

WEBVTT

NOTE duration: "00:58:37.781"

NOTE Confidence: 0.88772464

00:00:05.519 --> 00:00:06.019 Started.

NOTE Confidence: 0.99234647

00:00:08.160 --> 00:00:09.440 Everybody, you're in the right

NOTE Confidence: 0.99234647

00:00:09.440 --> 00:00:10.980 place. Thank you for joining.

NOTE Confidence: 0.9991192

00:00:11.599 --> 00:00:12.660 This is our

NOTE Confidence: 0.99255174

00:00:12.960 --> 00:00:14.320 next in a series of

NOTE Confidence: 0.99255174

00:00:14.320 --> 00:00:15.780 talks designed to

NOTE Confidence: 0.9252437

00:00:16.155 --> 00:00:17.935 address issues and the overlap

NOTE Confidence: 0.9252437

00:00:17.994 --> 00:00:18.494 between

NOTE Confidence: 0.9693939

00:00:19.435 --> 00:00:21.994 chronic pain, opioid misuse, and

NOTE Confidence: 0.9693939

00:00:21.994 --> 00:00:23.614 opioid use disorder.

NOTE Confidence: 0.9988998

00:00:24.154 --> 00:00:25.835 And we're really excited to

NOTE Confidence: 0.9988998

00:00:25.835 --> 00:00:27.855 focus on issues related to,

NOTE Confidence: 0.95155144

00:00:28.795 --> 00:00:29.295 cannabinoids

NOTE Confidence: 0.9730522

00:00:29.755 --> 00:00:30.255 today.

NOTE Confidence: 0.9974741

00:00:30.780 --> 00:00:32.480 We have an expert speaker,
NOTE Confidence: 0.9887424

00:00:32.860 --> 00:00:34.140 who I will introduce and
NOTE Confidence: 0.9887424

00:00:34.140 --> 00:00:35.580 then go ahead and let
NOTE Confidence: 0.9887424

00:00:35.580 --> 00:00:37.260 him talk. So our speaker
NOTE Confidence: 0.9887424

00:00:37.260 --> 00:00:38.880 today is Cyril D'Souza.
NOTE Confidence: 0.8895609

00:00:39.420 --> 00:00:41.040 He's the Vikram Soddy,
NOTE Confidence: 0.9742376

00:00:41.900 --> 00:00:43.500 professor of psychiatry here at
NOTE Confidence: 0.9742376

00:00:43.500 --> 00:00:44.960 the Yale School of Medicine
NOTE Confidence: 0.9040556

00:00:45.365 --> 00:00:46.885 and a psychiatrist at the
NOTE Confidence: 0.9040556

00:00:46.885 --> 00:00:48.905 VA Connecticut health care system.
NOTE Confidence: 0.8918385

00:00:49.445 --> 00:00:50.665 He directs the schizophrenia
NOTE Confidence: 0.9744079

00:00:52.165 --> 00:00:52.665 neuropharmacology
NOTE Confidence: 0.99370146

00:00:53.765 --> 00:00:55.684 research group at Yale, the
NOTE Confidence: 0.99370146

00:00:55.684 --> 00:00:56.184 neurobiologic
NOTE Confidence: 0.99875426

00:00:56.645 --> 00:00:58.405 studies unit at the VA
NOTE Confidence: 0.99875426

00:00:58.405 --> 00:00:58.905 Connecticut,

NOTE Confidence: 0.95681125
00:00:59.610 --> 00:01:00.829 the VA Schizophrenia
NOTE Confidence: 0.9126225
00:01:01.690 --> 00:01:03.449 Research Clinic, and also the
NOTE Confidence: 0.9126225
00:01:03.449 --> 00:01:04.970 Yale Center for the Science
NOTE Confidence: 0.9126225
00:01:04.970 --> 00:01:05.869 of Cannabis
NOTE Confidence: 0.93914473
00:01:06.330 --> 00:01:07.069 and Cannabinoids.
NOTE Confidence: 0.91150534
00:01:08.009 --> 00:01:09.369 This research is funded by
NOTE Confidence: 0.91150534
00:01:09.369 --> 00:01:11.049 the National Institutes on Drug
NOTE Confidence: 0.91150534
00:01:11.049 --> 00:01:12.970 Abuse, the National Institutes on
NOTE Confidence: 0.91150534
00:01:12.970 --> 00:01:13.790 Mental Health,
NOTE Confidence: 0.98315996
00:01:14.415 --> 00:01:16.355 the National Institute on Alcoholism
NOTE Confidence: 0.98315996
00:01:16.495 --> 00:01:17.635 and Alcohol Abuse,
NOTE Confidence: 0.9451548
00:01:18.095 --> 00:01:20.115 the VA Research and Development,
NOTE Confidence: 0.9451548
00:01:20.175 --> 00:01:21.395 and several foundations.
NOTE Confidence: 0.9098552
00:01:22.015 --> 00:01:23.694 And he's principal editor of
NOTE Confidence: 0.9098552
00:01:23.694 --> 00:01:25.235 the Journal of Pharmacology.
NOTE Confidence: 0.9767189

00:01:26.815 --> 00:01:28.740 Really excited to have doctor
NOTE Confidence: 0.9767189

00:01:28.740 --> 00:01:30.600 D'Souza today to speak to
NOTE Confidence: 0.9767189

00:01:30.819 --> 00:01:31.860 you about the need for
NOTE Confidence: 0.9767189

00:01:31.860 --> 00:01:34.120 research on cannabinoids and pain.
NOTE Confidence: 0.9767189

00:01:34.260 --> 00:01:35.160 Thank you, Cyril.
NOTE Confidence: 0.8046067

00:01:35.700 --> 00:01:37.240 Thanks for the invitation.
NOTE Confidence: 0.9005851

00:01:38.020 --> 00:01:38.340 And,
NOTE Confidence: 0.9946681

00:01:39.300 --> 00:01:40.920 I'm I'm I'm a psychiatrist
NOTE Confidence: 0.8549342

00:01:41.220 --> 00:01:42.580 as David mentioned, and my,
NOTE Confidence: 0.99062055

00:01:43.635 --> 00:01:45.075 focus over the last maybe
NOTE Confidence: 0.99062055

00:01:45.075 --> 00:01:46.194 twenty five years or so
NOTE Confidence: 0.99062055

00:01:46.194 --> 00:01:47.795 has been on cannabis and
NOTE Confidence: 0.99062055

00:01:47.795 --> 00:01:48.455 and cannabinoids.
NOTE Confidence: 0.93377894

00:01:50.034 --> 00:01:51.155 In the spirit of full
NOTE Confidence: 0.93377894

00:01:51.155 --> 00:01:53.555 disclosure, I'm not an expert
NOTE Confidence: 0.93377894

00:01:53.555 --> 00:01:55.155 on pain. There I see

NOTE Confidence: 0.93377894

00:01:55.155 --> 00:01:56.215 there are other experts

NOTE Confidence: 0.765744

00:01:56.755 --> 00:01:57.815 attending here,

NOTE Confidence: 0.78327674

00:01:58.390 --> 00:02:00.409 but I, hopefully provide,

NOTE Confidence: 0.88851017

00:02:01.750 --> 00:02:03.450 an overview of, cannabis,

NOTE Confidence: 0.8541709

00:02:04.310 --> 00:02:04.810 cannabinoids,

NOTE Confidence: 0.8908043

00:02:05.350 --> 00:02:06.649 and pain. So,

NOTE Confidence: 0.9977789

00:02:07.990 --> 00:02:08.709 let me see if I

NOTE Confidence: 0.9977789

00:02:08.709 --> 00:02:10.330 can move my slides.

NOTE Confidence: 0.96549827

00:02:11.030 --> 00:02:11.530 Yeah.

NOTE Confidence: 0.9542812

00:02:12.825 --> 00:02:13.485 So why,

NOTE Confidence: 0.99105227

00:02:14.264 --> 00:02:16.105 is it even interesting to

NOTE Confidence: 0.99105227

00:02:16.105 --> 00:02:18.345 talk about cannabis, cannabinoids, and

NOTE Confidence: 0.99105227

00:02:18.345 --> 00:02:20.105 and pain? It's because this

NOTE Confidence: 0.99105227

00:02:20.105 --> 00:02:21.065 is one of the most

NOTE Confidence: 0.99105227

00:02:21.065 --> 00:02:22.925 common reasons that people use

NOTE Confidence: 0.6868759

00:02:23.305 --> 00:02:24.025 for using,
NOTE Confidence: 0.9364176

00:02:24.345 --> 00:02:25.785 gift for using cannabis or
NOTE Confidence: 0.9364176

00:02:25.785 --> 00:02:26.285 cannabinoids.
NOTE Confidence: 0.995271

00:02:28.780 --> 00:02:29.819 I'm gonna give you an
NOTE Confidence: 0.995271

00:02:29.819 --> 00:02:30.879 overview of
NOTE Confidence: 0.9588967

00:02:31.180 --> 00:02:33.099 the of cannabis and and
NOTE Confidence: 0.9588967

00:02:33.099 --> 00:02:34.239 cannabinoid pharmacology,
NOTE Confidence: 0.9987544

00:02:35.019 --> 00:02:36.159 tell you about the endocannabinoid
NOTE Confidence: 0.9972725

00:02:36.540 --> 00:02:37.040 system,
NOTE Confidence: 0.89777607

00:02:38.379 --> 00:02:39.225 tell you about
NOTE Confidence: 0.96278495

00:02:39.705 --> 00:02:41.145 the products that are currently
NOTE Confidence: 0.96278495

00:02:41.145 --> 00:02:42.925 available and those in pipeline,
NOTE Confidence: 0.99499506

00:02:43.385 --> 00:02:45.225 and cover some information about
NOTE Confidence: 0.99499506

00:02:45.225 --> 00:02:46.905 the efficacy of cannabinoids in
NOTE Confidence: 0.99499506

00:02:46.905 --> 00:02:47.405 acute
NOTE Confidence: 0.9494398

00:02:47.705 --> 00:02:48.925 and chronic pain,

NOTE Confidence: 0.9705445

00:02:49.225 --> 00:02:49.965 and then,

NOTE Confidence: 0.839089

00:02:50.745 --> 00:02:52.709 find the clothes with gaps

NOTE Confidence: 0.839089

00:02:52.849 --> 00:02:53.830 in information

NOTE Confidence: 0.920393

00:02:54.450 --> 00:02:56.709 and, therefore, opportunities for research,

NOTE Confidence: 0.99771756

00:02:57.410 --> 00:02:58.709 on this topic. So

NOTE Confidence: 0.93454444

00:02:59.970 --> 00:03:00.770 everyone knows,

NOTE Confidence: 0.8645136

00:03:01.330 --> 00:03:02.870 about cannabinoids. Cannabis

NOTE Confidence: 0.98592067

00:03:03.410 --> 00:03:05.190 is ubiquitous now. It's available

NOTE Confidence: 0.98592067

00:03:05.250 --> 00:03:06.230 all over the place.

NOTE Confidence: 0.90988743

00:03:07.084 --> 00:03:08.284 But for those who of

NOTE Confidence: 0.90988743

00:03:08.284 --> 00:03:09.345 you are not familiar,

NOTE Confidence: 0.97658825

00:03:09.885 --> 00:03:12.364 most of the, interesting chemical

NOTE Confidence: 0.97658825

00:03:12.364 --> 00:03:14.364 compounds present in cannabis reside

NOTE Confidence: 0.97658825

00:03:14.364 --> 00:03:15.825 in these hair like trichomes,

NOTE Confidence: 0.88726085

00:03:16.685 --> 00:03:18.064 that are magnified here.

NOTE Confidence: 0.99420184

00:03:18.845 --> 00:03:20.704 And, cannabis contains
NOTE Confidence: 0.9524887

00:03:21.010 --> 00:03:23.030 about five hundred chemicals, including
NOTE Confidence: 0.99193805

00:03:23.410 --> 00:03:24.790 about a hundred cannabinoids.
NOTE Confidence: 0.9936811

00:03:25.330 --> 00:03:27.570 The ones that have, gotten
NOTE Confidence: 0.9936811

00:03:27.570 --> 00:03:29.170 most of our attention include
NOTE Confidence: 0.9936811

00:03:29.170 --> 00:03:30.470 delta nine tetrahydrocannabinol,
NOTE Confidence: 0.9887063

00:03:31.250 --> 00:03:32.630 which I'll refer to as
NOTE Confidence: 0.95127225

00:03:33.135 --> 00:03:34.435 THC from now on,
NOTE Confidence: 0.99842536

00:03:34.735 --> 00:03:35.555 and cannabidiol
NOTE Confidence: 0.9322565

00:03:36.015 --> 00:03:37.455 or CBD as I referred
NOTE Confidence: 0.9322565

00:03:37.455 --> 00:03:38.895 to. But beyond that, there
NOTE Confidence: 0.9322565

00:03:38.895 --> 00:03:40.435 are a number of other,
NOTE Confidence: 0.9993547

00:03:41.775 --> 00:03:42.675 minor cannabinoids
NOTE Confidence: 0.9578066

00:03:42.975 --> 00:03:44.575 present in the cannabis plant
NOTE Confidence: 0.9578066

00:03:44.575 --> 00:03:46.550 and then four hundred other,
NOTE Confidence: 0.9334693

00:03:47.330 --> 00:03:49.670 chemical constituents, including terpenes,

NOTE Confidence: 0.9932313

00:03:50.770 --> 00:03:51.590 and flavonoids.

NOTE Confidence: 0.948771

00:03:52.450 --> 00:03:53.750 But the ones that are

NOTE Confidence: 0.948771

00:03:53.810 --> 00:03:55.490 clearly of greatest interest, especially

NOTE Confidence: 0.948771

00:03:55.490 --> 00:03:57.350 to this topic, is, RTHC

NOTE Confidence: 0.948771

00:03:57.410 --> 00:03:58.070 and cannabidiol.

NOTE Confidence: 0.99868184

00:03:59.250 --> 00:03:59.750 So

NOTE Confidence: 0.9990363

00:04:00.965 --> 00:04:02.185 just to make this clear,

NOTE Confidence: 0.9499108

00:04:02.564 --> 00:04:04.504 the intoxicating or the psychoactive

NOTE Confidence: 0.9499108

00:04:04.724 --> 00:04:05.944 effects of cannabis

NOTE Confidence: 0.94728565

00:04:06.564 --> 00:04:08.345 can be attributed to THC.

NOTE Confidence: 0.8160656

00:04:08.885 --> 00:04:10.504 THC alters perception,

NOTE Confidence: 0.9860477

00:04:10.885 --> 00:04:13.224 produces euphoria, alters cognition,

NOTE Confidence: 0.88795584

00:04:13.910 --> 00:04:14.810 and also produces,

NOTE Confidence: 0.9973624

00:04:15.430 --> 00:04:16.169 some cardiovascular

NOTE Confidence: 0.9352296

00:04:16.470 --> 00:04:17.850 effects, including tachycardia,

NOTE Confidence: 0.9716053

00:04:18.710 --> 00:04:21.110 hypotension, and hypotension. In contrast,
NOTE Confidence: 0.9716053

00:04:21.110 --> 00:04:21.610 CBD
NOTE Confidence: 0.9991065

00:04:22.150 --> 00:04:23.750 does not produce any of
NOTE Confidence: 0.9991065

00:04:23.750 --> 00:04:24.490 those effects.
NOTE Confidence: 0.9994489

00:04:26.390 --> 00:04:27.830 CBD is not known to
NOTE Confidence: 0.9994489

00:04:27.830 --> 00:04:28.650 be a psychoactive
NOTE Confidence: 0.97529626

00:04:29.935 --> 00:04:31.775 cannabinoid. However, there's some data
NOTE Confidence: 0.97529626

00:04:31.775 --> 00:04:33.775 suggesting that on its own,
NOTE Confidence: 0.97529626

00:04:33.775 --> 00:04:35.134 at certain doses, it may
NOTE Confidence: 0.97529626

00:04:35.134 --> 00:04:36.595 have anxiolytic effects.
NOTE Confidence: 0.99768084

00:04:37.055 --> 00:04:38.574 And at certain doses, it
NOTE Confidence: 0.99768084

00:04:38.574 --> 00:04:39.634 might offset
NOTE Confidence: 0.96689504

00:04:40.255 --> 00:04:42.170 some of the less desirable
NOTE Confidence: 0.96689504

00:04:42.470 --> 00:04:44.150 effects of THC. And hopefully,
NOTE Confidence: 0.96689504

00:04:44.150 --> 00:04:45.190 we may get a chance
NOTE Confidence: 0.96689504

00:04:45.190 --> 00:04:46.170 to talk about it,

NOTE Confidence: 0.9972055
00:04:46.790 --> 00:04:47.610 later on.
NOTE Confidence: 0.9970374
00:04:48.390 --> 00:04:48.890 So
NOTE Confidence: 0.92245734
00:04:52.070 --> 00:04:53.770 that THC is a principal
NOTE Confidence: 0.92245734
00:04:53.830 --> 00:04:56.125 active constituent of cannabis was
NOTE Confidence: 0.92245734
00:04:56.125 --> 00:04:57.904 discovered in nineteen sixty three.
NOTE Confidence: 0.99712455
00:04:58.525 --> 00:04:59.485 But then for the next
NOTE Confidence: 0.99712455
00:04:59.485 --> 00:05:00.685 twenty five years or so,
NOTE Confidence: 0.99712455
00:05:00.685 --> 00:05:02.145 we really didn't know exactly
NOTE Confidence: 0.9572532
00:05:02.685 --> 00:05:04.865 how THC produced its effects
NOTE Confidence: 0.9572532
00:05:05.005 --> 00:05:06.925 until the late nineteen eighties
NOTE Confidence: 0.9572532
00:05:06.925 --> 00:05:07.425 when,
NOTE Confidence: 0.9996486
00:05:08.659 --> 00:05:10.120 when the first component
NOTE Confidence: 0.99952954
00:05:10.740 --> 00:05:11.639 of the endocannabinoid
NOTE Confidence: 0.9974663
00:05:12.020 --> 00:05:13.080 system was discovered.
NOTE Confidence: 0.9820935
00:05:14.020 --> 00:05:14.900 We now know a lot
NOTE Confidence: 0.9820935

00:05:14.900 --> 00:05:16.020 about that. I'm gonna spend
NOTE Confidence: 0.9820935

00:05:16.020 --> 00:05:16.819 quite a bit of time
NOTE Confidence: 0.9820935

00:05:16.819 --> 00:05:18.759 talking about the endocannabinoid system.
NOTE Confidence: 0.9160661

00:05:21.034 --> 00:05:22.714 There are two receptors. One
NOTE Confidence: 0.9160661

00:05:22.714 --> 00:05:24.634 is a mostly brain receptor,
NOTE Confidence: 0.9160661

00:05:24.634 --> 00:05:26.175 the c v one receptor,
NOTE Confidence: 0.9973636

00:05:26.555 --> 00:05:27.854 which mediates the
NOTE Confidence: 0.9603757

00:05:28.154 --> 00:05:30.474 psychoactive effects of of, cannabis
NOTE Confidence: 0.9603757

00:05:30.474 --> 00:05:31.134 and THC,
NOTE Confidence: 0.9752762

00:05:32.074 --> 00:05:33.194 and the other is the
NOTE Confidence: 0.9752762

00:05:33.194 --> 00:05:34.395 c v two receptor, which
NOTE Confidence: 0.9752762

00:05:34.395 --> 00:05:36.074 is mainly peripheral on immune
NOTE Confidence: 0.9752762

00:05:36.074 --> 00:05:38.000 cells and and may play
NOTE Confidence: 0.9752762

00:05:38.000 --> 00:05:39.520 a much more important role
NOTE Confidence: 0.9752762

00:05:39.520 --> 00:05:41.760 in in inflammation and immune
NOTE Confidence: 0.9752762

00:05:41.760 --> 00:05:44.020 responses rather than psychoactive effects.

NOTE Confidence: 0.9975688
00:05:47.040 --> 00:05:49.300 The distribution of cannabinoid receptors
NOTE Confidence: 0.9975688
00:05:49.520 --> 00:05:52.065 is in exactly those areas
NOTE Confidence: 0.9975688
00:05:52.065 --> 00:05:53.125 that we know,
NOTE Confidence: 0.99871117
00:05:53.745 --> 00:05:54.884 cannabis to produce
NOTE Confidence: 0.84093004
00:05:55.664 --> 00:05:56.884 its effects. So,
NOTE Confidence: 0.9137306
00:05:57.824 --> 00:05:59.125 cannabis can impair,
NOTE Confidence: 0.9413124
00:06:00.224 --> 00:06:02.404 attention, memory, and executive functions.
NOTE Confidence: 0.9413124
00:06:02.464 --> 00:06:03.585 There are higher densities of
NOTE Confidence: 0.9413124
00:06:03.585 --> 00:06:05.710 cannabinoid receptors in the in
NOTE Confidence: 0.9413124
00:06:05.710 --> 00:06:07.089 the prefrontal cortex.
NOTE Confidence: 0.9230177
00:06:08.509 --> 00:06:09.729 Cannabis can impair,
NOTE Confidence: 0.9876123
00:06:10.029 --> 00:06:11.870 memory, and we have there
NOTE Confidence: 0.9876123
00:06:11.870 --> 00:06:13.389 are high densities of cannabinoid
NOTE Confidence: 0.9876123
00:06:13.389 --> 00:06:14.610 receptors in the hippocampus.
NOTE Confidence: 0.9885041
00:06:15.789 --> 00:06:18.370 Cannabis can, can alter anxiety
NOTE Confidence: 0.9885041

00:06:18.430 --> 00:06:20.255 and produce fear and paranoia.
NOTE Confidence: 0.9885041

00:06:20.315 --> 00:06:21.115 We know there are high
NOTE Confidence: 0.9885041

00:06:21.115 --> 00:06:22.815 densities of cannabinoid receptors
NOTE Confidence: 0.9984068

00:06:23.195 --> 00:06:24.015 in the amygdala.
NOTE Confidence: 0.96357226

00:06:25.355 --> 00:06:27.115 Cannabis can alter appetite and
NOTE Confidence: 0.96357226

00:06:27.115 --> 00:06:28.395 sleep, and there are high
NOTE Confidence: 0.96357226

00:06:28.395 --> 00:06:30.154 densities of cannabinoids in the
NOTE Confidence: 0.96357226

00:06:30.154 --> 00:06:30.654 hypothalamus.
NOTE Confidence: 0.99375975

00:06:31.915 --> 00:06:32.575 And then
NOTE Confidence: 0.8415927

00:06:33.539 --> 00:06:35.379 cannabis and THC can impair
NOTE Confidence: 0.8415927

00:06:35.379 --> 00:06:35.879 coordination,
NOTE Confidence: 0.93541765

00:06:36.180 --> 00:06:38.020 reaction time, and balance. And
NOTE Confidence: 0.93541765

00:06:38.020 --> 00:06:39.220 there are very high densities
NOTE Confidence: 0.93541765

00:06:39.220 --> 00:06:40.819 of cannabinoid receptors in the
NOTE Confidence: 0.93541765

00:06:40.819 --> 00:06:41.319 cerebellum
NOTE Confidence: 0.9082711

00:06:41.860 --> 00:06:43.319 and the cerebellar cortex.

NOTE Confidence: 0.98216194

00:06:43.699 --> 00:06:45.300 There are some receptors in

NOTE Confidence: 0.98216194

00:06:45.300 --> 00:06:46.199 the brain stem,

NOTE Confidence: 0.99211246

00:06:46.574 --> 00:06:48.115 though the density of cannabinoid

NOTE Confidence: 0.99211246

00:06:48.175 --> 00:06:49.455 receptors in the brain stem

NOTE Confidence: 0.99211246

00:06:49.455 --> 00:06:51.535 is is relatively low compared

NOTE Confidence: 0.99211246

00:06:51.535 --> 00:06:52.654 to other areas of the

NOTE Confidence: 0.99211246

00:06:52.654 --> 00:06:53.154 brain.

