WEBVTT

NOTE duration:"01:09:56.4800000"

NOTE language:en-us

NOTE Confidence: 0.847765982151031

00:00:00.000 --> 00:00:02.954 Get started, it is my real pleasure

NOTE Confidence: 0.847765982151031

 $00:00:02.954 \dashrightarrow 00:00:05.305$ to welcome doctor Elliot Stein

NOTE Confidence: 0.847765982151031

 $00:00:05.305 \rightarrow 00:00:07.810$ to the psychiatry grand rounds.

NOTE Confidence: 0.847765982151031

00:00:07.810 --> 00:00:10.918 Today, Doctor Stein is chief of the

NOTE Confidence: 0.847765982151031

 $00:00:10.918 \rightarrow 00:00:13.291$ neuroimaging research branch and chief

NOTE Confidence: 0.847765982151031

 $00:00:13.291 \rightarrow 00:00:15.716$ of cognitive and affective neuroscience

NOTE Confidence: 0.847765982151031

 $00{:}00{:}15.716 \dashrightarrow 00{:}00{:}18.538$ of addiction section at the National

NOTE Confidence: 0.847765982151031

 $00:00:18.538 \rightarrow 00:00:21.118$ Institute of drug abuse is intramural

NOTE Confidence: 0.847765982151031

00:00:21.118 --> 00:00:23.290 research program in Baltimore.

NOTE Confidence: 0.847765982151031

 $00:00:23.290 \longrightarrow 00:00:25.030$ He interesting Lee.

NOTE Confidence: 0.847765982151031

00:00:25.030 --> 00:00:28.894 This is a little nugget I didn't know,

NOTE Confidence: 0.847765982151031

00:00:28.900 --> 00:00:31.600 but Doctor Stein actually started his

NOTE Confidence: 0.847765982151031

 $00:00:31.600 \rightarrow 00:00:34.489$ his post high school education here

NOTE Confidence: 0.847765982151031

 $00:00:34.489 \rightarrow 00:00:37.513$ in Connecticut and got his bachelors

00:00:37.513 --> 00:00:40.049 at Quinnipiac University in Biology

NOTE Confidence: 0.847765982151031

 $00:00:40.049 \rightarrow 00:00:42.935$ an completed a PhD in neurophysiology

NOTE Confidence: 0.847765982151031

00:00:42.935 - > 00:00:45.284 at the University of Maryland,

NOTE Confidence: 0.847765982151031

 $00:00:45.284 \longrightarrow 00:00:48.675$ School of Medicine and then did a

NOTE Confidence: 0.847765982151031

00:00:48.675 --> 00:00:51.240 postdoc in behavioral neurobiology at

NOTE Confidence: 0.847765982151031

 $00{:}00{:}51{.}240 \dashrightarrow 00{:}00{:}54{.}089$ Caltech with doctor James Olds who.

NOTE Confidence: 0.847765982151031

 $00{:}00{:}54.090 \dashrightarrow 00{:}00{:}57.586$ Many of you may recall was famous for

NOTE Confidence: 0.847765982151031

 $00:00:57.586 \rightarrow 00:00:59.851$ discovering what would got labeled

NOTE Confidence: 0.847765982151031

 $00:00:59.851 \dashrightarrow 00:01:02.910$ as the pleasure center in the brain.

NOTE Confidence: 0.847765982151031

00:01:02.910 --> 00:01:05.034 Doctor Olds is a psychologist who

NOTE Confidence: 0.847765982151031

 $00:01:05.034 \rightarrow 00:01:07.579$ firmly believed that the answer to

NOTE Confidence: 0.847765982151031

00:01:07.579 --> 00:01:09.169 understanding various psychological

NOTE Confidence: 0.847765982151031

 $00:01:09.169 \dashrightarrow 00:01:11.289$ processes like human motivation,

NOTE Confidence: 0.847765982151031

 $00{:}01{:}11{.}290 \dashrightarrow 00{:}01{:}14{.}377$ which he was very interested in studying,

NOTE Confidence: 0.847765982151031

 $00{:}01{:}14.380 \dashrightarrow 00{:}01{:}16.580$ and made big contributions on,

 $00:01:16.580 \longrightarrow 00:01:17.024$ needed,

NOTE Confidence: 0.847765982151031

 $00:01:17.024 \rightarrow 00:01:19.688$ needed study of the central nervous

NOTE Confidence: 0.847765982151031

 $00:01:19.688 \longrightarrow 00:01:21.869$ system and the brain.

