9925198

00:13:22.210 --> 00:13:23.110 use disorder

NOTE Confidence: 0.9148124

00:13:23.634 --> 00:13:25.815 using a validated FAW tracer

NOTE Confidence: 0.9148124

00:13:26.035 --> 00:13:27.014 called CRB.

NOTE Confidence: 0.9932528

00:13:28.194 --> 00:13:29.235 And so just to remind

NOTE Confidence: 0.9932528

00:13:29.235 --> 00:13:30.755 you that FAW degrades the

NOTE Confidence: 0.9932528

00:13:30.755 --> 00:13:31.255 endocannabinoid

NOTE Confidence: 0.8963623

00:13:31.714 --> 00:13:32.214 anandamide,

NOTE Confidence: 0.97614205

00:13:32.755 --> 00:13:33.554 and we used it as

NOTE Confidence: 0.97614205

00:13:33.554 --> 00:13:34.774 a proxy for endocannabinoid

NOTE Confidence: 0.991862

00:13:35.394 --> 00:13:36.774 activity or signaling.

NOTE Confidence: 0.9654083

00:13:37.250 --> 00:13:38.210 And so the question that

NOTE Confidence: 0.9654083

00:13:38.210 --> 00:13:39.649 we sought to answer was,

NOTE Confidence: 0.9654083

00:13:39.649 --> 00:13:40.850 do fall levels in the

NOTE Confidence: 0.9654083

00:13:40.850 --> 00:13:41.350 brain

NOTE Confidence: 0.97268677

00:13:41.890 --> 00:13:43.890 differ between individuals with co

NOTE Confidence: 0.97268677

00:13:43.890 --> 00:13:45.809 use compared to those with

NOTE Confidence: 0.97268677

00:13:45.809 --> 00:13:48.149 cannabis only use following overnight

NOTE Confidence: 0.97268677

00:13:48.210 --> 00:13:48.710 abstinence?

NOTE Confidence: 0.9937744

00:13:50.695 --> 00:13:52.135 And we also wanted to

NOTE Confidence: 0.9937744

00:13:52.135 --> 00:13:53.575 look to see if tobacco

NOTE Confidence: 0.9937744

00:13:53.575 --> 00:13:54.315 use independently

NOTE Confidence: 0.959082

00:13:54.695 --> 00:13:56.475 was associated with fall levels.

NOTE Confidence: 0.9812333

00:13:57.735 --> 00:13:59.735 So the sample was, we

NOTE Confidence: 0.9812333

00:13:59.735 --> 00:14:01.015 had five people in the

NOTE Confidence: 0.9812333

00:14:01.015 --> 00:14:02.535 co use group and eight

NOTE Confidence: 0.9812333

00:14:02.535 --> 00:14:03.895 people in the cannabis only

NOTE Confidence: 0.9812333

00:14:03.895 --> 00:14:04.860 group. And just to know

NOTE Confidence: 0.9812333

00:14:04.860 --> 00:14:05.900 that this is a different

NOTE Confidence: 0.9812333

00:14:05.900 --> 00:14:06.780 sample than the one I

NOTE Confidence: 0.9812333

00:14:06.780 --> 00:14:08.320 previously presented before.

NOTE Confidence: 0.95440674

00:14:08.700 --> 00:14:10.940 So these cannabis only users

NOTE Confidence: 0.95440674

00:14:10.940 --> 00:14:12.780 were were really only just

NOTE Confidence: 0.95440674

00:14:12.780 --> 00:14:13.760 using cannabis.

NOTE Confidence: 0.9569634

00:14:14.220 --> 00:14:15.420 And again, we had the

NOTE Confidence: 0.9569634

00:14:15.420 --> 00:14:16.860 groups very well matched on

NOTE Confidence: 0.9569634

00:14:16.860 --> 00:14:17.980 age as well as all

NOTE Confidence: 0.9569634

00:14:17.980 --> 00:14:19.600 the cannabis parameters.

NOTE Confidence: 0.93617314

00:14:20.265 --> 00:14:21.465 And again, they differed on

NOTE Confidence: 0.93617314

00:14:21.465 --> 00:14:23.145 tobacco use, so our CT

NOTE Confidence: 0.93617314

00:14:23.145 --> 00:14:24.825 plus group was using about

NOTE Confidence: 0.93617314

00:14:24.825 --> 00:14:26.665 six cigarettes per day and

NOTE Confidence: 0.93617314

00:14:26.665 --> 00:14:27.865 met for mild,

NOTE Confidence: 0.99902344

00:14:28.265 --> 00:14:29.325 nicotine dependence.

NOTE Confidence: 0.9834798

00:14:31.625 --> 00:14:33.225 So when we looked across

NOTE Confidence: 0.9834798

00:14:33.225 --> 00:14:34.505 regions of interest, and we

NOTE Confidence: 0.9834798

00:14:34.505 --> 00:14:36.610 looked at regions of interest

NOTE Confidence: 0.97365993

00:14:37.070 --> 00:14:38.430 that were that had high

NOTE Confidence: 0.97365993

00:14:38.430 --> 00:14:40.190 levels of cannabinoid one receptors

NOTE Confidence: 0.97365993

00:14:40.190 --> 00:14:41.550 and also had high levels

NOTE Confidence: 0.97365993

00:14:41.550 --> 00:14:43.010 of nicotine acetylcholine

NOTE Confidence: 0.9172363

00:14:43.470 --> 00:14:43.970 receptors.

NOTE Confidence: 0.9953613

00:14:44.590 --> 00:14:45.790 And you can see that

NOTE Confidence: 0.9953613

00:14:45.790 --> 00:14:47.090 across all regions

NOTE Confidence: 0.9911296

00:14:47.630 --> 00:14:48.690 that were examined,

NOTE Confidence: 0.9844401

00:14:49.445 --> 00:14:50.645 the co use group, which

NOTE Confidence: 0.9844401

00:14:50.645 --> 00:14:52.165 is the one denoted in

NOTE Confidence: 0.9844401

00:14:52.165 --> 00:14:54.185 orange, had higher fall levels

NOTE Confidence: 0.9940999

00:14:54.645 --> 00:14:56.964 than people with cannabis only

NOTE Confidence: 0.9940999

00:14:56.964 --> 00:14:57.464 use.

NOTE Confidence: 0.9941406

00:14:58.245 --> 00:14:58.745 And

NOTE Confidence: 0.99260604

00:14:59.285 --> 00:15:00.805 this even though the groups

NOTE Confidence: 0.99260604

00:15:00.805 --> 00:15:01.545 were small,

NOTE Confidence: 0.9746326

00:15:02.010 --> 00:15:04.170 significant differences emerged, in the

NOTE Confidence: 0.9746326

00:15:04.170 --> 00:15:06.410 cerebellum shown here, as well

NOTE Confidence: 0.9746326

00:15:06.410 --> 00:15:08.030 as the substantia nigra.

NOTE Confidence: 0.9501953

00:15:08.810 --> 00:15:10.090 But really this trend was

NOTE Confidence: 0.9501953

00:15:10.090 --> 00:15:12.430 present across all regions examined.

NOTE Confidence: 0.9612165

00:15:14.345 --> 00:15:15.704 And also, when we look

NOTE Confidence: 0.9612165

00:15:15.704 --> 00:15:16.345 to see,

NOTE Confidence: 0.97348946

00:15:17.144 --> 00:15:19.065 how tobacco use or cigarettes

NOTE Confidence: 0.97348946

00:15:19.065 --> 00:15:20.904 per day correlated with FAW,

NOTE Confidence: 0.97348946

00:15:20.904 --> 00:15:22.605 we saw a positive relationship

NOTE Confidence: 0.97348946

00:15:22.745 --> 00:15:24.665 where greater tobacco use actually

NOTE Confidence: 0.97348946

00:15:24.665 --> 00:15:25.165 correlated

NOTE Confidence: 0.9882987

00:15:25.704 --> 00:15:27.144 with higher FAW levels in

NOTE Confidence: 0.9882987

00:15:27.144 --> 00:15:27.884 the cerebellum.

NOTE Confidence: 0.9930061

00:15:29.040 --> 00:15:30.160 And it came out as

NOTE Confidence: 0.9930061

00:15:30.160 --> 00:15:31.360 trend level when we looked

NOTE Confidence: 0.9930061

00:15:31.360 --> 00:15:32.720 at the relationship in the

NOTE Confidence: 0.9930061

00:15:32.720 --> 00:15:33.940 substantia nigra.

NOTE Confidence: 0.959246

00:15:36.320 --> 00:15:37.440 So what this suggests is

NOTE Confidence: 0.959246

00:15:37.440 --> 00:15:38.960 that tobacco use may be

NOTE Confidence: 0.959246

00:15:38.960 --> 00:15:40.980 independently contributing to endocannabinoid

NOTE Confidence: 0.99902344

00:15:41.520 --> 00:15:42.020 dysfunction

NOTE Confidence: 0.99785155

00:15:42.654 --> 00:15:44.515 in people with cannabis use.

NOTE Confidence: 0.98148507

00:15:45.295 --> 00:15:46.735 So just to quickly summarize

NOTE Confidence: 0.98148507

00:15:46.735 --> 00:15:47.855 what I've shown so far

NOTE Confidence: 0.98148507

00:15:47.855 --> 00:15:49.455 is that people who co

NOTE Confidence: 0.98148507

00:15:49.455 --> 00:15:51.075 use have elevated and prolonged

NOTE Confidence: 0.98148507

00:15:51.135 --> 00:15:53.214 withdrawal severity compared to people

NOTE Confidence: 0.98148507

00:15:53.214 --> 00:15:55.270 with cannabis only use. People

NOTE Confidence: 0.98148507

00:15:55.270 --> 00:15:56.550 with co use have higher

NOTE Confidence: 0.98148507

00:15:56.550 --> 00:15:58.070 fall levels than people with

NOTE Confidence: 0.98148507

00:15:58.070 --> 00:15:59.370 cannabis only use.

NOTE Confidence: 0.9988281

00:15:59.750 --> 00:16:02.089 Tobacco use may independently predict

NOTE Confidence: 0.9144694

00:16:02.390 --> 00:16:03.610 greater fall levels,

NOTE Confidence: 0.9855957

00:16:04.070 --> 00:16:05.670 and greater withdrawal severity in

NOTE Confidence: 0.9855957

00:16:05.670 --> 00:16:07.365 co users may actually reflect

NOTE Confidence: 0.9855957

00:16:07.605 --> 00:16:09.065 an exacerbated endocannabinoid

NOTE Confidence: 0.99126524

00:16:09.605 --> 00:16:11.065 dysfunction or dysregulation.

NOTE Confidence: 0.83569336

00:16:12.725 --> 00:16:14.024 And so perhaps the

NOTE Confidence: 0.99035645

00:16:14.325 --> 00:16:14.825 endocannabinoid

NOTE Confidence: 0.9995117

00:16:15.285 --> 00:16:17.065 system is a promising therapeutic

NOTE Confidence: 0.9995117

00:16:17.285 --> 00:16:17.785 target

NOTE Confidence: 0.9715169

00:16:18.165 --> 00:16:19.945 to treat cannabis use disorder

NOTE Confidence: 0.9715169

00:16:20.005 --> 00:16:22.084 as well as people who

NOTE Confidence: 0.9715169

00:16:22.084 --> 00:16:22.904 co use.

NOTE Confidence: 0.99902344

00:16:24.300 --> 00:16:25.020 But one thing I do

NOTE Confidence: 0.99902344

00:16:25.020 --> 00:16:26.060 want to point out is

NOTE Confidence: 0.99902344

00:16:26.060 --> 00:16:26.960 that the endocannabinoid

NOTE Confidence: 0.9779367

00:16:27.420 --> 00:16:28.700 system is not a one

NOTE Confidence: 0.9779367

00:16:28.700 --> 00:16:30.860 size fits all. In fact,

NOTE Confidence: 0.9779367

00:16:30.860 --> 00:16:32.620 there's great variability, and one

NOTE Confidence: 0.9779367

00:16:32.620 --> 00:16:34.620 of theone of the sources

NOTE Confidence: 0.9779367

00:16:34.620 --> 00:16:36.540 of variability comes from sex.

NOTE Confidence: 0.9779367

00:16:36.540 --> 00:16:38.065 So, we see lots of

NOTE Confidence: 0.9779367

00:16:38.065 --> 00:16:40.485 sex differences across the endocannabinoid

NOTE Confidence: 0.9802246

00:16:41.024 --> 00:16:41.524 system.

NOTE Confidence: 0.9418132

00:16:42.144 --> 00:16:44.065 However, our understanding of cannabis

NOTE Confidence: 0.9418132

00:16:44.065 --> 00:16:45.125 use and the endocannabinoid

NOTE Confidence: 0.99958146

00:16:45.584 --> 00:16:47.365 system in females is actually

NOTE Confidence: 0.99958146

00:16:47.584 --> 00:16:48.404 quite limited.

NOTE Confidence: 0.9660516

00:16:50.400 --> 00:16:51.760 So, for people who are

NOTE Confidence: 0.9660516

00:16:51.760 --> 00:16:53.600 doing cannabis use research, I'm

NOTE Confidence: 0.9660516

00:16:53.600 --> 00:16:55.200 sure you're familiar with that

NOTE Confidence: 0.9660516

00:16:55.200 --> 00:16:57.220 females are very underrepresented

NOTE Confidence: 0.9781087

00:16:58.000 --> 00:16:59.220 in cannabis studies.

NOTE Confidence: 0.94003904

00:17:00.480 --> 00:17:01.665 And this is really a

NOTE Confidence: 0.94003904

00:17:01.824 --> 00:17:03.685 problem, especially these days because

NOTE Confidence: 0.94003904

00:17:03.745 --> 00:17:05.525 we're seeing that since legalization,

NOTE Confidence: 0.9937166

00:17:06.544 --> 00:17:07.825 rates of cannabis use in

NOTE Confidence: 0.9937166

00:17:07.825 --> 00:17:09.825 females are actually escalating at

NOTE Confidence: 0.9937166

00:17:09.825 --> 00:17:11.345 a much faster rate in

NOTE Confidence: 0.9937166

00:17:11.345 --> 00:17:13.365 females relative to males.

NOTE Confidence: 0.9714577

00:17:14.020 --> 00:17:15.220 And new data just came

NOTE Confidence: 0.9714577

00:17:15.220 --> 00:17:16.660 out from the states that

NOTE Confidence: 0.9714577

00:17:16.660 --> 00:17:19.000 actually showed that female adolescents

NOTE Confidence: 0.9714577

00:17:19.220 --> 00:17:21.140 now have higher rates of

NOTE Confidence: 0.9714577

00:17:21.140 --> 00:17:22.119 cannabis use

NOTE Confidence: 0.97664016

00:17:22.420 --> 00:17:24.500 compared to male adolescents. So

NOTE Confidence: 0.97664016

00:17:24.500 --> 00:17:26.980 this historical trend of males

NOTE Confidence: 0.97664016

00:17:26.980 --> 00:17:28.585 having higher rates of than

NOTE Confidence: 0.97664016

00:17:28.585 --> 00:17:30.025 females is we're now seeing

NOTE Confidence: 0.97664016

00:17:30.025 --> 00:17:30.685 a reversal

NOTE Confidence: 0.9966634

00:17:31.225 --> 00:17:32.205 in these patterns.

NOTE Confidence: 0.98431396

00:17:34.505 --> 00:17:35.885 And this is really concerning

NOTE Confidence: 0.98431396

00:17:36.025 --> 00:17:37.785 because females actually have worse

NOTE Confidence: 0.98431396

00:17:37.785 --> 00:17:40.025 cannabis treatment outcomes compared to

NOTE Confidence: 0.98431396

00:17:40.025 --> 00:17:40.525 males.

NOTE Confidence: 0.96950954

00:17:40.920 --> 00:17:41.800 So they tend to be

NOTE Confidence: 0.96950954

00:17:41.800 --> 00:17:43.180 less adherent to medications.

NOTE Confidence: 0.99902344

00:17:43.480 --> 00:17:45.100 They have reduced responsiveness

NOTE Confidence: 0.9970703

00:17:45.480 --> 00:17:46.140 to interventions.

NOTE Confidence: 0.986145

00:17:47.160 --> 00:17:49.080 They often demonstrate higher relapse

NOTE Confidence: 0.986145

00:17:49.080 --> 00:17:50.220 rates and lower

NOTE Confidence: 0.98657227

00:17:50.840 --> 00:17:52.060 cessation success.

NOTE Confidence: 0.83063823

00:17:52.840 --> 00:17:54.119 And so, again, it could

NOTE Confidence: 0.83063823

00:17:54.119 --> 00:17:54.462 be that cannabis withdrawal may

NOTE Confidence: 0.83063823

00:17:54.462 --> 00:17:54.840 underlie some of these sex

NOTE Confidence: 0.83063823

00:17:54.840 --> 00:17:55.275 specific effects.

NOTE Confidence: 0.90356445

00:18:06.155 --> 00:18:06.734 The data is quite mixed.

NOTE Confidence: 0.90356445

00:18:06.795 --> 00:18:08.010 There's some the data is

NOTE Confidence: 0.90356445

00:18:08.010 --> 00:18:09.450 quite mixed. There are some

NOTE Confidence: 0.90356445

00:18:09.450 --> 00:18:11.290 studies that show that females

NOTE Confidence: 0.90356445

00:18:11.290 --> 00:18:13.290 experience greater withdrawal burden than

NOTE Confidence: 0.90356445

00:18:13.290 --> 00:18:13.790 males,

NOTE Confidence: 0.9521077

00:18:14.250 --> 00:18:15.710 others that show the reverse

NOTE Confidence: 0.9521077

00:18:15.850 --> 00:18:16.350 relationship,

NOTE Confidence: 0.92685837

00:18:17.050 --> 00:18:18.330 and then many studies that

NOTE Confidence: 0.92685837

00:18:18.330 --> 00:18:19.690 actually show that there's no

NOTE Confidence: 0.92685837

00:18:19.690 --> 00:18:21.770 sex differences in cannabis withdrawal

NOTE Confidence: 0.92685837

00:18:21.770 --> 00:18:22.750 severity or

NOTE Confidence: 0.96069336

00:18:36.705 --> 00:18:38.109 And this is quite And

NOTE Confidence: 0.96069336

00:18:38.109 --> 00:18:40.029 this is quite problematic because

NOTE Confidence: 0.96069336

00:18:40.029 --> 00:18:41.230 what we see is that

NOTE Confidence: 0.96069336

00:18:41.230 --> 00:18:41.730 females

NOTE Confidence: 0.9810018

00:18:42.350 --> 00:18:43.869 with cannabis use disorder tend

NOTE Confidence: 0.9810018

00:18:43.869 --> 00:18:45.390 to have higher rates of

NOTE Confidence: 0.9810018

00:18:45.390 --> 00:18:46.609 psychiatric comorbidities,

NOTE Confidence: 0.99747723

00:18:47.549 --> 00:18:48.750 and the symptoms of these

NOTE Confidence: 0.99747723

00:18:48.750 --> 00:18:49.250 comorbidities

NOTE Confidence: 0.9880371

00:18:49.630 --> 00:18:50.690 actually overlap

NOTE Confidence: 0.9981864

00:18:51.149 --> 00:18:52.190 with a lot of the

NOTE Confidence: 0.9981864

00:18:52.190 --> 00:18:53.409 withdrawal symptoms.

NOTE Confidence: 0.95210403

00:18:55.205 --> 00:18:56.965 Second is that the evidence

NOTE Confidence: 0.95210403

00:18:56.965 --> 00:18:58.565 from these studies is derived

NOTE Confidence: 0.95210403

00:18:58.565 --> 00:18:59.065 from

NOTE Confidence: 0.96761066

00:18:59.445 --> 00:19:01.205 mostly studies that just have

NOTE Confidence: 0.96761066

00:19:01.205 --> 00:19:02.585 looked at one time point.

NOTE Confidence: 0.96761066

00:19:02.805 --> 00:19:03.625 They're predominantly

NOTE Confidence: 0.96173966

00:19:04.005 --> 00:19:05.685 cross sectional in nature, and

NOTE Confidence: 0.96173966

00:19:05.685 --> 00:19:06.805 they don't allow us to

NOTE Confidence: 0.96173966

00:19:06.805 --> 00:19:08.150 look at the dynamic

NOTE Confidence: 0.9802246

00:19:08.450 --> 00:19:09.590 or the time varying

NOTE Confidence: 0.99838865

00:19:10.050 --> 00:19:11.750 sex differences that may appear

NOTE Confidence: 0.99838865

00:19:11.890 --> 00:19:13.590 along the trajectory of withdrawal.

NOTE Confidence: 0.99194336

00:19:15.410 --> 00:19:16.450 And I also just wanted

NOTE Confidence: 0.99194336

00:19:16.450 --> 00:19:17.330 to point out that a

NOTE Confidence: 0.99194336

00:19:17.330 --> 00:19:18.130 lot of what we know

NOTE Confidence: 0.99194336

00:19:18.130 --> 00:19:19.890 about the cannabis withdrawal trajectory

NOTE Confidence: 0.99194336

00:19:19.890 --> 00:19:21.430 actually comes from studies

NOTE Confidence: 0.9393834

00:19:21.904 --> 00:19:23.605 that had been predominantly conducted

NOTE Confidence: 0.9393834

00:19:23.744 --> 00:19:24.484 in males.

NOTE Confidence: 0.80805117

00:19:25.664 --> 00:19:28.304 So Gabriela Malamud was a

NOTE Confidence: 0.80805117

00:19:28.304 --> 00:19:28.804 research,

NOTE Confidence: 0.9527995

00:19:29.105 --> 00:19:30.465 was a graduate student in

NOTE Confidence: 0.9527995

00:19:30.465 --> 00:19:31.825 my lab who recently finished

NOTE Confidence: 0.9527995

00:19:31.825 --> 00:19:32.565 her master's

NOTE Confidence: 0.82680666

00:19:33.264 --> 00:19:35.044 and she conducted, some preliminary

NOTE Confidence: 0.96085614

00:19:35.345 --> 00:19:37.500 analysis looking at how sex

NOTE Confidence: 0.96085614

00:19:37.500 --> 00:19:38.000 differences,

NOTE Confidence: 0.9892578

00:19:39.180 --> 00:19:39.680 portray

NOTE Confidence: 0.9958984

00:19:40.060 --> 00:19:42.560 across the cannabis withdrawal trajectory.