NOTE Confidence: 0.99857795

00:06:54.414 --> 00:06:55.794 We now have the capacity,

NOTE Confidence: 0.9976389

00:06:56.495 --> 00:06:57.714 to actually image

NOTE Confidence: 0.9953832

00:06:58.255 --> 00:07:00.175 cannabinoid receptors in in in

NOTE Confidence: 0.9953832

00:07:00.175 --> 00:07:00.675 vivo

NOTE Confidence: 0.9461045

00:07:01.000 --> 00:07:02.440 in in humans, and this

NOTE Confidence: 0.9461045

00:07:02.440 --> 00:07:03.900 is data from my lab

NOTE Confidence: 0.9876872

00:07:04.279 --> 00:07:05.800 looking at the distribution of

NOTE Confidence: 0.9876872

00:07:05.800 --> 00:07:08.120 cannabinoid receptors using positron emission

NOTE Confidence: 0.9876872

00:07:08.120 --> 00:07:08.620 tomography.
NOTE Confidence: 0.93556195

00:07:09.240 --> 00:07:10.680 And, again, what you see
NOTE Confidence: 0.93556195

00:07:10.680 --> 00:07:11.960 here is the distribution of
NOTE Confidence: 0.93556195

00:07:11.960 --> 00:07:13.639 these receptors, the highest densities
NOTE Confidence: 0.93556195

00:07:13.639 --> 00:07:14.139 on
NOTE Confidence: 0.9747601

00:07:14.455 --> 00:07:15.655 those areas that are shown
NOTE Confidence: 0.9747601

00:07:15.655 --> 00:07:17.415 in red seem to overlap
NOTE Confidence: 0.9747601

00:07:17.415 --> 00:07:18.635 with what we know from
NOTE Confidence: 0.9747601

00:07:18.775 --> 00:07:19.095 from,
NOTE Confidence: 0.6575098

00:07:20.375 --> 00:07:20.875 from,
NOTE Confidence: 0.9046729

00:07:22.135 --> 00:07:23.595 from postmortem studies,
NOTE Confidence: 0.9845702

00:07:24.135 --> 00:07:25.655 and from the known effects
NOTE Confidence: 0.9845702

00:07:25.655 --> 00:07:26.375 of of,
NOTE Confidence: 0.99639773

00:07:27.095 --> 00:07:27.595 cannabinoids.
NOTE Confidence: 0.9273518

00:07:30.340 --> 00:07:30.840 So
NOTE Confidence: 0.9920865

00:07:32.500 --> 00:07:33.540 with the discovery of the

NOTE Confidence: 0.9920865
00:07:33.540 --> 00:07:35.140 cannabinoid receptors in the late
NOTE Confidence: 0.9920865
00:07:35.140 --> 00:07:36.900 nineteen eighties, the next logical
NOTE Confidence: 0.9920865
00:07:36.900 --> 00:07:37.800 question was,
NOTE Confidence: 0.9569439
00:07:38.260 --> 00:07:39.560 are there endogenous,
NOTE Confidence: 0.96440107
00:07:40.580 --> 00:07:42.280 compounds acting in these cannabinoid
NOTE Confidence: 0.96440107
00:07:42.500 --> 00:07:44.995 receptors? So just as endorphins
NOTE Confidence: 0.96440107
00:07:45.135 --> 00:07:46.515 were discovered as the
NOTE Confidence: 0.9629985
00:07:47.215 --> 00:07:47.715 endogenous,
NOTE Confidence: 0.9490348
00:07:48.175 --> 00:07:50.275 ligands for, opioid receptors,
NOTE Confidence: 0.9856063
00:07:50.735 --> 00:07:51.775 we now know that there
NOTE Confidence: 0.9856063
00:07:51.775 --> 00:07:53.075 are at least two,
NOTE Confidence: 0.99677557
00:07:54.335 --> 00:07:54.835 endocannabinoids
NOTE Confidence: 0.9983726
00:07:55.375 --> 00:07:56.355 that have been discovered.
NOTE Confidence: 0.9969626
00:07:56.735 --> 00:07:57.715 The first one
NOTE Confidence: 0.93464136
00:07:58.210 --> 00:07:58.790 is anandamide
NOTE Confidence: 0.9583927

00:07:59.650 --> 00:08:00.870 and named after the Sanskrit
NOTE Confidence: 0.9583927

00:08:01.010 --> 00:08:02.790 word meaning bliss or anand,
NOTE Confidence: 0.9583927

00:08:03.090 --> 00:08:04.290 and the second is two
NOTE Confidence: 0.9583927

00:08:04.290 --> 00:08:05.889 AG. So these are the
NOTE Confidence: 0.9583927

00:08:05.889 --> 00:08:06.870 two endocannabinoids
NOTE Confidence: 0.99201006

00:08:07.650 --> 00:08:09.169 that have been, that are
NOTE Confidence: 0.99201006

00:08:09.169 --> 00:08:10.450 known to be part of
NOTE Confidence: 0.99201006

00:08:10.450 --> 00:08:11.990 the endocannabinoid machinery.
NOTE Confidence: 0.9750452

00:08:14.574 --> 00:08:16.094 We know a lot more
NOTE Confidence: 0.9750452

00:08:16.094 --> 00:08:17.875 now about this endocannabinoid
NOTE Confidence: 0.9839558

00:08:18.254 --> 00:08:19.775 system, and I'm I'm not
NOTE Confidence: 0.9839558

00:08:19.775 --> 00:08:20.735 going to go into all
NOTE Confidence: 0.9839558

00:08:20.735 --> 00:08:22.094 of the details, but I
NOTE Confidence: 0.9839558

00:08:22.094 --> 00:08:23.534 wanna point out some some
NOTE Confidence: 0.9839558

00:08:23.534 --> 00:08:24.974 really important things about the
NOTE Confidence: 0.9839558

00:08:24.974 --> 00:08:25.474 endocannabinoid

NOTE Confidence: 0.9998293
00:08:25.854 --> 00:08:26.354 system.
NOTE Confidence: 0.9825982
00:08:26.759 --> 00:08:28.199 We know the enzymes that
NOTE Confidence: 0.9825982
00:08:28.199 --> 00:08:28.860 are responsible
NOTE Confidence: 0.9996182
00:08:29.160 --> 00:08:29.819 for the
NOTE Confidence: 0.9890504
00:08:30.280 --> 00:08:31.740 synthesis of these endocannabinoids,
NOTE Confidence: 0.9992344
00:08:32.279 --> 00:08:33.500 and we know the enzymes
NOTE Confidence: 0.9992344
00:08:33.559 --> 00:08:35.080 that are responsible for the
NOTE Confidence: 0.9992344
00:08:35.080 --> 00:08:35.580 degradation
NOTE Confidence: 0.9900895
00:08:36.200 --> 00:08:37.100 of these endocannabinoids.
NOTE Confidence: 0.8528466
00:08:37.559 --> 00:08:39.820 And pharmaceutical companies have
NOTE Confidence: 0.9948381
00:08:40.254 --> 00:08:41.615 have seen these as targets
NOTE Confidence: 0.9948381
00:08:41.615 --> 00:08:43.054 and have developed drugs that
NOTE Confidence: 0.9948381
00:08:43.054 --> 00:08:44.254 have now been used in
NOTE Confidence: 0.9948381
00:08:44.254 --> 00:08:44.754 humans
NOTE Confidence: 0.9750984
00:08:45.454 --> 00:08:45.855 to,
NOTE Confidence: 0.998088

00:08:46.495 --> 00:08:48.194 to modulate the endocannabinoid
NOTE Confidence: 0.9919257

00:08:48.574 --> 00:08:49.554 system. So
NOTE Confidence: 0.97252965

00:08:49.934 --> 00:08:50.675 the enzyme
NOTE Confidence: 0.78569347

00:08:51.134 --> 00:08:53.295 fatty acid amide hydrolase or
NOTE Confidence: 0.78569347

00:08:53.295 --> 00:08:53.795 far,
NOTE Confidence: 0.9323288

00:08:54.899 --> 00:08:55.460 is what's,
NOTE Confidence: 0.9438969

00:08:56.020 --> 00:08:58.120 responsible for breaking down anamide
NOTE Confidence: 0.9227167

00:08:58.820 --> 00:08:59.559 to ethanolamine.
NOTE Confidence: 0.9820903

00:09:00.179 --> 00:09:02.020 And a number of companies,
NOTE Confidence: 0.9820903

00:09:02.020 --> 00:09:04.660 including Pfizer, developed inhibitors of
NOTE Confidence: 0.9820903

00:09:04.660 --> 00:09:06.584 these compounds that were that
NOTE Confidence: 0.9820903

00:09:06.584 --> 00:09:07.944 have been tested in humans
NOTE Confidence: 0.9820903

00:09:07.944 --> 00:09:09.064 and used for a number
NOTE Confidence: 0.9820903

00:09:09.064 --> 00:09:11.225 of indications, including, and I'll
NOTE Confidence: 0.9820903

00:09:11.225 --> 00:09:12.745 talk about that later on,
NOTE Confidence: 0.9820903

00:09:12.745 --> 00:09:12.824 pain.

NOTE Confidence: 0.9374928
00:09:14.904 --> 00:09:16.264 We know the enzyme that's
NOTE Confidence: 0.9374928
00:09:16.264 --> 00:09:16.764 responsible
NOTE Confidence: 0.9968538
00:09:17.545 --> 00:09:18.125 for the
NOTE Confidence: 0.7568654
00:09:19.064 --> 00:09:19.804 for the
NOTE Confidence: 0.98315763
00:09:20.700 --> 00:09:22.620 synthesis and degradation of the
NOTE Confidence: 0.98315763
00:09:22.620 --> 00:09:24.640 the other endocannabinoid two AG.
NOTE Confidence: 0.99945277
00:09:25.020 --> 00:09:26.540 Now what's peculiar about the
NOTE Confidence: 0.99945277
00:09:26.540 --> 00:09:27.040 endocannabinoid
NOTE Confidence: 0.99973816
00:09:27.420 --> 00:09:27.920 system
NOTE Confidence: 0.9420955
00:09:28.300 --> 00:09:30.220 is that unlike most other
NOTE Confidence: 0.9420955
00:09:30.220 --> 00:09:30.720 neurotransmitter
NOTE Confidence: 0.99911064
00:09:31.260 --> 00:09:31.760 systems,
NOTE Confidence: 0.9978659
00:09:32.220 --> 00:09:33.360 it is a retrograde
NOTE Confidence: 0.9830139
00:09:34.035 --> 00:09:35.394 messenger system. So let me
NOTE Confidence: 0.9830139
00:09:35.394 --> 00:09:36.995 try and explain this. So
NOTE Confidence: 0.9830139

00:09:36.995 --> 00:09:38.355 shown here in green is
NOTE Confidence: 0.9830139

00:09:38.355 --> 00:09:39.014 the presynaptic
NOTE Confidence: 0.8920546

00:09:39.315 --> 00:09:39.815 neuron,
NOTE Confidence: 0.9945078

00:09:40.675 --> 00:09:42.135 and shown here in pink
NOTE Confidence: 0.9945078

00:09:42.195 --> 00:09:43.575 is the postsynaptic
NOTE Confidence: 0.98379654

00:09:43.954 --> 00:09:45.495 neuron, and there's a synaptic
NOTE Confidence: 0.98379654

00:09:45.554 --> 00:09:47.255 cleft that's between them.
NOTE Confidence: 0.9734585

00:09:47.670 --> 00:09:48.710 So let's say there's a
NOTE Confidence: 0.9734585

00:09:48.710 --> 00:09:49.990 nerve impulse that comes down
NOTE Confidence: 0.9734585

00:09:49.990 --> 00:09:52.550 this presynaptic neuron resulting in
NOTE Confidence: 0.9734585

00:09:52.550 --> 00:09:54.070 the release of, let's say,
NOTE Confidence: 0.9734585

00:09:54.070 --> 00:09:54.570 these,
NOTE Confidence: 0.91566503

00:09:55.429 --> 00:09:55.929 glutamate,
NOTE Confidence: 0.94673085

00:09:57.750 --> 00:10:00.070 this this neurotransmitter glutamate shown
NOTE Confidence: 0.94673085

00:10:00.070 --> 00:10:01.450 here in these orange
NOTE Confidence: 0.96567065

00:10:02.315 --> 00:10:04.415 circles, and glutamate binds

NOTE Confidence: 0.9511614
00:10:05.115 --> 00:10:06.554 to a glutamate receptor on
NOTE Confidence: 0.9511614
00:10:06.554 --> 00:10:07.855 the postsynaptic neuron.
NOTE Confidence: 0.9991194
00:10:08.395 --> 00:10:09.915 What then happens is that
NOTE Confidence: 0.9991194
00:10:09.915 --> 00:10:10.735 it triggers
NOTE Confidence: 0.9979693
00:10:11.675 --> 00:10:13.455 the on demand synthesis
NOTE Confidence: 0.9486341
00:10:15.300 --> 00:10:15.960 of anandamide
NOTE Confidence: 0.9532745
00:10:16.340 --> 00:10:17.720 and two AG. So
NOTE Confidence: 0.9782319
00:10:18.340 --> 00:10:20.180 anandamide and two AG are
NOTE Confidence: 0.9782319
00:10:20.180 --> 00:10:21.860 not stored in vesicles. They
NOTE Confidence: 0.9782319
00:10:21.860 --> 00:10:23.540 are produced on demand, and
NOTE Confidence: 0.9782319
00:10:23.540 --> 00:10:25.000 they are produced on demand
NOTE Confidence: 0.9446647
00:10:25.540 --> 00:10:27.000 in response to,
NOTE Confidence: 0.977662
00:10:28.235 --> 00:10:30.714 activation of postsynaptic receptors. In
NOTE Confidence: 0.977662
00:10:30.714 --> 00:10:31.755 this case, I'm giving the
NOTE Confidence: 0.977662
00:10:31.755 --> 00:10:32.735 example of glutamate.
NOTE Confidence: 0.99456984

00:10:33.355 --> 00:10:35.195 What happens once they are
NOTE Confidence: 0.99456984

00:10:35.195 --> 00:10:36.954 produced and released is they
NOTE Confidence: 0.99456984

00:10:36.954 --> 00:10:38.014 travel back
NOTE Confidence: 0.99669456

00:10:39.355 --> 00:10:41.214 to bind to cannabinoid receptors
NOTE Confidence: 0.99669456

00:10:41.355 --> 00:10:42.554 that are present on the
NOTE Confidence: 0.99669456

00:10:42.554 --> 00:10:43.800 presynaptic neuron.
NOTE Confidence: 0.9993139

00:10:44.279 --> 00:10:45.660 So it's a retrograde
NOTE Confidence: 0.95036966

00:10:46.600 --> 00:10:47.660 messenger system.
NOTE Confidence: 0.9081081

00:10:48.360 --> 00:10:50.279 And what that does is
NOTE Confidence: 0.9081081

00:10:50.279 --> 00:10:51.480 when the c b one
NOTE Confidence: 0.9081081

00:10:51.480 --> 00:10:53.580 receptor shown here is activated
NOTE Confidence: 0.9081081

00:10:53.640 --> 00:10:54.860 or shown here is activated,
NOTE Confidence: 0.9961155

00:10:55.720 --> 00:10:56.459 it basically
NOTE Confidence: 0.999619

00:10:56.920 --> 00:10:57.420 prevents
NOTE Confidence: 0.99850386

00:10:57.815 --> 00:10:59.755 or inhibits the further release
NOTE Confidence: 0.99076635

00:11:00.135 --> 00:11:02.214 of the initial neurotransmitter, in

NOTE Confidence: 0.99076635

00:11:02.214 --> 00:11:03.195 this case, glutamate.

NOTE Confidence: 0.99963474

00:11:03.895 --> 00:11:04.395 So

NOTE Confidence: 0.9546154

00:11:04.934 --> 00:11:06.455 what is happening is, in

NOTE Confidence: 0.9546154

00:11:06.455 --> 00:11:08.075 in essence, is that the

NOTE Confidence: 0.9546154

00:11:08.375 --> 00:11:08.875 endocannabinoid

NOTE Confidence: 0.9839689

00:11:09.415 --> 00:11:11.415 system serves as a breaking

NOTE Confidence: 0.9839689

00:11:11.415 --> 00:11:11.915 function,

NOTE Confidence: 0.9892958

00:11:13.280 --> 00:11:15.200 preventing the release or inhibiting

NOTE Confidence: 0.9892958

00:11:15.200 --> 00:11:16.740 the release of further neurotransmitters.

NOTE Confidence: 0.9995782

00:11:18.320 --> 00:11:19.600 So this is something really

NOTE Confidence: 0.9995782

00:11:19.600 --> 00:11:20.800 important to keep in mind

NOTE Confidence: 0.9995782

00:11:20.800 --> 00:11:21.920 as we think about the

NOTE Confidence: 0.9995782

00:11:21.920 --> 00:11:22.420 physiology

NOTE Confidence: 0.9997428

00:11:23.120 --> 00:11:24.020 of the endocannabinoid

NOTE Confidence: 0.9995898

00:11:24.480 --> 00:11:24.980 system.

NOTE Confidence: 0.991613

00:11:26.885 --> 00:11:28.565 Something else that's really important

NOTE Confidence: 0.991613

00:11:28.565 --> 00:11:29.845 to keep in mind is

NOTE Confidence: 0.991613

00:11:29.845 --> 00:11:30.345 that

NOTE Confidence: 0.9578042

00:11:31.205 --> 00:11:32.265 once these endocannabinoids

NOTE Confidence: 0.992768

00:11:32.804 --> 00:11:34.165 are released and they bind

NOTE Confidence: 0.992768

00:11:34.165 --> 00:11:35.545 to cannabinoid receptors,

NOTE Confidence: 0.9966411

00:11:36.165 --> 00:11:37.225 they are inactivated

NOTE Confidence: 0.9631789

00:11:37.684 --> 00:11:39.705 almost immediately within milliseconds.

NOTE Confidence: 0.9885668

00:11:41.730 --> 00:11:43.010 That's one important point to

NOTE Confidence: 0.9885668

00:11:43.010 --> 00:11:44.210 keep in mind. Second is

NOTE Confidence: 0.9885668

00:11:44.210 --> 00:11:45.490 that the release of these

NOTE Confidence: 0.9885668

00:11:45.490 --> 00:11:45.990 endocannabinoids

NOTE Confidence: 0.9423434

00:11:47.010 --> 00:11:48.150 is very discreet.

NOTE Confidence: 0.881372

00:11:48.929 --> 00:11:50.470 They are they only release

NOTE Confidence: 0.881372

00:11:50.530 --> 00:11:52.390 in very, very small spaces.

NOTE Confidence: 0.881372

00:11:52.530 --> 00:11:53.995 And why am I want

NOTE Confidence: 0.881372
00:11:53.995 --> 00:11:55.834 to emphasize this is in
NOTE Confidence: 0.881372
00:11:55.834 --> 00:11:56.334 contrast,
NOTE Confidence: 0.9982095
00:11:56.714 --> 00:11:57.214 when
NOTE Confidence: 0.93365276
00:11:57.595 --> 00:11:59.774 someone smokes marijuana or weed,
NOTE Confidence: 0.99921197
00:12:01.115 --> 00:12:02.574 first thing is that THC
NOTE Confidence: 0.99921197
00:12:02.634 --> 00:12:04.334 floods the entire brain.
NOTE Confidence: 0.9419944
00:12:05.514 --> 00:12:07.355 THC does not just act
NOTE Confidence: 0.9419944
00:12:07.355 --> 00:12:08.954 on very discrete areas of
NOTE Confidence: 0.9419944
00:12:08.954 --> 00:12:10.050 the brain. It floods the
NOTE Confidence: 0.9419944
00:12:10.050 --> 00:12:12.790 entire brain and therefore activates
NOTE Confidence: 0.9419944
00:12:12.929 --> 00:12:14.530 c b one receptors all
NOTE Confidence: 0.9419944
00:12:14.530 --> 00:12:15.890 over the brain. That's number
NOTE Confidence: 0.9419944
00:12:15.890 --> 00:12:18.210 one. Second is that unlike
NOTE Confidence: 0.9419944
00:12:18.210 --> 00:12:18.710 endocannabinoids
NOTE Confidence: 0.99505866
00:12:19.250 --> 00:12:20.790 that are that are
NOTE Confidence: 0.96762764

00:12:21.570 --> 00:12:24.309 destroyed almost immediately after activating

NOTE Confidence: 0.96762764

00:12:24.370 --> 00:12:25.335 c b one receptors,

NOTE Confidence: 0.9827145

00:12:26.215 --> 00:12:26.715 THC

NOTE Confidence: 0.9912238

00:12:27.495 --> 00:12:29.415 will continue to activate c

NOTE Confidence: 0.9912238

00:12:29.415 --> 00:12:30.315 b one receptors.

NOTE Confidence: 0.9988869

00:12:30.695 --> 00:12:32.075 So the point here is

NOTE Confidence: 0.9865877

00:12:32.535 --> 00:12:34.875 that THC's effects are nonphysiological.

NOTE Confidence: 0.99610454

00:12:35.495 --> 00:12:36.395 They are different

NOTE Confidence: 0.98367214

00:12:36.775 --> 00:12:38.500 from the from the effects

NOTE Confidence: 0.98367214

00:12:38.500 --> 00:12:40.420 of the endocannabinoid system. By

NOTE Confidence: 0.98367214

00:12:40.420 --> 00:12:41.460 the way, please stop me

NOTE Confidence: 0.98367214

00:12:41.460 --> 00:12:42.500 at any time if you'd

NOTE Confidence: 0.98367214

00:12:42.500 --> 00:12:43.540 like to ask questions or

NOTE Confidence: 0.98367214

00:12:43.540 --> 00:12:44.500 if I'm if I'm not

NOTE Confidence: 0.98367214

00:12:44.500 --> 00:12:45.400 clear about,

NOTE Confidence: 0.96317124

00:12:45.940 --> 00:12:47.880 about, what I'm trying to

NOTE Confidence: 0.96317124
00:12:48.020 --> 00:12:49.800 trying to say. So, again,
NOTE Confidence: 0.96317124
00:12:49.955 --> 00:12:51.155 this is what we know
NOTE Confidence: 0.96317124
00:12:51.155 --> 00:12:52.355 about the this is a
NOTE Confidence: 0.96317124
00:12:52.355 --> 00:12:54.115 basic idea about about the
NOTE Confidence: 0.96317124
00:12:54.115 --> 00:12:54.615 endocannabinoid
NOTE Confidence: 0.9996946
00:12:54.995 --> 00:12:55.495 machinery.
NOTE Confidence: 0.9967902
00:12:58.915 --> 00:13:00.115 Another point to keep in
NOTE Confidence: 0.9967902
00:13:00.115 --> 00:13:01.795 mind is the idea that
NOTE Confidence: 0.9967902
00:13:01.795 --> 00:13:03.895 THC is a partial agonist
NOTE Confidence: 0.88510746
00:13:04.490 --> 00:13:05.769 at c b one receptors,
NOTE Confidence: 0.88510746
00:13:05.769 --> 00:13:06.730 and I'll try try and
NOTE Confidence: 0.88510746
00:13:06.730 --> 00:13:08.190 illustrate this. So,
NOTE Confidence: 0.96059054
00:13:10.170 --> 00:13:10.730 if a
NOTE Confidence: 0.99686503
00:13:11.370 --> 00:13:12.110 the endogenous
NOTE Confidence: 0.88500625
00:13:12.490 --> 00:13:14.269 of full agonist, which is
NOTE Confidence: 0.88500625

00:13:14.410 --> 00:13:16.569 a, anandamide or two AG
NOTE Confidence: 0.88500625

00:13:16.569 --> 00:13:17.949 is shown here in blue.
NOTE Confidence: 0.9997263

00:13:18.434 --> 00:13:20.115 And as you increase the
NOTE Confidence: 0.9997263

00:13:20.115 --> 00:13:20.615 dose
NOTE Confidence: 0.95300823

00:13:20.995 --> 00:13:22.355 of, say, anandamide or two
NOTE Confidence: 0.95300823

00:13:22.355 --> 00:13:23.575 AG, you get increasing
NOTE Confidence: 0.9754294

00:13:24.434 --> 00:13:26.115 effects that plateau off at
NOTE Confidence: 0.9754294

00:13:26.115 --> 00:13:27.655 around, let's say, hundred percent.
NOTE Confidence: 0.9850593

00:13:28.755 --> 00:13:29.795 What you may get with
NOTE Confidence: 0.9850593

00:13:29.795 --> 00:13:31.235 the with THC, which is
NOTE Confidence: 0.9850593

00:13:31.235 --> 00:13:32.215 a partial agonist,
NOTE Confidence: 0.9982942

00:13:32.660 --> 00:13:33.780 is that even at the
NOTE Confidence: 0.9982942

00:13:33.780 --> 00:13:35.380 highest dose of THC, it
NOTE Confidence: 0.9982942

00:13:35.380 --> 00:13:37.380 will never produce the same
NOTE Confidence: 0.9982942

00:13:37.380 --> 00:13:39.240 degree of efficacy or effects
NOTE Confidence: 0.9965449

00:13:39.860 --> 00:13:41.640 as the endogenous agonist.