NOTE Confidence: 0.847765982151031

 $00:01:21.870 \longrightarrow 00:01:25.006$ And this is all before image Ng.

NOTE Confidence: 0.847765982151031

00:01:25.010 --> 00:01:27.831 I say this because I think I

NOTE Confidence: 0.847765982151031

 $00:01:27.831 \longrightarrow 00:01:30.642$ think that this time has really

NOTE Confidence: 0.847765982151031

 $00:01:30.642 \rightarrow 00:01:33.660$ epitomized that sort of spirit and

NOTE Confidence: 0.847765982151031

 $00:01:33.660 \rightarrow 00:01:36.916$ goal in the work that he has done.

NOTE Confidence: 0.847765982151031

 $00:01:36.920 \rightarrow 00:01:39.075$ After getting if completing his

NOTE Confidence: 0.847765982151031

 $00:01:39.075 \longrightarrow 00:01:41.736$ post doc with Doctor Olds that

NOTE Confidence: 0.847765982151031

 $00{:}01{:}41.736 \dashrightarrow 00{:}01{:}43.876$ this time moved to Wisconsin,

NOTE Confidence: 0.847765982151031

 $00:01:43.880 \dashrightarrow 00:01:46.778$ he was on the faculty at Marquette

NOTE Confidence: 0.847765982151031

 $00:01:46.778 \dashrightarrow 00:01:49.455$ University and then on the faculty

NOTE Confidence: 0.847765982151031

00:01:49.455 --> 00:01:51.710 of Medical College of Wisconsin,

NOTE Confidence: 0.847765982151031

 $00{:}01{:}51{.}710 \dashrightarrow 00{:}01{:}53{.}885$ and during the birth of

NOTE Confidence: 0.847765982151031

00:01:53.885 - 00:01:54.755 functional neuroimaging,

- NOTE Confidence: 0.847765982151031
- 00:01:54.760 --> 00:01:58.669 an he was promoted all the way to full
- NOTE Confidence: 0.803226053714752
- $00:01:58.670 \longrightarrow 00:02:00.850$ professor. He was there for
- NOTE Confidence: 0.803226053714752
- $00{:}02{:}00{.}850 \dashrightarrow 00{:}02{:}04{.}585$ a long time and then in 2002 he joined
- NOTE Confidence: 0.803226053714752
- $00:02:04.585 \rightarrow 00:02:08.255$ the naida IRP as chief of the newly.
- NOTE Confidence: 0.803226053714752
- $00:02:08.260 \rightarrow 00:02:10.956$ Created neuroimaging research branch.
- NOTE Confidence: 0.803226053714752
- $00{:}02{:}10.956 \dashrightarrow 00{:}02{:}15.633$ This is really important because I think
- NOTE Confidence: 0.803226053714752
- $00:02:15.633 \rightarrow 00:02:18.837$ one of the real major contributions
- NOTE Confidence: 0.803226053714752
- $00:02:18.837 \longrightarrow 00:02:22.329$ of doctor Stein is that he used
- NOTE Confidence: 0.803226053714752
- $00:02:22.329 \rightarrow 00:02:25.023$ a number of different MRI tools,
- NOTE Confidence: 0.803226053714752
- 00:02:25.030 --> 00:02:27.830 both functional MRI NMR spectroscopy,
- NOTE Confidence: 0.803226053714752
- 00:02:27.830 --> 00:02:28.960 functional connectivity,
- NOTE Confidence: 0.803226053714752
- $00:02:28.960 \longrightarrow 00:02:31.785$ specially looking also at white
- NOTE Confidence: 0.803226053714752
- $00{:}02{:}31.785 \dashrightarrow 00{:}02{:}34.691$ matter tracks using diffusion tensor
- NOTE Confidence: 0.803226053714752
- $00{:}02{:}34{.}691 \dashrightarrow 00{:}02{:}37{.}516$ imaging and of course positive
- NOTE Confidence: 0.803226053714752
- $00:02:37.516 \rightarrow 00:02:39.590$ positive emission tomography pet.
- NOTE Confidence: 0.803226053714752