NOTE Confidence: 0.9703939

00:19:43.340 --> 00:19:44.460 So, in her project, she

NOTE Confidence: 0.9703939

00:19:44.460 --> 00:19:46.460 investigated how sex influences the

NOTE Confidence: 0.9703939

00:19:46.460 --> 00:19:48.480 severity of cannabis withdrawal symptoms

NOTE Confidence: 0.97821915

00:19:49.020 --> 00:19:50.140 in people with a current

NOTE Confidence: 0.97821915

00:19:50.140 --> 00:19:52.335 cannabis use disorder during twenty

NOTE Confidence: 0.97821915

00:19:52.335 --> 00:19:53.715 eight days of abstinence.

NOTE Confidence: 0.95801103

00:19:54.494 --> 00:19:56.255 And the inclusion exclusion criteria

NOTE Confidence: 0.95801103

00:19:56.255 --> 00:19:57.375 was pretty similar to the

NOTE Confidence: 0.95801103

00:19:57.375 --> 00:19:58.255 one that I showed you

NOTE Confidence: 0.95801103

00:19:58.255 --> 00:19:59.635 from the COUSE study,

NOTE Confidence: 0.9675781

00:19:59.935 --> 00:20:01.135 except here people had to

NOTE Confidence: 0.9675781

00:20:01.135 --> 00:20:02.675 identify as male or female.

NOTE Confidence: 0.9460217

00:20:03.160 --> 00:20:04.680 We also excluded people who

NOTE Confidence: 0.9460217

00:20:04.680 --> 00:20:06.780 smoked more than, ten cigarettes

NOTE Confidence: 0.9460217

00:20:06.840 --> 00:20:07.720 per day as well as

NOTE Confidence: 0.9460217

00:20:07.720 --> 00:20:09.640 females who were pregnant or

NOTE Confidence: 0.9460217

00:20:09.640 --> 00:20:10.140 breastfeeding.

NOTE Confidence: 0.92799884

00:20:12.200 --> 00:20:13.160 So it was the exact

NOTE Confidence: 0.92799884

00:20:13.160 --> 00:20:14.840 same study paradigm as I

NOTE Confidence: 0.92799884

00:20:14.840 --> 00:20:15.660 showed before.

NOTE Confidence: 0.9849243

00:20:16.585 --> 00:20:17.705 And in this study, we

NOTE Confidence: 0.9849243

00:20:17.705 --> 00:20:19.785 had twenty seven participants that

NOTE Confidence: 0.9849243

00:20:19.785 --> 00:20:20.845 completed abstinence,

NOTE Confidence: 0.9400635

00:20:21.305 --> 00:20:23.085 fifteen males, twelve females.

NOTE Confidence: 0.984167

00:20:23.705 --> 00:20:25.085 Two of the males relapsed,

NOTE Confidence: 0.984167

00:20:25.305 --> 00:20:26.744 three females relapsed, but there

NOTE Confidence: 0.984167

00:20:26.744 --> 00:20:28.505 was no sex difference in,

NOTE Confidence: 0.984167

00:20:28.825 --> 00:20:30.205 the abstinence rate.

NOTE Confidence: 0.9503581

00:20:31.859 --> 00:20:33.619 So the males and females

NOTE Confidence: 0.9503581

00:20:33.619 --> 00:20:35.700 were well matched across all

NOTE Confidence: 0.9503581

00:20:35.700 --> 00:20:37.640 parameters. So, age as well

NOTE Confidence: 0.9946289

00:20:38.100 --> 00:20:38.680 as cannabis

NOTE Confidence: 0.9760742

00:20:39.060 --> 00:20:41.540 parameters and cigarettes and alcohol

NOTE Confidence: 0.9760742

00:20:41.540 --> 00:20:42.680 use per day.

NOTE Confidence: 0.9526774

00:20:44.475 --> 00:20:45.355 But because we had a

NOTE Confidence: 0.9526774

00:20:45.355 --> 00:20:46.955 wide range of recency of

NOTE Confidence: 0.9526774

00:20:46.955 --> 00:20:48.555 use, we controlled for this

NOTE Confidence: 0.9526774

00:20:48.555 --> 00:20:49.855 in our analyses.

NOTE Confidence: 0.9862906

00:20:51.115 --> 00:20:52.155 And so when we looked

NOTE Confidence: 0.9862906

00:20:52.155 --> 00:20:53.675 at males, we saw again

NOTE Confidence: 0.9862906

00:20:53.675 --> 00:20:54.734 that they exhibited

NOTE Confidence: 0.9996745

00:20:55.115 --> 00:20:56.095 the very classic

NOTE Confidence: 0.9979553

00:20:56.760 --> 00:20:58.359 cannabis withdrawal trajectory that has

NOTE Confidence: 0.9979553

00:20:58.359 --> 00:20:59.740 been previously established.

NOTE Confidence: 0.9941782

00:21:01.000 --> 00:21:01.960 And when we looked at

NOTE Confidence: 0.9941782

00:21:01.960 --> 00:21:03.400 females, again, we saw a

NOTE Confidence: 0.9941782

00:21:03.400 --> 00:21:04.540 very different trajectory

NOTE Confidence: 0.9778276

00:21:05.000 --> 00:21:07.640 than males. So females experienced

NOTE Confidence: 0.9778276

00:21:07.640 --> 00:21:09.160 a more prolonged course of

NOTE Confidence: 0.9778276

00:21:09.160 --> 00:21:09.660 withdrawal.

NOTE Confidence: 0.9671875

00:21:10.255 --> 00:21:11.375 And at day twenty eight,

NOTE Confidence: 0.9671875

00:21:11.375 --> 00:21:13.075 they actually had greater withdrawal

NOTE Confidence: 0.9831543

00:21:13.375 --> 00:21:14.195 than males.

NOTE Confidence: 0.98046875

00:21:16.095 --> 00:21:17.135 And so when we first

NOTE Confidence: 0.98046875

00:21:17.135 --> 00:21:18.115 saw this data,

NOTE Confidence: 0.95346576

00:21:18.734 --> 00:21:20.355 I thought perhaps or we

NOTE Confidence: 0.95346576

00:21:20.575 --> 00:21:22.015 theorized that perhaps some of

NOTE Confidence: 0.95346576

00:21:22.015 --> 00:21:23.054 these effects were due to

NOTE Confidence: 0.95346576

00:21:23.054 --> 00:21:23.554 pharmacokinetic

NOTE Confidence: 0.94628906

00:21:24.420 --> 00:21:25.160 sex differences.

NOTE Confidence: 0.97843426

00:21:25.940 --> 00:21:26.740 And we had,

NOTE Confidence: 0.97539604

00:21:27.540 --> 00:21:29.400 data from our urine collection

NOTE Confidence: 0.97539604

00:21:29.540 --> 00:21:30.740 to confirm absence. So we

NOTE Confidence: 0.97539604

00:21:30.740 --> 00:21:32.200 could actually look at carboxy

NOTE Confidence: 0.97855633

00:21:32.740 --> 00:21:35.060 and hydroxy levels, these major

NOTE Confidence: 0.97855633

00:21:35.060 --> 00:21:35.560 metabolites

NOTE Confidence: 0.93693036

00:21:35.860 --> 00:21:37.060 of THC to see if

NOTE Confidence: 0.93693036

00:21:37.060 --> 00:21:38.520 they differed between sex,

NOTE Confidence: 0.9991319

00:21:39.184 --> 00:21:40.005 but they didn't.

NOTE Confidence: 0.9835612

00:21:41.345 --> 00:21:42.645 So perhaps pharmacodynamic

NOTE Confidence: 0.94641113

00:21:43.265 --> 00:21:44.804 effects may be better,

NOTE Confidence: 0.9682617

00:21:45.825 --> 00:21:47.424 suited to explain these sex

NOTE Confidence: 0.9682617

00:21:47.424 --> 00:21:47.924 differences.

NOTE Confidence: 0.939209

00:21:49.025 --> 00:21:49.345 And,

NOTE Confidence: 0.93588865

00:21:49.984 --> 00:21:50.785 we know that there are

NOTE Confidence: 0.93588865

00:21:50.785 --> 00:21:52.180 sex differences in the endocannabinoid

NOTE Confidence: 0.9862793

00:21:52.800 --> 00:21:54.640 system, although the direction of

NOTE Confidence: 0.9862793

00:21:54.640 --> 00:21:56.320 these effects are really not

NOTE Confidence: 0.9862793

00:21:56.320 --> 00:21:57.920 well established. So, you can

NOTE Confidence: 0.9862793

00:21:57.920 --> 00:21:59.380 find them in both directions

NOTE Confidence: 0.98502606

00:22:00.000 --> 00:22:00.820 in the literature.

NOTE Confidence: 0.98185223

00:22:01.520 --> 00:22:02.480 And we know that chronic

NOTE Confidence: 0.98185223

00:22:02.480 --> 00:22:04.255 cannabis use exerts pharmacodynamic

NOTE Confidence: 0.95820314

00:22:04.635 --> 00:22:06.235 effects, as I explained before.

NOTE Confidence: 0.95820314

00:22:06.235 --> 00:22:07.115 And this has been shown

NOTE Confidence: 0.95820314

00:22:07.115 --> 00:22:08.655 in both males and females.

NOTE Confidence: 0.97387695

00:22:09.275 --> 00:22:10.875 This idea that cannabinoid one

NOTE Confidence: 0.97387695

00:22:10.875 --> 00:22:11.855 receptor downregulation

NOTE Confidence: 0.998291

00:22:12.395 --> 00:22:13.935 occurs with chronic use.

NOTE Confidence: 0.988878

00:22:14.395 --> 00:22:15.515 It's also been shown in

NOTE Confidence: 0.988878

00:22:15.515 --> 00:22:16.975 males and females that,

NOTE Confidence: 0.97734374

00:22:17.520 --> 00:22:19.700 cannabinoid one receptor ability predicts

NOTE Confidence: 0.9556885

00:22:20.160 --> 00:22:21.220 withdrawal severity.

NOTE Confidence: 0.9990932

00:22:21.840 --> 00:22:23.200 But what hasn't been shown

NOTE Confidence: 0.9990932

00:22:23.200 --> 00:22:23.940 in females

NOTE Confidence: 0.9926758

00:22:24.720 --> 00:22:25.540 is that,

NOTE Confidence: 0.9995117

00:22:26.400 --> 00:22:26.900 normalization

NOTE Confidence: 0.9375

00:22:27.200 --> 00:22:27.940 or upregulation

NOTE Confidence: 0.99090576

00:22:28.640 --> 00:22:30.480 occurs with abstinence. So while

NOTE Confidence: 0.99090576

00:22:30.480 --> 00:22:31.300 this has been

NOTE Confidence: 0.9720154

00:22:31.654 --> 00:22:33.255 documented in two studies in

NOTE Confidence: 0.9720154

00:22:33.255 --> 00:22:34.934 males, it has not yet

NOTE Confidence: 0.9720154

00:22:34.934 --> 00:22:37.095 been examined in females and

NOTE Confidence: 0.9720154

00:22:37.095 --> 00:22:37.595 perhaps,

NOTE Confidence: 0.99401855

00:22:38.615 --> 00:22:40.075 dysregulation in the endocannabinoid

NOTE Confidence: 0.9985962

00:22:40.455 --> 00:22:42.615 system may persist longer in

NOTE Confidence: 0.9985962

00:22:42.615 --> 00:22:44.075 females than males.

NOTE Confidence: 0.9644653

00:22:45.580 --> 00:22:47.260 So another important piece of

NOTE Confidence: 0.9644653

00:22:47.260 --> 00:22:49.100 the puzzle to consider is

NOTE Confidence: 0.9644653

00:22:49.100 --> 00:22:51.200 the role of ovarian hormones.

NOTE Confidence: 0.9644653

00:22:51.260 --> 00:22:52.480 And we know that they

NOTE Confidence: 0.9928589

00:22:53.019 --> 00:22:54.080 influence endocannabinoid

NOTE Confidence: 0.92333984

00:22:54.460 --> 00:22:55.740 system as well as that

NOTE Confidence: 0.92333984

00:22:55.820 --> 00:22:56.859 is it as well as

NOTE Confidence: 0.92333984

00:22:56.859 --> 00:22:57.600 its activity.

NOTE Confidence: 0.97355145

00:22:58.065 --> 00:22:59.445 So they can actually modulate

NOTE Confidence: 0.97355145

00:22:59.504 --> 00:23:01.845 cannabinoid one receptor density or

NOTE Confidence: 0.97355145

00:23:01.984 --> 00:23:03.524 the affinity of these receptors.

NOTE Confidence: 0.9871582

00:23:04.304 --> 00:23:06.625 And these ovarian hormones obviously

NOTE Confidence: 0.9871582

00:23:06.625 --> 00:23:08.725 fluctuate across the menstrual system.

NOTE Confidence: 0.9919212

00:23:09.105 --> 00:23:10.565 So we can actually see

NOTE Confidence: 0.9919212

00:23:10.625 --> 00:23:11.984 across the menstrual system that

NOTE Confidence: 0.9919212

00:23:11.984 --> 00:23:12.484 endocannabinoid

NOTE Confidence: 0.99902344

00:23:13.024 --> 00:23:14.040 activity can

NOTE Confidence: 0.98706055

00:23:15.640 --> 00:23:15.960 change.

NOTE Confidence: 0.9832967

00:23:16.600 --> 00:23:18.119 But one one thing to

NOTE Confidence: 0.9832967

00:23:18.119 --> 00:23:19.660 note is that if hormones

NOTE Confidence: 0.9832967

00:23:19.800 --> 00:23:20.540 do change,

NOTE Confidence: 0.9555664

00:23:21.320 --> 00:23:21.820 across,

NOTE Confidence: 0.9578683

00:23:22.520 --> 00:23:24.220 the with the menstrual cycle,

NOTE Confidence: 0.9578683

00:23:24.520 --> 00:23:25.820 then we would have expected

NOTE Confidence: 0.9578683

00:23:26.040 --> 00:23:27.260 to see some variation

NOTE Confidence: 0.9798991

00:23:27.560 --> 00:23:29.160 in our withdrawal trajectory in

NOTE Confidence: 0.9798991

00:23:29.160 --> 00:23:29.660 females,

NOTE Confidence: 0.9871216

00:23:30.855 --> 00:23:32.475 even though the average,

NOTE Confidence: 0.99316406

00:23:33.095 --> 00:23:35.675 trajectory or severity was stagnant

NOTE Confidence: 0.99316406

00:23:35.734 --> 00:23:36.715 across females.

NOTE Confidence: 0.9980469

00:23:37.415 --> 00:23:37.915 So

NOTE Confidence: 0.99324036

00:23:38.695 --> 00:23:39.975 what we did next was

NOTE Confidence: 0.99324036

00:23:39.975 --> 00:23:41.175 we then looked at the

NOTE Confidence: 0.99324036

00:23:41.175 --> 00:23:43.494 individual trajectories of the females

NOTE Confidence: 0.99324036

00:23:43.494 --> 00:23:44.690 in the study. And when

NOTE Confidence: 0.99324036

00:23:44.690 --> 00:23:46.450 we unpack this data, we

NOTE Confidence: 0.99324036

00:23:46.450 --> 00:23:48.130 actually see that across the

NOTE Confidence: 0.99324036

00:23:48.130 --> 00:23:49.030 nine participants,

NOTE Confidence: 0.9944661

00:23:50.850 --> 00:23:52.390 the data was very heterogeneous.

NOTE Confidence: 0.9569336

00:23:52.690 --> 00:23:54.310 So all of the females

NOTE Confidence: 0.9760742

00:23:54.770 --> 00:23:56.210 looks like that they experienced

NOTE Confidence: 0.9760742

00:23:56.210 --> 00:23:57.650 a very different type of

NOTE Confidence: 0.9760742

00:23:57.650 --> 00:23:58.790 withdrawal trajectory,

NOTE Confidence: 0.9800347

00:24:00.075 --> 00:24:01.595 which suggests that hormones may

NOTE Confidence: 0.9800347

00:24:01.595 --> 00:24:03.054 indeed play a role

NOTE Confidence: 0.9977214

00:24:03.355 --> 00:24:04.395 in the severity of the

NOTE Confidence: 0.9977214

00:24:04.395 --> 00:24:04.895 symptoms.

NOTE Confidence: 0.96962893

00:24:05.434 --> 00:24:06.315 And one thing that we

NOTE Confidence: 0.96962893

00:24:06.315 --> 00:24:07.195 do see that we don't

NOTE Confidence: 0.96962893

00:24:07.195 --> 00:24:08.154 see in males is sort

NOTE Confidence: 0.96962893

00:24:08.154 --> 00:24:10.015 of this later phase elevation

NOTE Confidence: 0.96962893

00:24:10.075 --> 00:24:12.015 or surge in withdrawal severity,

NOTE Confidence: 0.9791626

00:24:13.210 --> 00:24:14.890 that's not present in males.

NOTE Confidence: 0.9791626

00:24:14.890 --> 00:24:16.090 And actually, when you look

NOTE Confidence: 0.9791626

00:24:16.090 --> 00:24:17.049 at males, and these are

NOTE Confidence: 0.9791626

00:24:17.049 --> 00:24:18.909 the thirteen males plotted out,

NOTE Confidence: 0.98375356

00:24:19.210 --> 00:24:20.570 you can actually see that

NOTE Confidence: 0.98375356

00:24:20.570 --> 00:24:22.250 the majority or seventy five

NOTE Confidence: 0.98375356

00:24:22.250 --> 00:24:22.750 percent

NOTE Confidence: 0.9260254

00:24:23.369 --> 00:24:24.990 of males actually showed

NOTE Confidence: 0.9572532

00:24:25.755 --> 00:24:27.195 the expected or the classic

NOTE Confidence: 0.9572532

00:24:27.195 --> 00:24:29.435 withdrawal trajectory. So it wasn't

NOTE Confidence: 0.9572532

00:24:29.435 --> 00:24:31.035 just an average effect, but

NOTE Confidence: 0.9572532

00:24:31.035 --> 00:24:32.395 most of these men are

NOTE Confidence: 0.9572532

00:24:32.395 --> 00:24:33.455 actually showing,

NOTE Confidence: 0.99088544

00:24:34.715 --> 00:24:36.555 this dissipation by day twenty

NOTE Confidence: 0.99088544

00:24:36.555 --> 00:24:37.835 eight and that peak at

NOTE Confidence: 0.99088544

00:24:37.835 --> 00:24:38.655 day seven.

NOTE Confidence: 0.9949951

00:24:40.409 --> 00:24:41.149 And so,

NOTE Confidence: 0.9741655

00:24:41.609 --> 00:24:42.730 what we see just to

NOTE Confidence: 0.9741655

00:24:42.730 --> 00:24:44.510 sum up is that females

NOTE Confidence: 0.9741655

00:24:44.570 --> 00:24:45.070 exhibit

NOTE Confidence: 0.9938287

00:24:45.369 --> 00:24:47.389 quite a different withdrawal trajectory

NOTE Confidence: 0.9938287

00:24:47.450 --> 00:24:48.889 than males. It's a lot

NOTE Confidence: 0.9938287

00:24:48.889 --> 00:24:49.630 more heterogeneous.

NOTE Confidence: 0.9987305

00:24:50.169 --> 00:24:51.549 It seems to be prolonged.

NOTE Confidence: 0.9671742

00:24:53.404 --> 00:24:55.664 These effects are likely mediated

NOTE Confidence: 0.9671742

00:24:55.725 --> 00:24:57.404 by some hormonal changes and

NOTE Confidence: 0.9671742

00:24:57.404 --> 00:24:57.904 endocannabinoid

NOTE Confidence: 0.9824707

00:24:58.365 --> 00:25:00.385 activity across the menstrual cycle.

NOTE Confidence: 0.92174184

00:25:01.885 --> 00:25:03.644 And really just sort of

NOTE Confidence: 0.92174184

00:25:03.644 --> 00:25:05.325 speaks to how much more

NOTE Confidence: 0.92174184

00:25:05.325 --> 00:25:05.825 investigations

NOTE Confidence: 0.99677736

00:25:06.125 --> 00:25:07.664 are needed in this area.

NOTE Confidence: 0.9959775

00:25:08.369 --> 00:25:09.970 So we need to start

NOTE Confidence: 0.9959775

00:25:09.970 --> 00:25:11.250 to look to see if

NOTE Confidence: 0.9959775

00:25:11.250 --> 00:25:13.090 hormones can influence or do

NOTE Confidence: 0.9959775

00:25:13.090 --> 00:25:15.410 influence cannabis withdrawal severity or

NOTE Confidence: 0.9959775

00:25:15.410 --> 00:25:15.910 endocannabinoid

NOTE Confidence: 0.97957355

00:25:16.290 --> 00:25:17.830 activity during abstinence.

NOTE Confidence: 0.9911431

00:25:18.850 --> 00:25:20.869 And, the real clinical relevance

NOTE Confidence: 0.9911431

00:25:21.010 --> 00:25:22.530 comes to speak to if

NOTE Confidence: 0.9911431

00:25:22.530 --> 00:25:24.105 treatments then need to be

NOTE Confidence: 0.9911431

00:25:24.265 --> 00:25:25.885 tailored towards sex.

NOTE Confidence: 0.9980469

00:25:27.304 --> 00:25:28.605 And so that's an area

NOTE Confidence: 0.9995117

00:25:28.905 --> 00:25:30.765 that we're continuing to pursue.

NOTE Confidence: 0.99614257

00:25:31.865 --> 00:25:33.244 So just to sum up,

NOTE Confidence: 0.9534505

00:25:34.345 --> 00:25:36.184 I just wanted to come

NOTE Confidence: 0.9534505

00:25:36.184 --> 00:25:37.544 back to this slide and

NOTE Confidence: 0.9534505

00:25:37.544 --> 00:25:38.605 show that,

NOTE Confidence: 0.97770995

00:25:40.500 --> 00:25:42.580 that we've identified withdrawal as

NOTE Confidence: 0.97770995

00:25:42.580 --> 00:25:44.280 a variable that predicts relapse,

NOTE Confidence: 0.9583808

00:25:44.900 --> 00:25:46.500 that tobacco co use as

NOTE Confidence: 0.9583808

00:25:46.500 --> 00:25:48.420 well as sex, do indeed

NOTE Confidence: 0.9583808

00:25:48.420 --> 00:25:50.500 moderate cannabis withdrawal severity as

NOTE Confidence: 0.9583808

00:25:50.500 --> 00:25:51.480 well as duration.