NOTE Confidence: 0.9815967
00:13:42.500 --> 00:13:43.940 So what what we mean
NOTE Confidence: 0.9815967
00:13:43.940 --> 00:13:44.900 to say here is that
NOTE Confidence: 0.9815967
00:13:44.900 --> 00:13:46.679 THC is a partial agonist.
NOTE Confidence: 0.98152477
00:13:47.085 --> 00:13:48.065 And in contrast,
NOTE Confidence: 0.9958694
00:13:48.684 --> 00:13:49.745 synthetic cannabinoids,
NOTE Confidence: 0.9750678
00:13:50.205 --> 00:13:51.325 and we'll talk about that
NOTE Confidence: 0.9750678
00:13:51.325 --> 00:13:53.025 later on, can produce,
NOTE Confidence: 0.83834124
00:13:53.565 --> 00:13:54.065 supranormal
NOTE Confidence: 0.9870889
00:13:54.445 --> 00:13:56.445 effects, effects that are higher
NOTE Confidence: 0.9870889
00:13:56.445 --> 00:13:58.465 than the endogenous agonist.
NOTE Confidence: 0.9909488
00:13:59.880 --> 00:14:01.240 So, again, this is just
NOTE Confidence: 0.9909488
00:14:01.240 --> 00:14:02.140 to show that
NOTE Confidence: 0.9920698
00:14:02.680 --> 00:14:03.880 the effects that you get
NOTE Confidence: 0.9920698
00:14:03.880 --> 00:14:05.100 with the full agonist
NOTE Confidence: 0.9942937
00:14:05.880 --> 00:14:07.320 is more than what you
NOTE Confidence: 0.9942937

00:14:07.320 --> 00:14:08.760 would get with THC, which
NOTE Confidence: 0.9942937

00:14:08.760 --> 00:14:09.980 is a partial agonist.
NOTE Confidence: 0.9097029

00:14:11.640 --> 00:14:12.380 And likewise,
NOTE Confidence: 0.976245

00:14:13.235 --> 00:14:14.775 when you talk about efficacy
NOTE Confidence: 0.976245

00:14:14.835 --> 00:14:15.815 and side effects,
NOTE Confidence: 0.99350286

00:14:16.195 --> 00:14:17.255 you see a difference
NOTE Confidence: 0.97110236

00:14:17.555 --> 00:14:20.215 between full agonists or synthetic
NOTE Confidence: 0.97110236

00:14:20.275 --> 00:14:22.835 agonists and, THC shown here.
NOTE Confidence: 0.97110236

00:14:22.835 --> 00:14:24.295 These are the clinical implications.
NOTE Confidence: 0.99494094

00:14:26.435 --> 00:14:27.415 Excuse me.
NOTE Confidence: 0.95229423

00:14:28.980 --> 00:14:29.960 Okay. So,
NOTE Confidence: 0.99960864

00:14:31.620 --> 00:14:33.540 something important to remember about
NOTE Confidence: 0.99960864

00:14:33.540 --> 00:14:34.280 the endocannabinoid
NOTE Confidence: 0.99970835

00:14:34.660 --> 00:14:35.780 system is that it's a
NOTE Confidence: 0.99970835

00:14:35.780 --> 00:14:37.240 highly dynamic system.
NOTE Confidence: 0.99872965

00:14:38.260 --> 00:14:39.220 What do I mean by

NOTE Confidence: 0.99872965
00:14:39.220 --> 00:14:39.720 that?
NOTE Confidence: 0.9965014
00:14:40.194 --> 00:14:42.375 With repeated exposure to THC
NOTE Confidence: 0.9965014
00:14:42.435 --> 00:14:43.014 or cannabis,
NOTE Confidence: 0.95608985
00:14:43.795 --> 00:14:44.535 there is
NOTE Confidence: 0.85417664
00:14:45.154 --> 00:14:46.454 a there is a remarkable
NOTE Confidence: 0.56156063
00:14:48.995 --> 00:14:49.495 downregulation
NOTE Confidence: 0.9987577
00:14:50.035 --> 00:14:50.774 and desensitization
NOTE Confidence: 0.9471847
00:14:51.315 --> 00:14:52.754 of the CB one receptor.
NOTE Confidence: 0.9471847
00:14:52.754 --> 00:14:54.214 It was previously only
NOTE Confidence: 0.9811386
00:14:54.760 --> 00:14:56.600 shown in animal studies, but,
NOTE Confidence: 0.9811386
00:14:56.839 --> 00:14:58.440 we again, because we have
NOTE Confidence: 0.9811386
00:14:58.440 --> 00:15:00.519 positron emission tomography available at
NOTE Confidence: 0.9811386
00:15:00.519 --> 00:15:02.519 Yale with a highly selective
NOTE Confidence: 0.9811386
00:15:02.519 --> 00:15:04.060 ligand for CB one receptors
NOTE Confidence: 0.9629168
00:15:04.600 --> 00:15:06.040 that allows us to actually
NOTE Confidence: 0.9629168

00:15:06.040 --> 00:15:07.320 look at the impact of
NOTE Confidence: 0.9629168

00:15:07.320 --> 00:15:08.940 repeated cannabis exposure
NOTE Confidence: 0.83466434

00:15:09.455 --> 00:15:10.515 on the endocannabinoid
NOTE Confidence: 0.9950437

00:15:10.975 --> 00:15:11.475 system.
NOTE Confidence: 0.9552182

00:15:12.095 --> 00:15:13.455 Shown here on in the
NOTE Confidence: 0.9552182

00:15:13.455 --> 00:15:14.435 top row,
NOTE Confidence: 0.9223836

00:15:15.295 --> 00:15:17.215 is CB one receptor binding
NOTE Confidence: 0.9223836

00:15:17.215 --> 00:15:17.955 or availability
NOTE Confidence: 0.8812504

00:15:18.495 --> 00:15:20.495 using measured using positron and
NOTE Confidence: 0.8812504

00:15:20.495 --> 00:15:21.315 sheet tomography
NOTE Confidence: 0.90875715

00:15:21.920 --> 00:15:23.600 and, and a ligand highly
NOTE Confidence: 0.90875715

00:15:23.600 --> 00:15:24.720 specific for the c v
NOTE Confidence: 0.90875715

00:15:24.720 --> 00:15:25.460 one receptor.
NOTE Confidence: 0.98039836

00:15:26.480 --> 00:15:28.640 And the middle panel shows
NOTE Confidence: 0.98039836

00:15:28.640 --> 00:15:30.560 you daily cannabis users. And,
NOTE Confidence: 0.98039836

00:15:30.560 --> 00:15:32.000 hopefully, to the naked eye,

NOTE Confidence: 0.98039836
00:15:32.000 --> 00:15:32.980 you can see that
NOTE Confidence: 0.99963677
00:15:34.095 --> 00:15:35.555 in response to repeated
NOTE Confidence: 0.95019543
00:15:35.935 --> 00:15:37.454 exposure to cannabis as in
NOTE Confidence: 0.95019543
00:15:37.454 --> 00:15:38.834 daily cannabis use,
NOTE Confidence: 0.99952567
00:15:39.295 --> 00:15:41.074 there is a reduction
NOTE Confidence: 0.9912365
00:15:41.454 --> 00:15:42.915 in the numbers of cannabinoid
NOTE Confidence: 0.9912365
00:15:43.055 --> 00:15:43.555 receptors,
NOTE Confidence: 0.8914598
00:15:45.135 --> 00:15:46.274 as as a consequence.
NOTE Confidence: 0.9759858
00:15:47.570 --> 00:15:49.590 What accompanies this is obviously
NOTE Confidence: 0.9717245
00:15:50.690 --> 00:15:52.290 tolerance. That is to say
NOTE Confidence: 0.9717245
00:15:52.290 --> 00:15:54.390 with repeated exposure to cannabis,
NOTE Confidence: 0.949806
00:15:54.770 --> 00:15:55.810 there will be the develop
NOTE Confidence: 0.949806
00:15:55.970 --> 00:15:57.430 there there is a development
NOTE Confidence: 0.949806
00:15:57.490 --> 00:15:58.150 of tolerance
NOTE Confidence: 0.98759604
00:15:58.770 --> 00:16:00.470 to the effects of cannabis,
NOTE Confidence: 0.99945974

00:16:00.985 --> 00:16:02.525 and the underlying biological

NOTE Confidence: 0.950496

00:16:03.225 --> 00:16:05.405 basis for that is downregulation

NOTE Confidence: 0.94223595

00:16:05.785 --> 00:16:07.225 of the CB one receptors,

NOTE Confidence: 0.94223595

00:16:07.225 --> 00:16:08.345 which we can see now

NOTE Confidence: 0.94223595

00:16:08.345 --> 00:16:09.165 using PEC,

NOTE Confidence: 0.9936388

00:16:09.705 --> 00:16:10.845 and also desensitization

NOTE Confidence: 0.9992649

00:16:11.545 --> 00:16:12.605 of these receptors.

NOTE Confidence: 0.9895502

00:16:13.880 --> 00:16:15.000 Of course, there are clinical

NOTE Confidence: 0.9895502

00:16:15.000 --> 00:16:16.380 implications for that.

NOTE Confidence: 0.99409056

00:16:17.080 --> 00:16:19.020 Based on on this biological

NOTE Confidence: 0.9948646

00:16:19.640 --> 00:16:21.660 data, one would expect that

NOTE Confidence: 0.9631796

00:16:22.200 --> 00:16:23.420 if you wanna target,

NOTE Confidence: 0.99837875

00:16:24.280 --> 00:16:24.940 a symptom

NOTE Confidence: 0.8768026

00:16:25.475 --> 00:16:26.675 or a tree or a

NOTE Confidence: 0.8768026

00:16:26.675 --> 00:16:27.175 condition,

NOTE Confidence: 0.9679398

00:16:27.875 --> 00:16:29.495 with THC or cannabinoids,

NOTE Confidence: 0.94675475
00:16:30.275 --> 00:16:31.735 with repeated administration,
NOTE Confidence: 0.999732
00:16:32.115 --> 00:16:33.095 you could expect
NOTE Confidence: 0.99879616
00:16:33.555 --> 00:16:34.675 that there would be some
NOTE Confidence: 0.99879616
00:16:34.675 --> 00:16:36.455 degree of loss of efficacy
NOTE Confidence: 0.99879616
00:16:36.675 --> 00:16:37.955 because of the development of
NOTE Confidence: 0.99879616
00:16:37.955 --> 00:16:38.455 tolerance.
NOTE Confidence: 0.96902
00:16:40.300 --> 00:16:42.560 Okay. Now what's also interesting
NOTE Confidence: 0.96902
00:16:42.620 --> 00:16:43.840 about this downregulation
NOTE Confidence: 0.9688722
00:16:44.380 --> 00:16:44.880 desensitization,
NOTE Confidence: 0.99981165
00:16:46.460 --> 00:16:47.280 is that
NOTE Confidence: 0.9654573
00:16:48.060 --> 00:16:49.420 this system is a highly
NOTE Confidence: 0.9654573
00:16:49.420 --> 00:16:50.400 dynamic system.
NOTE Confidence: 0.9914435
00:16:50.940 --> 00:16:52.475 So if you take heavy
NOTE Confidence: 0.9914435
00:16:52.475 --> 00:16:54.235 cannabis users and you ask
NOTE Confidence: 0.9914435
00:16:54.235 --> 00:16:55.935 them to stop using cannabis
NOTE Confidence: 0.9709593

00:16:56.795 --> 00:16:58.714 and you confirm that, you
NOTE Confidence: 0.9709593

00:16:58.714 --> 00:16:59.915 can see that within a
NOTE Confidence: 0.9709593

00:16:59.915 --> 00:17:01.695 fairly short period of time,
NOTE Confidence: 0.9970138

00:17:02.154 --> 00:17:03.214 there is recovery
NOTE Confidence: 0.933581

00:17:03.915 --> 00:17:05.680 of c v one receptors.
NOTE Confidence: 0.933581

00:17:05.680 --> 00:17:07.360 Again, this is data from
NOTE Confidence: 0.933581

00:17:07.360 --> 00:17:08.420 my lab using,
NOTE Confidence: 0.9669797

00:17:09.040 --> 00:17:10.240 PET and the c v
NOTE Confidence: 0.9669797

00:17:10.240 --> 00:17:10.880 one receptor,
NOTE Confidence: 0.9838266

00:17:11.440 --> 00:17:12.800 highly specific c v one
NOTE Confidence: 0.9838266

00:17:12.800 --> 00:17:14.800 receptor ligand. That is within
NOTE Confidence: 0.9838266

00:17:14.800 --> 00:17:16.000 four weeks or so, there
NOTE Confidence: 0.9838266

00:17:16.000 --> 00:17:18.020 is a pretty remarkable
NOTE Confidence: 0.99928087

00:17:18.480 --> 00:17:18.980 recovery
NOTE Confidence: 0.9148496

00:17:19.475 --> 00:17:20.855 of c v one receptors.
NOTE Confidence: 0.9148496

00:17:20.915 --> 00:17:22.515 And the clinical implications would

NOTE Confidence: 0.9148496
00:17:22.515 --> 00:17:23.255 be that,
NOTE Confidence: 0.941624
00:17:24.595 --> 00:17:25.815 if you were to,
NOTE Confidence: 0.9968802
00:17:27.555 --> 00:17:28.055 to
NOTE Confidence: 0.96710855
00:17:28.435 --> 00:17:29.494 devise a treatment,
NOTE Confidence: 0.9996326
00:17:29.955 --> 00:17:31.175 it might be important
NOTE Confidence: 0.9496905
00:17:33.029 --> 00:17:34.470 to give breaks in that
NOTE Confidence: 0.9496905
00:17:34.470 --> 00:17:36.470 treatment so there's recovery of
NOTE Confidence: 0.9496905
00:17:36.470 --> 00:17:37.750 that c of the of
NOTE Confidence: 0.9496905
00:17:37.750 --> 00:17:38.409 the system,
NOTE Confidence: 0.9844449
00:17:39.510 --> 00:17:40.630 or you may have to
NOTE Confidence: 0.9844449
00:17:40.630 --> 00:17:42.309 continue to increase the dose
NOTE Confidence: 0.9844449
00:17:42.309 --> 00:17:43.190 as we see with a
NOTE Confidence: 0.9844449
00:17:43.190 --> 00:17:44.390 number of other drugs that
NOTE Confidence: 0.9844449
00:17:44.390 --> 00:17:45.529 we use to treat
NOTE Confidence: 0.99403524
00:17:46.045 --> 00:17:47.425 pain, including opioids.
NOTE Confidence: 0.97201

00:17:49.325 --> 00:17:50.365 Okay. So what do we
NOTE Confidence: 0.97201

00:17:50.365 --> 00:17:52.225 know about the endocannabinoid system,
NOTE Confidence: 0.9515007

00:17:52.925 --> 00:17:53.885 and what you should you
NOTE Confidence: 0.9515007

00:17:53.885 --> 00:17:55.165 know about it? Because if
NOTE Confidence: 0.9515007

00:17:55.165 --> 00:17:56.305 you plan to use,
NOTE Confidence: 0.9974502

00:17:57.565 --> 00:17:59.005 cannabinoids in the treatment of
NOTE Confidence: 0.9974502

00:17:59.005 --> 00:17:59.665 a condition,
NOTE Confidence: 0.9997144

00:18:00.045 --> 00:18:00.945 if you understand
NOTE Confidence: 0.9990705

00:18:01.780 --> 00:18:03.140 the scope of its effects
NOTE Confidence: 0.9990705

00:18:03.140 --> 00:18:04.119 on other systems,
NOTE Confidence: 0.9995989

00:18:04.660 --> 00:18:05.780 you might be able to
NOTE Confidence: 0.9995989

00:18:05.780 --> 00:18:06.280 anticipate
NOTE Confidence: 0.99915534

00:18:06.740 --> 00:18:08.340 what side effects and other
NOTE Confidence: 0.99915534

00:18:08.340 --> 00:18:09.640 effects you might expect
NOTE Confidence: 0.9322299

00:18:10.020 --> 00:18:11.940 with repeated administration. We now
NOTE Confidence: 0.9322299

00:18:11.940 --> 00:18:12.980 know that the c v

NOTE Confidence: 0.9322299

00:18:12.980 --> 00:18:14.520 one system or the endocannabinoid

NOTE Confidence: 0.9996954

00:18:14.900 --> 00:18:15.400 system

NOTE Confidence: 0.9119461

00:18:16.105 --> 00:18:17.945 is plays an important role

NOTE Confidence: 0.9119461

00:18:17.945 --> 00:18:19.705 in stress regulation, in the

NOTE Confidence: 0.9119461

00:18:20.085 --> 00:18:21.725 in in regulating mood,

NOTE Confidence: 0.97067845

00:18:22.105 --> 00:18:23.565 in reward and reinforcement,

NOTE Confidence: 0.9532218

00:18:24.024 --> 00:18:25.325 in learning and memory,

NOTE Confidence: 0.98590434

00:18:26.505 --> 00:18:27.725 in sleep and appetite,

NOTE Confidence: 0.8667885

00:18:29.225 --> 00:18:31.085 pain modulation. We've talked about

NOTE Confidence: 0.9463017

00:18:31.810 --> 00:18:33.030 psychomotor control

NOTE Confidence: 0.938628

00:18:33.570 --> 00:18:34.070 and

NOTE Confidence: 0.85560703

00:18:34.530 --> 00:18:35.030 neurodevelopment,

NOTE Confidence: 0.9689148

00:18:35.650 --> 00:18:37.030 especially during adolescence

NOTE Confidence: 0.98626786

00:18:37.330 --> 00:18:38.310 and in utero.

NOTE Confidence: 0.8649994

00:18:40.770 --> 00:18:41.270 Peripherally,

NOTE Confidence: 0.8499814

00:18:41.970 --> 00:18:43.350 we are CB two receptors
NOTE Confidence: 0.8499814

00:18:43.490 --> 00:18:44.950 residing on immune cells.
NOTE Confidence: 0.9993379

00:18:45.655 --> 00:18:46.395 The endocannabinoid
NOTE Confidence: 0.9710211

00:18:46.775 --> 00:18:47.815 system may play a role
NOTE Confidence: 0.9710211

00:18:47.815 --> 00:18:49.734 in inflammation and immune cell
NOTE Confidence: 0.9710211

00:18:49.734 --> 00:18:50.234 signaling.
NOTE Confidence: 0.9761748

00:18:50.615 --> 00:18:52.075 And we also know that
NOTE Confidence: 0.9761748

00:18:52.135 --> 00:18:53.015 that there are,
NOTE Confidence: 0.99775904

00:18:54.695 --> 00:18:55.755 effects of the endocannabinoid
NOTE Confidence: 0.89284587

00:18:56.055 --> 00:18:58.215 system on energy balance and
NOTE Confidence: 0.89284587

00:18:58.215 --> 00:18:59.975 and glucosin glucose and lipid
NOTE Confidence: 0.89284587

00:18:59.975 --> 00:19:00.475 metabolism.
NOTE Confidence: 0.88229406

00:19:04.429 --> 00:19:04.929 So,
NOTE Confidence: 0.992052

00:19:06.990 --> 00:19:08.510 I wanna point out and
NOTE Confidence: 0.992052

00:19:08.510 --> 00:19:09.970 contrast the effects
NOTE Confidence: 0.89316916

00:19:10.270 --> 00:19:11.090 of the known

NOTE Confidence: 0.99969447
00:19:13.484 --> 00:19:13.984 endocannabinoid
NOTE Confidence: 0.98655707
00:19:14.285 --> 00:19:15.965 function and how that might
NOTE Confidence: 0.98655707
00:19:15.965 --> 00:19:18.045 differ from the effects of,
NOTE Confidence: 0.98655707
00:19:18.205 --> 00:19:20.125 cannabis and THC. If you
NOTE Confidence: 0.98655707
00:19:20.125 --> 00:19:21.165 recall, I mentioned to you
NOTE Confidence: 0.98655707
00:19:21.165 --> 00:19:22.305 that endocannabinoids
NOTE Confidence: 0.9933295
00:19:22.684 --> 00:19:24.305 are destroyed almost immediately,
NOTE Confidence: 0.9140727
00:19:25.244 --> 00:19:26.845 and are released in a
NOTE Confidence: 0.9140727
00:19:26.845 --> 00:19:28.865 very small area. In contrast,
NOTE Confidence: 0.9140727
00:19:29.140 --> 00:19:30.740 cannabis and THC present in
NOTE Confidence: 0.9140727
00:19:30.740 --> 00:19:31.240 cannabis
NOTE Confidence: 0.9474695
00:19:31.619 --> 00:19:33.000 floods the entire brain,
NOTE Confidence: 0.9940874
00:19:33.460 --> 00:19:34.440 in an indiscriminate
NOTE Confidence: 0.97151273
00:19:34.740 --> 00:19:35.240 way,
NOTE Confidence: 0.99492437
00:19:35.780 --> 00:19:38.200 and continues to activate receptors,
NOTE Confidence: 0.9708798

00:19:39.140 --> 00:19:40.820 for, minutes and up to
NOTE Confidence: 0.9708798

00:19:40.820 --> 00:19:41.320 hours.
NOTE Confidence: 0.9326342

00:19:42.740 --> 00:19:43.240 So
NOTE Confidence: 0.9994929

00:19:44.185 --> 00:19:45.484 what that means is
NOTE Confidence: 0.9976063

00:19:45.945 --> 00:19:46.685 that THC
NOTE Confidence: 0.9991131

00:19:47.385 --> 00:19:49.244 may actually convert a precise
NOTE Confidence: 0.9991131

00:19:49.305 --> 00:19:50.365 feedback system
NOTE Confidence: 0.9573598

00:19:50.665 --> 00:19:52.765 into a diffuse sustained signal,
NOTE Confidence: 0.9573598

00:19:52.825 --> 00:19:55.484 or THC is producing nonphysiological
NOTE Confidence: 0.9987118

00:19:56.185 --> 00:19:56.685 effects
NOTE Confidence: 0.68180424

00:19:57.369 --> 00:19:58.330 via via,
NOTE Confidence: 0.998827

00:19:58.730 --> 00:19:59.470 the endocannabinoid
NOTE Confidence: 0.79180956

00:20:00.169 --> 00:20:00.669 system.
NOTE Confidence: 0.99875855

00:20:03.530 --> 00:20:04.030 So
NOTE Confidence: 0.97559136

00:20:04.890 --> 00:20:06.330 what else would be interesting
NOTE Confidence: 0.97559136

00:20:06.330 --> 00:20:07.950 from the perspective of pain

NOTE Confidence: 0.97559136
00:20:08.169 --> 00:20:08.990 and the endocannabinoid
NOTE Confidence: 0.9902661
00:20:09.369 --> 00:20:09.869 system?
NOTE Confidence: 0.9514664
00:20:10.234 --> 00:20:11.535 We know of a peculiar
NOTE Confidence: 0.86334133
00:20:11.915 --> 00:20:12.415 polymorphism,
NOTE Confidence: 0.9442427
00:20:13.915 --> 00:20:14.315 of,
NOTE Confidence: 0.9980777
00:20:14.955 --> 00:20:15.615 the enzyme
NOTE Confidence: 0.98396784
00:20:15.994 --> 00:20:17.595 that's involved in the in
NOTE Confidence: 0.98396784
00:20:17.595 --> 00:20:18.255 the degradation
NOTE Confidence: 0.95449734
00:20:18.715 --> 00:20:19.035 of,
NOTE Confidence: 0.83996165
00:20:19.675 --> 00:20:21.695 of anandamide, the principal endogenous
NOTE Confidence: 0.985128
00:20:22.075 --> 00:20:22.575 cannabinoid.
NOTE Confidence: 0.94304156
00:20:23.700 --> 00:20:26.100 This polymorphism is associated with
NOTE Confidence: 0.94304156
00:20:26.100 --> 00:20:27.539 a reduction in the activity
NOTE Confidence: 0.94304156
00:20:27.539 --> 00:20:29.539 of that enzyme. So if
NOTE Confidence: 0.94304156
00:20:29.539 --> 00:20:30.840 the enzyme is responsive
NOTE Confidence: 0.9816357

00:20:31.380 --> 00:20:33.799 responsible for breaking down anandamide,
NOTE Confidence: 0.7536619

00:20:34.419 --> 00:20:34.919 a
NOTE Confidence: 0.9979334

00:20:35.539 --> 00:20:36.980 reduction in the activity of
NOTE Confidence: 0.9979334

00:20:36.980 --> 00:20:37.559 the enzyme
NOTE Confidence: 0.9078269

00:20:37.875 --> 00:20:39.155 results in an increase in
NOTE Confidence: 0.9078269

00:20:39.155 --> 00:20:39.655 anandamide
NOTE Confidence: 0.78254557

00:20:40.275 --> 00:20:41.715 present and increase in c
NOTE Confidence: 0.78254557

00:20:41.715 --> 00:20:43.494 b one receptor signaling.
NOTE Confidence: 0.9964187

00:20:44.035 --> 00:20:45.155 What they found is that
NOTE Confidence: 0.9964187

00:20:45.155 --> 00:20:46.775 individuals with this polymorphism
NOTE Confidence: 0.927466

00:20:47.395 --> 00:20:48.755 seem to have a an
NOTE Confidence: 0.927466

00:20:48.755 --> 00:20:51.095 unusually high pain tolerance.
NOTE Confidence: 0.9311015

00:20:52.030 --> 00:20:53.650 So this is really interesting
NOTE Confidence: 0.89407563

00:20:54.590 --> 00:20:55.809 clinical data
NOTE Confidence: 0.97606486

00:20:56.350 --> 00:20:56.850 supporting
NOTE Confidence: 0.99472225

00:20:57.710 --> 00:20:59.090 a role of the endocannabinoid

NOTE Confidence: 0.9995639
00:20:59.470 --> 00:20:59.970 system
NOTE Confidence: 0.9892413
00:21:00.430 --> 00:21:01.570 in pain signaling
NOTE Confidence: 0.84377563
00:21:01.950 --> 00:21:03.170 given the fact that,
NOTE Confidence: 0.9959135
00:21:04.350 --> 00:21:05.010 a polymorphism
NOTE Confidence: 0.9443056
00:21:05.390 --> 00:21:07.090 for the for, the
NOTE Confidence: 0.93371946
00:21:07.934 --> 00:21:09.855 of the far gene, which
NOTE Confidence: 0.93371946
00:21:09.855 --> 00:21:11.615 is which, results in a
NOTE Confidence: 0.93371946
00:21:11.615 --> 00:21:13.375 reduction in far activity and
NOTE Confidence: 0.93371946
00:21:13.375 --> 00:21:14.355 increased endocannabinoid
NOTE Confidence: 0.9687044
00:21:14.734 --> 00:21:17.234 tone is associated with higher
NOTE Confidence: 0.9687044
00:21:17.375 --> 00:21:18.595 pain, tolerance.
NOTE Confidence: 0.9842784
00:21:19.375 --> 00:21:21.070 And and, obviously, there are
NOTE Confidence: 0.9842784
00:21:21.070 --> 00:21:21.809 some pharmacological
NOTE Confidence: 0.9979243
00:21:22.190 --> 00:21:22.690 implications
NOTE Confidence: 0.93739957
00:21:23.309 --> 00:21:24.770 as I'll talk about later.
NOTE Confidence: 0.99604696

00:21:25.630 --> 00:21:26.929 There have been studies
NOTE Confidence: 0.8460744

00:21:27.230 --> 00:21:28.990 using a fine inhibitor in
NOTE Confidence: 0.8460744

00:21:28.990 --> 00:21:30.210 the treatment of pain.
NOTE Confidence: 0.97518766

00:21:30.750 --> 00:21:31.789 We'll talk about that,
NOTE Confidence: 0.9997963

00:21:32.270 --> 00:21:32.770 later.
NOTE Confidence: 0.99873

00:21:34.105 --> 00:21:36.205 So what would higher endocannabinoid
NOTE Confidence: 0.9988644