- $00:02:39.590 \longrightarrow 00:02:40.928$ Studies as well,
- NOTE Confidence: 0.803226053714752
- $00:02:40.928 \longrightarrow 00:02:42.266$ and most importantly,
- NOTE Confidence: 0.803226053714752
- $00:02:42.270 \rightarrow 00:02:45.830$ doing this both in humans and in animals,
- NOTE Confidence: 0.803226053714752
- $00:02:45.830 \longrightarrow 00:02:47.322$ which you can do.
- NOTE Confidence: 0.803226053714752
- $00{:}02{:}47.322 \dashrightarrow 00{:}02{:}50.163$ I think at using the naida IRP
- NOTE Confidence: 0.803226053714752
- $00{:}02{:}50{.}163 \dashrightarrow 00{:}02{:}53{.}265$ strengths of having both animal basic
- NOTE Confidence: 0.803226053714752
- 00:02:53.265 --> 00:02:56.088 scientists there as well as human,
- NOTE Confidence: 0.803226053714752
- $00:02:56.090 \rightarrow 00:02:58.320$ your scientists and this allowed
- NOTE Confidence: 0.803226053714752
- $00:02:58.320 \longrightarrow 00:03:00.550$ him to map an image.
- NOTE Confidence: 0.803226053714752
- 00:03:00.550 00:03:03.226 The brain in rodents in animals,
- NOTE Confidence: 0.803226053714752
- 00:03:03.230 --> 00:03:04.568 in nonhuman primates,
- NOTE Confidence: 0.803226053714752
- $00:03:04.568 \longrightarrow 00:03:06.798$ but also then translate that,
- NOTE Confidence: 0.803226053714752
- $00:03:06.800 \dashrightarrow 00:03:09.978$ and consider how to move that into.
- NOTE Confidence: 0.803226053714752
- 00:03:09.980 --> 00:03:12.320 The human brain imaging space,
- NOTE Confidence: 0.803226053714752
- $00:03:12.320 \dashrightarrow 00:03:16.390$ and I think that we benefited a lot from that
- NOTE Confidence: 0.803226053714752
- $00:03:16.481 \longrightarrow 00:03:20.275$ kind of Translational back and forth work.

- NOTE Confidence: 0.803226053714752
- $00:03:20.280 \longrightarrow 00:03:23.549$ The other thing that has has,
- NOTE Confidence: 0.803226053714752
- $00{:}03{:}23{.}550 \dashrightarrow 00{:}03{:}25{.}806$ I think pioneered has been what
- NOTE Confidence: 0.803226053714752
- $00{:}03{:}25.806 \dashrightarrow 00{:}03{:}28.061$ he identifies as event related
- NOTE Confidence: 0.803226053714752
- $00:03:28.061 \rightarrow 00:03:30.098$ cognitive neuroscience designs,
- NOTE Confidence: 0.803226053714752
- $00{:}03{:}30{.}100 \dashrightarrow 00{:}03{:}32{.}440$ which allowed us to look
- NOTE Confidence: 0.803226053714752
- $00:03:32.440 \longrightarrow 00:03:33.844$ at functional neuroimaging,
- NOTE Confidence: 0.803226053714752
- $00:03:33.850 \rightarrow 00:03:35.254$ meaning essentially understanding
- NOTE Confidence: 0.803226053714752
- $00:03:35.254 \longrightarrow 00:03:36.658$ different brain functions,
- NOTE Confidence: 0.803226053714752
- $00:03:36.660 \rightarrow 00:03:38.552$ an understanding the circuits
- NOTE Confidence: 0.803226053714752
- $00:03:38.552 \rightarrow 00:03:40.444$ from a systems science.
- NOTE Confidence: 0.803226053714752
- $00:03:40.450 \rightarrow 00:03:42.580$ And understanding different networks that
- NOTE Confidence: 0.803226053714752
- $00{:}03{:}42.580 \dashrightarrow 00{:}03{:}44.710$ contribute to those different functions.
- NOTE Confidence: 0.803226053714752
- $00:03:44.710 \dashrightarrow 00:03:48.200$ One of the key ones that that he started to
- NOTE Confidence: 0.803226053714752
- 00:03:48.289 --> 00:03:51.950 talk about was the executive control network,
- NOTE Confidence: 0.803226053714752
- $00:03:51.950 \longrightarrow 00:03:54.506$ based on findings that he had,
- NOTE Confidence: 0.803226053714752