NOTE Confidence: 0.9934082

00:25:52.294 --> 00:25:53.355 And that the endocannabinoid

NOTE Confidence: 0.98372394

00:25:53.734 --> 00:25:55.674 system may underlie the association

NOTE Confidence: 0.98372394

00:25:55.895 --> 00:25:57.975 between withdrawal and tobacco co

NOTE Confidence: 0.98372394

00:25:57.975 --> 00:26:00.154 use as well as sex.

NOTE Confidence: 0.9684448

00:26:00.775 --> 00:26:02.615 And hopefully, a better understanding

NOTE Confidence: 0.9684448

00:26:02.615 --> 00:26:03.595 of these relationships,

NOTE Confidence: 0.99930245

00:26:04.820 --> 00:26:06.920 can help identify novel therapeutics

NOTE Confidence: 0.99930245

00:26:07.140 --> 00:26:08.340 to overcome some of the

NOTE Confidence: 0.99930245

00:26:08.340 --> 00:26:09.720 barriers that we've had

NOTE Confidence: 0.96777344

00:26:10.340 --> 00:26:12.119 to cannabis treatment innovation.

NOTE Confidence: 0.9927246

00:26:13.940 --> 00:26:15.140 And with that, I'll just

NOTE Confidence: 0.9927246

00:26:15.140 --> 00:26:16.760 thank all of my collaborators,

NOTE Confidence: 0.99261475

00:26:18.274 --> 00:26:19.715 as well as all of

NOTE Confidence: 0.99261475

00:26:19.715 --> 00:26:21.174 my team members,

NOTE Confidence: 0.97831845

00:26:22.355 --> 00:26:24.355 and the funding agencies. And

NOTE Confidence: 0.97831845

00:26:24.355 --> 00:26:25.394 a real special thanks to

NOTE Confidence: 0.97831845

00:26:25.394 --> 00:26:26.294 all the participants

NOTE Confidence: 0.9819336

00:26:26.674 --> 00:26:27.174 who

NOTE Confidence: 0.9741618

00:26:27.554 --> 00:26:28.674 who go through a really

NOTE Confidence: 0.9741618

00:26:28.674 --> 00:26:29.174 intensive,

NOTE Confidence: 0.9937066

00:26:29.955 --> 00:26:32.195 laboratory paradigm to provide this

NOTE Confidence: 0.9937066

00:26:32.195 --> 00:26:34.054 data for us. So

NOTE Confidence: 0.96398926

00:26:34.410 --> 00:26:35.369 thank you all for your

NOTE Confidence: 0.96398926

00:26:35.369 --> 00:26:35.869 attention.

NOTE Confidence: 0.9991122

00:26:36.330 --> 00:26:37.450 And if there's time, I'll

NOTE Confidence: 0.9991122

00:26:37.450 --> 00:26:38.730 be happy to answer any

NOTE Confidence: 0.9991122

00:26:38.730 --> 00:26:39.230 questions.

NOTE Confidence: 0.52978516

00:26:40.650 --> 00:26:41.150 Thank

NOTE Confidence: 0.98463947

00:26:41.450 --> 00:26:44.010 you, Rachel. Great, talk. Maybe

NOTE Confidence: 0.98463947

00:26:44.010 --> 00:26:45.130 we'll have time only for

NOTE Confidence: 0.98463947

00:26:45.130 --> 00:26:45.710 two questions

NOTE Confidence: 0.9295654

00:26:47.210 --> 00:26:48.350 if you answer fast.

NOTE Confidence: 0.99560547

00:26:50.010 --> 00:26:51.125 I think there's a question

NOTE Confidence: 0.99560547

00:26:51.185 --> 00:26:52.085 in the chat.

NOTE Confidence: 0.975708

00:26:52.545 --> 00:26:53.525 Yeah. Okay.

NOTE Confidence: 0.8613281

00:26:54.225 --> 00:26:54.725 So,

NOTE Confidence: 0.9550171

00:26:56.865 --> 00:26:58.325 do you think, postmenopausal

NOTE Confidence: 0.9794515

00:26:58.785 --> 00:27:00.225 females would have a more

NOTE Confidence: 0.9794515

00:27:00.225 --> 00:27:00.725 uniform,

NOTE Confidence: 0.99572754

00:27:01.665 --> 00:27:03.505 pattern of withdrawal as compared

NOTE Confidence: 0.99572754

00:27:03.505 --> 00:27:04.005 to,

NOTE Confidence: 0.9373535

00:27:04.960 --> 00:27:06.820 well, women not during menopause?

NOTE Confidence: 0.9775954

00:27:08.480 --> 00:27:09.840 Yeah. I mean, I would

NOTE Confidence: 0.9775954

00:27:09.840 --> 00:27:11.840 speculate yes, but until we

NOTE Confidence: 0.9775954

00:27:11.840 --> 00:27:12.640 look at that,

NOTE Confidence: 0.99749756

00:27:13.360 --> 00:27:14.640 we really don't know. So

NOTE Confidence: 0.99749756

00:27:14.640 --> 00:27:16.240 there's just a lot of

NOTE Confidence: 0.99749756

00:27:16.240 --> 00:27:18.420 animal data showing that ovarian

NOTE Confidence: 0.99749756

00:27:18.480 --> 00:27:18.980 hormones

NOTE Confidence: 0.99365234

00:27:19.335 --> 00:27:20.315 influence endocannabinoid

NOTE Confidence: 0.97680664

00:27:20.855 --> 00:27:21.355 activity,

NOTE Confidence: 0.9961286

00:27:22.054 --> 00:27:23.174 but there's really not a

NOTE Confidence: 0.9961286

00:27:23.174 --> 00:27:24.215 lot of good studies in

NOTE Confidence: 0.9961286

00:27:24.215 --> 00:27:25.835 humans showing what happens

NOTE Confidence: 0.992513

00:27:26.135 --> 00:27:26.635 premenopausal

NOTE Confidence: 0.9951172

00:27:27.095 --> 00:27:27.595 or

NOTE Confidence: 1

00:27:27.895 --> 00:27:28.715 after menopause

NOTE Confidence: 0.9124756

00:27:29.414 --> 00:27:30.155 and even,

NOTE Confidence: 0.9663357

00:27:31.255 --> 00:27:33.335 while while while females are

NOTE Confidence: 0.9663357

00:27:33.335 --> 00:27:33.835 menstruating.

NOTE Confidence: 0.95265627

00:27:35.309 --> 00:27:36.269 Thank you. I have one

NOTE Confidence: 0.95265627

00:27:36.269 --> 00:27:37.649 question. And the last question,

NOTE Confidence: 0.95265627

00:27:37.869 --> 00:27:38.750 do you think there are

NOTE Confidence: 0.95265627

00:27:38.750 --> 00:27:41.169 specific times within the menstrual

NOTE Confidence: 0.95265627

00:27:41.230 --> 00:27:43.490 cycle that would predict better,

NOTE Confidence: 0.6430664

00:27:45.710 --> 00:27:46.210 success

NOTE Confidence: 0.9980469

00:27:46.510 --> 00:27:48.429 rate? Yeah. So we couldn't

NOTE Confidence: 0.9980469

00:27:48.429 --> 00:27:49.230 look at that from our

NOTE Confidence: 0.9980469

00:27:49.230 --> 00:27:50.289 data. In fact,

NOTE Confidence: 0.9302246

00:27:51.575 --> 00:27:52.295 we didn't have a lot

NOTE Confidence: 0.9302246

00:27:52.295 --> 00:27:54.155 of women on contraceptives, and,

NOTE Confidence: 0.99006

00:27:55.575 --> 00:27:57.015 females are not very good

NOTE Confidence: 0.99006

00:27:57.015 --> 00:27:57.835 at recalling,

NOTE Confidence: 0.95815206

00:27:58.855 --> 00:28:00.055 when the last day of

NOTE Confidence: 0.95815206

00:28:00.375 --> 00:28:01.095 the the first day of

NOTE Confidence: 0.95815206

00:28:01.095 --> 00:28:02.615 their last menstrual cycle was.

NOTE Confidence: 0.95815206

00:28:02.615 --> 00:28:03.415 So it was really hard

NOTE Confidence: 0.95815206

00:28:03.415 --> 00:28:04.075 to track

NOTE Confidence: 0.8755493

00:28:04.455 --> 00:28:05.415 where in their cycle they

NOTE Confidence: 0.8755493

00:28:05.415 --> 00:28:06.270 were during the

NOTE Confidence: 0.9771118

00:28:06.750 --> 00:28:07.950 study, but there is some

NOTE Confidence: 0.9771118

00:28:07.950 --> 00:28:09.650 evidence from the tobacco literature

NOTE Confidence: 0.9771118

00:28:09.710 --> 00:28:10.850 suggesting that,

NOTE Confidence: 0.95103234

00:28:11.630 --> 00:28:13.230 being in the early phase

NOTE Confidence: 0.95103234

00:28:13.230 --> 00:28:14.910 or late phase when estrogen

NOTE Confidence: 0.95103234

00:28:14.910 --> 00:28:16.030 levels are high or low,

NOTE Confidence: 0.95103234

00:28:16.030 --> 00:28:17.410 I mean, there's mixed evidence,

NOTE Confidence: 0.95103234

00:28:17.630 --> 00:28:19.410 may be beneficial and produce

NOTE Confidence: 0.95103234

00:28:19.550 --> 00:28:21.250 greater treatment success.

NOTE Confidence: 0.9800462

00:28:22.135 --> 00:28:23.575 Which phase that is, we

NOTE Confidence: 0.9800462

00:28:23.575 --> 00:28:24.855 don't know yet. And whether

NOTE Confidence: 0.9800462

00:28:24.855 --> 00:28:25.734 that's the same as the

NOTE Confidence: 0.9800462

00:28:25.734 --> 00:28:27.175 tobacco field or it's specific

NOTE Confidence: 0.9800462

00:28:27.175 --> 00:28:28.695 for cannabis, we also don't

NOTE Confidence: 0.9800462

00:28:28.695 --> 00:28:29.195 know.

NOTE Confidence: 0.985808

00:28:29.734 --> 00:28:31.015 So, like I said, we're

NOTE Confidence: 0.985808

00:28:31.015 --> 00:28:32.135 just sort of scratching the

NOTE Confidence: 0.985808

00:28:32.135 --> 00:28:33.415 surface here, and I think

NOTE Confidence: 0.985808

00:28:33.415 --> 00:28:34.855 there there remains a lot

NOTE Confidence: 0.985808

00:28:34.855 --> 00:28:36.234 of unanswered questions.

NOTE Confidence: 0.78515625

00:28:39.789 --> 00:28:40.289 Okay.

NOTE Confidence: 0.9160156

00:28:40.750 --> 00:28:42.610 I guess just one comment.

NOTE Confidence: 0.9160156

00:28:42.669 --> 00:28:43.549 One question. Do you think

NOTE Confidence: 0.9160156

00:28:43.549 --> 00:28:44.289 the tarpine,

NOTE Confidence: 0.9809977

00:28:44.669 --> 00:28:45.570 tarpine concentration,

NOTE Confidence: 0.99658203

00:28:46.510 --> 00:28:47.789 may have explained some of

NOTE Confidence: 0.99658203

00:28:47.789 --> 00:28:48.530 your findings?

NOTE Confidence: 0.9782959

00:28:51.295 --> 00:28:52.575 Yeah. I mean, cannabis is

NOTE Confidence: 0.9782959

00:28:52.575 --> 00:28:54.355 just such a complex plan,

NOTE Confidence: 0.9864343

00:28:54.895 --> 00:28:56.895 so we haven't really gotten

NOTE Confidence: 0.9864343

00:28:56.895 --> 00:28:58.895 into exactly what people are

NOTE Confidence: 0.9864343

00:28:58.895 --> 00:29:00.175 using. We're really trying to

NOTE Confidence: 0.9864343

00:29:00.175 --> 00:29:01.135 do a good job to

NOTE Confidence: 0.9864343

00:29:01.135 --> 00:29:02.035 try to document

NOTE Confidence: 0.9223633

00:29:02.575 --> 00:29:03.475 which strains,

NOTE Confidence: 0.9654541

00:29:04.060 --> 00:29:04.800 the potency.

NOTE Confidence: 0.95872146

00:29:05.660 --> 00:29:07.500 We're like, in Quebec, everything

NOTE Confidence: 0.95872146

00:29:07.500 --> 00:29:08.940 is really well regulated. So

NOTE Confidence: 0.95872146

00:29:08.940 --> 00:29:10.000 we're trying to

NOTE Confidence: 0.9690317

00:29:10.300 --> 00:29:11.820 get pictures of the products

NOTE Confidence: 0.9690317

00:29:11.820 --> 00:29:13.520 people are using, which sometimes

NOTE Confidence: 0.9690317

00:29:13.660 --> 00:29:14.640 lists the terpenes,

NOTE Confidence: 0.99960935

00:29:15.420 --> 00:29:16.800 but not always the concentrations

NOTE Confidence: 0.9845378

00:29:17.180 --> 00:29:18.240 of them. So

NOTE Confidence: 0.97466075

00:29:18.955 --> 00:29:20.395 so we're trying, but this

NOTE Confidence: 0.97466075

00:29:20.395 --> 00:29:21.835 is a really it's really

NOTE Confidence: 0.97466075

00:29:21.835 --> 00:29:23.275 hard to figure out exactly

NOTE Confidence: 0.97466075

00:29:23.275 --> 00:29:24.575 what people are using.

NOTE Confidence: 0.90273815

00:29:25.515 --> 00:29:26.475 Yeah. And I guess just

NOTE Confidence: 0.90273815

00:29:26.475 --> 00:29:28.395 the last comment from, doctor

NOTE Confidence: 0.90273815

00:29:28.395 --> 00:29:29.535 De Souza that,

NOTE Confidence: 0.92222375

00:29:29.835 --> 00:29:31.035 of course, c v one

NOTE Confidence: 0.92222375

00:29:31.035 --> 00:29:32.015 receptor availability

NOTE Confidence: 0.9869792

00:29:32.555 --> 00:29:33.240 is lower in

NOTE Confidence: 0.9906684

00:29:34.280 --> 00:29:35.960 tobacco smokers, which I'm sure

NOTE Confidence: 0.9906684

00:29:35.960 --> 00:29:37.820 you know. And, however,

NOTE Confidence: 0.9825614

00:29:38.120 --> 00:29:39.160 I don't think they're lower

NOTE Confidence: 0.9825614

00:29:39.160 --> 00:29:40.059 in alcohol

NOTE Confidence: 0.98217773

00:29:40.360 --> 00:29:41.260 use disorder,

NOTE Confidence: 0.9883789

00:29:41.800 --> 00:29:43.179 or at least not consistently.

NOTE Confidence: 0.9776893

00:29:43.960 --> 00:29:45.640 And I'm wondering with the

NOTE Confidence: 0.9776893

00:29:45.640 --> 00:29:47.080 last question whether you've looked

NOTE Confidence: 0.9776893

00:29:47.080 --> 00:29:48.460 into alcohol use.

NOTE Confidence: 0.95841473

00:29:49.215 --> 00:29:50.495 Yeah. I mean, our we

NOTE Confidence: 0.95841473

00:29:50.495 --> 00:29:51.775 exclude anyone with an alcohol

NOTE Confidence: 0.95841473

00:29:51.775 --> 00:29:52.674 use disorder.

NOTE Confidence: 0.9125163

00:29:53.375 --> 00:29:54.674 And, I mean,

NOTE Confidence: 1

00:29:54.975 --> 00:29:55.475 people

NOTE Confidence: 0.99624175

00:29:56.255 --> 00:29:58.174 are drinking recreationally, but the

NOTE Confidence: 0.99624175

00:29:58.174 --> 00:29:59.934 levels are very, very low.

NOTE Confidence: 0.99624175

00:29:59.934 --> 00:30:00.434 So,

NOTE Confidence: 0.95111954

00:30:01.215 --> 00:30:02.255 I think that the average

NOTE Confidence: 0.95111954

00:30:02.255 --> 00:30:03.375 works out to less than

NOTE Confidence: 0.95111954

00:30:03.375 --> 00:30:04.595 a drink a day.

NOTE Confidence: 0.9689646

00:30:05.240 --> 00:30:06.040 So we could look at

NOTE Confidence: 0.9689646

00:30:06.040 --> 00:30:07.720 that, but I again, because

NOTE Confidence: 0.9689646

00:30:07.720 --> 00:30:09.000 the the volume that people

NOTE Confidence: 0.9689646

00:30:09.000 --> 00:30:10.040 are consuming are quite low,

NOTE Confidence: 0.9689646

00:30:10.040 --> 00:30:11.320 I wouldn't expect in this

NOTE Confidence: 0.9689646

00:30:11.320 --> 00:30:12.360 sample for it it to

NOTE Confidence: 0.9689646

00:30:12.360 --> 00:30:13.180 have an effect.

NOTE Confidence: 1

00:30:13.720 --> 00:30:14.220 Excellent.

NOTE Confidence: 0.99088544

00:30:14.680 --> 00:30:16.120 Well, thank you very, very

NOTE Confidence: 0.99088544

00:30:16.120 --> 00:30:17.685 much, Rachel. Great talk.

NOTE Confidence: 0.99609375

00:30:18.325 --> 00:30:18.805 And,

NOTE Confidence: 0.99645996

00:30:19.205 --> 00:30:20.325 with that, we are going

NOTE Confidence: 0.99645996

00:30:20.325 --> 00:30:21.145 to be moving,

NOTE Confidence: 0.9748264

00:30:21.685 --> 00:30:22.745 on to Renato.

NOTE Confidence: 0.94940186

00:30:23.525 --> 00:30:24.585 Doctor Polimanti's

NOTE Confidence: 0.9892252

00:30:24.965 --> 00:30:26.965 research focuses on applying big

NOTE Confidence: 0.9892252

00:30:26.965 --> 00:30:29.785 data analytics, genomics, and computational

NOTE Confidence: 0.9157715

00:30:30.085 --> 00:30:32.040 biology to better understand the

NOTE Confidence: 0.9157715

00:30:32.040 --> 00:30:32.540 biological

NOTE Confidence: 0.9987793

00:30:32.840 --> 00:30:33.900 and epidemiological

NOTE Confidence: 0.9980469

00:30:34.280 --> 00:30:34.780 mechanisms

NOTE Confidence: 0.9748535

00:30:35.240 --> 00:30:36.220 underlying neuropsychiatric

NOTE Confidence: 0.9975586

00:30:36.760 --> 00:30:37.260 disorders,

NOTE Confidence: 0.9788005

00:30:37.880 --> 00:30:40.140 substance use, and complex behavioral

NOTE Confidence: 0.9788005

00:30:40.200 --> 00:30:40.700 traits.

NOTE Confidence: 0.85717773

00:30:41.080 --> 00:30:42.060 Doctor Polimanti

NOTE Confidence: 0.9812012

00:30:42.360 --> 00:30:43.480 is one of the recipients

NOTE Confidence: 0.9812012

00:30:43.480 --> 00:30:44.920 of the Yale Cannabis Research

NOTE Confidence: 0.9812012

00:30:44.920 --> 00:30:46.620 Center's pilot project award.

NOTE Confidence: 0.9941135

00:30:47.174 --> 00:30:48.934 His lecture will explore the

NOTE Confidence: 0.9941135

00:30:48.934 --> 00:30:49.434 neurobiological

NOTE Confidence: 0.9970703

00:30:50.054 --> 00:30:50.554 mechanism

NOTE Confidence: 0.9472656

00:30:50.855 --> 00:30:51.674 that distinguish

NOTE Confidence: 0.91584474

00:30:52.215 --> 00:30:53.914 the cannabis use from cannabis

NOTE Confidence: 0.91584474

00:30:53.975 --> 00:30:56.154 use from cannabis use disorder

NOTE Confidence: 0.9851717

00:30:56.455 --> 00:30:58.315 through the integration of genomics

NOTE Confidence: 0.9851717

00:30:58.455 --> 00:31:00.299 and brain imaging data. The

NOTE Confidence: 0.9851717

00:31:00.299 --> 00:31:02.720 presentation will highlight how listing

NOTE Confidence: 0.9851717

00:31:02.779 --> 00:31:04.399 patterns of brain connectivity

NOTE Confidence: 0.9996745

00:31:04.779 --> 00:31:06.240 and genetic architecture

NOTE Confidence: 0.9880676

00:31:06.700 --> 00:31:08.539 are associated with cannabis and

NOTE Confidence: 0.9880676

00:31:08.539 --> 00:31:09.759 cannabis use disorder,

NOTE Confidence: 0.99504745

00:31:10.139 --> 00:31:12.380 particularly within networks involved in

NOTE Confidence: 0.99504745

00:31:12.380 --> 00:31:13.440 cognitive control,

NOTE Confidence: 0.98653156

00:31:13.980 --> 00:31:16.275 salience processing, and default mode,

NOTE Confidence: 0.98653156

00:31:16.595 --> 00:31:17.095 functioning.

NOTE Confidence: 0.97476196

00:31:17.715 --> 00:31:19.235 Findings will also examine the

NOTE Confidence: 0.97476196

00:31:19.235 --> 00:31:20.215 role of neurodevelopmental,

NOTE Confidence: 0.99373955

00:31:21.315 --> 00:31:23.875 inflammatory, and immune related pathways

NOTE Confidence: 0.99373955

00:31:23.875 --> 00:31:25.415 in the progression from cannabis

NOTE Confidence: 0.99373955

00:31:25.475 --> 00:31:27.415 use to problematic use.