00:21:36.585 --> 00:21:37.484 tone do?
NOTE Confidence: 0.99948806

00:21:38.585 --> 00:21:39.725 It may reduce
NOTE Confidence: 0.91312134

00:21:40.105 --> 00:21:40.605 nociceptor
NOTE Confidence: 0.9342078

00:21:40.984 --> 00:21:41.484 firing.
NOTE Confidence: 0.93308926

00:21:41.865 --> 00:21:43.385 It may reduce glutamate and
NOTE Confidence: 0.93308926

00:21:43.385 --> 00:21:44.825 substance p release in the
NOTE Confidence: 0.93308926

00:21:44.825 --> 00:21:45.804 spinal cord.
NOTE Confidence: 0.97059375

00:21:46.150 --> 00:21:47.510 And at the central level,
NOTE Confidence: 0.97059375

00:21:47.510 --> 00:21:48.230 at the level of the
NOTE Confidence: 0.97059375

00:21:48.230 --> 00:21:50.390 brain, it might reduce pain

NOTE Confidence: 0.97059375
00:21:50.390 --> 00:21:50.890 savings.
NOTE Confidence: 0.99820995
00:21:53.270 --> 00:21:53.770 So
NOTE Confidence: 0.99493563
00:21:55.990 --> 00:21:58.490 how might THC modulate pain?
NOTE Confidence: 0.9684172
00:21:59.225 --> 00:22:00.265 Just going back to the
NOTE Confidence: 0.9684172
00:22:00.265 --> 00:22:02.125 earlier slide, THC may modulate
NOTE Confidence: 0.9684172
00:22:02.185 --> 00:22:02.685 pain
NOTE Confidence: 0.99232453
00:22:03.145 --> 00:22:05.065 by reducing the firing of
NOTE Confidence: 0.99232453
00:22:05.065 --> 00:22:05.565 nociceptors,
NOTE Confidence: 0.9698582
00:22:06.505 --> 00:22:08.505 by reducing inflammation that may
NOTE Confidence: 0.9698582
00:22:08.505 --> 00:22:10.585 be contributing to pain. So
NOTE Confidence: 0.9698582
00:22:10.585 --> 00:22:11.865 at a very peripheral level,
NOTE Confidence: 0.9698582
00:22:11.865 --> 00:22:13.385 at the spinal cord level,
NOTE Confidence: 0.9698582
00:22:13.385 --> 00:22:14.040 it could,
NOTE Confidence: 0.9271807
00:22:14.920 --> 00:22:15.560 THC can,
NOTE Confidence: 0.99843127
00:22:15.960 --> 00:22:17.420 reduce glutamate release
NOTE Confidence: 0.9870493

00:22:17.800 --> 00:22:19.640 and reduce signal transmission. And
NOTE Confidence: 0.9870493

00:22:19.640 --> 00:22:20.600 then at the level of
NOTE Confidence: 0.9870493

00:22:20.600 --> 00:22:21.260 the brain,
NOTE Confidence: 0.99015504

00:22:22.040 --> 00:22:24.859 THC may reduce pain salience
NOTE Confidence: 0.99232656

00:22:25.640 --> 00:22:27.980 and increase descending inhibition. So
NOTE Confidence: 0.9936725

00:22:28.525 --> 00:22:29.905 it is at these multiple
NOTE Confidence: 0.9936725

00:22:29.965 --> 00:22:31.744 levels that one might hypothesize,
NOTE Confidence: 0.9587014

00:22:33.085 --> 00:22:34.705 THC to modulate,
NOTE Confidence: 0.99960756

00:22:35.325 --> 00:22:35.825 pain.
NOTE Confidence: 0.9991819

00:22:38.365 --> 00:22:38.865 So
NOTE Confidence: 0.99572706

00:22:39.244 --> 00:22:40.525 I've spoken a lot about
NOTE Confidence: 0.99572706

00:22:40.525 --> 00:22:41.965 THC, but cannabis is a
NOTE Confidence: 0.99572706

00:22:41.965 --> 00:22:43.340 lot more than THC. As
NOTE Confidence: 0.99572706

00:22:43.340 --> 00:22:44.780 I mentioned earlier, there are
NOTE Confidence: 0.99572706

00:22:44.780 --> 00:22:46.080 at least hundred cannabinoids,
NOTE Confidence: 0.97439057

00:22:47.420 --> 00:22:49.020 present in cannabis and at

NOTE Confidence: 0.97439057
00:22:49.020 --> 00:22:50.400 least four hundred other,
NOTE Confidence: 0.7721496
00:22:50.859 --> 00:22:51.359 chemical
NOTE Confidence: 0.9628723
00:22:51.660 --> 00:22:53.580 constituents of cannabinoids, and some
NOTE Confidence: 0.9628723
00:22:53.580 --> 00:22:55.740 of those include terpenoids and
NOTE Confidence: 0.9628723
00:22:55.740 --> 00:22:56.240 flavonoids.
NOTE Confidence: 0.9587508
00:22:57.375 --> 00:22:59.055 We know that terpenoids are
NOTE Confidence: 0.9587508
00:22:59.055 --> 00:22:59.875 what impart
NOTE Confidence: 0.9992125
00:23:00.175 --> 00:23:01.715 the distinct aroma
NOTE Confidence: 0.936352
00:23:02.175 --> 00:23:02.835 of cannabis,
NOTE Confidence: 0.94842046
00:23:04.415 --> 00:23:06.015 and there's some interest now
NOTE Confidence: 0.94842046
00:23:06.015 --> 00:23:07.135 in looking at these at
NOTE Confidence: 0.94842046
00:23:07.135 --> 00:23:07.635 pharmacological
NOTE Confidence: 0.9967782
00:23:08.095 --> 00:23:08.595 doses.
NOTE Confidence: 0.9904872
00:23:09.359 --> 00:23:10.100 We acknowledge
NOTE Confidence: 0.9788949
00:23:10.480 --> 00:23:12.660 that THC is the dominant
NOTE Confidence: 0.9788949

00:23:12.720 --> 00:23:14.640 driver of the psychoactive effects
NOTE Confidence: 0.9788949

00:23:14.640 --> 00:23:15.380 of cannabis,
NOTE Confidence: 0.88918877

00:23:16.320 --> 00:23:17.140 and THC,
NOTE Confidence: 0.99220246

00:23:17.680 --> 00:23:18.820 together with CBD,
NOTE Confidence: 0.9513262

00:23:19.440 --> 00:23:20.400 seem to account for the
NOTE Confidence: 0.9513262

00:23:20.400 --> 00:23:22.100 majority of the known clinically
NOTE Confidence: 0.916206

00:23:22.640 --> 00:23:24.500 relevant effects of, cannabis.
NOTE Confidence: 0.9206691

00:23:25.174 --> 00:23:26.534 And these other compounds, these
NOTE Confidence: 0.9206691

00:23:26.534 --> 00:23:27.835 terpenoids and flavonoids,
NOTE Confidence: 0.9543806

00:23:28.534 --> 00:23:30.455 play a mostly secondary or
NOTE Confidence: 0.9543806

00:23:30.455 --> 00:23:30.955 modulatory
NOTE Confidence: 0.9964098

00:23:31.255 --> 00:23:31.755 role.
NOTE Confidence: 0.98220116

00:23:33.655 --> 00:23:34.635 Some have argued
NOTE Confidence: 0.9998221

00:23:35.015 --> 00:23:35.515 that
NOTE Confidence: 0.99923396

00:23:35.895 --> 00:23:37.275 these other constituents
NOTE Confidence: 0.983221

00:23:38.220 --> 00:23:40.159 of cannabis, including terpenes,

NOTE Confidence: 0.98821354
00:23:40.539 --> 00:23:42.480 flavonoids, and the minor cannabinoids,
NOTE Confidence: 0.9242477
00:23:44.140 --> 00:23:46.400 play something of an entourage
NOTE Confidence: 0.9242477
00:23:46.460 --> 00:23:46.960 effect.
NOTE Confidence: 0.99725866
00:23:47.740 --> 00:23:49.280 This is the idea of,
NOTE Confidence: 0.88064605
00:23:49.900 --> 00:23:52.159 let's say, illustrating here a
NOTE Confidence: 0.78108066
00:23:52.865 --> 00:23:53.925 a movie stars
NOTE Confidence: 0.89536333
00:23:54.305 --> 00:23:55.925 surrounded by an entourage
NOTE Confidence: 0.9355156
00:23:56.305 --> 00:23:58.145 where the entourage themselves may
NOTE Confidence: 0.9355156
00:23:58.145 --> 00:23:59.045 not have effects,
NOTE Confidence: 0.97854376
00:23:59.505 --> 00:24:00.005 but,
NOTE Confidence: 0.9764822
00:24:00.785 --> 00:24:01.285 they
NOTE Confidence: 0.95961136
00:24:01.665 --> 00:24:02.165 embellish,
NOTE Confidence: 0.99860644
00:24:02.865 --> 00:24:03.605 the aura
NOTE Confidence: 0.9359677
00:24:04.065 --> 00:24:04.565 of,
NOTE Confidence: 0.94653636
00:24:05.025 --> 00:24:06.485 of the, of the superstar.
NOTE Confidence: 0.9397314

00:24:08.450 --> 00:24:10.710 There's some data suggesting that
NOTE Confidence: 0.9397314

00:24:10.850 --> 00:24:12.470 some of the minor cannabinoids
NOTE Confidence: 0.9397314

00:24:12.530 --> 00:24:13.750 including cannabidural,
NOTE Confidence: 0.9522907

00:24:14.770 --> 00:24:15.270 cannabinol,
NOTE Confidence: 0.98756546

00:24:15.730 --> 00:24:17.430 and terpenes may modulate
NOTE Confidence: 0.9918394

00:24:18.210 --> 00:24:19.650 some of the effects of
NOTE Confidence: 0.9918394

00:24:19.650 --> 00:24:20.150 THC,
NOTE Confidence: 0.9936337

00:24:21.170 --> 00:24:23.030 and contribute in a subtle
NOTE Confidence: 0.9936337

00:24:23.244 --> 00:24:25.325 and context dependent way on
NOTE Confidence: 0.9936337

00:24:25.325 --> 00:24:25.984 the overall
NOTE Confidence: 0.91955304

00:24:26.445 --> 00:24:27.804 effects or the net effects
NOTE Confidence: 0.91955304

00:24:27.804 --> 00:24:29.744 of of cannabis. However,
NOTE Confidence: 0.9330425

00:24:32.284 --> 00:24:33.265 on their own,
NOTE Confidence: 0.98448133

00:24:33.725 --> 00:24:34.705 that is independently,
NOTE Confidence: 0.96472454

00:24:35.804 --> 00:24:37.005 there is not that much
NOTE Confidence: 0.96472454

00:24:37.005 --> 00:24:37.505 data

NOTE Confidence: 0.9658617
00:24:39.410 --> 00:24:41.830 and and very, very inconsistent
NOTE Confidence: 0.9895172
00:24:42.130 --> 00:24:43.970 data. So this concept of
NOTE Confidence: 0.9895172
00:24:43.970 --> 00:24:45.490 the entourage effect, which you
NOTE Confidence: 0.9895172
00:24:45.490 --> 00:24:46.609 might hear about a lot
NOTE Confidence: 0.9895172
00:24:46.609 --> 00:24:47.990 in the cannabinoid field,
NOTE Confidence: 0.9802468
00:24:48.530 --> 00:24:50.530 is not universally accepted and
NOTE Confidence: 0.9802468
00:24:50.530 --> 00:24:51.030 remains
NOTE Confidence: 0.9667192
00:24:51.410 --> 00:24:52.549 incompletely proven
NOTE Confidence: 0.99948215
00:24:52.850 --> 00:24:53.590 in humans.
NOTE Confidence: 0.85666347
00:24:56.405 --> 00:24:56.885 So,
NOTE Confidence: 0.9587841
00:24:59.525 --> 00:25:01.765 two minor cannabinoids that I,
NOTE Confidence: 0.89281404
00:25:02.725 --> 00:25:03.925 I want to point out,
NOTE Confidence: 0.94006544
00:25:04.325 --> 00:25:05.145 one is,
NOTE Confidence: 0.7970395
00:25:05.925 --> 00:25:06.425 cannabidural
NOTE Confidence: 0.889497
00:25:06.805 --> 00:25:08.025 and the other is cannabinol.
NOTE Confidence: 0.9434665

00:25:09.430 --> 00:25:10.890 One is a very weak
NOTE Confidence: 0.59885925

00:25:11.270 --> 00:25:11.770 potentially,
NOTE Confidence: 0.8775356

00:25:12.390 --> 00:25:13.750 c b one antagonist and
NOTE Confidence: 0.8775356

00:25:13.750 --> 00:25:14.550 the other is a weak
NOTE Confidence: 0.8775356

00:25:14.550 --> 00:25:15.450 partial agonist.
NOTE Confidence: 0.9556496

00:25:16.470 --> 00:25:17.930 They may reduce anxiety,
NOTE Confidence: 0.9708071

00:25:19.670 --> 00:25:21.450 and may have minimal sedating
NOTE Confidence: 0.9708071

00:25:21.510 --> 00:25:22.010 effects.
NOTE Confidence: 0.9171637

00:25:23.345 --> 00:25:24.865 The net effect on THC
NOTE Confidence: 0.9171637

00:25:24.865 --> 00:25:25.845 may be that cannabagiol
NOTE Confidence: 0.96495295

00:25:26.385 --> 00:25:28.225 might attenuate its effects, and
NOTE Confidence: 0.96495295

00:25:28.225 --> 00:25:30.865 cannabinol might slightly enhance the
NOTE Confidence: 0.96495295

00:25:30.865 --> 00:25:32.484 sedating effects of THC.
NOTE Confidence: 0.98851746

00:25:34.780 --> 00:25:36.140 Something else that you'd hear
NOTE Confidence: 0.98851746

00:25:36.140 --> 00:25:37.040 from your patients
NOTE Confidence: 0.9019148

00:25:37.660 --> 00:25:40.480 is this distinction between cannabis

NOTE Confidence: 0.9019148
00:25:40.540 --> 00:25:43.200 indica and can cannabis sativa.
NOTE Confidence: 0.99226725
00:25:44.220 --> 00:25:45.280 And I would argue,
NOTE Confidence: 0.9570356
00:25:45.980 --> 00:25:47.835 that we are struggling still
NOTE Confidence: 0.9570356
00:25:47.835 --> 00:25:49.195 struggling with whether this is
NOTE Confidence: 0.9570356
00:25:49.195 --> 00:25:50.815 science or or myth.
NOTE Confidence: 0.9982681
00:25:51.275 --> 00:25:52.494 The idea is that,
NOTE Confidence: 0.9434049
00:25:53.435 --> 00:25:53.835 that,
NOTE Confidence: 0.9848247
00:25:55.115 --> 00:25:56.655 if that that
NOTE Confidence: 0.88907486
00:25:57.115 --> 00:25:58.255 cannabis indica,
NOTE Confidence: 0.93922234
00:25:59.340 --> 00:26:00.859 may be more of a
NOTE Confidence: 0.93922234
00:26:00.859 --> 00:26:01.359 downer,
NOTE Confidence: 0.99783826
00:26:01.900 --> 00:26:03.900 whereas cannabis sativa might be
NOTE Confidence: 0.99783826
00:26:03.900 --> 00:26:05.200 more of an upper.
NOTE Confidence: 0.9951036
00:26:06.220 --> 00:26:08.140 The problem with this is
NOTE Confidence: 0.9951036
00:26:08.140 --> 00:26:09.520 that most of the cannabis
NOTE Confidence: 0.9951036

00:26:09.580 --> 00:26:10.559 that's available
NOTE Confidence: 0.9988303

00:26:11.505 --> 00:26:12.645 is highly mixed.
NOTE Confidence: 0.94874334

00:26:13.105 --> 00:26:15.105 It's not distinctly indica or
NOTE Confidence: 0.94874334

00:26:15.105 --> 00:26:15.605 sativa.
NOTE Confidence: 0.9617594

00:26:16.945 --> 00:26:18.405 And if you talk to,
NOTE Confidence: 0.9303917

00:26:19.905 --> 00:26:21.665 folks who, do research in
NOTE Confidence: 0.9303917

00:26:21.665 --> 00:26:22.405 this space,
NOTE Confidence: 0.9678715

00:26:22.785 --> 00:26:25.205 they are extremely skeptic skeptical
NOTE Confidence: 0.9678715

00:26:25.345 --> 00:26:25.744 of this,
NOTE Confidence: 0.9991742

00:26:26.500 --> 00:26:27.559 of this distinction.
NOTE Confidence: 0.9850428

00:26:29.059 --> 00:26:30.700 There's a feeling in in
NOTE Confidence: 0.9850428

00:26:30.980 --> 00:26:32.580 amongst researchers that this is
NOTE Confidence: 0.9850428

00:26:32.580 --> 00:26:33.080 really
NOTE Confidence: 0.9373139

00:26:33.539 --> 00:26:35.380 something that is exploited for
NOTE Confidence: 0.9373139

00:26:35.380 --> 00:26:36.440 marketing purposes,
NOTE Confidence: 0.9987683

00:26:37.220 --> 00:26:38.440 rather than pharmacological

NOTE Confidence: 0.9993405
00:26:38.820 --> 00:26:39.320 purposes.
NOTE Confidence: 0.99970526
00:26:41.804 --> 00:26:42.304 So
NOTE Confidence: 0.986024
00:26:42.605 --> 00:26:43.725 how do we think about
NOTE Confidence: 0.986024
00:26:43.725 --> 00:26:44.784 cannabis then?
NOTE Confidence: 0.9658188
00:26:46.284 --> 00:26:47.484 Many would argue that we
NOTE Confidence: 0.9658188
00:26:47.484 --> 00:26:49.725 might divide cannabis into three
NOTE Confidence: 0.9658188
00:26:49.725 --> 00:26:50.945 distinct types.
NOTE Confidence: 0.94247675
00:26:51.644 --> 00:26:53.725 One is THC dominant, the
NOTE Confidence: 0.94247675
00:26:53.725 --> 00:26:55.024 other CBD dominant,
NOTE Confidence: 0.99618566
00:26:55.519 --> 00:26:56.720 and the third is a
NOTE Confidence: 0.99618566
00:26:56.720 --> 00:26:58.899 balance between THC and CBD.
NOTE Confidence: 0.9475128
00:27:00.960 --> 00:27:02.340 As the names would suggest,
NOTE Confidence: 0.9475128
00:27:02.559 --> 00:27:04.000 the THC dominant has a
NOTE Confidence: 0.9475128
00:27:04.000 --> 00:27:05.679 very high THC content, low
NOTE Confidence: 0.9475128
00:27:05.679 --> 00:27:06.820 CBD content,
NOTE Confidence: 0.81590277

00:27:07.919 --> 00:27:08.419 and,
NOTE Confidence: 0.97380483
00:27:09.234 --> 00:27:10.595 has a variable content of
NOTE Confidence: 0.97380483
00:27:10.595 --> 00:27:11.575 other cannabinoids.
NOTE Confidence: 0.92886996
00:27:12.674 --> 00:27:14.914 Its typical effects include significant
NOTE Confidence: 0.92886996
00:27:14.914 --> 00:27:15.414 intoxication,
NOTE Confidence: 0.99598235
00:27:16.274 --> 00:27:16.774 euphoria,
NOTE Confidence: 0.79923767
00:27:17.395 --> 00:27:18.914 maybe analgesia as we talk
NOTE Confidence: 0.79923767
00:27:18.914 --> 00:27:19.414 about,
NOTE Confidence: 0.98362607
00:27:19.875 --> 00:27:21.715 but there's also a risk
NOTE Confidence: 0.98362607
00:27:21.715 --> 00:27:23.895 for more unpleasant effects, including
NOTE Confidence: 0.9945934
00:27:24.330 --> 00:27:25.150 anxiety, paranoia,
NOTE Confidence: 0.99732065
00:27:26.330 --> 00:27:26.830 psychosis.
NOTE Confidence: 0.9995091
00:27:27.450 --> 00:27:28.190 In contrast,
NOTE Confidence: 0.99759465
00:27:28.650 --> 00:27:30.270 CBD dominant cannabis
NOTE Confidence: 0.94577414
00:27:31.289 --> 00:27:32.830 produces minimal intoxication
NOTE Confidence: 0.9274328
00:27:33.850 --> 00:27:34.350 and

NOTE Confidence: 0.7645316
00:27:35.130 --> 00:27:35.950 is generally
NOTE Confidence: 0.99725336
00:27:36.625 --> 00:27:39.025 well tolerated relative to THC
NOTE Confidence: 0.99725336
00:27:39.025 --> 00:27:39.924 dominant cannabis.
NOTE Confidence: 0.9889774
00:27:40.785 --> 00:27:42.725 Also, THC dominant cannabis
NOTE Confidence: 0.74722874
00:27:43.424 --> 00:27:43.924 may
NOTE Confidence: 0.92151004
00:27:45.424 --> 00:27:47.585 be more abuse liable relative
NOTE Confidence: 0.92151004
00:27:47.585 --> 00:27:49.125 to CBD dominant cannabis,
NOTE Confidence: 0.9982098
00:27:49.730 --> 00:27:50.550 and the balanced version
NOTE Confidence: 0.95338315
00:27:51.090 --> 00:27:52.950 is falls somewhere in between.
NOTE Confidence: 0.9837211
00:27:57.170 --> 00:27:58.930 So what has changed over
NOTE Confidence: 0.9837211
00:27:58.930 --> 00:28:00.530 the last maybe three decades
NOTE Confidence: 0.9837211
00:28:00.530 --> 00:28:01.730 or so is that the
NOTE Confidence: 0.9837211
00:28:01.730 --> 00:28:03.350 THC content of cannabis
NOTE Confidence: 0.99798244
00:28:04.125 --> 00:28:05.425 continues to increase.
NOTE Confidence: 0.9577284
00:28:06.365 --> 00:28:08.845 This is, data from University
NOTE Confidence: 0.9577284

00:28:08.845 --> 00:28:09.665 of Mississippi,
NOTE Confidence: 0.97670496

00:28:10.525 --> 00:28:11.585 which has been tasked
NOTE Confidence: 0.9945845

00:28:12.045 --> 00:28:13.565 for the last forty years
NOTE Confidence: 0.9945845

00:28:13.565 --> 00:28:14.065 to
NOTE Confidence: 0.99539006

00:28:14.525 --> 00:28:16.445 to test the THC and
NOTE Confidence: 0.99539006

00:28:16.445 --> 00:28:17.585 CBD content
NOTE Confidence: 0.96696854

00:28:18.010 --> 00:28:19.789 of cannabis that's been seized
NOTE Confidence: 0.96696854

00:28:19.850 --> 00:28:21.789 by the Drug Enforcement Agency.
NOTE Confidence: 0.98607284

00:28:22.330 --> 00:28:23.289 And you can see here
NOTE Confidence: 0.98607284

00:28:23.289 --> 00:28:23.770 that,
NOTE Confidence: 0.98473376

00:28:24.330 --> 00:28:25.690 in nineteen ninety five, the
NOTE Confidence: 0.98473376

00:28:25.690 --> 00:28:27.530 average THC content was about
NOTE Confidence: 0.98473376

00:28:27.530 --> 00:28:28.270 four percent.
NOTE Confidence: 0.98429835

00:28:28.970 --> 00:28:30.490 In twenty twenty two, it
NOTE Confidence: 0.98429835

00:28:30.490 --> 00:28:32.350 was closer to sixteen percent,
NOTE Confidence: 0.9767192

00:28:33.015 --> 00:28:34.455 and it continues to grow.

NOTE Confidence: 0.9767192

00:28:34.455 --> 00:28:36.135 In contrast, the CBD content

NOTE Confidence: 0.9767192

00:28:36.135 --> 00:28:38.075 of cannabis has remained relatively

NOTE Confidence: 0.97975796

00:28:39.015 --> 00:28:40.315 stable over time.

NOTE Confidence: 0.9644398

00:28:42.455 --> 00:28:44.475 Now cannabis is only one

NOTE Confidence: 0.9644398

00:28:44.615 --> 00:28:45.809 of the many ways that

NOTE Confidence: 0.9644398

00:28:45.809 --> 00:28:47.650 people can use cannabinoids, and

NOTE Confidence: 0.9644398

00:28:47.650 --> 00:28:49.169 then a staggering array of

NOTE Confidence: 0.9644398

00:28:49.169 --> 00:28:51.110 other products derived from cannabis

NOTE Confidence: 0.9644398

00:28:51.169 --> 00:28:52.530 that you should be aware

NOTE Confidence: 0.9644398

00:28:52.530 --> 00:28:53.030 of.