NOTE Confidence: 0.993571

00:31:28.190 --> 00:31:29.870 Additionally, the talk will discuss

NOTE Confidence: 0.993571

00:31:29.870 --> 00:31:31.630 how these discoveries may inform

NOTE Confidence: 0.993571

00:31:31.630 --> 00:31:32.530 future therapeutic

NOTE Confidence: 0.9519043

00:31:32.910 --> 00:31:35.010 strategies, including the identification

NOTE Confidence: 0.98776037

00:31:35.710 --> 00:31:38.050 of potential drug repurposing candidates

NOTE Confidence: 0.95778

00:31:38.670 --> 00:31:40.770 targeting pathways linked to COD.

NOTE Confidence: 0.90045166

00:31:42.455 --> 00:31:43.595 Doctor Bolimanti,

NOTE Confidence: 1

00:31:43.975 --> 00:31:45.195 the floor is yours.

NOTE Confidence: 0.98876953

00:31:46.215 --> 00:31:46.715 Great.

NOTE Confidence: 0.9622581

00:31:47.575 --> 00:31:48.535 Thank you so much for

NOTE Confidence: 0.9622581

00:31:48.535 --> 00:31:49.975 the invite. I'm very happy

NOTE Confidence: 0.9622581

00:31:49.975 --> 00:31:51.655 to present this project. And

NOTE Confidence: 0.9622581

00:31:51.655 --> 00:31:52.855 now I should be in

NOTE Confidence: 0.9622581

00:31:52.855 --> 00:31:54.155 presentation mode,

NOTE Confidence: 0.9980469

00:31:55.070 --> 00:31:56.350 And so I'm not seeing

NOTE Confidence: 0.9980469

00:31:56.350 --> 00:31:58.670 anyone right now. Great. Okay.

NOTE Confidence: 0.9980469

00:31:58.670 --> 00:31:59.170 So,

NOTE Confidence: 0.97927517

00:31:59.550 --> 00:32:00.510 this is the study that

NOTE Confidence: 0.97927517

00:32:00.510 --> 00:32:01.809 I'm going to present.

NOTE Confidence: 0.8938927

00:32:03.309 --> 00:32:04.750 And, again, here are my

NOTE Confidence: 0.8938927

00:32:04.750 --> 00:32:06.510 competing interest, which are not

NOTE Confidence: 0.8938927

00:32:06.510 --> 00:32:07.570 related to cannabis

NOTE Confidence: 0.7873535

00:32:07.870 --> 00:32:08.370 research.

NOTE Confidence: 0.9131557

00:32:09.315 --> 00:32:10.835 And, this is my group.

NOTE Confidence: 0.9131557

00:32:11.075 --> 00:32:12.274 Usually, I like to start

NOTE Confidence: 0.9131557

00:32:12.274 --> 00:32:13.414 with with their picture,

NOTE Confidence: 0.9735635

00:32:13.875 --> 00:32:14.995 also because, again, they do

NOTE Confidence: 0.9735635

00:32:14.995 --> 00:32:15.955 most of the work. In

NOTE Confidence: 0.9735635

00:32:15.955 --> 00:32:17.315 this case, like, most of

NOTE Confidence: 0.9735635

00:32:17.315 --> 00:32:18.755 the analysis that I'm going

NOTE Confidence: 0.9735635

00:32:18.755 --> 00:32:19.955 to present were done by

NOTE Confidence: 0.9735635

00:32:19.955 --> 00:32:21.014 Rapunzel Chen.

NOTE Confidence: 0.929362

00:32:21.809 --> 00:32:23.650 And so, like, as mentioned,

NOTE Confidence: 0.929362

00:32:23.650 --> 00:32:25.190 like, this study was,

NOTE Confidence: 0.9145752

00:32:25.730 --> 00:32:27.730 funded by a pilot award,

NOTE Confidence: 0.9145752

00:32:27.730 --> 00:32:30.070 which, I'm very grateful for.

NOTE Confidence: 0.96533203

00:32:30.610 --> 00:32:31.090 And,

NOTE Confidence: 0.94056535

00:32:31.650 --> 00:32:33.570 so before getting started, since

NOTE Confidence: 0.94056535

00:32:33.570 --> 00:32:34.789 I know how diverse

NOTE Confidence: 0.93155926

00:32:35.225 --> 00:32:37.225 is the audience attending these

NOTE Confidence: 0.93155926

00:32:37.225 --> 00:32:37.725 webinars,

NOTE Confidence: 0.97036743

00:32:38.105 --> 00:32:38.985 I would like to give

NOTE Confidence: 0.97036743

00:32:38.985 --> 00:32:40.125 you, like, some,

NOTE Confidence: 0.9938151

00:32:40.905 --> 00:32:42.525 basic concept about

NOTE Confidence: 0.89127606

00:32:42.985 --> 00:32:44.665 human genetic research, which is

NOTE Confidence: 0.89127606

00:32:44.665 --> 00:32:45.165 the,

NOTE Confidence: 0.93178713

00:32:46.185 --> 00:32:47.945 base of the study that,

NOTE Confidence: 0.9267578

00:32:48.985 --> 00:32:49.645 we did.

NOTE Confidence: 0.90851384

00:32:50.090 --> 00:32:52.250 And so, like, our starting

NOTE Confidence: 0.90851384

00:32:52.250 --> 00:32:54.250 step are genome wide association

NOTE Confidence: 0.90851384

00:32:54.250 --> 00:32:54.750 studies.

NOTE Confidence: 0.9089233

00:32:55.370 --> 00:32:57.150 These are brute force experiments

NOTE Confidence: 0.9089233

00:32:57.210 --> 00:32:58.570 and why they are, why

NOTE Confidence: 0.9089233

00:32:58.570 --> 00:33:00.350 I'm calling them like this

NOTE Confidence: 0.9089233

00:33:00.410 --> 00:33:01.950 is because we are testing

NOTE Confidence: 0.91786027

00:33:02.330 --> 00:33:04.010 all the variants across the

NOTE Confidence: 0.91786027

00:33:04.010 --> 00:33:05.295 genome to find the

NOTE Confidence: 0.91726506

00:33:05.615 --> 00:33:07.375 associations. And what this means,

NOTE Confidence: 0.91726506

00:33:07.375 --> 00:33:08.175 it means that we are

NOTE Confidence: 0.91726506

00:33:08.175 --> 00:33:10.175 finding for variants that are

NOTE Confidence: 0.91726506

00:33:10.175 --> 00:33:10.995 more frequent.

NOTE Confidence: 0.9204245

00:33:11.295 --> 00:33:12.735 For example, if exact case

NOTE Confidence: 0.9204245

00:33:12.735 --> 00:33:14.255 control definition, more frequent in

NOTE Confidence: 0.9204245

00:33:14.255 --> 00:33:15.375 people with the disease than

NOTE Confidence: 0.9204245

00:33:15.375 --> 00:33:16.975 people without. In this case,

NOTE Confidence: 0.9204245

00:33:16.975 --> 00:33:18.590 it would be the SNP

NOTE Confidence: 0.9204245

00:33:18.650 --> 00:33:19.770 number three where you see

NOTE Confidence: 0.9204245

00:33:19.770 --> 00:33:21.230 that there are more,

NOTE Confidence: 0.18444824

00:33:22.570 --> 00:33:23.070 allele

NOTE Confidence: 0.9281142

00:33:23.450 --> 00:33:24.809 in the case group than

NOTE Confidence: 0.9281142

00:33:24.809 --> 00:33:26.110 in the control group.

NOTE Confidence: 0.978418

00:33:27.210 --> 00:33:28.250 And, again, like, this is

NOTE Confidence: 0.978418

00:33:28.250 --> 00:33:29.850 a technology that now has,

NOTE Confidence: 0.95703125

00:33:30.475 --> 00:33:32.575 I think, almost twenty years

NOTE Confidence: 0.95703125

00:33:32.634 --> 00:33:33.294 of age.

NOTE Confidence: 0.98809814

00:33:34.075 --> 00:33:35.695 And, in twenty years,

NOTE Confidence: 0.9995117

00:33:36.075 --> 00:33:37.695 more than seventy thousand

NOTE Confidence: 0.97642684

00:33:37.995 --> 00:33:39.514 study have been published, and

NOTE Confidence: 0.97642684

00:33:39.514 --> 00:33:40.654 more than one million

NOTE Confidence: 0.92089844

00:33:41.195 --> 00:33:41.695 association

NOTE Confidence: 0.9757487

00:33:42.235 --> 00:33:43.215 have been reported.

NOTE Confidence: 0.9150255

00:33:43.595 --> 00:33:45.570 Here is a a plot

NOTE Confidence: 0.9150255

00:33:45.649 --> 00:33:47.250 from the GWAS catalog for

NOTE Confidence: 0.9150255

00:33:47.250 --> 00:33:48.289 people that work in human

NOTE Confidence: 0.9150255

00:33:48.289 --> 00:33:49.269 genetics. This is,

NOTE Confidence: 0.9397244

00:33:49.970 --> 00:33:51.409 something that people showed all

NOTE Confidence: 0.9397244

00:33:51.409 --> 00:33:52.610 the time, but, again, it's

NOTE Confidence: 0.9397244

00:33:52.610 --> 00:33:53.970 it's all looks so what

NOTE Confidence: 0.9397244

00:33:53.970 --> 00:33:55.649 what you see here is

NOTE Confidence: 0.9397244

00:33:55.649 --> 00:33:57.090 the chromosome, which is are

NOTE Confidence: 0.9397244

00:33:57.090 --> 00:33:57.909 these tiny

NOTE Confidence: 0.92093915

00:33:58.435 --> 00:34:00.035 streams, and then all these

NOTE Confidence: 0.92093915

00:34:00.035 --> 00:34:02.195 dots are genetic associations. So

NOTE Confidence: 0.92093915

00:34:02.195 --> 00:34:03.495 you can see here that,

NOTE Confidence: 0.89416504

00:34:04.035 --> 00:34:06.195 variants are associated with complex

NOTE Confidence: 0.89416504

00:34:06.195 --> 00:34:07.495 traits are everywhere.

NOTE Confidence: 0.9609819

00:34:08.355 --> 00:34:09.635 And so, like, because the

NOTE Confidence: 0.9609819

00:34:09.635 --> 00:34:11.555 architecture of common traits and

NOTE Confidence: 0.9609819

00:34:11.555 --> 00:34:12.055 disease

NOTE Confidence: 0.99194336

00:34:12.730 --> 00:34:13.770 is due to,

NOTE Confidence: 0.9749756

00:34:14.250 --> 00:34:16.250 the contribution of many variants

NOTE Confidence: 0.9749756

00:34:16.250 --> 00:34:17.469 with very small

NOTE Confidence: 0.98514813

00:34:17.850 --> 00:34:20.010 effect size. And with respect

NOTE Confidence: 0.98514813

00:34:20.010 --> 00:34:20.410 to,

NOTE Confidence: 0.9539659

00:34:21.370 --> 00:34:22.810 what we can do with

NOTE Confidence: 0.9539659

00:34:22.810 --> 00:34:24.030 this kind of information,

NOTE Confidence: 0.98429364

00:34:24.489 --> 00:34:25.710 we can use this genetic

NOTE Confidence: 0.98429364

00:34:25.770 --> 00:34:26.270 association

NOTE Confidence: 0.9798584

00:34:26.570 --> 00:34:28.350 to investigate both the epidemiology

NOTE Confidence: 0.9798584

00:34:28.645 --> 00:34:29.465 and then biology

NOTE Confidence: 0.86968994

00:34:30.005 --> 00:34:31.545 of human traits and disease.

NOTE Confidence: 0.86968994

00:34:31.685 --> 00:34:32.505 This is another

NOTE Confidence: 0.91994405

00:34:33.125 --> 00:34:35.445 very famous plot in, in

NOTE Confidence: 0.91994405

00:34:35.445 --> 00:34:37.045 genetic research. It's a Manhattan

NOTE Confidence: 0.91994405

00:34:37.045 --> 00:34:38.405 plot. And here on the

NOTE Confidence: 0.91994405

00:34:38.405 --> 00:34:39.925 x axis, you have, like,

NOTE Confidence: 0.91994405

00:34:39.925 --> 00:34:40.745 our chromosomes.

NOTE Confidence: 0.93104386

00:34:41.205 --> 00:34:42.405 And then here, you have,

NOTE Confidence: 0.93104386

00:34:42.405 --> 00:34:44.105 like, a statistical significance.

NOTE Confidence: 0.9526367

00:34:44.510 --> 00:34:44.829 The highest

NOTE Confidence: 0.8855713

00:34:46.190 --> 00:34:47.069 the the the dot here,

NOTE Confidence: 0.8855713

00:34:47.069 --> 00:34:49.170 the strongest is the statistical

NOTE Confidence: 0.8855713

00:34:49.230 --> 00:34:50.750 significance, and this each dot

NOTE Confidence: 0.8855713

00:34:50.750 --> 00:34:52.210 is a is a variant.

NOTE Confidence: 0.9852973

00:34:52.510 --> 00:34:53.790 And so depending on how

NOTE Confidence: 0.9852973

00:34:53.790 --> 00:34:55.170 many variants we get,

NOTE Confidence: 0.88688964

00:34:55.630 --> 00:34:57.969 surviving our multiple testing correction,

NOTE Confidence: 0.88688964

00:34:58.109 --> 00:35:00.210 which is this banded line,

NOTE Confidence: 0.97956544

00:35:01.205 --> 00:35:02.725 We can detect, like, information

NOTE Confidence: 0.97956544

00:35:02.725 --> 00:35:04.265 about which are the pathways

NOTE Confidence: 0.97249347

00:35:04.885 --> 00:35:06.405 involved in our disease of

NOTE Confidence: 0.97249347

00:35:06.405 --> 00:35:07.925 interest. We can create a

NOTE Confidence: 0.97249347

00:35:07.925 --> 00:35:09.945 polygenic risk score to distinguish

NOTE Confidence: 0.97249347

00:35:10.085 --> 00:35:11.145 case and controls.

NOTE Confidence: 0.9200963

00:35:11.685 --> 00:35:13.410 We can perform a causal

NOTE Confidence: 0.9200963

00:35:13.410 --> 00:35:14.469 inference analysis.

NOTE Confidence: 0.9996745

00:35:15.010 --> 00:35:15.910 We can integrate

NOTE Confidence: 0.95180666

00:35:16.369 --> 00:35:18.230 other omic domains to understand

NOTE Confidence: 0.94455296

00:35:18.609 --> 00:35:20.450 how a genetic variance can

NOTE Confidence: 0.94455296

00:35:20.450 --> 00:35:21.430 lead to the disease

NOTE Confidence: 0.8781738

00:35:21.809 --> 00:35:23.510 through which molecular mechanism

NOTE Confidence: 0.9458008

00:35:24.210 --> 00:35:25.410 in the brain or in

NOTE Confidence: 0.9458008

00:35:25.410 --> 00:35:26.150 other organs,

NOTE Confidence: 0.9595467

00:35:27.155 --> 00:35:29.094 can affect the disease risk

NOTE Confidence: 0.9595467

00:35:29.234 --> 00:35:31.555 or conduct multivariable analysis to

NOTE Confidence: 0.9595467

00:35:31.555 --> 00:35:32.055 understand

NOTE Confidence: 0.77441406

00:35:32.355 --> 00:35:32.855 how

NOTE Confidence: 0.8742676

00:35:33.234 --> 00:35:35.415 two traits, two different diseases

NOTE Confidence: 0.8742676

00:35:35.635 --> 00:35:36.535 that we observe

NOTE Confidence: 0.9911295

00:35:36.835 --> 00:35:37.575 as comorbid

NOTE Confidence: 0.7738037

00:35:38.195 --> 00:35:39.494 share genetic,

NOTE Confidence: 0.81347656

00:35:39.954 --> 00:35:40.380 factors.

NOTE Confidence: 0.717041

00:35:40.779 --> 00:35:41.279 So,

NOTE Confidence: 0.96990967

00:35:41.579 --> 00:35:43.739 with respect to cannabis research,

NOTE Confidence: 0.96990967

00:35:43.739 --> 00:35:44.799 here are the,

NOTE Confidence: 0.99902344

00:35:45.259 --> 00:35:45.759 five

NOTE Confidence: 0.9946289

00:35:46.299 --> 00:35:47.119 large scale

NOTE Confidence: 0.9553613

00:35:47.500 --> 00:35:49.660 GWAS published in the last

NOTE Confidence: 0.9553613

00:35:49.660 --> 00:35:51.180 few years. And here you

NOTE Confidence: 0.9553613

00:35:51.180 --> 00:35:51.980 can see that we have

NOTE Confidence: 0.9553613

00:35:51.980 --> 00:35:53.739 three for cannabis use and

NOTE Confidence: 0.9553613

00:35:53.739 --> 00:35:56.000 two for, cannabis use disorder.

NOTE Confidence: 0.9596122

00:35:57.204 --> 00:35:58.645 And so, like, again, several

NOTE Confidence: 0.9596122

00:35:58.645 --> 00:35:59.385 of these,

NOTE Confidence: 0.743103

00:36:00.244 --> 00:36:02.085 saw, like, Joel Scalenta Group

NOTE Confidence: 0.743103

00:36:02.085 --> 00:36:03.145 as the primary,

NOTE Confidence: 0.9809007

00:36:04.244 --> 00:36:06.244 leader in these studies. And

NOTE Confidence: 0.9809007

00:36:06.244 --> 00:36:07.204 so what we can do

NOTE Confidence: 0.9809007

00:36:07.204 --> 00:36:08.105 with this information?

NOTE Confidence: 0.99816895

00:36:08.405 --> 00:36:09.685 With this information, we can

NOTE Confidence: 0.99816895

00:36:09.685 --> 00:36:11.300 understand the difference

NOTE Confidence: 0.9980469

00:36:11.600 --> 00:36:12.100 between

NOTE Confidence: 0.9599202

00:36:12.560 --> 00:36:14.320 cannabis use and cannabis use

NOTE Confidence: 0.9599202

00:36:14.320 --> 00:36:14.820 disorder,

NOTE Confidence: 0.9712853

00:36:15.120 --> 00:36:16.880 how strong is the genetic

NOTE Confidence: 0.9712853

00:36:16.880 --> 00:36:18.640 overlap between these two, and

NOTE Confidence: 0.9712853

00:36:18.640 --> 00:36:19.940 how these two

NOTE Confidence: 0.9819336

00:36:20.320 --> 00:36:21.780 differ in their relationship

NOTE Confidence: 0.9482422

00:36:22.080 --> 00:36:22.820 with other,

NOTE Confidence: 1

00:36:23.360 --> 00:36:23.860 psychiatric

NOTE Confidence: 0.99658203

00:36:24.160 --> 00:36:24.900 and behavioral

NOTE Confidence: 0.97749835

00:36:25.280 --> 00:36:26.955 traits. And so this is

NOTE Confidence: 0.97749835

00:36:26.955 --> 00:36:27.455 another

NOTE Confidence: 0.92077637

00:36:27.755 --> 00:36:28.875 plot from one of the

NOTE Confidence: 0.92077637

00:36:28.875 --> 00:36:30.395 study. Again, it's one of

NOTE Confidence: 0.92077637

00:36:30.395 --> 00:36:31.755 the study which was led

NOTE Confidence: 0.92077637

00:36:31.755 --> 00:36:34.155 by, Joel Skeleton group. And

NOTE Confidence: 0.92077637

00:36:34.155 --> 00:36:35.435 you can see here that

NOTE Confidence: 0.92077637

00:36:35.435 --> 00:36:36.415 we have multiple,

NOTE Confidence: 0.9663086

00:36:37.435 --> 00:36:38.495 secondary disorders

NOTE Confidence: 0.9970703

00:36:38.930 --> 00:36:39.910 and other behavioral

NOTE Confidence: 0.98860675

00:36:40.370 --> 00:36:40.870 phenotypes.

NOTE Confidence: 0.9309082

00:36:41.170 --> 00:36:42.370 And so this is, an

NOTE Confidence: 0.9309082

00:36:42.370 --> 00:36:44.290 analysis called a genomic structural

NOTE Confidence: 0.9309082

00:36:44.290 --> 00:36:46.210 equation modeling. And so it

NOTE Confidence: 0.9309082

00:36:46.210 --> 00:36:47.190 tries to converge,

NOTE Confidence: 0.4506836

00:36:48.250 --> 00:36:48.750 con

NOTE Confidence: 0.871024

00:36:49.090 --> 00:36:51.810 converge, like, genetic correlation across

NOTE Confidence: 0.871024

00:36:51.810 --> 00:36:52.550 these traits

NOTE Confidence: 0.9800781

00:36:52.985 --> 00:36:55.645 in latent factors that underline

NOTE Confidence: 0.56225586

00:36:56.265 --> 00:36:57.245 the genetic

NOTE Confidence: 0.9273437

00:36:57.785 --> 00:37:00.185 relationship among these these different

NOTE Confidence: 0.9273437

00:37:00.185 --> 00:37:01.465 conditions. And so here I

NOTE Confidence: 0.9273437

00:37:01.465 --> 00:37:03.325 highlighted the cannabis use disorder

NOTE Confidence: 0.90907913

00:37:03.625 --> 00:37:05.330 and then cannabis use. You

NOTE Confidence: 0.90907913

00:37:05.330 --> 00:37:06.770 can see that cannabis use

NOTE Confidence: 0.90907913

00:37:06.770 --> 00:37:09.190 disorder cluster together other substance

NOTE Confidence: 0.90907913

00:37:09.250 --> 00:37:09.910 use disorder,

NOTE Confidence: 0.9604899

00:37:10.210 --> 00:37:12.050 opioid use disorder, alcohol use

NOTE Confidence: 0.9604899

00:37:12.050 --> 00:37:12.550 disorder.

NOTE Confidence: 0.9157049

00:37:13.650 --> 00:37:15.270 And we start away from

NOTE Confidence: 0.9157049

00:37:15.489 --> 00:37:17.330 cannabis use, and cannabis use

NOTE Confidence: 0.9157049

00:37:17.330 --> 00:37:17.830 cluster

NOTE Confidence: 0.8829753

00:37:18.335 --> 00:37:19.775 with other traits, like a

NOTE Confidence: 0.8829753

00:37:19.775 --> 00:37:21.234 number of sexual partner,

NOTE Confidence: 0.677124

00:37:21.535 --> 00:37:22.594 smoke initiation,

NOTE Confidence: 0.8863352

00:37:23.934 --> 00:37:25.855 Townsend Deprivation Inserts, which is

NOTE Confidence: 0.8863352

00:37:25.855 --> 00:37:27.614 a material deprivation, and they

NOTE Confidence: 0.8863352

00:37:27.614 --> 00:37:29.795 cluster on this impulsivity,

NOTE Confidence: 0.8757324

00:37:30.255 --> 00:37:31.154 a risk taking,

NOTE Confidence: 0.98093486

00:37:32.414 --> 00:37:33.570 factor. And so you can

NOTE Confidence: 0.98093486

00:37:33.570 --> 00:37:35.270 see here that these two

NOTE Confidence: 0.98093486

00:37:35.330 --> 00:37:35.830 traits

NOTE Confidence: 0.9918213

00:37:36.450 --> 00:37:37.270 are partially,

NOTE Confidence: 0.92089844

00:37:37.810 --> 00:37:38.310 genetically,

NOTE Confidence: 0.9037598

00:37:39.250 --> 00:37:40.770 correlated. And so here here

NOTE Confidence: 0.9037598

00:37:40.770 --> 00:37:41.570 you can see, like, the

NOTE Confidence: 0.9037598

00:37:41.570 --> 00:37:43.270 genetic correlation between the impulsivity

NOTE Confidence: 0.8892299

00:37:43.810 --> 00:37:45.170 risk taking factor and the

NOTE Confidence: 0.8892299

00:37:45.170 --> 00:37:46.230 substance dependence

NOTE Confidence: 0.98759764

00:37:46.530 --> 00:37:48.230 factor, which is about six

NOTE Confidence: 0.9740989

00:37:48.825 --> 00:37:50.344 point sixty five. And so

NOTE Confidence: 0.9740989

00:37:50.344 --> 00:37:51.465 you can see how different

NOTE Confidence: 0.9740989

00:37:51.465 --> 00:37:52.825 they are. And then we

NOTE Confidence: 0.9740989

00:37:52.825 --> 00:37:53.705 can look up to our

NOTE Confidence: 0.9740989

00:37:53.705 --> 00:37:54.685 recent preprint

NOTE Confidence: 0.92854816

00:37:55.224 --> 00:37:56.364 where they increased

NOTE Confidence: 0.94384766

00:37:57.705 --> 00:37:58.844 the the study

NOTE Confidence: 0.9436035

00:37:59.145 --> 00:37:59.645 of,

NOTE Confidence: 0.90457153

00:38:00.585 --> 00:38:02.685 different cannabis trait, including

NOTE Confidence: 0.63986206

00:38:03.180 --> 00:38:04.560 adverse use of cannabis,

NOTE Confidence: 0.9970703

00:38:05.099 --> 00:38:05.599 frequency

NOTE Confidence: 0.92300034

00:38:05.980 --> 00:38:07.660 of use of cannabis, and

NOTE Confidence: 0.92300034

00:38:07.660 --> 00:38:09.420 cannabis use disorder. And, yeah,

NOTE Confidence: 0.92300034

00:38:09.420 --> 00:38:10.780 you can see, like, different

NOTE Confidence: 0.92300034

00:38:10.780 --> 00:38:12.780 trends of this relationship. As

NOTE Confidence: 0.92300034

00:38:12.780 --> 00:38:13.980 I mentioned, this is the

NOTE Confidence: 0.92300034

00:38:14.219 --> 00:38:15.980 for example, looking to a

NOTE Confidence: 0.92300034

00:38:15.980 --> 00:38:17.200 condition and

NOTE Confidence: 0.9160156

00:38:17.575 --> 00:38:18.075 social,

NOTE Confidence: 0.96209717

00:38:18.775 --> 00:38:20.375 determinants of health, we have

NOTE Confidence: 0.96209717

00:38:20.375 --> 00:38:22.295 material deprivation here, and we

NOTE Confidence: 0.96209717

00:38:22.295 --> 00:38:23.575 can see that there is

NOTE Confidence: 0.96209717

00:38:23.575 --> 00:38:25.815 a positive genetic correlation, which

NOTE Confidence: 0.96209717

00:38:25.815 --> 00:38:27.415 is stronger for cannabis use

NOTE Confidence: 0.96209717

00:38:27.415 --> 00:38:29.335 disorder and less stronger for

NOTE Confidence: 0.96209717

00:38:29.335 --> 00:38:30.315 cannabis use,

NOTE Confidence: 0.92578125

00:38:31.025 --> 00:38:31.525 ever

NOTE Confidence: 0.9374884

00:38:31.940 --> 00:38:34.180 cannabis use, and frequency is

NOTE Confidence: 0.9374884

00:38:34.180 --> 00:38:35.300 kind of in the middle.

NOTE Confidence: 0.9374884

00:38:35.300 --> 00:38:36.420 Most of the time, we

NOTE Confidence: 0.9374884

00:38:36.420 --> 00:38:37.960 we can see that frequency

NOTE Confidence: 0.9374884

00:38:38.260 --> 00:38:38.760 is

NOTE Confidence: 0.99483234

00:38:39.140 --> 00:38:40.660 somehow in the middle between

NOTE Confidence: 0.99483234

00:38:40.660 --> 00:38:41.620 the fact that we see

NOTE Confidence: 0.99483234

00:38:41.620 --> 00:38:43.220 for cannabis use disorder and

NOTE Confidence: 0.99483234

00:38:43.220 --> 00:38:44.340 the fact that we see

NOTE Confidence: 0.99483234

00:38:44.340 --> 00:38:46.375 for ever using cannabis.

NOTE Confidence: 0.9635304

00:38:46.994 --> 00:38:48.355 But, okay, in some cases,

NOTE Confidence: 0.9635304

00:38:48.355 --> 00:38:49.395 like, we can see, like,

NOTE Confidence: 0.9635304

00:38:49.395 --> 00:38:50.915 something that is reversed. For

NOTE Confidence: 0.9635304

00:38:50.915 --> 00:38:53.315 example, for working memory, we

NOTE Confidence: 0.9635304

00:38:53.315 --> 00:38:55.155 see, like, a positive genetic

NOTE Confidence: 0.9635304

00:38:55.155 --> 00:38:56.614 correlation, which is lower

NOTE Confidence: 0.9073283

00:38:57.119 --> 00:38:59.359 for cannabis use disorder, but

NOTE Confidence: 0.9073283

00:38:59.359 --> 00:39:01.359 is higher for frequency and

NOTE Confidence: 0.9073283

00:39:01.359 --> 00:39:02.259 ever use.

NOTE Confidence: 0.95143723

00:39:02.640 --> 00:39:04.719 Verbal reasoning, we see opposite

NOTE Confidence: 0.95143723

00:39:04.719 --> 00:39:06.880 collection for ever use and

NOTE Confidence: 0.95143723

00:39:06.880 --> 00:39:08.319 cannabis use disorder. And so,

NOTE Confidence: 0.95143723

00:39:08.319 --> 00:39:10.160 like, similar pattern also for

NOTE Confidence: 0.95143723

00:39:10.160 --> 00:39:11.700 IQ, educational attainment,

NOTE Confidence: 0.9491043

00:39:12.285 --> 00:39:14.844 income. Again, childhood IQ, we

NOTE Confidence: 0.9491043

00:39:14.844 --> 00:39:16.765 see, like, it's probably due

NOTE Confidence: 0.9491043

00:39:16.765 --> 00:39:18.045 to less power, but we

NOTE Confidence: 0.9491043

00:39:18.045 --> 00:39:19.805 see a similar trend. Reaction

NOTE Confidence: 0.9491043

00:39:19.805 --> 00:39:21.484 time, the effect is basically

NOTE Confidence: 0.9491043

00:39:21.484 --> 00:39:23.905 null. With respect to mental

NOTE Confidence: 0.9491043

00:39:23.964 --> 00:39:24.944 health outcomes,

NOTE Confidence: 0.9735456

00:39:25.739 --> 00:39:27.100 we can see a similar

NOTE Confidence: 0.9735456

00:39:27.100 --> 00:39:29.180 trend where the cannabis use

NOTE Confidence: 0.9735456

00:39:29.180 --> 00:39:31.040 disorder is most strongly,

NOTE Confidence: 0.9975586

00:39:31.660 --> 00:39:32.800 genetically correlated

NOTE Confidence: 0.73030597

00:39:33.340 --> 00:39:34.640 with a psychiatric

NOTE Confidence: 0.93959963

00:39:35.020 --> 00:39:37.040 condition and also, like, negative

NOTE Confidence: 0.9512451

00:39:37.660 --> 00:39:39.500 mental health outcomes, but we

NOTE Confidence: 0.9512451

00:39:39.500 --> 00:39:41.200 have some exceptions. For example,

NOTE Confidence: 0.78437865

00:39:41.715 --> 00:39:43.075 with the autism and the

NOTE Confidence: 0.78437865

00:39:43.075 --> 00:39:44.855 Noroxera nervosa, it's actually

NOTE Confidence: 0.86173505

00:39:45.155 --> 00:39:46.515 ever cannabis use that has

NOTE Confidence: 0.86173505

00:39:46.515 --> 00:39:48.035 stronger genetic relation. So you

NOTE Confidence: 0.86173505

00:39:48.114 --> 00:39:49.175 we we can see how

NOTE Confidence: 0.86173505

00:39:49.235 --> 00:39:50.295 these two traits,

NOTE Confidence: 0.97417533

00:39:51.075 --> 00:39:52.835 are different, and they're different

NOTE Confidence: 0.97417533

00:39:52.835 --> 00:39:54.535 in their relationship with

NOTE Confidence: 0.98828125

00:39:54.849 --> 00:39:55.349 other

NOTE Confidence: 0.9113525

00:39:55.650 --> 00:39:57.569 brain related outcomes. And here,

NOTE Confidence: 0.9113525

00:39:57.569 --> 00:39:58.869 we can see, like, some

NOTE Confidence: 0.8203125

00:39:59.170 --> 00:40:00.069 substance use,

NOTE Confidence: 0.9309082

00:40:00.770 --> 00:40:01.589 use disorder,

NOTE Confidence: 0.94247586

00:40:02.050 --> 00:40:03.569 phenotypes, and when we look

NOTE Confidence: 0.94247586

00:40:03.569 --> 00:40:04.469 for dependence,

NOTE Confidence: 0.8342285

00:40:05.569 --> 00:40:05.969 and,

NOTE Confidence: 0.9980469

00:40:06.530 --> 00:40:07.030 other

NOTE Confidence: 0.93408203

00:40:07.695 --> 00:40:08.675 strongly related,

NOTE Confidence: 0.76538086

00:40:09.535 --> 00:40:10.035 behavioral,

NOTE Confidence: 0.95273435

00:40:10.895 --> 00:40:12.094 linked to addiction, we can

NOTE Confidence: 0.95273435

00:40:12.094 --> 00:40:13.855 see that cannabis use disorder

NOTE Confidence: 0.95273435

00:40:13.855 --> 00:40:15.795 is the most strongly related.

NOTE Confidence: 0.97387695

00:40:17.295 --> 00:40:18.094 And so, like,

NOTE Confidence: 0.98286945

00:40:18.735 --> 00:40:20.015 our goal in this study

NOTE Confidence: 0.98286945

00:40:20.015 --> 00:40:21.235 was to try to understand

NOTE Confidence: 0.98286945

00:40:21.295 --> 00:40:22.200 better the

NOTE Confidence: 0.9980469

00:40:22.680 --> 00:40:23.500 brain biology

NOTE Confidence: 0.93555325

00:40:23.880 --> 00:40:25.960 underlying this difference between cannabis

NOTE Confidence: 0.93555325

00:40:25.960 --> 00:40:27.800 use disorder and cannabis use.

NOTE Confidence: 0.93555325

00:40:27.800 --> 00:40:29.320 And to do that, we

NOTE Confidence: 0.93555325

00:40:29.320 --> 00:40:31.079 use the UK Biobank. This

NOTE Confidence: 0.93555325

00:40:31.079 --> 00:40:33.079 is a a large quarter

NOTE Confidence: 0.93555325

00:40:33.079 --> 00:40:35.025 that enrolled more than five

NOTE Confidence: 0.93555325

00:40:35.025 --> 00:40:36.545 hundred thousand people in the

NOTE Confidence: 0.93555325

00:40:36.545 --> 00:40:38.625 UK, and they generated the,

NOTE Confidence: 0.93555325

00:40:38.944 --> 00:40:41.364 brain multimodal brain imaging data,

NOTE Confidence: 0.8598633

00:40:41.905 --> 00:40:42.724 for for

NOTE Confidence: 0.99035066

00:40:43.105 --> 00:40:44.385 a large chunk of this

NOTE Confidence: 0.99035066

00:40:44.385 --> 00:40:46.305 population. In twenty twenty five,

NOTE Confidence: 0.99035066

00:40:46.305 --> 00:40:47.924 the UK Biobank released

NOTE Confidence: 0.7763672

00:40:49.299 --> 00:40:49.799 brain,

NOTE Confidence: 0.9444716

00:40:50.660 --> 00:40:52.500 body, and bone scans for

NOTE Confidence: 0.9444716

00:40:52.500 --> 00:40:54.039 one hundred thousand volunteers.

NOTE Confidence: 0.9676921

00:40:54.339 --> 00:40:55.380 In the analysis that I'm

NOTE Confidence: 0.9676921

00:40:55.380 --> 00:40:57.160 presenting today, we used

NOTE Confidence: 0.93455

00:40:57.539 --> 00:40:59.219 a previous release of the

NOTE Confidence: 0.93455

00:40:59.219 --> 00:41:01.059 data, which included thirty three

NOTE Confidence: 0.93455

00:41:01.059 --> 00:41:01.960 thousand participants

NOTE Confidence: 0.9159546

00:41:02.795 --> 00:41:04.795 and almost four thousand brain

NOTE Confidence: 0.9159546

00:41:04.795 --> 00:41:06.175 imaging derived phenotypes

NOTE Confidence: 0.9315796

00:41:06.715 --> 00:41:09.035 derived from six different brain

NOTE Confidence: 0.9315796

00:41:09.035 --> 00:41:10.395 modalities that can give us

NOTE Confidence: 0.9315796

00:41:10.395 --> 00:41:11.535 information about,

NOTE Confidence: 0.9550781

00:41:12.315 --> 00:41:12.815 variation

NOTE Confidence: 0.9962891

00:41:13.355 --> 00:41:15.535 in brain structure and function.

NOTE Confidence: 0.87890625

00:41:16.520 --> 00:41:18.280 And yet we report like

NOTE Confidence: 0.87890625

00:41:18.280 --> 00:41:20.520 this, this plot about the

NOTE Confidence: 0.87890625

00:41:20.520 --> 00:41:21.660 genetic component

NOTE Confidence: 0.81396484

00:41:22.119 --> 00:41:23.339 of these different,

NOTE Confidence: 0.94940865

00:41:23.800 --> 00:41:25.480 brain imaging phenotype. And so

NOTE Confidence: 0.94940865

00:41:25.480 --> 00:41:26.940 we have genetic information,

NOTE Confidence: 0.9648205

00:41:27.880 --> 00:41:29.960 regarding cannabis use disorder, cannabis

NOTE Confidence: 0.9648205

00:41:29.960 --> 00:41:32.075 use, and genetic information about

NOTE Confidence: 0.9648205

00:41:32.215 --> 00:41:33.755 these brain imaging phenotypes.

NOTE Confidence: 0.9890137

00:41:34.775 --> 00:41:35.995 In a previous study,

NOTE Confidence: 0.9760335

00:41:36.375 --> 00:41:37.975 which was based mostly on

NOTE Confidence: 0.9760335

00:41:37.975 --> 00:41:38.475 observational,

NOTE Confidence: 0.9807129

00:41:39.975 --> 00:41:40.475 analysis,

NOTE Confidence: 0.9212782

00:41:42.295 --> 00:41:43.655 the was the UK Biobank

NOTE Confidence: 0.9212782

00:41:43.655 --> 00:41:44.935 was used to understand the

NOTE Confidence: 0.9212782

00:41:44.935 --> 00:41:45.835 difference between,

NOTE Confidence: 0.93618375

00:41:46.569 --> 00:41:49.210 cannabis users and controls. And

NOTE Confidence: 0.93618375

00:41:49.210 --> 00:41:50.329 you can see here that

NOTE Confidence: 0.93618375

00:41:50.329 --> 00:41:51.930 the sample size is much

NOTE Confidence: 0.93618375

00:41:51.930 --> 00:41:54.089 smaller because the this study

NOTE Confidence: 0.93618375

00:41:54.089 --> 00:41:55.469 focused mostly on

NOTE Confidence: 0.94417316

00:41:55.770 --> 00:41:58.170 individuals that have actual information

NOTE Confidence: 0.94417316

00:41:58.170 --> 00:41:58.670 about

NOTE Confidence: 0.9115767

00:41:59.145 --> 00:42:00.665 cannabis use. And in this

NOTE Confidence: 0.9115767

00:42:00.665 --> 00:42:02.905 study, they identified that people

NOTE Confidence: 0.9115767

00:42:02.905 --> 00:42:03.225 with,

NOTE Confidence: 0.8189087

00:42:03.864 --> 00:42:05.465 that use cannabis in their

NOTE Confidence: 0.8189087

00:42:05.465 --> 00:42:06.844 life have lower,

NOTE Confidence: 0.96655273

00:42:07.145 --> 00:42:08.285 white matter integrity,

NOTE Confidence: 0.875

00:42:09.465 --> 00:42:10.685 higher immunity

NOTE Confidence: 0.9692993

00:42:11.305 --> 00:42:12.525 in the corpus callosus,

NOTE Confidence: 0.6853841

00:42:12.920 --> 00:42:14.219 and reduced connectivity

NOTE Confidence: 0.8267456

00:42:14.760 --> 00:42:16.280 in the default mode and

NOTE Confidence: 0.8267456

00:42:16.280 --> 00:42:18.380 the same internal executive networks.

NOTE Confidence: 0.9829915

00:42:18.920 --> 00:42:20.200 And so, like, in this

NOTE Confidence: 0.9829915

00:42:20.200 --> 00:42:20.700 study,

NOTE Confidence: 0.8249512

00:42:21.080 --> 00:42:21.820 they use

NOTE Confidence: 0.93636066

00:42:22.200 --> 00:42:24.040 individual level information to try

NOTE Confidence: 0.93636066

00:42:24.040 --> 00:42:25.640 to understand the association between

NOTE Confidence: 0.93636066

00:42:25.640 --> 00:42:26.380 brain variation

NOTE Confidence: 0.971654

00:42:27.125 --> 00:42:28.885 and cannabis use. They were

NOTE Confidence: 0.971654

00:42:28.885 --> 00:42:29.844 not able to do an

NOTE Confidence: 0.971654

00:42:29.844 --> 00:42:31.525 analysis for cannabis use disorder

NOTE Confidence: 0.971654

00:42:31.525 --> 00:42:32.984 because cannabis use disorder

NOTE Confidence: 0.96324056

00:42:33.525 --> 00:42:34.825 doesn't have a high prevalence

NOTE Confidence: 0.96324056

00:42:34.885 --> 00:42:36.085 in the UK Biobank. We

NOTE Confidence: 0.96324056

00:42:36.085 --> 00:42:37.625 don't have that that information.

NOTE Confidence: 0.94990236

00:42:38.165 --> 00:42:39.545 And so in the study

NOTE Confidence: 0.9764579

00:42:40.530 --> 00:42:41.730 that was funded by this

NOTE Confidence: 0.9764579

00:42:41.730 --> 00:42:42.550 pilot award,

NOTE Confidence: 0.94013673

00:42:42.930 --> 00:42:44.950 instead of using information about

NOTE Confidence: 0.8925781

00:42:45.330 --> 00:42:46.550 individual participants,

NOTE Confidence: 0.9091797

00:42:46.930 --> 00:42:47.750 we modeled

NOTE Confidence: 0.9432373

00:42:48.210 --> 00:42:49.270 genetic effects.

NOTE Confidence: 0.98986816

00:42:49.650 --> 00:42:50.630 Genetic effects,

NOTE Confidence: 0.9016879

00:42:51.410 --> 00:42:53.090 for related to cannabis use

NOTE Confidence: 0.9016879

00:42:53.090 --> 00:42:55.175 disorder, to cannabis use, and

NOTE Confidence: 0.9016879

00:42:55.175 --> 00:42:57.094 to this four thousand brain

NOTE Confidence: 0.9016879

00:42:57.094 --> 00:42:58.075 imaging phenotypes.

NOTE Confidence: 0.95928484

00:42:58.614 --> 00:43:00.135 And our first goal was

NOTE Confidence: 0.95928484

00:43:00.135 --> 00:43:01.655 to understand if there is

NOTE Confidence: 0.95928484

00:43:01.655 --> 00:43:02.795 a different relationship

NOTE Confidence: 0.99902344

00:43:03.255 --> 00:43:03.755 between

NOTE Confidence: 0.9291992

00:43:04.215 --> 00:43:05.275 the genetic effects

NOTE Confidence: 0.9722377

00:43:05.655 --> 00:43:07.815 linking cannabis use disorder to

NOTE Confidence: 0.9722377

00:43:07.815 --> 00:43:08.555 brain variation

NOTE Confidence: 0.904012

00:43:08.870 --> 00:43:10.469 and those related to cannabis

NOTE Confidence: 0.904012

00:43:10.469 --> 00:43:10.969 use.

NOTE Confidence: 0.9567348

00:43:11.430 --> 00:43:13.030 And then to follow-up this

NOTE Confidence: 0.9567348

00:43:13.030 --> 00:43:14.550 first analysis, we want to

NOTE Confidence: 0.9567348

00:43:14.550 --> 00:43:16.170 understand if the biology

NOTE Confidence: 0.95825195

00:43:16.630 --> 00:43:17.690 underlying this

NOTE Confidence: 0.9295044

00:43:17.989 --> 00:43:19.210 pleiotropic effect,

NOTE Confidence: 0.9138794

00:43:19.510 --> 00:43:21.130 effect that are shared between

NOTE Confidence: 0.9138794

00:43:21.350 --> 00:43:22.170 a brain variation

NOTE Confidence: 0.94628906

00:43:22.469 --> 00:43:23.930 and this cannabis phenotype

NOTE Confidence: 0.99776787

00:43:24.505 --> 00:43:26.685 could be targeted by existing

NOTE Confidence: 0.99776787

00:43:26.744 --> 00:43:27.885 molecular compounds.