NOTE Confidence: 0.9972785

00:28:54.690 --> 00:28:55.650 And to put that in

NOTE Confidence: 0.9972785

00:28:55.650 --> 00:28:56.150 perspective,

NOTE Confidence: 0.9558919

00:28:58.049 --> 00:28:58.549 the

NOTE Confidence: 0.9722358

00:28:59.395 --> 00:29:01.815 the THC content of cannabis,

NOTE Confidence: 0.9722358

00:29:02.035 --> 00:29:03.155 for example, in the state

NOTE Confidence: 0.9722358

00:29:03.155 --> 00:29:04.595 of Connecticut that's shown in

NOTE Confidence: 0.9722358

00:29:04.595 --> 00:29:05.095 dispensaries,

NOTE Confidence: 0.973425

00:29:06.434 --> 00:29:07.795 has a cap at thirty

NOTE Confidence: 0.973425

00:29:07.795 --> 00:29:09.635 five percent THC. So this

NOTE Confidence: 0.973425

00:29:09.635 --> 00:29:11.235 is cannabis that you can

NOTE Confidence: 0.973425

00:29:11.235 --> 00:29:12.675 buy at a dispensary in

NOTE Confidence: 0.973425

00:29:12.675 --> 00:29:14.195 the state of Connecticut. In

NOTE Confidence: 0.973425

00:29:14.195 --> 00:29:14.934 other states,

NOTE Confidence: 0.99528456

00:29:15.820 --> 00:29:17.580 other states do allow the

NOTE Confidence: 0.99528456

00:29:17.580 --> 00:29:19.419 THC content of cannabis to

NOTE Confidence: 0.99528456

00:29:19.419 --> 00:29:20.620 be even higher than thirty

NOTE Confidence: 0.99528456

00:29:20.620 --> 00:29:21.360 five percent.

NOTE Confidence: 0.94786406

00:29:22.139 --> 00:29:23.100 And to put that in

NOTE Confidence: 0.94786406

00:29:23.100 --> 00:29:25.019 perspective, that's about ten ten

NOTE Confidence: 0.94786406

00:29:25.019 --> 00:29:26.860 times higher than what the

NOTE Confidence: 0.94786406

00:29:26.860 --> 00:29:28.779 average THC content was in

NOTE Confidence: 0.94786406

00:29:28.779 --> 00:29:30.915 cannabis in nineteen ninety five.

NOTE Confidence: 0.9913844

00:29:31.395 --> 00:29:32.835 And beyond that, we now

NOTE Confidence: 0.9913844

00:29:32.835 --> 00:29:34.055 have a number of,

NOTE Confidence: 0.9912098

00:29:34.835 --> 00:29:35.955 products that we refer to

NOTE Confidence: 0.9912098

00:29:35.955 --> 00:29:36.695 as concentrates

NOTE Confidence: 0.98521614

00:29:37.555 --> 00:29:39.255 that may have a THC

NOTE Confidence: 0.98521614

00:29:39.315 --> 00:29:41.635 content of ninety percent. So

NOTE Confidence: 0.98521614

00:29:41.635 --> 00:29:42.135 that's,

NOTE Confidence: 0.9922643

00:29:43.170 --> 00:29:44.770 almost twenty times twenty to

NOTE Confidence: 0.9922643

00:29:44.770 --> 00:29:46.450 thirty times more than the

NOTE Confidence: 0.9922643

00:29:46.450 --> 00:29:47.910 THC content of cannabis,

NOTE Confidence: 0.97610795

00:29:48.930 --> 00:29:50.230 in the nineteen nineties.

NOTE Confidence: 0.96245706

00:29:51.010 --> 00:29:52.290 Why is that important? It's

NOTE Confidence: 0.96245706

00:29:52.290 --> 00:29:53.810 important because for from a

NOTE Confidence: 0.96245706

00:29:53.810 --> 00:29:55.410 number of different perspectives. That

NOTE Confidence: 0.96245706

00:29:55.410 --> 00:29:56.955 is that if we believe
NOTE Confidence: 0.96245706

00:29:56.955 --> 00:29:58.735 that the effects of cannabis
NOTE Confidence: 0.84533995

00:29:59.195 --> 00:30:00.495 THC are dose related,
NOTE Confidence: 0.98717546

00:30:00.875 --> 00:30:01.775 then as,
NOTE Confidence: 0.99076146

00:30:02.475 --> 00:30:04.235 people use these more potent
NOTE Confidence: 0.99076146

00:30:04.235 --> 00:30:05.535 products, you might expect,
NOTE Confidence: 0.9992146

00:30:06.395 --> 00:30:08.555 greater effects. That's number one.
NOTE Confidence: 0.9992146

00:30:08.555 --> 00:30:09.295 The second
NOTE Confidence: 0.9918771

00:30:10.380 --> 00:30:11.820 important issue to keep in
NOTE Confidence: 0.9918771

00:30:11.820 --> 00:30:12.800 mind is that
NOTE Confidence: 0.9190365

00:30:13.180 --> 00:30:14.960 studies would that were done
NOTE Confidence: 0.9190365

00:30:15.020 --> 00:30:15.760 on the
NOTE Confidence: 0.9988663

00:30:16.380 --> 00:30:16.880 consequences
NOTE Confidence: 0.98677933

00:30:17.180 --> 00:30:18.620 of cannabis use from the
NOTE Confidence: 0.98677933

00:30:18.620 --> 00:30:20.480 nineteen eighties and nineteen nineties
NOTE Confidence: 0.98677933

00:30:20.540 --> 00:30:21.520 may not extrapolate

NOTE Confidence: 0.9632667

00:30:22.125 --> 00:30:23.565 to the current landscape of

NOTE Confidence: 0.9632667

00:30:23.565 --> 00:30:25.565 cannabis where cannabis is much

NOTE Confidence: 0.9632667

00:30:25.565 --> 00:30:27.025 more potent than it was

NOTE Confidence: 0.9632667

00:30:27.245 --> 00:30:28.445 back in the eighties and

NOTE Confidence: 0.9632667

00:30:28.445 --> 00:30:28.945 nineties,

NOTE Confidence: 0.9976799

00:30:29.245 --> 00:30:30.865 and we have these really

NOTE Confidence: 0.99673206

00:30:31.165 --> 00:30:33.405 potent products available, which have

NOTE Confidence: 0.99673206

00:30:33.405 --> 00:30:35.425 about ninety percent THC content.

NOTE Confidence: 0.78810257

00:30:36.580 --> 00:30:36.980 And and and the

NOTE Confidence: 0.9973025

00:30:38.419 --> 00:30:40.340 another consequence of that is

NOTE Confidence: 0.9973025

00:30:40.340 --> 00:30:40.840 that

NOTE Confidence: 0.99422455

00:30:41.220 --> 00:30:42.659 studies that were done back

NOTE Confidence: 0.99422455

00:30:42.659 --> 00:30:44.200 in the seventies and eighties,

NOTE Confidence: 0.97503257

00:30:45.460 --> 00:30:46.980 that showed that only one

NOTE Confidence: 0.97503257

00:30:46.980 --> 00:30:48.100 in ten people who use

NOTE Confidence: 0.97503257

00:30:48.100 --> 00:30:50.360 cannabis developed cannabis use disorder.

NOTE Confidence: 0.9933281

00:30:52.115 --> 00:30:53.715 The the more recent studies

NOTE Confidence: 0.9933281

00:30:53.715 --> 00:30:55.235 looking at the current landscape

NOTE Confidence: 0.9933281

00:30:55.235 --> 00:30:57.014 of cannabis would suggest that

NOTE Confidence: 0.9838386

00:30:57.554 --> 00:30:58.755 one in three people who

NOTE Confidence: 0.9838386

00:30:58.755 --> 00:31:00.595 use cannabis will develop cannabis

NOTE Confidence: 0.9838386

00:31:00.595 --> 00:31:01.414 use disorder.

NOTE Confidence: 0.99406856

00:31:01.715 --> 00:31:02.395 And that's,

NOTE Confidence: 0.9827309

00:31:02.835 --> 00:31:04.914 I think, directly related to

NOTE Confidence: 0.9827309

00:31:04.914 --> 00:31:06.135 the THC content

NOTE Confidence: 0.9420246

00:31:06.520 --> 00:31:07.260 of Canvas.

NOTE Confidence: 0.9234137

00:31:08.120 --> 00:31:09.559 So these are some of

NOTE Confidence: 0.9234137

00:31:09.559 --> 00:31:11.240 the products that are available

NOTE Confidence: 0.9234137

00:31:11.240 --> 00:31:13.660 with unusual names like, shatter,

NOTE Confidence: 0.9049908

00:31:14.280 --> 00:31:15.100 and DHL.

NOTE Confidence: 0.95956296

00:31:16.200 --> 00:31:17.720 The basic idea behind these

NOTE Confidence: 0.95956296

00:31:17.720 --> 00:31:19.900 studies these products is that,

NOTE Confidence: 0.9703769

00:31:20.395 --> 00:31:22.415 they use different techniques, including

NOTE Confidence: 0.9703769

00:31:22.715 --> 00:31:23.615 using butane

NOTE Confidence: 0.9775554

00:31:24.075 --> 00:31:25.355 to leach out all the

NOTE Confidence: 0.9775554

00:31:25.355 --> 00:31:27.615 THC from herbal cannabis material

NOTE Confidence: 0.9887167

00:31:27.995 --> 00:31:29.434 and to extract this wax

NOTE Confidence: 0.9887167

00:31:29.434 --> 00:31:30.175 like substance.

NOTE Confidence: 0.983789

00:31:31.355 --> 00:31:32.315 The way that,

NOTE Confidence: 0.96179205

00:31:32.795 --> 00:31:34.555 these compounds are used is

NOTE Confidence: 0.96179205

00:31:34.555 --> 00:31:35.615 either in a,

NOTE Confidence: 0.9626439

00:31:36.049 --> 00:31:37.410 in a in a a

NOTE Confidence: 0.9626439

00:31:37.410 --> 00:31:38.309 vaping cartridge

NOTE Confidence: 0.99484605

00:31:38.770 --> 00:31:40.049 or by heating up a

NOTE Confidence: 0.99484605

00:31:40.049 --> 00:31:40.870 glass rod,

NOTE Confidence: 0.956776

00:31:41.330 --> 00:31:42.630 dipping it in there, and

NOTE Confidence: 0.956776

00:31:42.850 --> 00:31:43.990 inhaling the vapors.
NOTE Confidence: 0.9995233

00:31:44.370 --> 00:31:44.870 Again,
NOTE Confidence: 0.9987049

00:31:45.250 --> 00:31:46.470 these products contain
NOTE Confidence: 0.9592182

00:31:47.570 --> 00:31:49.030 up to ninety five percent,
NOTE Confidence: 0.9375725

00:31:49.410 --> 00:31:50.610 THC and so are really
NOTE Confidence: 0.9375725

00:31:50.610 --> 00:31:52.005 potent, and we are seeing
NOTE Confidence: 0.9375725

00:31:52.005 --> 00:31:53.305 some negative consequences,
NOTE Confidence: 0.99949265

00:31:53.925 --> 00:31:55.125 associated with the use of
NOTE Confidence: 0.99949265

00:31:55.125 --> 00:31:55.865 these products.
NOTE Confidence: 0.9766039

00:31:57.925 --> 00:31:58.425 So
NOTE Confidence: 0.95428485

00:31:59.845 --> 00:32:01.605 route of administration is really
NOTE Confidence: 0.95428485

00:32:01.605 --> 00:32:03.285 important, and I'll get to
NOTE Confidence: 0.95428485

00:32:03.285 --> 00:32:04.610 to that in a in
NOTE Confidence: 0.95428485

00:32:04.610 --> 00:32:05.890 a minute, especially if you're
NOTE Confidence: 0.95428485

00:32:05.890 --> 00:32:07.430 thinking about designing studies.
NOTE Confidence: 0.91822296

00:32:07.810 --> 00:32:08.610 Of course, you know, the

NOTE Confidence: 0.91822296
00:32:08.610 --> 00:32:10.050 typical the most common way
NOTE Confidence: 0.91822296
00:32:10.050 --> 00:32:11.730 that people use consume cannabis
NOTE Confidence: 0.91822296
00:32:11.730 --> 00:32:12.630 is by inhalation,
NOTE Confidence: 0.98390967
00:32:13.810 --> 00:32:15.250 and why that might be
NOTE Confidence: 0.98390967
00:32:15.250 --> 00:32:16.450 important for you for you
NOTE Confidence: 0.98390967
00:32:16.450 --> 00:32:17.650 all if you're thinking about
NOTE Confidence: 0.98390967
00:32:17.650 --> 00:32:18.150 doing,
NOTE Confidence: 0.79779994
00:32:19.895 --> 00:32:20.554 you know,
NOTE Confidence: 0.9640319
00:32:21.015 --> 00:32:22.934 conducting clinical trials is that
NOTE Confidence: 0.9640319
00:32:22.934 --> 00:32:24.535 it's unlikely the that the
NOTE Confidence: 0.9640319
00:32:24.535 --> 00:32:26.075 FDA will ever approve
NOTE Confidence: 0.90746874
00:32:26.615 --> 00:32:27.975 any product that needs to
NOTE Confidence: 0.90746874
00:32:27.975 --> 00:32:29.195 be in smoke.
NOTE Confidence: 0.9806421
00:32:29.735 --> 00:32:30.855 So that's clearly off the
NOTE Confidence: 0.9806421
00:32:30.855 --> 00:32:31.355 table.
NOTE Confidence: 0.9632665

00:32:32.930 --> 00:32:34.850 Another more common way of
NOTE Confidence: 0.9632665

00:32:34.850 --> 00:32:35.430 of using,
NOTE Confidence: 0.9607897

00:32:35.810 --> 00:32:37.190 cannabis products is,
NOTE Confidence: 0.99108255

00:32:37.650 --> 00:32:39.350 by by using it orally,
NOTE Confidence: 0.9780433

00:32:40.210 --> 00:32:41.990 especially amongst older individuals,
NOTE Confidence: 0.97092754

00:32:42.930 --> 00:32:44.390 who prefer using edibles,
NOTE Confidence: 0.982823

00:32:45.315 --> 00:32:46.595 that are sold in in
NOTE Confidence: 0.982823

00:32:46.595 --> 00:32:48.455 doses of anywhere from five,
NOTE Confidence: 0.99516124

00:32:48.835 --> 00:32:49.335 ten
NOTE Confidence: 0.89515734

00:32:49.635 --> 00:32:50.695 milligram increments.
NOTE Confidence: 0.9759888

00:32:52.355 --> 00:32:52.855 But
NOTE Confidence: 0.7866204

00:32:53.315 --> 00:32:53.715 but,
NOTE Confidence: 0.89683276

00:32:54.195 --> 00:32:55.395 there are a number of
NOTE Confidence: 0.89683276

00:32:55.395 --> 00:32:56.455 other oral products
NOTE Confidence: 0.9785051

00:32:56.835 --> 00:32:57.335 available.
NOTE Confidence: 0.96630126

00:32:58.260 --> 00:32:59.620 There are topical products that

NOTE Confidence: 0.96630126

00:32:59.620 --> 00:33:00.980 are also available. I don't

NOTE Confidence: 0.96630126

00:33:00.980 --> 00:33:02.260 really know too much about

NOTE Confidence: 0.96630126

00:33:02.260 --> 00:33:03.140 them. And then, of course,

NOTE Confidence: 0.96630126

00:33:03.140 --> 00:33:04.820 there are also some rectal

NOTE Confidence: 0.96630126

00:33:04.820 --> 00:33:07.060 and vaginal support suppositories that

NOTE Confidence: 0.96630126

00:33:07.060 --> 00:33:08.520 are available, and that's pretty,

NOTE Confidence: 0.79336244

00:33:09.300 --> 00:33:10.500 the use of this product

NOTE Confidence: 0.79336244

00:33:10.500 --> 00:33:11.140 is pretty,

NOTE Confidence: 0.9995345

00:33:11.620 --> 00:33:12.120 rare.

NOTE Confidence: 0.96130186

00:33:13.215 --> 00:33:14.434 So what are the implications

NOTE Confidence: 0.96130186

00:33:14.495 --> 00:33:15.535 of this from a drug

NOTE Confidence: 0.96130186

00:33:15.535 --> 00:33:16.655 development point of view or

NOTE Confidence: 0.96130186

00:33:16.655 --> 00:33:18.095 from the point of view

NOTE Confidence: 0.96130186

00:33:18.095 --> 00:33:18.755 of treating,

NOTE Confidence: 0.9220217

00:33:19.615 --> 00:33:20.815 treating pain? I'm gonna skip

NOTE Confidence: 0.9220217

00:33:20.815 --> 00:33:22.115 this slide since I've already
NOTE Confidence: 0.9380079

00:33:22.815 --> 00:33:23.955 told you about it.
NOTE Confidence: 0.99537665

00:33:24.415 --> 00:33:25.475 Is that the pharmacokinetics
NOTE Confidence: 0.9474735

00:33:27.610 --> 00:33:29.470 of palming and oral THC
NOTE Confidence: 0.99904513

00:33:29.770 --> 00:33:30.669 are quite different.
NOTE Confidence: 0.9794514

00:33:31.450 --> 00:33:33.850 So when someone smokes or
NOTE Confidence: 0.9794514

00:33:33.850 --> 00:33:34.350 vapes,
NOTE Confidence: 0.9991353

00:33:35.370 --> 00:33:35.530 THC,
NOTE Confidence: 0.96223384

00:33:37.370 --> 00:33:38.910 the time to peak plasma
NOTE Confidence: 0.96223384

00:33:39.049 --> 00:33:41.290 levels is within minutes, three
NOTE Confidence: 0.96223384

00:33:41.290 --> 00:33:42.190 to ten minutes,
NOTE Confidence: 0.96109885

00:33:43.505 --> 00:33:45.105 And so people experience the
NOTE Confidence: 0.96109885

00:33:45.105 --> 00:33:45.605 effects
NOTE Confidence: 0.81886816

00:33:46.065 --> 00:33:46.885 fairly quickly,
NOTE Confidence: 0.98840964

00:33:47.745 --> 00:33:49.924 the psychotropic effects fairly quickly.
NOTE Confidence: 0.9974055

00:33:50.465 --> 00:33:52.225 The effects usually peak about

NOTE Confidence: 0.9974055
00:33:52.225 --> 00:33:53.845 fifteen to thirty minutes later
NOTE Confidence: 0.91011184
00:33:54.304 --> 00:33:55.585 and last for a hundred
NOTE Confidence: 0.91011184
00:33:55.585 --> 00:33:56.865 and twenty two two hours
NOTE Confidence: 0.91011184
00:33:56.865 --> 00:33:58.325 to two to three hours.
NOTE Confidence: 0.99470025
00:33:59.320 --> 00:34:00.220 And the bioavailability
NOTE Confidence: 0.9378086
00:34:00.759 --> 00:34:02.360 of THC when smoked or
NOTE Confidence: 0.9378086
00:34:02.360 --> 00:34:03.659 vaped is fairly high.
NOTE Confidence: 0.94618875
00:34:04.200 --> 00:34:05.559 The other important piece of
NOTE Confidence: 0.94618875
00:34:05.559 --> 00:34:06.919 this is that when a
NOTE Confidence: 0.94618875
00:34:06.919 --> 00:34:08.440 person smokes or in or
NOTE Confidence: 0.94618875
00:34:08.440 --> 00:34:08.940 vapes,
NOTE Confidence: 0.99898756
00:34:09.480 --> 00:34:11.180 they have the capacity to
NOTE Confidence: 0.9662783
00:34:11.744 --> 00:34:13.684 titrate the dose with exquisite
NOTE Confidence: 0.9662783
00:34:13.904 --> 00:34:14.404 precision
NOTE Confidence: 0.94588715
00:34:14.944 --> 00:34:16.244 in real time. Because
NOTE Confidence: 0.99912566

00:34:16.625 --> 00:34:18.305 if someone hasn't had too
NOTE Confidence: 0.99912566

00:34:18.305 --> 00:34:19.344 much of an effect, they
NOTE Confidence: 0.99912566

00:34:19.344 --> 00:34:20.565 can take another hit
NOTE Confidence: 0.95399857

00:34:21.025 --> 00:34:22.545 and get to that desired
NOTE Confidence: 0.95399857

00:34:22.545 --> 00:34:24.384 effect. If someone has had
NOTE Confidence: 0.95399857

00:34:24.384 --> 00:34:24.900 too much
NOTE Confidence: 0.99788886

00:34:25.859 --> 00:34:26.819 if the effects are too
NOTE Confidence: 0.99788886

00:34:26.819 --> 00:34:27.319 intense,
NOTE Confidence: 0.96393794

00:34:27.619 --> 00:34:28.819 they just hold off on
NOTE Confidence: 0.96393794

00:34:28.819 --> 00:34:30.200 when their next hit is.
NOTE Confidence: 0.9989668

00:34:30.500 --> 00:34:31.319 In contrast,
NOTE Confidence: 0.97051007

00:34:31.779 --> 00:34:33.880 when someone consumes an edible
NOTE Confidence: 0.97051007

00:34:33.940 --> 00:34:35.239 shown here in red,
NOTE Confidence: 0.9650936

00:34:35.940 --> 00:34:37.859 the effects only emerge about
NOTE Confidence: 0.9650936

00:34:37.859 --> 00:34:39.400 two to three hours later.
NOTE Confidence: 0.96046084

00:34:41.744 --> 00:34:43.344 The peak effects are two

NOTE Confidence: 0.96046084

00:34:43.344 --> 00:34:44.945 to three hours later. The

NOTE Confidence: 0.96046084

00:34:44.945 --> 00:34:46.945 onset of psychotropic effects is

NOTE Confidence: 0.96046084

00:34:46.945 --> 00:34:47.905 an hour to an hour

NOTE Confidence: 0.96046084

00:34:47.905 --> 00:34:48.805 and a half later,

NOTE Confidence: 0.9524016

00:34:49.825 --> 00:34:51.344 and the duration of effects

NOTE Confidence: 0.9524016

00:34:51.344 --> 00:34:53.605 is highly variable, anywhere from

NOTE Confidence: 0.9524016

00:34:53.825 --> 00:34:54.325 four

NOTE Confidence: 0.9976089

00:34:56.410 --> 00:34:57.230 to six

NOTE Confidence: 0.96120757

00:34:57.770 --> 00:34:59.210 to to to more than,

NOTE Confidence: 0.9554651

00:35:00.570 --> 00:35:01.310 eight hours,

NOTE Confidence: 0.9982888

00:35:02.090 --> 00:35:03.310 depending on the

NOTE Confidence: 0.9814539

00:35:03.930 --> 00:35:04.590 the metabolism

NOTE Confidence: 0.9985201

00:35:04.890 --> 00:35:06.110 of the of the drug.

NOTE Confidence: 0.9233435

00:35:06.810 --> 00:35:08.190 And, again, here, the bioavailability

NOTE Confidence: 0.9899909

00:35:08.730 --> 00:35:10.489 of THC when consumed orally

NOTE Confidence: 0.9899909

00:35:10.489 --> 00:35:12.315 is is quite slow.
NOTE Confidence: 0.999637

00:35:12.614 --> 00:35:13.114 So
NOTE Confidence: 0.99725956

00:35:14.055 --> 00:35:15.255 there are some pros and
NOTE Confidence: 0.99725956

00:35:15.255 --> 00:35:16.155 cons to,
NOTE Confidence: 0.9862013

00:35:16.935 --> 00:35:17.995 the route of administration.
NOTE Confidence: 0.87097657

00:35:20.215 --> 00:35:21.915 When smoked or vaped,
NOTE Confidence: 0.991283

00:35:22.455 --> 00:35:24.295 people feel in control of
NOTE Confidence: 0.991283

00:35:24.295 --> 00:35:25.415 the effects, and they can
NOTE Confidence: 0.991283

00:35:25.415 --> 00:35:27.730 control it with exquisite precision.
NOTE Confidence: 0.99745435

00:35:28.510 --> 00:35:30.290 When people consume an edible,
NOTE Confidence: 0.99745435

00:35:30.510 --> 00:35:31.969 they don't have control.
NOTE Confidence: 0.9862699

00:35:32.670 --> 00:35:34.190 On the other hand, the
NOTE Confidence: 0.9862699

00:35:34.190 --> 00:35:35.790 effects of the edible last
NOTE Confidence: 0.9862699

00:35:35.790 --> 00:35:36.849 for much longer.
NOTE Confidence: 0.9806614

00:35:37.310 --> 00:35:39.010 The onset and the slope
NOTE Confidence: 0.9806614

00:35:39.150 --> 00:35:40.190 of the or the rise

NOTE Confidence: 0.9806614
00:35:40.190 --> 00:35:41.569 in the in effects
NOTE Confidence: 0.9769455
00:35:42.114 --> 00:35:43.955 also tends to be, much
NOTE Confidence: 0.9769455
00:35:43.955 --> 00:35:45.555 slower. And so, therefore, it's
NOTE Confidence: 0.9769455
00:35:45.555 --> 00:35:47.094 not by accident that
NOTE Confidence: 0.9218775
00:35:47.715 --> 00:35:49.255 in in general, people
NOTE Confidence: 0.9972663
00:35:50.114 --> 00:35:51.175 don't abuse
NOTE Confidence: 0.99967134
00:35:51.475 --> 00:35:53.335 edibles to the same extent
NOTE Confidence: 0.9061861
00:35:53.795 --> 00:35:55.015 as they may have used
NOTE Confidence: 0.9061861
00:35:55.075 --> 00:35:57.094 smoked or baked products.
NOTE Confidence: 0.99514973
00:36:00.460 --> 00:36:01.900 Okay. So what are the
NOTE Confidence: 0.99514973
00:36:01.900 --> 00:36:03.279 cannabinoids that are currently
NOTE Confidence: 0.9417813
00:36:03.579 --> 00:36:05.579 in use on in, in
NOTE Confidence: 0.9417813
00:36:05.739 --> 00:36:06.640 or in the pipeline?
NOTE Confidence: 0.9874629
00:36:09.260 --> 00:36:09.660 So,
NOTE Confidence: 0.9800164
00:36:10.219 --> 00:36:10.619 these
NOTE Confidence: 0.99044514

00:36:11.525 --> 00:36:13.205 the three columns show drugs
NOTE Confidence: 0.99044514

00:36:13.205 --> 00:36:13.864 that are
NOTE Confidence: 0.974807

00:36:14.165 --> 00:36:15.705 already approved and marketed,
NOTE Confidence: 0.9195446

00:36:16.245 --> 00:36:17.605 those that are in clinical
NOTE Confidence: 0.9195446

00:36:17.605 --> 00:36:18.965 development, and those that are
NOTE Confidence: 0.9195446

00:36:18.965 --> 00:36:20.965 in preclinical development. So there
NOTE Confidence: 0.9195446

00:36:20.965 --> 00:36:21.925 are a number of c
NOTE Confidence: 0.9195446

00:36:21.925 --> 00:36:23.844 d one are agonists that
NOTE Confidence: 0.9195446

00:36:23.844 --> 00:36:24.505 are available.
NOTE Confidence: 0.9176178

00:36:25.640 --> 00:36:27.739 They include dronabinol, which is
NOTE Confidence: 0.9176178

00:36:27.800 --> 00:36:28.300 THC,
NOTE Confidence: 0.9481081

00:36:28.920 --> 00:36:30.760 and nabilone, which is a
NOTE Confidence: 0.9481081

00:36:30.760 --> 00:36:31.820 synthetic analog
NOTE Confidence: 0.95846903

00:36:32.280 --> 00:36:32.940 of THC.
NOTE Confidence: 0.9746583

00:36:33.560 --> 00:36:35.000 Both those drugs are FDA
NOTE Confidence: 0.9746583

00:36:35.000 --> 00:36:35.500 approved,

NOTE Confidence: 0.9986846

00:36:35.960 --> 00:36:37.640 and the primary indication is

NOTE Confidence: 0.9986846

00:36:37.640 --> 00:36:38.140 for

NOTE Confidence: 0.9940532

00:36:38.475 --> 00:36:40.655 chemotherapy induced nausea and vomiting.