NOTE Confidence: 0.9584961

00:43:29.945 --> 00:43:31.885 And here are some, initial,

NOTE Confidence: 0.96153677

00:43:32.344 --> 00:43:33.945 results. And so, like, here,

NOTE Confidence: 0.96153677

00:43:33.945 --> 00:43:35.224 we can see, like, some

NOTE Confidence: 0.96153677

00:43:35.224 --> 00:43:35.724 statistics

NOTE Confidence: 0.9871419

00:43:36.265 --> 00:43:38.525 about global genetic correlation. So

NOTE Confidence: 0.9871419

00:43:38.820 --> 00:43:39.320 correlation

NOTE Confidence: 0.9470215

00:43:39.780 --> 00:43:40.280 across,

NOTE Confidence: 0.96203613

00:43:40.900 --> 00:43:42.900 genetic factor in the whole

NOTE Confidence: 0.96203613

00:43:42.900 --> 00:43:44.340 genome. And here we can

NOTE Confidence: 0.96203613

00:43:44.340 --> 00:43:45.160 see that

NOTE Confidence: 0.9515991

00:43:45.540 --> 00:43:47.460 several of these are related

NOTE Confidence: 0.9515991

00:43:47.460 --> 00:43:48.680 to functional connectivity

NOTE Confidence: 0.9229329

00:43:49.300 --> 00:43:50.820 and mostly relate to the

NOTE Confidence: 0.9229329

00:43:50.820 --> 00:43:51.320 default

NOTE Confidence: 0.95336914

00:43:52.235 --> 00:43:53.295 mode network.

NOTE Confidence: 0.99698895

00:43:53.755 --> 00:43:54.895 We also see,

NOTE Confidence: 0.82580566

00:43:55.835 --> 00:43:57.775 like, a white matter,

NOTE Confidence: 0.7117513

00:43:58.395 --> 00:43:58.895 microstructure

NOTE Confidence: 0.99121094

00:43:59.275 --> 00:43:59.775 association

NOTE Confidence: 0.97260535

00:44:00.155 --> 00:44:01.915 in the right superior thalamic

NOTE Confidence: 0.97260535

00:44:01.915 --> 00:44:03.614 region. And but the important

NOTE Confidence: 0.97260535

00:44:03.675 --> 00:44:05.355 part here is that this

NOTE Confidence: 0.97260535

00:44:05.355 --> 00:44:05.855 effect

NOTE Confidence: 0.93066406

00:44:06.155 --> 00:44:07.455 appears to be specific

NOTE Confidence: 0.97084147

00:44:07.910 --> 00:44:09.110 with only one of the

NOTE Confidence: 0.97084147

00:44:09.110 --> 00:44:10.790 two cannabis phenotype. So they

NOTE Confidence: 0.97084147

00:44:10.790 --> 00:44:12.170 don't appear to be shared.

NOTE Confidence: 0.9238185

00:44:12.710 --> 00:44:13.670 And so, like, we can

NOTE Confidence: 0.9238185

00:44:13.670 --> 00:44:15.350 see, for example, like, for

NOTE Confidence: 0.9238185

00:44:15.350 --> 00:44:17.190 this first brain function, the

NOTE Confidence: 0.9238185

00:44:17.190 --> 00:44:18.710 effect is specific to cannabis

NOTE Confidence: 0.9238185

00:44:18.710 --> 00:44:19.910 use disorder, but it's not

NOTE Confidence: 0.9238185

00:44:19.910 --> 00:44:21.974 present for cannabis use. And

NOTE Confidence: 0.9238185

00:44:21.974 --> 00:44:23.255 the same things follow the

NOTE Confidence: 0.9238185

00:44:23.255 --> 00:44:24.375 others. And in the first

NOTE Confidence: 0.9238185

00:44:24.614 --> 00:44:25.654 and in all these cases,

NOTE Confidence: 0.9238185

00:44:25.654 --> 00:44:26.934 we can see that the

NOTE Confidence: 0.9238185

00:44:26.934 --> 00:44:27.434 statistical

NOTE Confidence: 0.9270172

00:44:27.734 --> 00:44:29.734 difference between the cannabis use

NOTE Confidence: 0.9270172

00:44:29.734 --> 00:44:31.575 versus cannabis use disorder or

NOTE Confidence: 0.9270172

00:44:31.575 --> 00:44:33.674 genetic correlation aspect is statistically

NOTE Confidence: 0.9270172

00:44:33.895 --> 00:44:34.395 significant.

NOTE Confidence: 0.97031814

00:44:34.950 --> 00:44:36.150 But, again, this is only

NOTE Confidence: 0.97031814

00:44:36.150 --> 00:44:37.430 the the first step of

NOTE Confidence: 0.97031814

00:44:37.430 --> 00:44:39.050 our analysis. We wanted to

NOTE Confidence: 0.97031814

00:44:39.109 --> 00:44:40.869 go deeper. And so what

NOTE Confidence: 0.97031814

00:44:41.030 --> 00:44:42.630 and here is, like, again,

NOTE Confidence: 0.97031814

00:44:42.630 --> 00:44:43.130 like,

NOTE Confidence: 0.8780692

00:44:43.910 --> 00:44:45.510 a a plot about one

NOTE Confidence: 0.8780692

00:44:45.510 --> 00:44:45.910 of these,

NOTE Confidence: 0.9781494

00:44:47.484 --> 00:44:48.305 functional connectivity,

NOTE Confidence: 0.97540283

00:44:49.085 --> 00:44:50.464 phenotypes that we identified.

NOTE Confidence: 0.9207194

00:44:51.165 --> 00:44:52.364 And this is particularly related

NOTE Confidence: 0.9207194

00:44:52.364 --> 00:44:54.224 to the fourth mode network.

NOTE Confidence: 0.9207194

00:44:54.364 --> 00:44:55.984 And, again, if we compare

NOTE Confidence: 0.9916992

00:44:56.605 --> 00:44:58.844 the, genetic correlation between cannabis

NOTE Confidence: 0.9916992

00:44:58.844 --> 00:45:00.364 use and cannabis use disorder,

NOTE Confidence: 0.9916992

00:45:00.364 --> 00:45:01.165 we can see that there

NOTE Confidence: 0.9916992

00:45:01.165 --> 00:45:02.670 is a strong and statistically

NOTE Confidence: 0.9916992

00:45:02.810 --> 00:45:03.310 significant

NOTE Confidence: 0.9703776

00:45:03.770 --> 00:45:06.010 relationship with cannabis use, but

NOTE Confidence: 0.9703776

00:45:06.010 --> 00:45:07.950 not for cannabis use disorder.

NOTE Confidence: 0.9703776

00:45:08.170 --> 00:45:09.370 But as I was mentioning,

NOTE Confidence: 0.9703776

00:45:09.370 --> 00:45:10.890 we wanted to do, a

NOTE Confidence: 0.9703776

00:45:10.890 --> 00:45:12.570 deeper analysis. And so we

NOTE Confidence: 0.9703776

00:45:12.570 --> 00:45:13.390 moved from,

NOTE Confidence: 0.9741211

00:45:13.850 --> 00:45:15.469 a genetic correlation analysis

NOTE Confidence: 0.96931964

00:45:16.015 --> 00:45:17.535 to a latent causal variable

NOTE Confidence: 0.96931964

00:45:17.535 --> 00:45:18.035 analysis.

NOTE Confidence: 0.9718628

00:45:18.335 --> 00:45:19.775 So in this approach, we

NOTE Confidence: 0.9718628

00:45:19.775 --> 00:45:20.594 try to identify

NOTE Confidence: 0.99609375

00:45:21.135 --> 00:45:23.235 if the genetic effect

NOTE Confidence: 0.99869794

00:45:23.935 --> 00:45:24.915 that is shared

NOTE Confidence: 0.8709717

00:45:25.295 --> 00:45:27.155 between two different phenotypes,

NOTE Confidence: 0.98669434

00:45:27.535 --> 00:45:28.994 in this case, between

NOTE Confidence: 0.94018555

00:45:29.750 --> 00:45:31.589 cannabis phenotype and a brain

NOTE Confidence: 0.94018555

00:45:31.589 --> 00:45:32.489 imaging derived,

NOTE Confidence: 0.99609375

00:45:33.109 --> 00:45:33.609 phenotype

NOTE Confidence: 0.9680894

00:45:34.069 --> 00:45:35.430 is due to a latent

NOTE Confidence: 0.9680894

00:45:35.430 --> 00:45:37.349 causal variable. And if this

NOTE Confidence: 0.9680894

00:45:37.349 --> 00:45:38.950 causal variable has a full

NOTE Confidence: 0.9680894

00:45:38.950 --> 00:45:39.770 causal effect,

NOTE Confidence: 0.91204834

00:45:40.230 --> 00:45:41.829 it could negate partial,

NOTE Confidence: 0.96173096

00:45:42.150 --> 00:45:43.545 partially this this effect.

NOTE Confidence: 0.9486178

00:45:44.105 --> 00:45:45.224 And so we run this

NOTE Confidence: 0.9486178

00:45:45.224 --> 00:45:46.344 analysis, and we were able

NOTE Confidence: 0.9486178

00:45:46.344 --> 00:45:47.724 to identify additional,

NOTE Confidence: 0.90393066

00:45:50.025 --> 00:45:52.025 brain imaging phenotypes. And also

NOTE Confidence: 0.90393066

00:45:52.025 --> 00:45:52.844 in this case,

NOTE Confidence: 0.9134766

00:45:53.464 --> 00:45:55.405 what we observed is that

NOTE Confidence: 0.8645833

00:45:56.140 --> 00:45:56.940 each of these,

NOTE Confidence: 0.92822266

00:45:57.500 --> 00:45:58.000 relationship

NOTE Confidence: 0.9947374

00:45:58.300 --> 00:45:59.900 was specific to only one

NOTE Confidence: 0.9947374

00:45:59.900 --> 00:46:01.359 of the cannabis phenotype.

NOTE Confidence: 0.9074707

00:46:01.739 --> 00:46:02.560 So we found,

NOTE Confidence: 0.97753906

00:46:02.940 --> 00:46:04.000 genetic relationship

NOTE Confidence: 0.9873047

00:46:04.859 --> 00:46:05.359 specific

NOTE Confidence: 0.98339844

00:46:05.739 --> 00:46:07.600 to cannabis use and genetic

NOTE Confidence: 0.98339844

00:46:07.660 --> 00:46:08.160 relationship

NOTE Confidence: 0.9984375

00:46:08.505 --> 00:46:10.285 specific to cannabis use disorder.

NOTE Confidence: 0.950236

00:46:10.664 --> 00:46:11.944 Also, in this case, there

NOTE Confidence: 0.950236

00:46:11.944 --> 00:46:12.444 was,

NOTE Confidence: 0.92220056

00:46:12.744 --> 00:46:13.565 an overrepresentation

NOTE Confidence: 0.9345703

00:46:14.344 --> 00:46:14.424 of,

NOTE Confidence: 0.9975586

00:46:16.025 --> 00:46:17.164 functional connectivity

NOTE Confidence: 0.91661245

00:46:17.464 --> 00:46:19.625 phenotypes. But we also observed,

NOTE Confidence: 0.91661245

00:46:19.625 --> 00:46:19.944 like,

NOTE Confidence: 0.92626953

00:46:20.505 --> 00:46:21.644 cortical thickness

NOTE Confidence: 0.8737793

00:46:22.150 --> 00:46:22.650 and,

NOTE Confidence: 0.9666341

00:46:23.110 --> 00:46:24.489 again, white matter,

NOTE Confidence: 0.90722656

00:46:25.910 --> 00:46:26.410 microstructure,

NOTE Confidence: 0.8597005

00:46:27.350 --> 00:46:27.850 phenotypes,

NOTE Confidence: 0.9841657

00:46:28.310 --> 00:46:30.410 again, specifically related to cannabis

NOTE Confidence: 0.9841657

00:46:30.469 --> 00:46:31.210 use disorder.

NOTE Confidence: 0.8613281

00:46:31.910 --> 00:46:32.969 Also in this case,

NOTE Confidence: 0.86017114

00:46:33.270 --> 00:46:34.994 again, I want to show

NOTE Confidence: 0.86017114

00:46:34.994 --> 00:46:36.674 one of these brain imaging

NOTE Confidence: 0.86017114

00:46:36.674 --> 00:46:38.614 brain imaging brain imaging phenotype

NOTE Confidence: 0.86017114

00:46:38.674 --> 00:46:40.194 and specifically one, again, related

NOTE Confidence: 0.86017114

00:46:40.194 --> 00:46:41.094 to the default,

NOTE Confidence: 0.93981934

00:46:41.714 --> 00:46:43.315 model network. And in this

NOTE Confidence: 0.93981934

00:46:43.315 --> 00:46:44.934 case, you can see how

NOTE Confidence: 0.9502716

00:46:45.315 --> 00:46:46.914 stronger is the relationship with

NOTE Confidence: 0.9502716

00:46:46.914 --> 00:46:48.750 cannabis use disorder while it's

NOTE Confidence: 0.9502716

00:46:48.750 --> 00:46:50.750 null for the cannabis use

NOTE Confidence: 0.9502716

00:46:50.750 --> 00:46:51.250 disorder,

NOTE Confidence: 0.99365234

00:46:52.430 --> 00:46:52.930 phenotype.

NOTE Confidence: 0.95926106

00:46:54.510 --> 00:46:56.210 And here is, again, summarizing,

NOTE Confidence: 0.9891881

00:46:57.070 --> 00:46:59.469 our different genetic relationship that

NOTE Confidence: 0.9891881

00:46:59.469 --> 00:47:00.130 we observed

NOTE Confidence: 0.98515624

00:47:00.614 --> 00:47:02.235 with respect to the connectivity

NOTE Confidence: 0.99275714

00:47:02.614 --> 00:47:04.075 between different networks.

NOTE Confidence: 0.9508464

00:47:04.375 --> 00:47:05.655 And so, like, we have

NOTE Confidence: 0.9508464

00:47:05.655 --> 00:47:06.155 different,

NOTE Confidence: 0.92567664

00:47:06.775 --> 00:47:08.295 nodes and the edge that

NOTE Confidence: 0.92567664

00:47:08.295 --> 00:47:09.114 we identified.

NOTE Confidence: 0.9547526

00:47:09.575 --> 00:47:11.655 And so, like, again, color

NOTE Confidence: 0.9547526

00:47:11.655 --> 00:47:13.655 coding based on if these

NOTE Confidence: 0.9547526

00:47:13.655 --> 00:47:14.875 were genetic

NOTE Confidence: 0.99609375

00:47:15.175 --> 00:47:15.675 correlation

NOTE Confidence: 0.9920247

00:47:16.050 --> 00:47:17.030 or if these

NOTE Confidence: 0.88256836

00:47:17.370 --> 00:47:17.870 were,

NOTE Confidence: 0.91748047

00:47:18.450 --> 00:47:18.770 genetic

NOTE Confidence: 0.93544006

00:47:19.250 --> 00:47:21.810 genetically causal proportion. So potential

NOTE Confidence: 0.93544006

00:47:21.810 --> 00:47:23.430 causal relationship within,

NOTE Confidence: 0.95088124

00:47:25.250 --> 00:47:27.010 the BRAIN imaging phenotype and

NOTE Confidence: 0.95088124

00:47:27.010 --> 00:47:28.464 one of the phenotype. As

NOTE Confidence: 0.95088124

00:47:28.464 --> 00:47:29.425 you can see, as I

NOTE Confidence: 0.95088124

00:47:29.425 --> 00:47:31.505 mentioned, like, we observe both

NOTE Confidence: 0.95088124

00:47:31.505 --> 00:47:32.005 differences

NOTE Confidence: 0.93280584

00:47:32.385 --> 00:47:34.325 between the two, cannabis phenotype,

NOTE Confidence: 0.93280584

00:47:34.464 --> 00:47:36.944 cannabis use versus cannabis use

NOTE Confidence: 0.93280584

00:47:36.944 --> 00:47:38.704 disorder. But, also, we observe

NOTE Confidence: 0.93280584

00:47:38.704 --> 00:47:40.305 that there are differences between,

NOTE Confidence: 0.93280584

00:47:40.305 --> 00:47:41.125 like, the

NOTE Confidence: 0.94628906

00:47:42.130 --> 00:47:42.630 genetic,

NOTE Confidence: 0.86279297

00:47:43.650 --> 00:47:44.150 correlation,

NOTE Confidence: 0.95527786

00:47:44.850 --> 00:47:46.290 the phenotypes identified by the

NOTE Confidence: 0.95527786

00:47:46.290 --> 00:47:48.130 genetic correlation and the phenotypes

NOTE Confidence: 0.95527786

00:47:48.130 --> 00:47:48.630 identified

NOTE Confidence: 0.8198868

00:47:48.930 --> 00:47:50.210 by the Ladd and Kousser

NOTE Confidence: 0.8198868

00:47:50.210 --> 00:47:52.230 variables. So those phenotype with

NOTE Confidence: 0.8198868

00:47:52.290 --> 00:47:53.989 genetically Kousser proportion.

NOTE Confidence: 0.9859484

00:47:55.464 --> 00:47:57.385 And so to follow-up even

NOTE Confidence: 0.9859484

00:47:57.385 --> 00:47:57.885 more,

NOTE Confidence: 0.9219971

00:47:58.585 --> 00:47:59.405 this analysis,

NOTE Confidence: 0.95247877

00:47:59.864 --> 00:48:01.305 we decided to do a

NOTE Confidence: 0.95247877

00:48:01.305 --> 00:48:03.625 local genetic correlation analysis. In

NOTE Confidence: 0.95247877

00:48:03.625 --> 00:48:04.744 particular, we want to do

NOTE Confidence: 0.95247877

00:48:04.744 --> 00:48:05.565 this because,

NOTE Confidence: 0.93038505

00:48:06.344 --> 00:48:08.230 to follow-up on the possible

NOTE Confidence: 0.93038505

00:48:08.230 --> 00:48:10.630 causal relationship identified in our

NOTE Confidence: 0.93038505

00:48:10.630 --> 00:48:12.170 study, we also performed

NOTE Confidence: 0.9546034

00:48:12.470 --> 00:48:14.790 Mendelian randomization approach. This is

NOTE Confidence: 0.9546034

00:48:14.790 --> 00:48:15.290 another,

NOTE Confidence: 0.939621

00:48:16.230 --> 00:48:18.630 genetically informed causal inference method,

NOTE Confidence: 0.939621

00:48:18.630 --> 00:48:20.170 and we didn't find consistent

NOTE Confidence: 0.939621

00:48:20.230 --> 00:48:22.150 between the latent causal variable

NOTE Confidence: 0.939621

00:48:22.150 --> 00:48:22.650 analysis

NOTE Confidence: 0.9091797

00:48:23.125 --> 00:48:23.864 and the,

NOTE Confidence: 0.94628906

00:48:24.485 --> 00:48:26.105 Mendelian randomization results.

NOTE Confidence: 0.86568195

00:48:26.645 --> 00:48:27.705 So we politicized

NOTE Confidence: 0.91015625

00:48:28.325 --> 00:48:30.005 that there may be specific

NOTE Confidence: 0.91015625

00:48:30.005 --> 00:48:30.505 loci

NOTE Confidence: 0.99902344

00:48:31.045 --> 00:48:31.545 that

NOTE Confidence: 0.73498535

00:48:32.085 --> 00:48:32.905 are linking

NOTE Confidence: 0.80048287

00:48:33.205 --> 00:48:34.965 brain variation with one of

NOTE Confidence: 0.80048287

00:48:34.965 --> 00:48:36.265 these gamma disc phenotype.

NOTE Confidence: 0.9967448

00:48:36.645 --> 00:48:37.625 And we identified

NOTE Confidence: 0.9485677

00:48:38.250 --> 00:48:39.850 five different region in the

NOTE Confidence: 0.9485677

00:48:39.850 --> 00:48:41.790 genome where we observed

NOTE Confidence: 0.817688

00:48:42.330 --> 00:48:44.270 this local genetic correlation.

NOTE Confidence: 0.94766515

00:48:44.650 --> 00:48:45.770 In this case, again, if

NOTE Confidence: 0.94766515

00:48:45.770 --> 00:48:47.610 we consider only results that

NOTE Confidence: 0.94766515

00:48:47.610 --> 00:48:48.110 survive,

NOTE Confidence: 0.9069824

00:48:48.969 --> 00:48:51.210 false discovery rate, multiple testing

NOTE Confidence: 0.9069824

00:48:51.210 --> 00:48:52.489 correction, we can see that

NOTE Confidence: 0.9069824

00:48:52.489 --> 00:48:53.630 there is some specificity.

NOTE Confidence: 0.9476788

00:48:54.225 --> 00:48:55.345 But in this case, we

NOTE Confidence: 0.9476788

00:48:55.345 --> 00:48:57.185 also identified that there may

NOTE Confidence: 0.9476788

00:48:57.185 --> 00:48:58.245 be some overlap

NOTE Confidence: 0.93662107

00:48:58.785 --> 00:49:00.485 that link the same region,

NOTE Confidence: 0.93858844

00:49:01.425 --> 00:49:03.525 to the other cannabis phenotype

NOTE Confidence: 0.93858844

00:49:03.665 --> 00:49:05.364 in relation to one other

NOTE Confidence: 0.93858844

00:49:05.585 --> 00:49:07.845 of the functional connectivity phenotype.

NOTE Confidence: 0.93858844

00:49:08.020 --> 00:49:09.140 Also, one thing that I

NOTE Confidence: 0.93858844

00:49:09.140 --> 00:49:10.360 want to highlight that

NOTE Confidence: 0.8994838

00:49:10.820 --> 00:49:12.660 the brain imaging phenotype that

NOTE Confidence: 0.8994838

00:49:12.660 --> 00:49:13.400 we identified,

NOTE Confidence: 0.9241333

00:49:15.300 --> 00:49:16.920 in the local genetic correlation

NOTE Confidence: 0.9241333

00:49:16.980 --> 00:49:18.180 analysis were all related to

NOTE Confidence: 0.9241333

00:49:18.180 --> 00:49:19.080 functional connectivity.