NOTE Confidence: 0.9939866

00:36:41.355 --> 00:36:42.495 There's another product,

NOTE Confidence: 0.93798584

00:36:43.035 --> 00:36:44.795 that's available but outside the

NOTE Confidence: 0.93798584

00:36:44.795 --> 00:36:46.475 US and Canada, Mexico, and

NOTE Confidence: 0.93798584

00:36:46.475 --> 00:36:47.215 and Europe,

NOTE Confidence: 0.9501573

00:36:48.795 --> 00:36:50.235 known under the brand name

NOTE Confidence: 0.9501573

00:36:50.235 --> 00:36:51.614 Sativex or nabiximans.

NOTE Confidence: 0.9835125

00:36:52.075 --> 00:36:53.135 This is a balance

NOTE Confidence: 0.93229944

00:36:53.719 --> 00:36:55.079 of one of near one

NOTE Confidence: 0.93229944

00:36:55.079 --> 00:36:56.680 to one ratio of THC

NOTE Confidence: 0.93229944

00:36:56.680 --> 00:36:57.420 and CBD,

NOTE Confidence: 0.8565526

00:36:59.000 --> 00:37:00.140 sold as a as

NOTE Confidence: 0.94541925

00:37:01.079 --> 00:37:01.819 a as a spray,

NOTE Confidence: 0.8892786

00:37:02.599 --> 00:37:04.380 as an oral mucosal spray.
NOTE Confidence: 0.9929162

00:37:05.239 --> 00:37:06.735 And it seems like
NOTE Confidence: 0.9661361

00:37:07.295 --> 00:37:09.475 from reports it's better tolerated
NOTE Confidence: 0.9661361

00:37:09.695 --> 00:37:10.915 than THC alone.
NOTE Confidence: 0.97068626

00:37:11.935 --> 00:37:13.715 Now in what's in clinical
NOTE Confidence: 0.97068626

00:37:13.855 --> 00:37:15.375 development include a number of
NOTE Confidence: 0.97068626

00:37:15.375 --> 00:37:16.915 other THC rich formulations,
NOTE Confidence: 0.9042873

00:37:17.775 --> 00:37:18.595 and historically,
NOTE Confidence: 0.9765559

00:37:19.550 --> 00:37:20.510 there have been a number
NOTE Confidence: 0.9765559

00:37:20.510 --> 00:37:21.869 of other drugs that were
NOTE Confidence: 0.9765559

00:37:21.869 --> 00:37:23.250 developed that were abandoned,
NOTE Confidence: 0.9412294

00:37:23.710 --> 00:37:25.410 including the drug levonantrodal.
NOTE Confidence: 0.9978932

00:37:26.190 --> 00:37:27.730 It was developed by Pfizer.
NOTE Confidence: 0.9978932

00:37:27.950 --> 00:37:29.170 It was found to
NOTE Confidence: 0.96563375

00:37:29.630 --> 00:37:31.170 be a very potent analgesic,
NOTE Confidence: 0.9706249

00:37:31.725 --> 00:37:33.405 but was dropped from further

NOTE Confidence: 0.9706249
00:37:33.405 --> 00:37:35.665 development because of an unacceptably
NOTE Confidence: 0.95035595
00:37:36.045 --> 00:37:36.545 high,
NOTE Confidence: 0.8840549
00:37:37.325 --> 00:37:37.965 level of,
NOTE Confidence: 0.9993189
00:37:38.685 --> 00:37:39.185 psychotropic
NOTE Confidence: 0.98352784
00:37:39.485 --> 00:37:41.405 side effects, including psychosis and
NOTE Confidence: 0.98352784
00:37:41.405 --> 00:37:41.905 paranoia.
NOTE Confidence: 0.9474095
00:37:42.925 --> 00:37:44.205 Of course, what's interesting is
NOTE Confidence: 0.9474095
00:37:44.205 --> 00:37:45.425 at the time that levonantradiol
NOTE Confidence: 0.99718165
00:37:45.725 --> 00:37:46.465 was developed,
NOTE Confidence: 0.96632296
00:37:47.310 --> 00:37:48.670 the CB one receptor had
NOTE Confidence: 0.96632296
00:37:48.670 --> 00:37:50.110 not been discovered. It's only
NOTE Confidence: 0.96632296
00:37:50.110 --> 00:37:51.550 later that they discovered that
NOTE Confidence: 0.96632296
00:37:51.550 --> 00:37:52.210 this drug,
NOTE Confidence: 0.97201383
00:37:52.830 --> 00:37:54.830 bound produced its effects by,
NOTE Confidence: 0.97201383
00:37:55.230 --> 00:37:57.230 by by, activating CB one
NOTE Confidence: 0.97201383

00:37:57.230 --> 00:37:57.730 receptors.
NOTE Confidence: 0.9493562

00:37:59.070 --> 00:38:00.285 There are a number of,
NOTE Confidence: 0.99814284

00:38:01.325 --> 00:38:01.825 endocannabinoid
NOTE Confidence: 0.99183923

00:38:02.605 --> 00:38:03.105 modulators.
NOTE Confidence: 0.98595685

00:38:03.645 --> 00:38:04.765 If you recall, I spoke
NOTE Confidence: 0.98595685

00:38:04.765 --> 00:38:05.964 to you about the enzymes
NOTE Confidence: 0.98595685

00:38:05.964 --> 00:38:07.265 that are involved in the
NOTE Confidence: 0.97962

00:38:07.645 --> 00:38:09.484 synthesis and degradation of,
NOTE Confidence: 0.9412406

00:38:10.125 --> 00:38:11.905 of anandamide in two AG.
NOTE Confidence: 0.9412406

00:38:12.204 --> 00:38:13.645 One of those enzymes is
NOTE Confidence: 0.9412406

00:38:13.645 --> 00:38:15.184 fatty acid amide hydrolase.
NOTE Confidence: 0.9481384

00:38:16.089 --> 00:38:17.450 A number of fatty acid
NOTE Confidence: 0.9481384

00:38:17.450 --> 00:38:19.290 amide hydrolase inhibitors had been
NOTE Confidence: 0.9481384

00:38:19.290 --> 00:38:19.790 developed.
NOTE Confidence: 0.8657999

00:38:20.250 --> 00:38:21.310 Pfizer tested,
NOTE Confidence: 0.9736861

00:38:21.849 --> 00:38:23.950 fatty acid amide hydrolase inhibitor

NOTE Confidence: 0.9736861

00:38:24.010 --> 00:38:26.010 for the treatment of pain

NOTE Confidence: 0.9736861

00:38:26.010 --> 00:38:27.310 associated with osteoarthritis,

NOTE Confidence: 0.98657066

00:38:28.089 --> 00:38:29.130 and we'll come to that,

NOTE Confidence: 0.98657066

00:38:29.290 --> 00:38:30.430 in a minute now.

NOTE Confidence: 0.93158597

00:38:30.825 --> 00:38:32.265 Companies are trying to develop

NOTE Confidence: 0.93158597

00:38:32.265 --> 00:38:33.705 a second generation, a new

NOTE Confidence: 0.93158597

00:38:33.705 --> 00:38:35.565 generation of, five inhibitors,

NOTE Confidence: 0.9694591

00:38:36.025 --> 00:38:37.065 and I believe there are

NOTE Confidence: 0.9694591

00:38:37.065 --> 00:38:38.905 also MagLytease inhibitors that have

NOTE Confidence: 0.9694591

00:38:38.905 --> 00:38:40.364 been administered to humans.

NOTE Confidence: 0.9941393

00:38:41.545 --> 00:38:42.825 There are also drugs that

NOTE Confidence: 0.9941393

00:38:42.825 --> 00:38:43.484 have been

NOTE Confidence: 0.99944377

00:38:43.830 --> 00:38:44.890 developed as

NOTE Confidence: 0.9373099

00:38:45.270 --> 00:38:46.950 only peripheral c v one

NOTE Confidence: 0.9373099

00:38:46.950 --> 00:38:49.030 agonists, so they only have

NOTE Confidence: 0.9373099

00:38:49.030 --> 00:38:50.230 effects on c v one
NOTE Confidence: 0.9373099

00:38:50.230 --> 00:38:50.730 receptors
NOTE Confidence: 0.9981079

00:38:51.030 --> 00:38:51.530 peripherally
NOTE Confidence: 0.9909411

00:38:51.910 --> 00:38:52.969 and not centrally.
NOTE Confidence: 0.9850605

00:38:53.350 --> 00:38:54.630 The advantage of that would
NOTE Confidence: 0.9850605

00:38:54.630 --> 00:38:56.070 be that these drugs, in
NOTE Confidence: 0.9850605

00:38:56.070 --> 00:38:57.770 theory, should not produce psychoactive
NOTE Confidence: 0.96232116

00:38:58.070 --> 00:38:59.655 effects, which tend to be
NOTE Confidence: 0.96232116

00:38:59.655 --> 00:39:01.515 the rate limiting, side effects,
NOTE Confidence: 0.9702858

00:39:02.455 --> 00:39:04.155 in using these drugs to,
NOTE Confidence: 0.99568146

00:39:04.695 --> 00:39:06.235 as as potential treatments.
NOTE Confidence: 0.84960604

00:39:07.255 --> 00:39:08.455 There are also c v
NOTE Confidence: 0.84960604

00:39:08.455 --> 00:39:08.955 two
NOTE Confidence: 0.9795212

00:39:09.735 --> 00:39:11.415 agonists. And as you may
NOTE Confidence: 0.9795212

00:39:11.415 --> 00:39:13.094 recall, c v two receptors
NOTE Confidence: 0.9795212

00:39:13.094 --> 00:39:14.930 are mostly present on immune

NOTE Confidence: 0.9795212

00:39:14.930 --> 00:39:15.989 cells in the periphery

NOTE Confidence: 0.94569

00:39:16.369 --> 00:39:17.430 and may contribute,

NOTE Confidence: 0.9936715

00:39:18.690 --> 00:39:21.190 to reducing pain by modulating

NOTE Confidence: 0.9936715

00:39:21.410 --> 00:39:21.910 inflammation.

NOTE Confidence: 0.89810723

00:39:22.529 --> 00:39:23.809 And then there are CB

NOTE Confidence: 0.89810723

00:39:23.809 --> 00:39:25.589 one r and antagonists.

NOTE Confidence: 0.91228575

00:39:27.585 --> 00:39:28.545 You some of you may

NOTE Confidence: 0.91228575

00:39:28.545 --> 00:39:29.984 recall from the from the

NOTE Confidence: 0.91228575

00:39:29.984 --> 00:39:31.585 early two thousand drug called

NOTE Confidence: 0.91228575

00:39:31.585 --> 00:39:32.085 rimonovant

NOTE Confidence: 0.89363307

00:39:32.385 --> 00:39:32.885 that

NOTE Confidence: 0.9314033

00:39:33.185 --> 00:39:33.505 was,

NOTE Confidence: 0.97863936

00:39:34.305 --> 00:39:36.465 that became commercially available. It

NOTE Confidence: 0.97863936

00:39:36.465 --> 00:39:37.685 was used in the treatment

NOTE Confidence: 0.97863936

00:39:37.744 --> 00:39:38.244 of,

NOTE Confidence: 0.94695187

00:39:38.785 --> 00:39:39.445 of obesity.
NOTE Confidence: 0.93787396

00:39:40.625 --> 00:39:41.125 The
NOTE Confidence: 0.99865973

00:39:41.640 --> 00:39:42.140 simple
NOTE Confidence: 0.5704247

00:39:42.760 --> 00:39:43.260 messages,
NOTE Confidence: 0.99001104

00:39:43.640 --> 00:39:44.920 if cannabis gives you the
NOTE Confidence: 0.99001104

00:39:44.920 --> 00:39:45.420 munchies,
NOTE Confidence: 0.70618814

00:39:45.719 --> 00:39:46.460 a CB1R
NOTE Confidence: 0.99756086

00:39:46.839 --> 00:39:47.339 antagonist
NOTE Confidence: 0.9727977

00:39:47.880 --> 00:39:49.880 will, will reduce appetite. And
NOTE Confidence: 0.9727977

00:39:49.880 --> 00:39:51.400 indeed, it did reduce appetite
NOTE Confidence: 0.9727977

00:39:51.400 --> 00:39:52.940 and people did lose weight.
NOTE Confidence: 0.9727977

00:39:53.160 --> 00:39:53.660 Unfortunately,
NOTE Confidence: 0.94574106

00:39:54.614 --> 00:39:55.355 some patients,
NOTE Confidence: 0.9922283

00:39:56.295 --> 00:39:56.795 developed
NOTE Confidence: 0.4851163

00:39:57.094 --> 00:39:57.594 suicidal
NOTE Confidence: 0.89833444

00:39:57.895 --> 00:39:59.495 ideation and depression, and that's

NOTE Confidence: 0.89833444

00:39:59.495 --> 00:40:01.415 what really killed the rimono

NOTE Confidence: 0.89833444

00:40:01.415 --> 00:40:02.775 band program. There are a

NOTE Confidence: 0.89833444

00:40:02.775 --> 00:40:04.315 couple of other CB one,

NOTE Confidence: 0.89833444

00:40:04.375 --> 00:40:06.315 CB one receptor antagonists

NOTE Confidence: 0.9952195

00:40:07.015 --> 00:40:08.535 that are in development. These

NOTE Confidence: 0.9952195

00:40:08.535 --> 00:40:09.835 are drugs that are

NOTE Confidence: 0.986746

00:40:10.480 --> 00:40:12.739 basically being developed to reverse

NOTE Confidence: 0.94987416

00:40:15.120 --> 00:40:17.620 cannabis intoxication or THC intoxication

NOTE Confidence: 0.94987416

00:40:17.840 --> 00:40:19.680 and to reverse, say, acute

NOTE Confidence: 0.94987416

00:40:19.680 --> 00:40:22.080 paranoia and panic attacks, that

NOTE Confidence: 0.94987416

00:40:22.080 --> 00:40:23.440 often lead people to go

NOTE Confidence: 0.94987416

00:40:23.440 --> 00:40:24.739 to the emergency room.

NOTE Confidence: 0.93914264

00:40:26.205 --> 00:40:26.705 So

NOTE Confidence: 0.9899931

00:40:27.485 --> 00:40:29.245 the the current philosophy in

NOTE Confidence: 0.9899931

00:40:29.245 --> 00:40:30.545 terms of drug development,

NOTE Confidence: 0.9864274

00:40:31.245 --> 00:40:31.745 involving,
NOTE Confidence: 0.9614436

00:40:33.245 --> 00:40:35.645 cannabinoids is not for stronger
NOTE Confidence: 0.9614436

00:40:35.645 --> 00:40:37.485 cannabinoids, but to make them
NOTE Confidence: 0.9614436

00:40:37.485 --> 00:40:38.305 more selective.
NOTE Confidence: 0.80131584

00:40:39.810 --> 00:40:41.650 And so that's that's the
NOTE Confidence: 0.80131584

00:40:41.650 --> 00:40:42.150 general,
NOTE Confidence: 0.9922245

00:40:42.930 --> 00:40:44.530 direction that these drugs are
NOTE Confidence: 0.9922245

00:40:44.530 --> 00:40:45.270 being developed.
NOTE Confidence: 0.99916106

00:40:47.810 --> 00:40:49.110 There are also some
NOTE Confidence: 0.93497866

00:40:50.370 --> 00:40:52.770 minor cannabinoids that are receiving
NOTE Confidence: 0.93497866

00:40:52.770 --> 00:40:53.235 some
NOTE Confidence: 0.82501215

00:40:53.715 --> 00:40:55.335 attention, including cannabagirals,
NOTE Confidence: 0.96133995

00:40:57.475 --> 00:40:59.255 and, and a few others,
NOTE Confidence: 0.96133995

00:40:59.395 --> 00:41:01.255 these are fairly early on
NOTE Confidence: 0.8819154

00:41:01.635 --> 00:41:01.955 in,
NOTE Confidence: 0.9944959

00:41:02.435 --> 00:41:03.495 in in development.

NOTE Confidence: 0.96174014

00:41:04.435 --> 00:41:05.555 They have not yet been

NOTE Confidence: 0.96174014

00:41:05.555 --> 00:41:07.310 established, and they are mostly,

NOTE Confidence: 0.96174014

00:41:07.310 --> 00:41:08.130 as I mentioned,

NOTE Confidence: 0.9966817

00:41:08.510 --> 00:41:10.370 in early translational work.

NOTE Confidence: 0.88811696

00:41:13.390 --> 00:41:13.890 So,

NOTE Confidence: 0.9992822

00:41:15.070 --> 00:41:16.910 in terms of acute pain,

NOTE Confidence: 0.9992822

00:41:16.910 --> 00:41:18.050 what is the evidence

NOTE Confidence: 0.99867165

00:41:19.155 --> 00:41:19.635 for,

NOTE Confidence: 0.98265713

00:41:20.114 --> 00:41:21.815 cannabinoids in acute pain?

NOTE Confidence: 0.98395544

00:41:22.114 --> 00:41:23.395 And I make this distinction

NOTE Confidence: 0.98395544

00:41:23.395 --> 00:41:24.835 between acute pain and chronic

NOTE Confidence: 0.98395544

00:41:24.835 --> 00:41:25.335 pain,

NOTE Confidence: 0.9623287

00:41:25.955 --> 00:41:26.755 and I'm sure there are

NOTE Confidence: 0.9623287

00:41:26.755 --> 00:41:27.955 others on this call who

NOTE Confidence: 0.9623287

00:41:27.955 --> 00:41:29.075 who probably know a lot

NOTE Confidence: 0.9623287

00:41:29.075 --> 00:41:30.295 more about this. But
NOTE Confidence: 0.99430203

00:41:30.675 --> 00:41:31.955 in terms of acute pain,
NOTE Confidence: 0.99430203

00:41:31.955 --> 00:41:33.300 what is the data? I'm
NOTE Confidence: 0.99430203

00:41:33.300 --> 00:41:34.660 gonna draw your attention to
NOTE Confidence: 0.99430203

00:41:34.660 --> 00:41:36.260 a study that that I
NOTE Confidence: 0.99430203

00:41:36.260 --> 00:41:37.700 did in my lab in
NOTE Confidence: 0.99430203

00:41:37.700 --> 00:41:38.440 in collaboration
NOTE Confidence: 0.92792994

00:41:38.820 --> 00:41:39.140 with,
NOTE Confidence: 0.880281

00:41:39.940 --> 00:41:41.780 with colleagues in anesthesia and
NOTE Confidence: 0.880281

00:41:41.780 --> 00:41:42.280 neurology.
NOTE Confidence: 0.9673689

00:41:43.380 --> 00:41:44.680 And this was a study,
NOTE Confidence: 0.9653947

00:41:46.020 --> 00:41:47.480 where we tested,
NOTE Confidence: 0.847956

00:41:49.515 --> 00:41:50.714 it was a double blind,
NOTE Confidence: 0.847956

00:41:50.714 --> 00:41:51.214 randomized,
NOTE Confidence: 0.93327236

00:41:51.594 --> 00:41:53.835 placebo controlled crossover study, so
NOTE Confidence: 0.93327236

00:41:53.835 --> 00:41:55.214 each subject served as

NOTE Confidence: 0.9970856
00:41:55.515 --> 00:41:57.375 his or her own control.
NOTE Confidence: 0.98277646
00:41:58.234 --> 00:41:59.675 This was done in healthy
NOTE Confidence: 0.98277646
00:41:59.675 --> 00:42:00.175 volunteers,
NOTE Confidence: 0.96783733
00:42:00.714 --> 00:42:02.714 and we used, we tested
NOTE Confidence: 0.96783733
00:42:02.714 --> 00:42:03.214 placebo,
NOTE Confidence: 0.95121235
00:42:04.040 --> 00:42:05.560 low and medium dose of
NOTE Confidence: 0.95121235
00:42:05.560 --> 00:42:07.180 THC, and we inflicted
NOTE Confidence: 0.879613
00:42:07.800 --> 00:42:09.980 five different kinds of experimental
NOTE Confidence: 0.879613
00:42:10.119 --> 00:42:11.020 pain, including
NOTE Confidence: 0.9330711
00:42:11.560 --> 00:42:13.000 heat and cold pain using
NOTE Confidence: 0.9330711
00:42:13.000 --> 00:42:13.660 a thermode.
NOTE Confidence: 0.99247575
00:42:14.840 --> 00:42:15.580 We injected
NOTE Confidence: 0.7909571
00:42:16.359 --> 00:42:16.859 capsaicin,
NOTE Confidence: 0.8999063
00:42:17.875 --> 00:42:18.375 into,
NOTE Confidence: 0.99452156
00:42:19.235 --> 00:42:19.735 subcutaneously
NOTE Confidence: 0.766824

00:42:20.035 --> 00:42:20.775 and that,
NOTE Confidence: 0.93022233

00:42:21.875 --> 00:42:23.975 intradermally, sorry, and that induces
NOTE Confidence: 0.93022233

00:42:24.114 --> 00:42:24.614 a,
NOTE Confidence: 0.99598837

00:42:25.155 --> 00:42:27.735 reliable zone of hyper hyperalgesia.
NOTE Confidence: 0.89276344

00:42:29.075 --> 00:42:29.955 We also had,
NOTE Confidence: 0.9986246

00:42:30.355 --> 00:42:31.875 we looked at mechanical and
NOTE Confidence: 0.9986246

00:42:31.875 --> 00:42:33.015 electrical pain.
NOTE Confidence: 0.95326835

00:42:33.770 --> 00:42:35.050 This was the basic design
NOTE Confidence: 0.95326835

00:42:35.050 --> 00:42:36.330 of the study. There was
NOTE Confidence: 0.95326835

00:42:36.330 --> 00:42:38.089 a baseline phase. We did
NOTE Confidence: 0.95326835

00:42:38.089 --> 00:42:39.609 some pace pain assessments at
NOTE Confidence: 0.95326835

00:42:39.609 --> 00:42:40.109 baseline,
NOTE Confidence: 0.970346

00:42:41.210 --> 00:42:42.510 and then we administered,
NOTE Confidence: 0.972304

00:42:43.369 --> 00:42:43.869 THC,
NOTE Confidence: 0.9530791

00:42:45.530 --> 00:42:47.050 have the pain paradigms, and
NOTE Confidence: 0.9530791

00:42:47.050 --> 00:42:49.070 then we looked at pain

NOTE Confidence: 0.98526996
00:42:49.715 --> 00:42:50.915 at the peak of THC
NOTE Confidence: 0.98526996
00:42:50.915 --> 00:42:51.415 effects
NOTE Confidence: 0.94582546
00:42:51.795 --> 00:42:53.715 and sometime later during the,
NOTE Confidence: 0.9887078
00:42:54.515 --> 00:42:55.255 the study.
NOTE Confidence: 0.9639455
00:42:57.155 --> 00:42:58.355 And what we found was
NOTE Confidence: 0.9639455
00:42:58.355 --> 00:43:00.195 that at these doses, THC
NOTE Confidence: 0.9639455
00:43:00.195 --> 00:43:02.135 produced effects that are consistent
NOTE Confidence: 0.9078676
00:43:02.700 --> 00:43:03.900 with the known effects of
NOTE Confidence: 0.9078676
00:43:03.900 --> 00:43:05.020 cannabis, as in they made
NOTE Confidence: 0.9078676
00:43:05.020 --> 00:43:06.780 a person feel high, the
NOTE Confidence: 0.9078676
00:43:06.780 --> 00:43:08.140 people felt more calm and
NOTE Confidence: 0.9078676
00:43:08.140 --> 00:43:08.640 relaxed.
NOTE Confidence: 0.88853717
00:43:09.500 --> 00:43:11.339 They had some alteration in
NOTE Confidence: 0.88853717
00:43:11.339 --> 00:43:12.800 cognitive test performance,
NOTE Confidence: 0.9283714
00:43:14.219 --> 00:43:16.060 and heart had an increase
NOTE Confidence: 0.9283714

00:43:16.060 --> 00:43:17.280 in heart rate. But
NOTE Confidence: 0.987968

00:43:17.815 --> 00:43:19.175 at none of these doses
NOTE Confidence: 0.987968

00:43:19.175 --> 00:43:21.195 did THC have any significant
NOTE Confidence: 0.987968

00:43:21.335 --> 00:43:21.835 effects
NOTE Confidence: 0.9885373

00:43:22.455 --> 00:43:24.075 on experimentally induced
NOTE Confidence: 0.9659746

00:43:24.455 --> 00:43:26.235 chemical, mechanical, thermal,
NOTE Confidence: 0.9692054

00:43:26.935 --> 00:43:27.435 electrical,
NOTE Confidence: 0.969168

00:43:28.215 --> 00:43:30.555 pain, or capsaicin induced hyperalgesia.
NOTE Confidence: 0.9916773

00:43:31.335 --> 00:43:32.535 So at least in our
NOTE Confidence: 0.9916773

00:43:32.535 --> 00:43:33.035 hands,
NOTE Confidence: 0.99635094

00:43:33.430 --> 00:43:34.730 we did not find,
NOTE Confidence: 0.9766427

00:43:35.350 --> 00:43:36.950 that THC in this,
NOTE Confidence: 0.92862445

00:43:37.350 --> 00:43:39.510 highly controlled, double blind, randomized,
NOTE Confidence: 0.92862445

00:43:39.510 --> 00:43:40.810 placebo controlled study,
NOTE Confidence: 0.97460693

00:43:42.630 --> 00:43:44.390 have any effects on acute
NOTE Confidence: 0.97460693

00:43:44.390 --> 00:43:45.770 pain in healthy individuals.

NOTE Confidence: 0.9655277

00:43:47.895 --> 00:43:48.935 There have been a couple

NOTE Confidence: 0.9655277

00:43:48.935 --> 00:43:49.594 of other,

NOTE Confidence: 0.9083273

00:43:51.495 --> 00:43:53.655 meta analyses done, systematic reviews

NOTE Confidence: 0.9083273

00:43:53.655 --> 00:43:55.015 and meta analyses that have

NOTE Confidence: 0.9083273

00:43:55.015 --> 00:43:55.675 been done,

NOTE Confidence: 0.9709382

00:43:56.135 --> 00:43:57.435 which have shown that,

NOTE Confidence: 0.9937241

00:43:58.775 --> 00:44:00.155 there may be a small

NOTE Confidence: 0.9937241

00:44:00.215 --> 00:44:01.755 increase in pain threshold,

NOTE Confidence: 0.9930135

00:44:03.309 --> 00:44:05.010 a small to medium increase

NOTE Confidence: 0.9930135

00:44:05.069 --> 00:44:06.130 in pain tolerance,

NOTE Confidence: 0.9986035

00:44:06.750 --> 00:44:08.430 and a small to medium

NOTE Confidence: 0.9986035

00:44:08.430 --> 00:44:09.969 reduction in the unpleasantness

NOTE Confidence: 0.8959491

00:44:10.910 --> 00:44:12.989 of ongoing experiment pain in

NOTE Confidence: 0.8959491

00:44:12.989 --> 00:44:14.450 these experimental studies.

NOTE Confidence: 0.9981383

00:44:15.055 --> 00:44:15.555 But,

NOTE Confidence: 0.995059

00:44:16.175 --> 00:44:18.755 cannabinoids did not decrease experimental

NOTE Confidence: 0.995059

00:44:18.895 --> 00:44:20.995 pain or mechanical hyperalgesia.

NOTE Confidence: 0.9863938

00:44:22.415 --> 00:44:22.915 So,

NOTE Confidence: 0.96692884

00:44:23.775 --> 00:44:24.975 I draw your attention to

NOTE Confidence: 0.96692884

00:44:24.975 --> 00:44:26.015 the last line of their

NOTE Confidence: 0.96692884

00:44:26.015 --> 00:44:27.570 conclusions, which is that they

NOTE Confidence: 0.96692884

00:44:27.570 --> 00:44:29.510 see that cannabis induced improvements

NOTE Confidence: 0.96692884

00:44:29.650 --> 00:44:31.830 in pain related negative affect

NOTE Confidence: 0.97803277

00:44:32.450 --> 00:44:34.130 may underlie the widely held

NOTE Confidence: 0.97803277

00:44:34.130 --> 00:44:36.310 belief that cannabis relieves pain.

NOTE Confidence: 0.9981074

00:44:37.570 --> 00:44:38.770 This was followed by a

NOTE Confidence: 0.9981074

00:44:38.770 --> 00:44:39.510 more recent

NOTE Confidence: 0.7230562

00:44:40.450 --> 00:44:41.510 systematic review,

NOTE Confidence: 0.9803168

00:44:42.085 --> 00:44:42.405 which,

NOTE Confidence: 0.9989973

00:44:43.045 --> 00:44:44.505 which concluded that

NOTE Confidence: 0.99974483

00:44:44.885 --> 00:44:46.405 the evidence was all over

NOTE Confidence: 0.99974483
00:44:46.405 --> 00:44:47.065 the place
NOTE Confidence: 0.9145096
00:44:47.445 --> 00:44:48.505 and not consistent,
NOTE Confidence: 0.8979646
00:44:49.925 --> 00:44:50.245 of,
NOTE Confidence: 0.9905679
00:44:50.885 --> 00:44:52.725 efficacy of cannabinoids as an
NOTE Confidence: 0.9905679
00:44:52.725 --> 00:44:54.505 analgesic agent for acute,
NOTE Confidence: 0.9987255
00:44:55.445 --> 00:44:56.344 acute pain.
NOTE Confidence: 0.99942696
00:44:58.120 --> 00:44:58.620 So
NOTE Confidence: 0.98689216
00:44:59.000 --> 00:45:00.600 just to summarize the data
NOTE Confidence: 0.98689216
00:45:00.600 --> 00:45:02.440 on acute pain with THC
NOTE Confidence: 0.98689216
00:45:02.440 --> 00:45:03.180 and CBD,
NOTE Confidence: 0.99464726
00:45:03.640 --> 00:45:05.100 there may be some evidence
NOTE Confidence: 0.99464726
00:45:05.160 --> 00:45:06.360 to suggest that there's an
NOTE Confidence: 0.99464726
00:45:06.360 --> 00:45:07.420 increase in threshold
NOTE Confidence: 0.98494
00:45:07.880 --> 00:45:09.320 pain threshold and a decrease
NOTE Confidence: 0.98494
00:45:09.320 --> 00:45:10.380 in pain unpleasantness.
NOTE Confidence: 0.97717667

00:45:11.815 --> 00:45:13.815 There's some questionable evidence about

NOTE Confidence: 0.97717667

00:45:14.055 --> 00:45:15.355 of hyper hyperalgesia

NOTE Confidence: 0.97230023

00:45:15.975 --> 00:45:16.795 at higher doses,

NOTE Confidence: 0.87375575

00:45:17.495 --> 00:45:18.955 and there may be biphasic

NOTE Confidence: 0.87375575

00:45:19.094 --> 00:45:20.695 effects that is at at

NOTE Confidence: 0.87375575

00:45:20.695 --> 00:45:21.435 low doses.

NOTE Confidence: 0.92657775

00:45:21.815 --> 00:45:23.335 THC may have effects going

NOTE Confidence: 0.92657775

00:45:23.335 --> 00:45:24.455 in one direction and a

NOTE Confidence: 0.92657775

00:45:24.455 --> 00:45:25.575 higher dose is a different

NOTE Confidence: 0.92657775

00:45:25.575 --> 00:45:26.075 direction.

NOTE Confidence: 0.9069024

00:45:26.600 --> 00:45:27.500 But they are limiting

NOTE Confidence: 0.58911264

00:45:27.880 --> 00:45:28.360 if,

NOTE Confidence: 0.98204154

00:45:28.760 --> 00:45:30.440 the limiting factor is that

NOTE Confidence: 0.98204154

00:45:30.440 --> 00:45:32.040 at doses that might produce

NOTE Confidence: 0.98204154

00:45:32.040 --> 00:45:33.320 some of these effects on

NOTE Confidence: 0.98204154

00:45:33.320 --> 00:45:34.140 pain threshold,

NOTE Confidence: 0.96588653
00:45:34.840 --> 00:45:36.140 they may also produce,
NOTE Confidence: 0.99853843
00:45:36.680 --> 00:45:38.300 psychoactive adverse events.
NOTE Confidence: 0.92262954
00:45:39.225 --> 00:45:41.065 In fact, the psychoactive adverse
NOTE Confidence: 0.92262954
00:45:41.065 --> 00:45:42.205 events may emerge
NOTE Confidence: 0.9942923
00:45:42.825 --> 00:45:44.125 at at or below
NOTE Confidence: 0.9313287
00:45:44.585 --> 00:45:45.085 analgesic,
NOTE Confidence: 0.9795287
00:45:46.025 --> 00:45:47.865 doses, suggesting a very narrow
NOTE Confidence: 0.9795287
00:45:47.865 --> 00:45:48.365 therapeutic
NOTE Confidence: 0.9927119
00:45:48.745 --> 00:45:49.245 window.
NOTE Confidence: 0.99509406
00:45:49.625 --> 00:45:50.905 And then in terms of
NOTE Confidence: 0.99509406
00:45:50.905 --> 00:45:51.405 CBD,
NOTE Confidence: 0.96588
00:45:52.119 --> 00:45:53.640 at least in acute pain,
NOTE Confidence: 0.96588
00:45:53.640 --> 00:45:55.239 there's very little, if any,
NOTE Confidence: 0.96588
00:45:55.239 --> 00:45:57.339 data to suggest that CBD
NOTE Confidence: 0.96588
00:45:57.400 --> 00:45:59.080 has any effects on acute
NOTE Confidence: 0.96588

00:45:59.080 --> 00:45:59.580 pain.
NOTE Confidence: 0.99798435

00:46:01.640 --> 00:46:02.920 Now what about the effects
NOTE Confidence: 0.99798435

00:46:02.920 --> 00:46:03.980 of, cannabinoids
NOTE Confidence: 0.88513255

00:46:04.280 --> 00:46:05.339 and chronic pain?
NOTE Confidence: 0.9796901

00:46:06.565 --> 00:46:08.325 There's a lot more research
NOTE Confidence: 0.9796901

00:46:08.325 --> 00:46:09.285 that has been done on
NOTE Confidence: 0.9796901

00:46:09.285 --> 00:46:10.185 chronic pain,
NOTE Confidence: 0.98964775

00:46:10.805 --> 00:46:12.185 and I'm not going to
NOTE Confidence: 0.98964775

00:46:12.325 --> 00:46:13.705 review all that literature.
NOTE Confidence: 0.993106

00:46:14.165 --> 00:46:15.525 If you're interested, I would
NOTE Confidence: 0.993106

00:46:15.525 --> 00:46:17.045 point you to a very
NOTE Confidence: 0.993106

00:46:17.045 --> 00:46:19.205 interesting collaboration between the Department
NOTE Confidence: 0.993106

00:46:19.205 --> 00:46:20.344 of Veterans Affairs
NOTE Confidence: 0.94849586

00:46:21.000 --> 00:46:21.480 and,
NOTE Confidence: 0.9603263

00:46:21.960 --> 00:46:23.820 Oregon Health Sciences University,
NOTE Confidence: 0.94988114

00:46:24.280 --> 00:46:25.580 where they have a program

NOTE Confidence: 0.94988114
00:46:25.640 --> 00:46:26.460 called systematically
NOTE Confidence: 0.94652987
00:46:26.840 --> 00:46:28.540 testing the evidence on marijuana.
NOTE Confidence: 0.9717893
00:46:29.160 --> 00:46:30.060 And they published,
NOTE Confidence: 0.76697344
00:46:30.600 --> 00:46:31.340 they published,
NOTE Confidence: 0.9771986
00:46:33.585 --> 00:46:35.665 live reviews. These are ongoing
NOTE Confidence: 0.9771986
00:46:35.665 --> 00:46:37.605 reviews of different topics such
NOTE Confidence: 0.95695496
00:46:37.905 --> 00:46:39.505 as cannabis and pain, cannabis
NOTE Confidence: 0.95695496
00:46:39.505 --> 00:46:41.605 and PTSD, cannabis and pregnancy,
NOTE Confidence: 0.96286774
00:46:41.984 --> 00:46:43.744 and they're basically one page
NOTE Confidence: 0.96286774
00:46:43.744 --> 00:46:44.805 summaries that
NOTE Confidence: 0.96158826
00:46:45.105 --> 00:46:46.705 make it easy for people
NOTE Confidence: 0.96158826
00:46:46.705 --> 00:46:48.180 who are not familiar with
NOTE Confidence: 0.96158826
00:46:48.180 --> 00:46:49.880 the the cannabis field
NOTE Confidence: 0.9949215
00:46:50.180 --> 00:46:50.920 to understand
NOTE Confidence: 0.9871182
00:46:51.219 --> 00:46:52.660 exactly what the evidence is
NOTE Confidence: 0.9871182

00:46:52.660 --> 00:46:53.619 out there, and it's really

NOTE Confidence: 0.9871182

00:46:53.619 --> 00:46:55.080 also useful for patients

NOTE Confidence: 0.98892045

00:46:55.460 --> 00:46:56.760 in addition to clinicians.

NOTE Confidence: 0.8944453

00:46:57.300 --> 00:46:57.700 This is,

NOTE Confidence: 0.9289791

00:46:58.420 --> 00:47:00.119 this is their summary

NOTE Confidence: 0.9935354

00:47:00.744 --> 00:47:02.285 of the evidence of cannabis,

NOTE Confidence: 0.93538904

00:47:02.984 --> 00:47:03.805 for pain.

NOTE Confidence: 0.9606953

00:47:04.505 --> 00:47:05.005 And,

NOTE Confidence: 0.99868745

00:47:06.585 --> 00:47:07.484 they look at

NOTE Confidence: 0.8946344

00:47:07.785 --> 00:47:08.605 both benefits,

NOTE Confidence: 0.9490412

00:47:09.065 --> 00:47:10.445 and they look at harms.

NOTE Confidence: 0.95964515

00:47:11.945 --> 00:47:13.625 And they've looked at, this

NOTE Confidence: 0.95964515

00:47:13.625 --> 00:47:15.005 in a in an ongoing

NOTE Confidence: 0.95964515

00:47:15.120 --> 00:47:16.400 fashion. I think this review

NOTE Confidence: 0.95964515

00:47:16.400 --> 00:47:17.940 was from maybe last year.

NOTE Confidence: 0.87481916

00:47:18.560 --> 00:47:19.680 And I'll just read out

NOTE Confidence: 0.87481916

00:47:19.680 --> 00:47:21.200 the bottom line, which is

NOTE Confidence: 0.87481916

00:47:21.200 --> 00:47:23.040 there's moderate certainty evidence that

NOTE Confidence: 0.87481916

00:47:23.040 --> 00:47:24.800 a product come with compact

NOTE Confidence: 0.87481916

00:47:25.040 --> 00:47:27.140 comparable THC to CBD ratios

NOTE Confidence: 0.9134889

00:47:28.005 --> 00:47:30.244 probably improves pain but not

NOTE Confidence: 0.9134889

00:47:30.244 --> 00:47:30.744 functioning,

NOTE Confidence: 0.9907503

00:47:31.605 --> 00:47:33.285 and that oral CBD alone

NOTE Confidence: 0.9907503

00:47:33.285 --> 00:47:35.125 probably does not affect pain

NOTE Confidence: 0.9907503

00:47:35.125 --> 00:47:35.785 or function.

NOTE Confidence: 0.9987354

00:47:36.404 --> 00:47:37.224 Some formulations

NOTE Confidence: 0.9977127

00:47:37.525 --> 00:47:38.644 increase the risk of side

NOTE Confidence: 0.9977127

00:47:38.644 --> 00:47:39.144 effects,

NOTE Confidence: 0.99941

00:47:40.244 --> 00:47:41.464 and several formulations

NOTE Confidence: 0.982255

00:47:41.765 --> 00:47:42.825 remain understudied.

NOTE Confidence: 0.99901664

00:47:43.640 --> 00:47:45.020 So there you have it.

NOTE Confidence: 0.84135455

00:47:47.880 --> 00:47:49.560 So oral t h oral
NOTE Confidence: 0.84135455

00:47:49.560 --> 00:47:50.940 CBD doesn't affect,
NOTE Confidence: 0.97432166

00:47:51.320 --> 00:47:52.700 the strength of the evidence
NOTE Confidence: 0.97432166

00:47:52.760 --> 00:47:54.280 for all other benefits is
NOTE Confidence: 0.97432166

00:47:54.280 --> 00:47:55.420 low or insufficient.
NOTE Confidence: 0.9280455

00:47:56.744 --> 00:47:59.065 Compared to placebo, cannabis related
NOTE Confidence: 0.9280455

00:47:59.065 --> 00:47:59.565 interventions
NOTE Confidence: 0.98989123

00:48:00.424 --> 00:48:01.484 result in greater
NOTE Confidence: 0.99320096

00:48:02.025 --> 00:48:02.924 risk of common
NOTE Confidence: 0.9389943

00:48:03.305 --> 00:48:04.924 side effects, but not severe
NOTE Confidence: 0.85758436

00:48:05.704 --> 00:48:06.525 adverse events,
NOTE Confidence: 0.917809

00:48:07.704 --> 00:48:09.964 and there's little data on
NOTE Confidence: 0.9869039

00:48:11.150 --> 00:48:12.530 the effects of these compounds
NOTE Confidence: 0.9869039

00:48:12.670 --> 00:48:14.210 in children or adolescents.
NOTE Confidence: 0.92403316

00:48:17.870 --> 00:48:19.790 The International Association for the
NOTE Confidence: 0.92403316

00:48:19.790 --> 00:48:21.330 Study of Pain presidential

NOTE Confidence: 0.91605717

00:48:21.630 --> 00:48:23.570 task for force had a

NOTE Confidence: 0.91605717

00:48:23.710 --> 00:48:24.770 consent statement,

NOTE Confidence: 0.99810106

00:48:25.325 --> 00:48:27.585 and they basically concluded that

NOTE Confidence: 0.99810106

00:48:27.805 --> 00:48:28.765 there was a lack of

NOTE Confidence: 0.99810106

00:48:28.765 --> 00:48:30.465 high quality clinical evidence

NOTE Confidence: 0.98353565

00:48:30.765 --> 00:48:32.525 and that they do not

NOTE Confidence: 0.98353565

00:48:32.525 --> 00:48:34.365 currently endorse the general use

NOTE Confidence: 0.98353565

00:48:34.365 --> 00:48:35.885 of cannabis or cannabinoids for

NOTE Confidence: 0.98353565

00:48:35.885 --> 00:48:36.625 pain relief.

NOTE Confidence: 0.9595114

00:48:37.005 --> 00:48:38.045 And they further go on

NOTE Confidence: 0.9595114

00:48:38.045 --> 00:48:38.845 to say there is a

NOTE Confidence: 0.9595114

00:48:38.845 --> 00:48:40.690 pressing need for preclinical

NOTE Confidence: 0.994641

00:48:40.990 --> 00:48:42.750 and clinical studies to fill

NOTE Confidence: 0.994641

00:48:42.750 --> 00:48:43.490 this gap.

NOTE Confidence: 0.9924383

00:48:44.190 --> 00:48:45.150 Now some of you may

NOTE Confidence: 0.9924383

00:48:45.150 --> 00:48:46.130 also be aware
NOTE Confidence: 0.99867797

00:48:46.510 --> 00:48:47.870 of a recent study that
NOTE Confidence: 0.99867797

00:48:47.870 --> 00:48:48.910 received quite a bit of
NOTE Confidence: 0.99867797

00:48:48.910 --> 00:48:49.410 attention.
NOTE Confidence: 0.9909821

00:48:50.350 --> 00:48:51.710 This was a very large
NOTE Confidence: 0.9909821

00:48:51.710 --> 00:48:52.210 study,
NOTE Confidence: 0.99819887

00:48:52.670 --> 00:48:53.890 staggeringly large
NOTE Confidence: 0.99562705

00:48:54.915 --> 00:48:56.035 study that had more than
NOTE Confidence: 0.99562705

00:48:56.035 --> 00:48:57.094 eight hundred adults
NOTE Confidence: 0.95876294

00:48:57.395 --> 00:48:58.755 enrolled. This is far bigger
NOTE Confidence: 0.95876294

00:48:58.755 --> 00:49:00.195 than any other study that's
NOTE Confidence: 0.95876294

00:49:00.195 --> 00:49:01.795 ever been done where they
NOTE Confidence: 0.95876294

00:49:01.795 --> 00:49:03.575 used an oral full spectrum
NOTE Confidence: 0.95876294

00:49:03.715 --> 00:49:04.935 cannabis extract,
NOTE Confidence: 0.9793814

00:49:06.275 --> 00:49:08.114 versus placebo in a in
NOTE Confidence: 0.9793814

00:49:08.114 --> 00:49:09.719 a in a study that

NOTE Confidence: 0.9793814
00:49:09.719 --> 00:49:11.239 was quite complicated. I'll just
NOTE Confidence: 0.9793814
00:49:11.239 --> 00:49:12.840 focus on the first twelve
NOTE Confidence: 0.9793814
00:49:12.840 --> 00:49:13.739 weeks of treatment.
NOTE Confidence: 0.9964254
00:49:14.600 --> 00:49:15.900 And in that study,
NOTE Confidence: 0.9747938
00:49:16.200 --> 00:49:17.400 they showed that there was
NOTE Confidence: 0.9747938
00:49:17.400 --> 00:49:18.780 a two to three point,
NOTE Confidence: 0.9916829
00:49:19.880 --> 00:49:22.140 reduction in pain versus baseline
NOTE Confidence: 0.9974801
00:49:22.745 --> 00:49:23.945 in the group that received
NOTE Confidence: 0.9974801
00:49:23.945 --> 00:49:24.605 the cannabis
NOTE Confidence: 0.80986446
00:49:24.985 --> 00:49:25.485 extract,
NOTE Confidence: 0.9607308
00:49:26.505 --> 00:49:28.185 and the primary outcome measure
NOTE Confidence: 0.9607308
00:49:28.185 --> 00:49:29.645 here was NRS.
NOTE Confidence: 0.8514668
00:49:30.585 --> 00:49:31.325 In addition
NOTE Confidence: 0.9850335
00:49:32.025 --> 00:49:33.705 to improvements in pain, they
NOTE Confidence: 0.9850335
00:49:33.705 --> 00:49:35.864 saw improvements in function and
NOTE Confidence: 0.9850335

00:49:35.864 --> 00:49:37.290 sleep, which has not been
NOTE Confidence: 0.9850335

00:49:37.290 --> 00:49:38.590 shown in previous studies,
NOTE Confidence: 0.9921792

00:49:38.890 --> 00:49:40.510 and these effects were sustained
NOTE Confidence: 0.9921792

00:49:40.570 --> 00:49:41.310 over time.
NOTE Confidence: 0.9957789

00:49:41.690 --> 00:49:43.130 And while these effects were
NOTE Confidence: 0.9957789

00:49:43.130 --> 00:49:44.350 modest, they were clinically,
NOTE Confidence: 0.9997026

00:49:45.050 --> 00:49:45.550 meaningful.
NOTE Confidence: 0.95301574

00:49:45.850 --> 00:49:47.310 Now what caught my attention
NOTE Confidence: 0.95301574

00:49:47.370 --> 00:49:48.110 was that
NOTE Confidence: 0.98872864

00:49:49.094 --> 00:49:50.235 at the time that,
NOTE Confidence: 0.99040663

00:49:51.655 --> 00:49:53.114 at least until recently,
NOTE Confidence: 0.98783934

00:49:53.975 --> 00:49:55.494 the one kind of pain
NOTE Confidence: 0.98783934

00:49:55.494 --> 00:49:57.494 that was seemed most likely
NOTE Confidence: 0.98783934

00:49:57.494 --> 00:49:59.815 to benefit from cannabis or
NOTE Confidence: 0.98783934

00:49:59.815 --> 00:50:01.835 cannabinoids was neuropathic pain.
NOTE Confidence: 0.9537502

00:50:02.540 --> 00:50:03.900 When we did a literature

NOTE Confidence: 0.9537502

00:50:03.900 --> 00:50:05.359 review several years ago,

NOTE Confidence: 0.967848

00:50:06.219 --> 00:50:07.739 in thinking about designing a

NOTE Confidence: 0.967848

00:50:07.739 --> 00:50:09.920 study to address pain, we,

NOTE Confidence: 0.9602455

00:50:10.380 --> 00:50:11.500 one of our first tasks

NOTE Confidence: 0.9602455

00:50:11.500 --> 00:50:12.960 was what kind of pain

NOTE Confidence: 0.9602455

00:50:13.099 --> 00:50:14.859 would we want to target?

NOTE Confidence: 0.9602455

00:50:14.859 --> 00:50:16.560 And it became clear that

NOTE Confidence: 0.9953988

00:50:17.625 --> 00:50:18.985 even though there was limited

NOTE Confidence: 0.9953988

00:50:18.985 --> 00:50:21.325 evidence, that limited evidence suggested

NOTE Confidence: 0.9953988

00:50:21.385 --> 00:50:22.505 that the kind of pain

NOTE Confidence: 0.9953988

00:50:22.505 --> 00:50:23.785 that was most likely to

NOTE Confidence: 0.9953988

00:50:23.785 --> 00:50:24.765 respond to cannabinoids

NOTE Confidence: 0.99714464

00:50:25.305 --> 00:50:27.085 was chronic neuropathic pain.