NOTE Confidence: 0.96899414

00:49:19.540 --> 00:49:20.680 And some of these,

NOTE Confidence: 0.9873047

00:49:21.300 --> 00:49:21.800 were

NOTE Confidence: 0.9968262

00:49:22.725 --> 00:49:24.405 interesting with respect to brain

NOTE Confidence: 0.9968262

00:49:24.405 --> 00:49:24.905 biology.

NOTE Confidence: 0.9929199

00:49:25.605 --> 00:49:26.345 For example,

NOTE Confidence: 0.8761161

00:49:27.285 --> 00:49:29.605 in in some in for

NOTE Confidence: 0.8761161

00:49:29.605 --> 00:49:30.425 the ENPP

NOTE Confidence: 0.8718262

00:49:31.045 --> 00:49:31.864 six gene

NOTE Confidence: 0.9352417

00:49:32.245 --> 00:49:34.005 is involved in the,

NOTE Confidence: 0.8754883

00:49:34.485 --> 00:49:34.985 neurogenesis.

NOTE Confidence: 0.99316406

00:49:36.245 --> 00:49:36.745 The

NOTE Confidence: 0.98746747

00:49:38.340 --> 00:49:40.920 gene is involved in axon

NOTE Confidence: 0.98746747

00:49:40.980 --> 00:49:41.480 guidance.

NOTE Confidence: 0.9650879

00:49:41.940 --> 00:49:42.840 The SMHC

NOTE Confidence: 0.9592285

00:49:43.140 --> 00:49:43.640 two,

NOTE Confidence: 0.99790037

00:49:44.260 --> 00:49:46.280 gene is involved in neurogenesis.

NOTE Confidence: 0.91365564

00:49:47.780 --> 00:49:48.680 The LHPP

NOTE Confidence: 0.9315257

00:49:49.060 --> 00:49:50.500 and the FAM fifty three

NOTE Confidence: 0.9315257

00:49:50.500 --> 00:49:52.260 b gene are both genes

NOTE Confidence: 0.9315257

00:49:52.260 --> 00:49:54.785 that were previously identified in

NOTE Confidence: 0.9315257

00:49:54.785 --> 00:49:55.525 large scale,

NOTE Confidence: 0.96831053

00:49:56.065 --> 00:49:57.825 genome wide analysis of other,

NOTE Confidence: 0.84583235

00:49:58.864 --> 00:50:01.025 substance use disorder. For example,

NOTE Confidence: 0.84583235

00:50:01.025 --> 00:50:02.785 the FAM fifty two b

NOTE Confidence: 0.84583235

00:50:02.785 --> 00:50:04.385 gene was identified in a

NOTE Confidence: 0.84583235

00:50:04.385 --> 00:50:05.605 coven dependence

NOTE Confidence: 0.89485675

00:50:06.065 --> 00:50:06.565 GWAS.

NOTE Confidence: 0.7967936

00:50:07.320 --> 00:50:08.300 The LHPP

NOTE Confidence: 0.9977214

00:50:08.680 --> 00:50:09.660 gene was identified

NOTE Confidence: 0.99476844

00:50:10.040 --> 00:50:11.719 in a study investigating risk

NOTE Confidence: 0.99476844

00:50:11.719 --> 00:50:12.620 taking behavior

NOTE Confidence: 0.93168133

00:50:12.920 --> 00:50:14.360 with respect in the context

NOTE Confidence: 0.93168133

00:50:14.360 --> 00:50:14.860 of,

NOTE Confidence: 0.9885254

00:50:15.480 --> 00:50:16.620 alcohol dependence.

NOTE Confidence: 0.9066569

00:50:17.000 --> 00:50:17.900 But again, like,

NOTE Confidence: 0.95840615

00:50:18.760 --> 00:50:19.640 here, we can see there

NOTE Confidence: 0.95840615

00:50:19.640 --> 00:50:21.234 are many other genes. And

NOTE Confidence: 0.95840615

00:50:21.234 --> 00:50:22.355 so, like, there may be

NOTE Confidence: 0.95840615

00:50:22.355 --> 00:50:23.875 other kind of, like,

NOTE Confidence: 0.8774414

00:50:24.515 --> 00:50:25.015 dynamics

NOTE Confidence: 0.9814453

00:50:25.474 --> 00:50:26.375 that go beyond

NOTE Confidence: 0.78841144

00:50:27.075 --> 00:50:28.695 specific brain biology

NOTE Confidence: 0.9980469

00:50:29.075 --> 00:50:30.055 that could link

NOTE Confidence: 0.9187012

00:50:30.355 --> 00:50:31.094 brain variation

NOTE Confidence: 0.88082886

00:50:31.954 --> 00:50:33.474 to, one of these kind

NOTE Confidence: 0.88082886

00:50:33.474 --> 00:50:34.295 of this phenotype.

NOTE Confidence: 0.9515381

00:50:34.915 --> 00:50:35.395 And so,

NOTE Confidence: 0.9465448

00:50:36.549 --> 00:50:37.910 we try to do also

NOTE Confidence: 0.9465448

00:50:37.910 --> 00:50:38.650 a colocalization

NOTE Confidence: 0.98791504

00:50:39.109 --> 00:50:40.869 analysis to identify if there

NOTE Confidence: 0.98791504

00:50:40.869 --> 00:50:42.710 was a specific variant in

NOTE Confidence: 0.98791504

00:50:42.710 --> 00:50:43.609 this region

NOTE Confidence: 0.9002511

00:50:43.989 --> 00:50:45.930 that was adding causal effect

NOTE Confidence: 0.9002511

00:50:46.150 --> 00:50:46.890 on both

NOTE Confidence: 0.6222331

00:50:47.269 --> 00:50:48.410 brain imaging variation

NOTE Confidence: 0.9406738

00:50:49.565 --> 00:50:51.404 and the cannabis phenotype, and

NOTE Confidence: 0.9406738

00:50:51.404 --> 00:50:52.684 we didn't see that. So

NOTE Confidence: 0.9406738

00:50:52.684 --> 00:50:54.364 there wasn't a single causal

NOTE Confidence: 0.9406738

00:50:54.364 --> 00:50:54.864 variant

NOTE Confidence: 0.9873047

00:50:55.244 --> 00:50:55.744 underlying

NOTE Confidence: 0.98028564

00:50:56.045 --> 00:50:57.744 this local genetic correlation.

NOTE Confidence: 0.855962

00:50:58.605 --> 00:51:00.045 We also didn't see a

NOTE Confidence: 0.855962

00:51:00.045 --> 00:51:00.944 mediate petrioplaiotomy.

NOTE Confidence: 0.9170503

00:51:01.565 --> 00:51:02.605 At least, we didn't see

NOTE Confidence: 0.9170503

00:51:02.605 --> 00:51:04.364 strong evidence of it because

NOTE Confidence: 0.9170503

00:51:04.364 --> 00:51:06.660 of the, null results that

NOTE Confidence: 0.9170503

00:51:06.660 --> 00:51:08.200 we observe in the Mendelian

NOTE Confidence: 0.9170503

00:51:08.340 --> 00:51:08.840 normalization.

NOTE Confidence: 0.95528156

00:51:09.460 --> 00:51:10.900 In this case, we don't

NOTE Confidence: 0.95528156

00:51:10.900 --> 00:51:11.400 expect,

NOTE Confidence: 0.93551433

00:51:12.420 --> 00:51:14.680 to, be biased by misclassification

NOTE Confidence: 0.9375226

00:51:15.540 --> 00:51:17.219 because, actually, we are observing

NOTE Confidence: 0.9375226

00:51:17.219 --> 00:51:19.380 two different dynamic between cannabis

NOTE Confidence: 0.9375226

00:51:19.380 --> 00:51:21.275 use and cannabis use disorder.

NOTE Confidence: 0.9375226

00:51:21.415 --> 00:51:22.315 So the misclassification

NOTE Confidence: 0.99482423

00:51:22.614 --> 00:51:24.234 should have increased the likelihood

NOTE Confidence: 0.9715576

00:51:24.775 --> 00:51:25.435 to see,

NOTE Confidence: 0.88952637

00:51:25.895 --> 00:51:27.994 convergence between two different phenotype.

NOTE Confidence: 0.9988281

00:51:28.775 --> 00:51:30.155 And so what we expect

NOTE Confidence: 0.89172363

00:51:30.535 --> 00:51:32.315 is that pleiotropic mechanism

NOTE Confidence: 0.9715169

00:51:32.855 --> 00:51:34.234 linking brain variation

NOTE Confidence: 0.9892578

00:51:34.800 --> 00:51:35.540 to cannabis,

NOTE Confidence: 0.99902344

00:51:36.719 --> 00:51:37.219 phenotypes

NOTE Confidence: 0.8807843

00:51:37.600 --> 00:51:39.520 should be, due to different

NOTE Confidence: 0.8807843

00:51:39.520 --> 00:51:41.320 type of a pleiotropy. To

NOTE Confidence: 0.8807843

00:51:41.320 --> 00:51:42.820 a pleiotropy where

NOTE Confidence: 0.8823242

00:51:43.200 --> 00:51:44.420 a variance located

NOTE Confidence: 0.86083984

00:51:44.800 --> 00:51:45.620 in the

NOTE Confidence: 0.98451453

00:51:46.400 --> 00:51:48.080 same genes or in two

NOTE Confidence: 0.98451453

00:51:48.080 --> 00:51:48.980 different genes

NOTE Confidence: 0.7023926

00:51:49.285 --> 00:51:51.065 in strong link and disequilibrium

NOTE Confidence: 0.8885498

00:51:51.605 --> 00:51:52.085 may be,

NOTE Confidence: 0.99214685

00:51:53.045 --> 00:51:55.364 responsible for the pleiotropy that

NOTE Confidence: 0.99214685

00:51:55.364 --> 00:51:57.125 we are observing. And so

NOTE Confidence: 0.99214685

00:51:57.125 --> 00:51:58.905 to further investigate this,

NOTE Confidence: 0.93014866

00:51:59.285 --> 00:52:01.065 we did a gene ontology

NOTE Confidence: 0.93014866

00:52:01.125 --> 00:52:02.645 analysis. And so what are

NOTE Confidence: 0.93014866

00:52:02.645 --> 00:52:03.305 gene ontologies?

NOTE Confidence: 0.98295087

00:52:03.620 --> 00:52:05.060 Gene ontologies are is a

NOTE Confidence: 0.98295087

00:52:05.060 --> 00:52:05.560 classification

NOTE Confidence: 0.9932455

00:52:06.260 --> 00:52:07.080 to categorize,

NOTE Confidence: 0.9642741

00:52:08.180 --> 00:52:09.780 loci depending on,

NOTE Confidence: 0.9838867

00:52:10.580 --> 00:52:11.480 which processes

NOTE Confidence: 0.9945313

00:52:11.860 --> 00:52:13.239 they play a role in,

NOTE Confidence: 0.9760742

00:52:13.780 --> 00:52:14.280 where

NOTE Confidence: 0.97669816

00:52:14.580 --> 00:52:16.280 the gene products are expressed,

NOTE Confidence: 0.97669816

00:52:16.565 --> 00:52:18.005 or what type of action

NOTE Confidence: 0.97669816

00:52:18.005 --> 00:52:18.965 they do. And so, like,

NOTE Confidence: 0.97669816

00:52:18.965 --> 00:52:20.665 there are three main categories,

NOTE Confidence: 0.97669816

00:52:20.885 --> 00:52:23.765 biological processes, molecular function, and

NOTE Confidence: 0.97669816

00:52:23.765 --> 00:52:24.825 cellular components.

NOTE Confidence: 0.92071533

00:52:25.205 --> 00:52:27.205 And so we run these

NOTE Confidence: 0.92071533

00:52:27.205 --> 00:52:28.425 gene ontology analysis,

NOTE Confidence: 0.9279785

00:52:28.770 --> 00:52:29.270 identified,

NOTE Confidence: 1

00:52:30.130 --> 00:52:31.350 more than five hundred

NOTE Confidence: 0.95251465

00:52:31.730 --> 00:52:33.830 gene ontology terms surviving

NOTE Confidence: 0.7974121

00:52:34.370 --> 00:52:35.590 a strict Bonferroni,

NOTE Confidence: 0.93896484

00:52:36.530 --> 00:52:37.030 significance.

NOTE Confidence: 0.95029294

00:52:37.489 --> 00:52:40.310 And these were shared across

NOTE Confidence: 0.95029294

00:52:40.370 --> 00:52:43.045 cannabis use, cannabis use disorder,

NOTE Confidence: 0.95222473

00:52:43.344 --> 00:52:45.025 and the pleiotropic brain imaging

NOTE Confidence: 0.95222473

00:52:45.025 --> 00:52:46.704 phenotype. And here is the

NOTE Confidence: 0.95222473

00:52:46.704 --> 00:52:48.384 distribution across the three different

NOTE Confidence: 0.95222473

00:52:48.384 --> 00:52:48.884 categories,

NOTE Confidence: 0.99532646

00:52:49.424 --> 00:52:51.984 biological processes, molecular function, and

NOTE Confidence: 0.99532646

00:52:51.984 --> 00:52:52.964 cellular components.

NOTE Confidence: 0.92252606

00:52:53.424 --> 00:52:54.464 Of course, in these five

NOTE Confidence: 0.92252606

00:52:54.464 --> 00:52:54.964 hundred

NOTE Confidence: 0.71746826

00:52:55.505 --> 00:52:56.005 geotems,

NOTE Confidence: 0.98413086

00:52:56.464 --> 00:52:57.125 we identified

NOTE Confidence: 0.9980469

00:52:57.719 --> 00:52:58.219 several

NOTE Confidence: 0.97843426

00:52:59.000 --> 00:53:00.440 that were related to brain

NOTE Confidence: 0.97843426

00:53:00.440 --> 00:53:00.940 biology.

NOTE Confidence: 0.97558594

00:53:01.400 --> 00:53:02.760 But the things that was

NOTE Confidence: 0.97558594

00:53:02.760 --> 00:53:05.500 interesting is that the, top

NOTE Confidence: 0.88671875

00:53:05.960 --> 00:53:06.460 terms,

NOTE Confidence: 0.96325684

00:53:07.160 --> 00:53:07.800 for both,

NOTE Confidence: 0.9937337

00:53:08.359 --> 00:53:10.440 cannabis use and cannabis use

NOTE Confidence: 0.9937337

00:53:10.440 --> 00:53:10.940 disorder

NOTE Confidence: 0.9493519

00:53:11.335 --> 00:53:12.935 were related to immune functions.

NOTE Confidence: 0.9493519

00:53:12.935 --> 00:53:15.094 Specifically, for cannabis use, the

NOTE Confidence: 0.9493519

00:53:15.094 --> 00:53:15.594 top

NOTE Confidence: 0.6824112

00:53:16.855 --> 00:53:18.955 genotype terms were related to

NOTE Confidence: 0.6824112

00:53:19.094 --> 00:53:20.315 regulation of inflammatory

NOTE Confidence: 0.94628906

00:53:20.614 --> 00:53:21.114 response

NOTE Confidence: 0.8959961

00:53:21.495 --> 00:53:22.715 and cell activation

NOTE Confidence: 0.9058838

00:53:23.015 --> 00:53:24.555 involved in immune response.

NOTE Confidence: 0.9563423

00:53:24.980 --> 00:53:26.500 And for cannabis use disorder,

NOTE Confidence: 0.9563423

00:53:26.500 --> 00:53:28.839 the top terms were apoptotic

NOTE Confidence: 0.9563423

00:53:29.059 --> 00:53:31.400 signaling pathway and leukocyte differentiation.

NOTE Confidence: 0.9842122

00:53:32.260 --> 00:53:33.239 We also identified

NOTE Confidence: 0.87577313

00:53:33.779 --> 00:53:35.460 some gene ontology that were

NOTE Confidence: 0.87577313

00:53:35.460 --> 00:53:35.960 specific

NOTE Confidence: 0.978007

00:53:36.260 --> 00:53:37.940 to cannabis use and the

NOTE Confidence: 0.978007

00:53:37.940 --> 00:53:38.440 pleiotropic

NOTE Confidence: 0.9296085

00:53:38.980 --> 00:53:40.875 brain imaging derived phenotypes, but

NOTE Confidence: 0.9296085

00:53:40.955 --> 00:53:42.155 but they were not shared

NOTE Confidence: 0.9296085

00:53:42.155 --> 00:53:44.155 with cannabis use disorder. And

NOTE Confidence: 0.9296085

00:53:44.155 --> 00:53:45.275 in this case, we found,

NOTE Confidence: 0.9296085

00:53:45.275 --> 00:53:46.875 like, things that are linked

NOTE Confidence: 0.9296085

00:53:46.875 --> 00:53:48.315 to brain biology and in

NOTE Confidence: 0.9296085

00:53:48.315 --> 00:53:50.015 particularly about cell communication

NOTE Confidence: 0.98828125

00:53:50.395 --> 00:53:50.895 and

NOTE Confidence: 0.9177246

00:53:51.275 --> 00:53:51.775 synapse

NOTE Confidence: 0.9746094

00:53:52.155 --> 00:53:52.655 assembly.

NOTE Confidence: 0.9227905

00:53:53.870 --> 00:53:54.989 And so like what we

NOTE Confidence: 0.9227905

00:53:54.989 --> 00:53:56.510 want to do next is

NOTE Confidence: 0.9227905

00:53:56.510 --> 00:53:57.710 to try to understand if

NOTE Confidence: 0.9227905

00:53:57.710 --> 00:53:58.210 these

NOTE Confidence: 0.8968994

00:53:58.590 --> 00:54:00.989 molecular pathways and molecular function,

NOTE Confidence: 0.8968994

00:54:00.989 --> 00:54:03.170 biological processes, and cellular component

NOTE Confidence: 0.9733887

00:54:03.950 --> 00:54:05.650 could give us some insight

NOTE Confidence: 0.9733887

00:54:05.790 --> 00:54:06.290 about

NOTE Confidence: 0.91904294

00:54:06.750 --> 00:54:09.330 molecular compounds that could target

NOTE Confidence: 0.8071289

00:54:10.644 --> 00:54:10.885 this,

NOTE Confidence: 0.87184966

00:54:11.525 --> 00:54:14.184 pleiotropic mechanism linking brain variation

NOTE Confidence: 0.87184966

00:54:14.325 --> 00:54:16.164 with canary spenotype. So what

NOTE Confidence: 0.87184966

00:54:16.164 --> 00:54:17.065 we did was

NOTE Confidence: 0.8394572

00:54:17.364 --> 00:54:19.444 a genetically inform drug report

NOTE Confidence: 0.8394572

00:54:19.444 --> 00:54:21.684 processing analysis. And specifically, what

NOTE Confidence: 0.8394572

00:54:21.684 --> 00:54:22.424 we did

NOTE Confidence: 0.98828125

00:54:22.724 --> 00:54:23.224 was

NOTE Confidence: 0.95874023

00:54:23.684 --> 00:54:24.585 using these

NOTE Confidence: 0.9797363

00:54:25.020 --> 00:54:25.680 pathways and

NOTE Confidence: 0.8331299

00:54:26.219 --> 00:54:27.680 try to identify if,

NOTE Confidence: 0.8186701

00:54:29.900 --> 00:54:31.900 non molecular compounds and in

NOTE Confidence: 0.8186701

00:54:31.900 --> 00:54:34.620 particular, their transcriptomic profiles was

NOTE Confidence: 0.8186701

00:54:34.620 --> 00:54:35.120 somehow,

NOTE Confidence: 0.98532444

00:54:35.980 --> 00:54:37.739 statistically matching what we were

NOTE Confidence: 0.98532444

00:54:37.739 --> 00:54:39.100 observing with respect to,

NOTE Confidence: 0.99853516

00:54:40.085 --> 00:54:40.904 the genetically

NOTE Confidence: 0.68726397

00:54:42.085 --> 00:54:43.765 regulated mechanism led to this

NOTE Confidence: 0.68726397

00:54:43.765 --> 00:54:44.265 plaiotomy.

NOTE Confidence: 0.97314453

00:54:45.444 --> 00:54:46.404 And this is what we

NOTE Confidence: 0.97314453

00:54:46.404 --> 00:54:48.105 found. And so we identified

NOTE Confidence: 0.97314453

00:54:48.244 --> 00:54:49.384 different compounds,

NOTE Confidence: 0.9740931

00:54:50.164 --> 00:54:51.765 and, we did the analysis

NOTE Confidence: 0.9740931

00:54:51.765 --> 00:54:53.204 stratified by different type of

NOTE Confidence: 0.9740931

00:54:53.204 --> 00:54:54.940 gene ontologies. And so we

NOTE Confidence: 0.9740931

00:54:54.940 --> 00:54:57.200 did, one analysis for biological

NOTE Confidence: 0.9740931

00:54:57.260 --> 00:54:59.180 processes, one analysis for molecular

NOTE Confidence: 0.9740931

00:54:59.180 --> 00:55:00.860 function, and one analysis for

NOTE Confidence: 0.9740931

00:55:00.860 --> 00:55:01.840 cellular components.

NOTE Confidence: 0.9641113

00:55:02.219 --> 00:55:03.280 So, of course,

NOTE Confidence: 0.9323033

00:55:03.820 --> 00:55:05.020 there is some kind of,

NOTE Confidence: 0.9323033

00:55:05.020 --> 00:55:05.840 like, relationship

NOTE Confidence: 0.87886554

00:55:06.219 --> 00:55:08.214 across these three these three

NOTE Confidence: 0.87886554

00:55:08.214 --> 00:55:08.714 different,

NOTE Confidence: 0.91842216

00:55:09.335 --> 00:55:10.855 categories, so they are not

NOTE Confidence: 0.91842216

00:55:10.855 --> 00:55:11.994 completely independent.

NOTE Confidence: 0.9490497

00:55:12.535 --> 00:55:14.295 But the fact that for

NOTE Confidence: 0.9490497

00:55:14.295 --> 00:55:15.734 most of the genes, we

NOTE Confidence: 0.9490497

00:55:15.734 --> 00:55:17.594 observe consistent evidence

NOTE Confidence: 0.96972656

00:55:17.974 --> 00:55:20.155 across different gene ontology category

NOTE Confidence: 0.87719727

00:55:20.580 --> 00:55:22.760 further support the reliability

NOTE Confidence: 0.99454755

00:55:23.219 --> 00:55:24.040 of the results.

NOTE Confidence: 0.99853516

00:55:24.420 --> 00:55:24.920 Interestingly,

NOTE Confidence: 0.89791167

00:55:25.780 --> 00:55:27.780 we identified different type of

NOTE Confidence: 0.89791167

00:55:27.780 --> 00:55:29.620 of of drugs. And so

NOTE Confidence: 0.89791167

00:55:29.620 --> 00:55:30.760 for example, the,

NOTE Confidence: 0.5824585

00:55:31.780 --> 00:55:32.840 methylated benzatholium

NOTE Confidence: 1

00:55:33.140 --> 00:55:33.640 chloride

NOTE Confidence: 0.93562824

00:55:34.020 --> 00:55:34.920 is an antiseptic.

NOTE Confidence: 0.64485675

00:55:36.464 --> 00:55:37.924 The zinc cocaine

NOTE Confidence: 0.9806722

00:55:38.305 --> 00:55:39.204 is an anesthetics.

NOTE Confidence: 0.9098036

00:55:40.224 --> 00:55:41.825 And so, like, there are,

NOTE Confidence: 0.9098036

00:55:42.144 --> 00:55:42.644 Danazole

NOTE Confidence: 0.9335205

00:55:42.944 --> 00:55:44.085 and Raloxifen

NOTE Confidence: 0.83414716

00:55:44.704 --> 00:55:45.605 that are in.

NOTE Confidence: 0.9117839

00:55:46.224 --> 00:55:46.724 Modulator,

NOTE Confidence: 0.8548177

00:55:47.105 --> 00:55:48.005 there is a

NOTE Confidence: 0.72216797

00:55:49.200 --> 00:55:49.700 antidepressant

NOTE Confidence: 0.83709717

00:55:50.000 --> 00:55:51.440 that is con currently was,

NOTE Confidence: 0.83709717

00:55:51.599 --> 00:55:52.099 recently,

NOTE Confidence: 0.4300537

00:55:52.640 --> 00:55:53.140 discontinued,

NOTE Confidence: 0.6448161

00:55:54.239 --> 00:55:54.739 maprotrelin.

NOTE Confidence: 0.98431396

00:55:55.520 --> 00:55:56.640 And so, like, you can

NOTE Confidence: 0.98431396

00:55:56.640 --> 00:55:57.760 see there are different kind

NOTE Confidence: 0.98431396

00:55:57.760 --> 00:55:58.420 of, like,

NOTE Confidence: 0.96240234

00:56:00.080 --> 00:56:01.219 molecular compounds

NOTE Confidence: 0.9970703

00:56:01.599 --> 00:56:03.060 that appears to target

NOTE Confidence: 0.86059344

00:56:03.645 --> 00:56:05.325 this pleiotropic mechanism that we

NOTE Confidence: 0.86059344

00:56:05.325 --> 00:56:07.185 identified between canopy sphenotype

NOTE Confidence: 0.98828125

00:56:07.725 --> 00:56:08.785 and brain variation.

NOTE Confidence: 0.9680583

00:56:10.205 --> 00:56:12.045 And so, like, here is

NOTE Confidence: 0.9680583

00:56:12.045 --> 00:56:13.425 kind of, like, a summary

NOTE Confidence: 0.9680583

00:56:13.645 --> 00:56:14.385 of the

NOTE Confidence: 0.9463379

00:56:14.685 --> 00:56:16.525 key method key findings from

NOTE Confidence: 0.9463379

00:56:16.525 --> 00:56:18.785 this study. We identified that,

NOTE Confidence: 0.9777832

00:56:19.510 --> 00:56:21.370 there are distinct brain connectivity

NOTE Confidence: 0.9777832

00:56:21.510 --> 00:56:22.010 patterns,

NOTE Confidence: 0.9812622

00:56:22.630 --> 00:56:24.650 related to cannabis use versus

NOTE Confidence: 0.9812622

00:56:24.710 --> 00:56:25.930 cannabis use disorder.

NOTE Confidence: 0.9410592

00:56:27.030 --> 00:56:28.870 The pleiotropy of this cannabis

NOTE Confidence: 0.9410592

00:56:28.870 --> 00:56:30.710 phenotype with brain variation doesn't

NOTE Confidence: 0.9410592

00:56:30.710 --> 00:56:31.875 seem to be due to

NOTE Confidence: 0.9410592

00:56:32.114 --> 00:56:32.855 causal relationship,

NOTE Confidence: 0.9241455

00:56:33.395 --> 00:56:34.755 but actually, it could be

NOTE Confidence: 0.9241455

00:56:34.755 --> 00:56:36.935 due to local genetic correlation

NOTE Confidence: 0.9552571

00:56:37.395 --> 00:56:39.315 driven by shared pathway and

NOTE Confidence: 0.9552571

00:56:39.315 --> 00:56:41.155 not by specific causal variants

NOTE Confidence: 0.9552571

00:56:41.155 --> 00:56:42.915 that have effect on both

NOTE Confidence: 0.9552571

00:56:42.915 --> 00:56:45.094 brain variation and cannabis phenotypes.

NOTE Confidence: 0.93226624

00:56:46.275 --> 00:56:47.820 We saw an arrangement for

NOTE Confidence: 0.93226624

00:56:48.060 --> 00:56:49.900 immune pathways, and so this

NOTE Confidence: 0.93226624

00:56:49.900 --> 00:56:51.420 may open new direction in

NOTE Confidence: 0.93226624

00:56:51.420 --> 00:56:51.920 cannabis

NOTE Confidence: 0.94876534

00:56:52.380 --> 00:56:53.900 research. And, also, we found

NOTE Confidence: 0.94876534

00:56:53.900 --> 00:56:54.560 some evidence

NOTE Confidence: 0.9951172

00:56:55.020 --> 00:56:55.520 supporting

NOTE Confidence: 0.8964844

00:56:56.219 --> 00:56:57.520 that brain imaging

NOTE Confidence: 0.8673502

00:56:58.380 --> 00:57:00.320 integrated in brain imaging with

NOTE Confidence: 0.8673502

00:57:00.380 --> 00:57:02.400 a genetically informed drug repurposing

NOTE Confidence: 0.8673502

00:57:02.540 --> 00:57:03.040 analysis

NOTE Confidence: 0.87524414

00:57:04.275 --> 00:57:04.855 could uncover

NOTE Confidence: 0.9805908

00:57:05.155 --> 00:57:06.994 new dark targets for for

NOTE Confidence: 0.9805908

00:57:06.994 --> 00:57:07.494 cannabis,

NOTE Confidence: 0.9946289

00:57:08.355 --> 00:57:08.855 treatments.

NOTE Confidence: 0.9973416

00:57:09.315 --> 00:57:10.594 And with respect to what

NOTE Confidence: 0.9973416

00:57:10.594 --> 00:57:11.734 we are doing now,

NOTE Confidence: 0.91276044

00:57:12.835 --> 00:57:13.555 currently, we are,

NOTE Confidence: 0.9102376

00:57:14.194 --> 00:57:15.734 working on the much larger

NOTE Confidence: 0.9102376

00:57:15.954 --> 00:57:16.454 expanded

NOTE Confidence: 0.94235027

00:57:17.120 --> 00:57:18.880 UK Biobank brain imaging. So

NOTE Confidence: 0.94235027

00:57:18.880 --> 00:57:20.660 moving from thirty three thousand

NOTE Confidence: 0.99159074

00:57:21.040 --> 00:57:22.640 individuals to one hundred thousand

NOTE Confidence: 0.99159074

00:57:22.640 --> 00:57:24.500 individuals to understand better

NOTE Confidence: 0.99412435

00:57:25.440 --> 00:57:27.040 the relationship of the polygenic

NOTE Confidence: 0.99412435

00:57:27.040 --> 00:57:28.640 risk of cannabis use disorder

NOTE Confidence: 0.99412435

00:57:28.640 --> 00:57:30.815 and cannabis use on different

NOTE Confidence: 0.9536133

00:57:31.675 --> 00:57:32.655 brain wide,

NOTE Confidence: 0.988878

00:57:33.595 --> 00:57:34.955 patterns. And so, like, the

NOTE Confidence: 0.988878

00:57:34.955 --> 00:57:36.494 goal is to identify

NOTE Confidence: 0.9926758

00:57:37.035 --> 00:57:37.615 a mechanism

NOTE Confidence: 0.9975586

00:57:37.915 --> 00:57:38.575 that are

NOTE Confidence: 0.9921875

00:57:38.875 --> 00:57:39.375 both

NOTE Confidence: 0.97265625

00:57:39.755 --> 00:57:40.255 specific

NOTE Confidence: 0.9232835

00:57:40.714 --> 00:57:41.915 for one of these cannabis

NOTE Confidence: 0.9232835

00:57:41.915 --> 00:57:43.515 phenotype, but also those that

NOTE Confidence: 0.9232835

00:57:43.515 --> 00:57:44.820 are shared. And because of

NOTE Confidence: 0.9232835

00:57:44.820 --> 00:57:46.260 the larger sample size, we

NOTE Confidence: 0.9232835

00:57:46.260 --> 00:57:47.540 also would be able to

NOTE Confidence: 0.9232835

00:57:47.540 --> 00:57:48.040 investigate

NOTE Confidence: 0.84106445

00:57:48.420 --> 00:57:48.920 better,

NOTE Confidence: 0.98095703

00:57:49.780 --> 00:57:51.620 potential sex differences, which we

NOTE Confidence: 0.98095703

00:57:51.620 --> 00:57:53.320 didn't do in this initial

NOTE Confidence: 0.9500122

00:57:53.620 --> 00:57:55.540 study. Another aspect that,

NOTE Confidence: 0.9994141

00:57:56.020 --> 00:57:57.320 we would like to expand

NOTE Confidence: 0.97558594

00:57:57.780 --> 00:57:58.600 is to understand

NOTE Confidence: 0.9244385

00:58:00.465 --> 00:58:01.685 how single,

NOTE Confidence: 0.98323566

00:58:02.065 --> 00:58:03.445 cell specific mechanism

NOTE Confidence: 0.9995117

00:58:03.985 --> 00:58:05.125 may play a role

NOTE Confidence: 0.96484375

00:58:05.425 --> 00:58:06.165 in linking,

NOTE Confidence: 0.97110325

00:58:06.945 --> 00:58:08.785 brain variation to cannabis use

NOTE Confidence: 0.97110325

00:58:08.785 --> 00:58:10.865 disorder and cannabis use. And

NOTE Confidence: 0.97110325

00:58:10.865 --> 00:58:11.905 so we are going to

NOTE Confidence: 0.97110325

00:58:11.905 --> 00:58:13.205 perform a transcriptome

NOTE Confidence: 0.9970703

00:58:13.505 --> 00:58:14.245 wide analysis

NOTE Confidence: 0.99902344

00:58:14.625 --> 00:58:15.205 to understand

NOTE Confidence: 0.923584

00:58:15.710 --> 00:58:16.210 how,

NOTE Confidence: 0.9822998

00:58:16.829 --> 00:58:19.089 genetically regulated transcriptomic changes

NOTE Confidence: 0.9996745

00:58:19.470 --> 00:58:20.369 can be associated

NOTE Confidence: 0.9180036

00:58:20.990 --> 00:58:22.750 to brain variation and to

NOTE Confidence: 0.9180036

00:58:22.750 --> 00:58:23.650 cannabis phenotype.

NOTE Confidence: 0.93896484

00:58:23.950 --> 00:58:26.049 Also, because we identified some,

NOTE Confidence: 0.97164917

00:58:27.230 --> 00:58:29.089 drugs that are currently used,

NOTE Confidence: 0.97164917

00:58:29.225 --> 00:58:30.125 We are planning,

NOTE Confidence: 0.9110585

00:58:30.825 --> 00:58:32.185 target trial elimination in the

NOTE Confidence: 0.9110585

00:58:32.185 --> 00:58:34.025 robust research program, which include

NOTE Confidence: 0.9110585

00:58:34.025 --> 00:58:35.945 around ten thousand cases of

NOTE Confidence: 0.9110585

00:58:35.945 --> 00:58:38.125 cannabis use disorder to see

NOTE Confidence: 0.9110585

00:58:38.345 --> 00:58:39.225 which are the,

NOTE Confidence: 0.9975586

00:58:40.105 --> 00:58:41.245 outcome associated

NOTE Confidence: 0.9758301

00:58:42.710 --> 00:58:43.910 among the people that you're

NOTE Confidence: 0.9758301

00:58:43.910 --> 00:58:45.510 already using are already using

NOTE Confidence: 0.9758301

00:58:45.510 --> 00:58:46.250 these drugs,

NOTE Confidence: 0.9580892

00:58:46.789 --> 00:58:47.930 with respect to,

NOTE Confidence: 0.97206336

00:58:48.390 --> 00:58:50.069 and also affected by cannabis

NOTE Confidence: 0.97206336

00:58:50.069 --> 00:58:50.730 use disorder.

NOTE Confidence: 0.90614825

00:58:51.750 --> 00:58:52.869 Again, I I need to

NOTE Confidence: 0.90614825

00:58:52.869 --> 00:58:54.230 thank, like, my group and,

NOTE Confidence: 0.90614825

00:58:54.230 --> 00:58:55.049 again, for

NOTE Confidence: 0.9246419

00:58:56.025 --> 00:58:57.085 leading this analysis,

NOTE Confidence: 0.93918777

00:58:58.184 --> 00:58:59.625 the Yale Center for, the

NOTE Confidence: 0.93918777

00:58:59.625 --> 00:59:01.164 Science of Cannabis and Cannabinoids

NOTE Confidence: 0.93918777

00:59:01.385 --> 00:59:02.984 for giving us this pilot

NOTE Confidence: 0.93918777

00:59:02.984 --> 00:59:04.265 award, and I'm happy to

NOTE Confidence: 0.93918777

00:59:04.265 --> 00:59:05.244 take any question.

NOTE Confidence: 0.97600764

00:59:06.664 --> 00:59:08.424 Excellent work. Thank you very

NOTE Confidence: 0.97600764

00:59:08.424 --> 00:59:09.625 much. We have very little

NOTE Confidence: 0.97600764

00:59:09.625 --> 00:59:10.105 time,

NOTE Confidence: 0.98986816

00:59:10.730 --> 00:59:11.630 if there is any

NOTE Confidence: 0.8310547

00:59:15.369 --> 00:59:15.869 questions?

NOTE Confidence: 0.9152832

00:59:16.650 --> 00:59:17.150 No?

NOTE Confidence: 0.9801595

00:59:19.369 --> 00:59:20.809 Okay. Just one question I

NOTE Confidence: 0.9801595

00:59:20.809 --> 00:59:22.730 have. Yeah. I I've seen

NOTE Confidence: 0.9801595

00:59:22.730 --> 00:59:25.230 in your, initial background section,

NOTE Confidence: 0.95592153

00:59:25.645 --> 00:59:27.325 in your results that for

NOTE Confidence: 0.95592153

00:59:27.325 --> 00:59:28.365 some reason, there was a

NOTE Confidence: 0.95592153

00:59:28.365 --> 00:59:28.845 negative,

NOTE Confidence: 0.9987793

00:59:29.245 --> 00:59:30.285 association with,

NOTE Confidence: 0.86865234

00:59:31.165 --> 00:59:32.305 ASD spectrum.

NOTE Confidence: 0.995223

00:59:33.165 --> 00:59:34.125 I mean, this is in

NOTE Confidence: 0.995223

00:59:34.125 --> 00:59:35.905 the context of some studies

NOTE Confidence: 0.995223

00:59:36.045 --> 00:59:38.305 suggesting that targeting the endocannabinoid

NOTE Confidence: 0.99061805

00:59:38.685 --> 00:59:40.550 system may may be beneficial

NOTE Confidence: 0.99061805

00:59:40.770 --> 00:59:41.510 for ASD.

NOTE Confidence: 0.97452796

00:59:41.970 --> 00:59:43.730 So it's curious that, none

NOTE Confidence: 0.97452796

00:59:43.730 --> 00:59:44.850 of these people are self

NOTE Confidence: 0.97452796

00:59:44.850 --> 00:59:45.350 medicating.

NOTE Confidence: 0.663208

00:59:47.650 --> 00:59:48.530 Also, their,

NOTE Confidence: 0.91552734

00:59:49.010 --> 00:59:49.510 potential,

NOTE Confidence: 0.9433594

00:59:50.290 --> 00:59:50.790 shared,

NOTE Confidence: 0.80810547

00:59:51.250 --> 00:59:51.750 neuroinflammatory

NOTE Confidence: 0.8754883

00:59:52.290 --> 00:59:52.790 profile.

NOTE Confidence: 0.97381884

00:59:54.204 --> 00:59:55.244 So I wonder whether you

NOTE Confidence: 0.97381884

00:59:55.244 --> 00:59:56.204 have Yeah. No. That's that's

NOTE Confidence: 0.97381884

00:59:56.204 --> 00:59:57.165 a good point. And when

NOTE Confidence: 0.97381884

00:59:57.165 --> 00:59:58.285 I when I was putting

NOTE Confidence: 0.97381884

00:59:58.285 --> 00:59:58.785 together,

NOTE Confidence: 0.92439777

00:59:59.085 --> 01:00:00.525 these these slides, I was

NOTE Confidence: 0.92439777

01:00:00.525 --> 01:00:02.065 also interested about this,

NOTE Confidence: 0.82833254

01:00:02.365 --> 01:00:04.204 again, because all this more

NOTE Confidence: 0.82833254

01:00:04.285 --> 01:00:06.065 the relationship between the autism

NOTE Confidence: 0.82833254

01:00:06.204 --> 01:00:07.964 and this cannabis phenotype was

NOTE Confidence: 0.82833254

01:00:07.964 --> 01:00:09.665 different from other secondary disorders.

NOTE Confidence: 0.9818115

01:00:10.089 --> 01:00:11.130 There is also, like,

NOTE Confidence: 0.9877116

01:00:12.010 --> 01:00:13.470 one possible aspect,

NOTE Confidence: 0.8439767

01:00:14.250 --> 01:00:16.250 that, like, people with the

NOTE Confidence: 0.8439767

01:00:16.250 --> 01:00:16.910 old ishmm,

NOTE Confidence: 0.956901

01:00:17.210 --> 01:00:18.730 they may have more risk

NOTE Confidence: 0.956901

01:00:18.730 --> 01:00:20.089 at birth, and this could

NOTE Confidence: 0.956901

01:00:20.089 --> 01:00:21.710 lead, like, to less exposure.

NOTE Confidence: 0.91516113

01:00:22.185 --> 01:00:23.065 But I've also, like, there

NOTE Confidence: 0.91516113

01:00:23.065 --> 01:00:24.665 could be other molecular mechanisms

NOTE Confidence: 0.91516113

01:00:24.665 --> 01:00:26.345 that are underlying this relationship.

NOTE Confidence: 0.91516113

01:00:26.345 --> 01:00:27.565 So, like, I think that

NOTE Confidence: 0.91516113

01:00:27.705 --> 01:00:28.825 there is need for more

NOTE Confidence: 0.91516113

01:00:28.825 --> 01:00:30.365 more studies about autism

NOTE Confidence: 0.90126956

01:00:30.665 --> 01:00:32.345 and cannabis to understand that

NOTE Confidence: 0.90126956

01:00:32.345 --> 01:00:33.485 there could be some treatment,

NOTE Confidence: 0.9720917

01:00:33.785 --> 01:00:35.385 or it is simply driven

NOTE Confidence: 0.9720917

01:00:35.385 --> 01:00:37.330 by population dynamics that affect,

NOTE Confidence: 0.9720917

01:00:37.330 --> 01:00:38.609 like, the participants that are

NOTE Confidence: 0.9720917

01:00:38.609 --> 01:00:39.109 enrolled

NOTE Confidence: 0.9677124

01:00:39.410 --> 01:00:40.470 and things like that.

NOTE Confidence: 0.9048767

01:00:40.770 --> 01:00:41.890 Yeah. Also because of the

NOTE Confidence: 0.9048767

01:00:41.890 --> 01:00:43.430 shared potential neuroinflammatory

NOTE Confidence: 0.94226074

01:00:43.970 --> 01:00:45.810 profile is well studied in

NOTE Confidence: 0.94226074

01:00:45.810 --> 01:00:47.410 one and is now emerging

NOTE Confidence: 0.94226074

01:00:47.410 --> 01:00:48.070 in calories.

NOTE Confidence: 0.9628906

01:00:49.945 --> 01:00:52.105 Okay. So that's my question.

NOTE Confidence: 0.9628906

01:00:52.105 --> 01:00:53.145 If there is no other

NOTE Confidence: 0.9628906

01:00:53.145 --> 01:00:53.645 question

NOTE Confidence: 0.97356546

01:00:55.785 --> 01:00:58.585 Yes. Thanks, both, Renato and,

NOTE Confidence: 0.97356546

01:00:58.744 --> 01:01:00.984 Rachel for wonderful talks. I'm

NOTE Confidence: 0.97356546

01:01:00.984 --> 01:01:02.025 I'm sure I'll reach out

NOTE Confidence: 0.97356546

01:01:02.025 --> 01:01:02.825 to you all. I have

NOTE Confidence: 0.97356546

01:01:02.825 --> 01:01:04.910 some ideas that I'd like

NOTE Confidence: 0.97356546

01:01:05.050 --> 01:01:06.270 to talk about. Thanks.

NOTE Confidence: 0.8318413

01:01:06.570 --> 01:01:07.770 Appreciate it. Thank you. Ex

NOTE Confidence: 0.8318413

01:01:07.930 --> 01:01:08.430 excellent,

NOTE Confidence: 0.9411621

01:01:08.810 --> 01:01:09.849 Tom. Thank you very much,

NOTE Confidence: 0.9411621

01:01:09.849 --> 01:01:10.349 everyone.

NOTE Confidence: 0.95581055

01:01:10.890 --> 01:01:12.170 Thank you. Bye. Have a

NOTE Confidence: 0.95581055

01:01:12.170 --> 01:01:12.829 good day.