NOTE Confidence: 0.9997056

00:50:27.545 --> 00:50:28.605 So I was surprised

NOTE Confidence: 0.96832436

00:50:29.559 --> 00:50:30.680 by the results of this

NOTE Confidence: 0.96832436

00:50:30.680 --> 00:50:32.200 study that was published in,
NOTE Confidence: 0.9216053

00:50:32.599 --> 00:50:33.739 in Nature Medicine.
NOTE Confidence: 0.8824678

00:50:37.719 --> 00:50:39.020 So I think that
NOTE Confidence: 0.9991311

00:50:40.200 --> 00:50:40.940 we still
NOTE Confidence: 0.9531598

00:50:41.614 --> 00:50:42.895 don't have a good idea
NOTE Confidence: 0.9531598

00:50:42.895 --> 00:50:44.835 about the risk benefit ratio
NOTE Confidence: 0.9531598

00:50:44.895 --> 00:50:46.895 of, cannabinoids and the treatment
NOTE Confidence: 0.9531598

00:50:46.895 --> 00:50:47.555 of pain.
NOTE Confidence: 0.9435488

00:50:48.734 --> 00:50:49.375 We have,
NOTE Confidence: 0.9212947

00:50:50.815 --> 00:50:52.194 I just wanna point out
NOTE Confidence: 0.9212947

00:50:52.335 --> 00:50:53.614 one study that was done
NOTE Confidence: 0.9212947

00:50:53.614 --> 00:50:55.214 several years ago with the
NOTE Confidence: 0.9212947

00:50:55.214 --> 00:50:55.714 inhibitor.
NOTE Confidence: 0.9425225

00:50:56.900 --> 00:50:57.780 There was quite a bit
NOTE Confidence: 0.9425225

00:50:57.780 --> 00:51:00.100 of excitement because, of the
NOTE Confidence: 0.9425225

00:51:00.100 --> 00:51:02.400 mechanism of action of fine

NOTE Confidence: 0.9425225
00:51:02.400 --> 00:51:03.400 inhibition increasing
NOTE Confidence: 0.93334556
00:51:03.860 --> 00:51:04.360 endocannabinoid
NOTE Confidence: 0.99102086
00:51:04.739 --> 00:51:06.020 levels in the brain without
NOTE Confidence: 0.99102086
00:51:06.020 --> 00:51:07.080 producing intoxication.
NOTE Confidence: 0.94552594
00:51:07.700 --> 00:51:09.800 Unfortunately, this drug did not,
NOTE Confidence: 0.9802135
00:51:10.994 --> 00:51:12.674 did not produce pain in,
NOTE Confidence: 0.9802135
00:51:12.994 --> 00:51:13.815 in osteoarthritis,
NOTE Confidence: 0.9299432
00:51:14.914 --> 00:51:16.194 though it was very well
NOTE Confidence: 0.9299432
00:51:16.194 --> 00:51:17.474 tolerated. And then drug was
NOTE Confidence: 0.9299432
00:51:17.474 --> 00:51:18.775 abandoned by Pfizer,
NOTE Confidence: 0.99665064
00:51:20.035 --> 00:51:20.855 at the time.
NOTE Confidence: 0.8141314
00:51:22.035 --> 00:51:22.535 So,
NOTE Confidence: 0.99124295
00:51:23.719 --> 00:51:24.680 there are a number of
NOTE Confidence: 0.99124295
00:51:24.680 --> 00:51:26.519 research gaps and opportunities for
NOTE Confidence: 0.99124295
00:51:26.519 --> 00:51:27.600 cannabinoids. I know we have
NOTE Confidence: 0.99124295

00:51:27.600 --> 00:51:28.700 a few minutes left.
NOTE Confidence: 0.96381176

00:51:29.719 --> 00:51:31.160 I just want to summarize
NOTE Confidence: 0.96381176

00:51:31.160 --> 00:51:32.059 some of the limitations
NOTE Confidence: 0.9599835

00:51:32.359 --> 00:51:33.640 as some of you may
NOTE Confidence: 0.9599835

00:51:33.640 --> 00:51:35.480 be thinking about designing studies
NOTE Confidence: 0.9599835

00:51:35.480 --> 00:51:37.079 to look at the effects
NOTE Confidence: 0.9599835

00:51:37.079 --> 00:51:38.680 of cannabis or cannabinoids with
NOTE Confidence: 0.9599835

00:51:38.680 --> 00:51:40.594 pain. The first is sample
NOTE Confidence: 0.9599835

00:51:40.594 --> 00:51:41.954 sizes. Most of the studies
NOTE Confidence: 0.9599835

00:51:41.954 --> 00:51:43.575 had very small sample sizes.
NOTE Confidence: 0.99770033

00:51:44.114 --> 00:51:45.575 Blinding is a big issue.
NOTE Confidence: 0.99770033

00:51:45.795 --> 00:51:47.234 If you use doses that
NOTE Confidence: 0.99770033

00:51:47.234 --> 00:51:49.234 are clearly psychotropic, you really
NOTE Confidence: 0.99770033

00:51:49.234 --> 00:51:50.435 need to think about using
NOTE Confidence: 0.99770033

00:51:50.435 --> 00:51:51.954 a dose that is on
NOTE Confidence: 0.99770033

00:51:51.954 --> 00:51:52.454 the

NOTE Confidence: 0.9934609
00:51:53.030 --> 00:51:54.730 on the threshold of psychotropic
NOTE Confidence: 0.9934609
00:51:54.869 --> 00:51:55.369 effects.
NOTE Confidence: 0.9817193
00:51:56.790 --> 00:51:58.150 Many of these studies, and
NOTE Confidence: 0.9817193
00:51:58.150 --> 00:51:59.750 it's so important in pain
NOTE Confidence: 0.9817193
00:51:59.750 --> 00:52:01.849 and depression and PTSD research
NOTE Confidence: 0.9461829
00:52:02.150 --> 00:52:03.910 to measure expectancy and take
NOTE Confidence: 0.9461829
00:52:03.910 --> 00:52:05.450 that into account in studies.
NOTE Confidence: 0.92357194
00:52:06.515 --> 00:52:07.955 Many studies do not take
NOTE Confidence: 0.92357194
00:52:07.955 --> 00:52:10.515 into account previous cannabis exposure
NOTE Confidence: 0.92357194
00:52:10.515 --> 00:52:11.815 as I showed you in
NOTE Confidence: 0.92357194
00:52:11.955 --> 00:52:13.315 we have pet data showing
NOTE Confidence: 0.92357194
00:52:13.315 --> 00:52:15.155 that there's down regulation and
NOTE Confidence: 0.92357194
00:52:15.155 --> 00:52:15.655 desensitization
NOTE Confidence: 0.85650617
00:52:16.035 --> 00:52:17.335 of c b one receptors.
NOTE Confidence: 0.9879264
00:52:18.360 --> 00:52:19.640 Most of the studies have
NOTE Confidence: 0.9879264

00:52:19.640 --> 00:52:22.060 relied almost exclusively on subjective
NOTE Confidence: 0.9879264

00:52:22.120 --> 00:52:22.620 effects,
NOTE Confidence: 0.9779787

00:52:23.400 --> 00:52:24.360 and did not look at
NOTE Confidence: 0.9779787

00:52:24.360 --> 00:52:26.300 other measures, including functioning.
NOTE Confidence: 0.9484051

00:52:27.560 --> 00:52:29.080 The literature is a mess
NOTE Confidence: 0.9484051

00:52:29.080 --> 00:52:30.680 because there's so many different
NOTE Confidence: 0.9484051

00:52:30.680 --> 00:52:31.880 compounds that have been tested,
NOTE Confidence: 0.9484051

00:52:31.880 --> 00:52:33.020 that have been administered.
NOTE Confidence: 0.57111067

00:52:33.465 --> 00:52:33.965 We
NOTE Confidence: 0.8372199

00:52:34.344 --> 00:52:35.385 we have different routes of
NOTE Confidence: 0.8372199

00:52:35.385 --> 00:52:35.885 administration
NOTE Confidence: 0.9320621

00:52:36.265 --> 00:52:37.325 and different doses.
NOTE Confidence: 0.9462979

00:52:38.665 --> 00:52:40.505 And, and most studies looked
NOTE Confidence: 0.9462979

00:52:40.505 --> 00:52:41.965 at isolated cannabinoids
NOTE Confidence: 0.90802306

00:52:42.585 --> 00:52:44.105 with one exception. That is
NOTE Confidence: 0.90802306

00:52:44.105 --> 00:52:45.785 the last study published from,

NOTE Confidence: 0.7704497
00:52:46.185 --> 00:52:47.485 in Germany in nature,
NOTE Confidence: 0.8260548
00:52:48.759 --> 00:52:49.579 nature medicine
NOTE Confidence: 0.980463
00:52:50.039 --> 00:52:52.059 that used whole plant cannabis
NOTE Confidence: 0.92336166
00:52:52.359 --> 00:52:53.019 that contained,
NOTE Confidence: 0.9502408
00:52:53.799 --> 00:52:55.160 not just THC, but many
NOTE Confidence: 0.9502408
00:52:55.160 --> 00:52:57.180 other cannabinoids, terpenes, and flavonoids.
NOTE Confidence: 0.97671247
00:52:58.119 --> 00:52:58.599 So,
NOTE Confidence: 0.99825764
00:52:58.920 --> 00:53:00.680 we are actually trying to
NOTE Confidence: 0.99825764
00:53:00.680 --> 00:53:02.460 address many of these limitations
NOTE Confidence: 0.99825764
00:53:02.680 --> 00:53:03.180 in
NOTE Confidence: 0.9900916
00:53:03.515 --> 00:53:04.955 what is the first VA
NOTE Confidence: 0.9900916
00:53:04.955 --> 00:53:05.775 funded study,
NOTE Confidence: 0.9773092
00:53:06.475 --> 00:53:06.795 that,
NOTE Confidence: 0.83650744
00:53:07.435 --> 00:53:09.115 Don McGarry and I are
NOTE Confidence: 0.83650744
00:53:09.115 --> 00:53:09.695 are are
NOTE Confidence: 0.8957714

00:53:10.475 --> 00:53:10.975 leading,
NOTE Confidence: 0.96681297
00:53:11.675 --> 00:53:13.835 involving five VAs. We are
NOTE Confidence: 0.96681297
00:53:13.835 --> 00:53:15.195 going to study a very
NOTE Confidence: 0.96681297
00:53:15.195 --> 00:53:16.715 large number of subjects larger
NOTE Confidence: 0.96681297
00:53:16.875 --> 00:53:18.155 the sample size is larger
NOTE Confidence: 0.96681297
00:53:18.155 --> 00:53:18.655 than
NOTE Confidence: 0.98661613
00:53:19.080 --> 00:53:20.440 any other study that's been
NOTE Confidence: 0.98661613
00:53:20.440 --> 00:53:21.420 done recently.
NOTE Confidence: 0.9672119
00:53:22.200 --> 00:53:23.560 We are gonna study chronic
NOTE Confidence: 0.9672119
00:53:23.560 --> 00:53:25.640 neuropathic pain, and we are
NOTE Confidence: 0.9672119
00:53:25.640 --> 00:53:26.140 testing
NOTE Confidence: 0.9815259
00:53:26.840 --> 00:53:27.340 THC,
NOTE Confidence: 0.9642284
00:53:27.719 --> 00:53:28.219 CBD,
NOTE Confidence: 0.90811366
00:53:28.760 --> 00:53:29.960 the combination of the t
NOTE Confidence: 0.90811366
00:53:30.120 --> 00:53:31.340 of the two and placebo,
NOTE Confidence: 0.95677847
00:53:32.175 --> 00:53:33.375 in an eight week long

NOTE Confidence: 0.95677847

00:53:33.375 --> 00:53:34.415 trial. We're looking at a

NOTE Confidence: 0.95677847

00:53:34.415 --> 00:53:35.875 number of measures, including

NOTE Confidence: 0.878874

00:53:36.335 --> 00:53:37.775 measures of pain, measures of

NOTE Confidence: 0.878874

00:53:37.775 --> 00:53:39.635 function, and measures of mood,

NOTE Confidence: 0.97809523

00:53:40.335 --> 00:53:41.795 and, of course, side effects.

NOTE Confidence: 0.96539235

00:53:42.255 --> 00:53:43.695 The study is ongoing. We

NOTE Confidence: 0.96539235

00:53:43.695 --> 00:53:44.735 are about a third of

NOTE Confidence: 0.96539235

00:53:44.735 --> 00:53:45.715 the way through.

NOTE Confidence: 0.93209016

00:53:46.119 --> 00:53:47.500 Hopefully, we have results,

NOTE Confidence: 0.93787116

00:53:49.080 --> 00:53:50.119 in in a couple of

NOTE Confidence: 0.93787116

00:53:50.119 --> 00:53:50.619 years.

NOTE Confidence: 0.9907895

00:53:51.800 --> 00:53:53.080 So thank you for your

NOTE Confidence: 0.9907895

00:53:53.080 --> 00:53:54.119 attention. I'm happy to take

NOTE Confidence: 0.9907895

00:53:54.119 --> 00:53:55.580 questions if you have any.

NOTE Confidence: 0.98195744

00:54:01.075 --> 00:54:02.055 I think you're muted.

NOTE Confidence: 0.98705804

00:54:04.194 --> 00:54:05.335 Oh, I can't hear you.
NOTE Confidence: 0.9555101

00:54:11.760 --> 00:54:12.880 I can't hear you. I
NOTE Confidence: 0.9555101

00:54:12.880 --> 00:54:13.920 don't know if anyone else
NOTE Confidence: 0.9555101

00:54:13.920 --> 00:54:14.420 can.
NOTE Confidence: 0.95249915

00:54:46.640 --> 00:54:48.160 I can definitely see the
NOTE Confidence: 0.95249915

00:54:48.160 --> 00:54:48.660 chat.
NOTE Confidence: 0.975137

00:54:49.119 --> 00:54:50.160 So if you have questions,
NOTE Confidence: 0.975137

00:54:50.160 --> 00:54:51.539 happy to answer questions.
NOTE Confidence: 0.93547475

00:54:58.375 --> 00:54:59.594 Oh, can you hear me?
NOTE Confidence: 0.67571914

00:55:00.215 --> 00:55:01.195 Yeah. Yeah.
NOTE Confidence: 0.96009034

00:55:01.655 --> 00:55:03.735 Oh, great talk. You mentioned
NOTE Confidence: 0.96009034

00:55:03.735 --> 00:55:04.235 that
NOTE Confidence: 0.9994894

00:55:04.614 --> 00:55:05.114 edibles
NOTE Confidence: 0.95948887

00:55:06.215 --> 00:55:06.715 are
NOTE Confidence: 0.93552506

00:55:08.000 --> 00:55:09.839 are good but less potent
NOTE Confidence: 0.93552506

00:55:09.839 --> 00:55:10.739 than smoking.

NOTE Confidence: 0.978429
00:55:11.599 --> 00:55:13.359 Did you also mention edibles
NOTE Confidence: 0.978429
00:55:13.359 --> 00:55:14.640 are good for pain but
NOTE Confidence: 0.978429
00:55:14.640 --> 00:55:15.780 not function?
NOTE Confidence: 0.9551651
00:55:16.559 --> 00:55:17.700 Did I get that right?
NOTE Confidence: 0.9551651
00:55:17.920 --> 00:55:19.280 So I I I I
NOTE Confidence: 0.9551651
00:55:19.280 --> 00:55:20.480 would not say good or
NOTE Confidence: 0.9551651
00:55:20.480 --> 00:55:22.185 bad. I I try and
NOTE Confidence: 0.9551651
00:55:22.185 --> 00:55:23.945 steal care from using those
NOTE Confidence: 0.9551651
00:55:23.945 --> 00:55:24.925 kinds of adjectives.
NOTE Confidence: 0.98270804
00:55:25.385 --> 00:55:26.345 I I would I would
NOTE Confidence: 0.98270804
00:55:26.345 --> 00:55:27.085 say that,
NOTE Confidence: 0.94333804
00:55:30.585 --> 00:55:31.885 that there are differences,
NOTE Confidence: 0.99815947
00:55:32.265 --> 00:55:32.765 pharmacokinetic
NOTE Confidence: 0.8412453
00:55:33.145 --> 00:55:34.285 differences between
NOTE Confidence: 0.9995005
00:55:34.930 --> 00:55:35.430 edibles
NOTE Confidence: 0.9225949

00:55:35.810 --> 00:55:37.010 and, of course, smoke and
NOTE Confidence: 0.9225949

00:55:37.010 --> 00:55:38.370 vape, which and there are
NOTE Confidence: 0.9225949

00:55:38.370 --> 00:55:39.910 some advantages and disadvantages
NOTE Confidence: 0.9929727

00:55:40.450 --> 00:55:41.750 to to both.
NOTE Confidence: 0.99100953

00:55:42.370 --> 00:55:44.290 When one consumes an edible,
NOTE Confidence: 0.99100953

00:55:44.290 --> 00:55:44.790 the
NOTE Confidence: 0.9972729

00:55:45.730 --> 00:55:47.570 the duration of exposure is
NOTE Confidence: 0.9972729

00:55:47.570 --> 00:55:48.390 a lot longer
NOTE Confidence: 0.9486893

00:55:49.215 --> 00:55:49.655 than,
NOTE Confidence: 0.97993815

00:55:50.095 --> 00:55:51.635 when one smokes or vapes.
NOTE Confidence: 0.9825443

00:55:52.015 --> 00:55:52.915 Also, the
NOTE Confidence: 0.99244267

00:55:53.455 --> 00:55:53.955 the
NOTE Confidence: 0.9719936

00:55:54.255 --> 00:55:55.775 the effects emerge a lot
NOTE Confidence: 0.9719936

00:55:55.775 --> 00:55:57.375 slower, but then, of course,
NOTE Confidence: 0.9719936

00:55:57.375 --> 00:55:58.515 last a lot longer.
NOTE Confidence: 0.9974046

00:55:59.135 --> 00:55:59.795 The disadvantages

NOTE Confidence: 0.9968807
00:56:00.335 --> 00:56:01.475 of of consuming
NOTE Confidence: 0.95497155
00:56:01.935 --> 00:56:02.755 these products,
NOTE Confidence: 0.99074847
00:56:03.375 --> 00:56:03.875 orally
NOTE Confidence: 0.99369025
00:56:04.190 --> 00:56:05.470 is that there's there's a
NOTE Confidence: 0.99369025
00:56:05.470 --> 00:56:05.970 lot
NOTE Confidence: 0.99893785
00:56:06.350 --> 00:56:07.010 of variability
NOTE Confidence: 0.9684167
00:56:07.950 --> 00:56:09.170 in the bioavailability
NOTE Confidence: 0.9932739
00:56:09.950 --> 00:56:11.570 of the of of THC.
NOTE Confidence: 0.99612117
00:56:12.750 --> 00:56:14.370 Also, when you consume
NOTE Confidence: 0.99984574
00:56:14.670 --> 00:56:15.170 THC
NOTE Confidence: 0.98012686
00:56:15.470 --> 00:56:17.570 orally or cannabis products orally,
NOTE Confidence: 0.99769914
00:56:18.430 --> 00:56:19.330 there is
NOTE Confidence: 0.9980229
00:56:19.935 --> 00:56:20.915 a greater
NOTE Confidence: 0.89996624
00:56:25.614 --> 00:56:27.795 synthesis of an active metabolite
NOTE Confidence: 0.89996624
00:56:27.935 --> 00:56:28.675 of THC,
NOTE Confidence: 0.9960708

00:56:29.775 --> 00:56:31.535 and that active metabolite of

NOTE Confidence: 0.9960708

00:56:31.535 --> 00:56:33.614 THC tends to be more

NOTE Confidence: 0.9960708

00:56:33.614 --> 00:56:35.475 potent than THC itself.

NOTE Confidence: 0.9966304

00:56:36.230 --> 00:56:38.569 So some people might experience,

NOTE Confidence: 0.95363903

00:56:40.869 --> 00:56:43.030 more negative psychotropic effects in

NOTE Confidence: 0.95363903

00:56:43.030 --> 00:56:43.530 theory,

NOTE Confidence: 0.9991456

00:56:44.069 --> 00:56:45.530 when they consume edibles.

NOTE Confidence: 0.9675344

00:56:46.789 --> 00:56:48.069 I don't think there's been

NOTE Confidence: 0.9675344

00:56:48.069 --> 00:56:49.530 any study to my knowledge

NOTE Confidence: 0.97026205

00:56:49.864 --> 00:56:52.204 that has compared oral versus,

NOTE Confidence: 0.6897388

00:56:52.825 --> 00:56:53.805 vague to smoked

NOTE Confidence: 0.7540307

00:56:54.265 --> 00:56:54.765 THC,

NOTE Confidence: 0.9995186

00:56:55.385 --> 00:56:56.204 for pain.

NOTE Confidence: 0.99929905

00:56:59.305 --> 00:57:00.744 And the study that you're

NOTE Confidence: 0.99929905

00:57:00.744 --> 00:57:02.364 proposing will do that?

NOTE Confidence: 0.99831

00:57:03.650 --> 00:57:04.930 The study that we are

NOTE Confidence: 0.99831
00:57:04.930 --> 00:57:05.430 proposing,
NOTE Confidence: 0.995845
00:57:06.530 --> 00:57:07.270 the THC
NOTE Confidence: 0.99630517
00:57:07.730 --> 00:57:09.350 is in an oral form.
NOTE Confidence: 0.9804337
00:57:10.530 --> 00:57:11.410 Like I mentioned to you
NOTE Confidence: 0.9804337
00:57:11.410 --> 00:57:13.250 earlier, it's very unlikely the
NOTE Confidence: 0.9804337
00:57:13.410 --> 00:57:14.690 that the FDA is going
NOTE Confidence: 0.9804337
00:57:14.690 --> 00:57:16.585 to approve of any drug
NOTE Confidence: 0.9804337
00:57:16.585 --> 00:57:17.705 that's going that would that
NOTE Confidence: 0.9804337
00:57:17.705 --> 00:57:18.845 needs to be smoked.
NOTE Confidence: 0.993456
00:57:19.465 --> 00:57:21.245 That's just not gonna happen.
NOTE Confidence: 0.9814274
00:57:21.705 --> 00:57:22.585 And so that's one of
NOTE Confidence: 0.9814274
00:57:22.585 --> 00:57:24.265 the one of the interesting
NOTE Confidence: 0.9814274
00:57:24.265 --> 00:57:26.045 things about this space that,
NOTE Confidence: 0.97723883
00:57:26.825 --> 00:57:28.285 people who are using cannabis
NOTE Confidence: 0.97723883
00:57:28.425 --> 00:57:29.705 are mostly using it by
NOTE Confidence: 0.97723883

00:57:29.705 --> 00:57:30.205 smoking,
NOTE Confidence: 0.9875428

00:57:30.970 --> 00:57:32.490 but research that's being done
NOTE Confidence: 0.9875428

00:57:32.490 --> 00:57:33.790 on cannabis and smoking
NOTE Confidence: 0.9980986

00:57:34.250 --> 00:57:35.930 cannot use smoking as a
NOTE Confidence: 0.9980986

00:57:35.930 --> 00:57:37.790 way of delivering cannabis. So
NOTE Confidence: 0.9980986

00:57:37.930 --> 00:57:39.210 there's always going to be
NOTE Confidence: 0.9980986

00:57:39.210 --> 00:57:40.590 this mismatch between
NOTE Confidence: 0.9995192

00:57:41.210 --> 00:57:42.990 the real world evidence
NOTE Confidence: 0.8996265

00:57:43.370 --> 00:57:44.970 and what we as clinical
NOTE Confidence: 0.8996265

00:57:44.970 --> 00:57:46.510 scientists are trying to
NOTE Confidence: 0.98808146

00:57:47.265 --> 00:57:48.005 to determine.
NOTE Confidence: 0.9433437

00:57:52.704 --> 00:57:53.984 Yeah. For the last study,
NOTE Confidence: 0.9433437

00:57:53.984 --> 00:57:55.744 was it oral? Which, the
NOTE Confidence: 0.9433437

00:57:55.744 --> 00:57:57.345 study in Germany with the
NOTE Confidence: 0.9433437

00:57:57.345 --> 00:57:58.704 eight hundred subjects? Yes. That
NOTE Confidence: 0.9433437

00:57:58.704 --> 00:57:59.444 was oral.

NOTE Confidence: 0.8820549
00:58:00.960 --> 00:58:02.580 And they call their product
NOTE Confidence: 0.8658789
00:58:03.280 --> 00:58:04.500 VER one.
NOTE Confidence: 0.9149274
00:58:06.800 --> 00:58:08.400 I I I'm you I'm
NOTE Confidence: 0.9149274
00:58:08.400 --> 00:58:10.080 happy to send the paper
NOTE Confidence: 0.9149274
00:58:10.080 --> 00:58:10.880 to you. It's in nature
NOTE Confidence: 0.9149274
00:58:10.880 --> 00:58:12.800 and, medicine, so it's easily
NOTE Confidence: 0.9149274
00:58:12.800 --> 00:58:13.300 accessible.
NOTE Confidence: 0.9949857
00:58:23.055 --> 00:58:24.355 Are there any more questions?
NOTE Confidence: 0.9378659
00:58:27.466 --> 00:58:28.746 Thank you so much, doctor
NOTE Confidence: 0.9378659
00:58:28.746 --> 00:58:30.846 D'Souza and everyone for joining.
NOTE Confidence: 0.9378659
00:58:30.986 --> 00:58:31.726 Have a wonderful
NOTE Confidence: 0.9915012
00:58:32.106 --> 00:58:33.326 day. Bye.
NOTE Confidence: 0.9991013
00:58:34.026 --> 00:58:34.526 Bye.