 $00:03:54.510 \rightarrow 00:03:56.964$ which showed the chronic drug use

NOTE Confidence: 0.803226053714752

 $00:03:56.964 \rightarrow 00:03:59.190$ alters this executive control network.

NOTE Confidence: 0.803226053714752

 $00:03:59.190 \longrightarrow 00:04:01.746$ In addition to that he has.

NOTE Confidence: 0.803226053714752

 $00{:}04{:}01.750 \dashrightarrow 00{:}04{:}04.870$ I would credit him with a lot of

NOTE Confidence: 0.803226053714752

00:04:04.870 --> 00:04:06.664 really critical work identifying

NOTE Confidence: 0.803226053714752

 $00:04:06.664 \rightarrow 00:04:08.984$ the role of the insula,

NOTE Confidence: 0.803226053714752

 $00:04:08.990 \longrightarrow 00:04:11.180$ which is an int receptive.

NOTE Confidence: 0.803226053714752

 $00:04:11.180 \rightarrow 00:04:15.698$ Hub in the brain for feelings in the body.

NOTE Confidence: 0.803226053714752

 $00{:}04{:}15{.}700 \dashrightarrow 00{:}04{:}18{.}430$ Signals that coming from inside of

NOTE Confidence: 0.803226053714752

 $00:04:18.430 \rightarrow 00:04:21.655$ the body and his work has really

NOTE Confidence: 0.803226053714752

 $00{:}04{:}21.655 \dashrightarrow 00{:}04{:}24.714$ sort of move the field forward in

NOTE Confidence: 0.803226053714752

 $00:04:24.809 \rightarrow 00:04:26.951$ addiction around understanding

NOTE Confidence: 0.803226053714752

 $00:04:26.951 \longrightarrow 00:04:29.807$ insulin networks as well.

NOTE Confidence: 0.803226053714752

 $00:04:29.810 \longrightarrow 00:04:32.778$ I think the since 2002 if we think

NOTE Confidence: 0.803226053714752

 $00:04:32.778 \dashrightarrow 00:04:35.600$ back the last two decades there has

NOTE Confidence: 0.803226053714752

 $00:04:35.600 \longrightarrow 00:04:38.651$ been a lot of signs showing sort

00:04:38.651 --> 00:04:41.567 of addiction as a brain disease,

NOTE Confidence: 0.803226053714752

 $00:04:41.570 \longrightarrow 00:04:42.704$ so to speak.

NOTE Confidence: 0.803226053714752

00:04:42.704 --> 00:04:44.972 And doctor sign has really brought

NOTE Confidence: 0.803226053714752

 $00:04:44.972 \longrightarrow 00:04:47.322$ that home with translating the

NOTE Confidence: 0.803226053714752

 $00{:}04{:}47{.}322 \dashrightarrow 00{:}04{:}49{.}687$ work from animal experiments to

NOTE Confidence: 0.803226053714752

 $00{:}04{:}49.687 \dashrightarrow 00{:}04{:}52.202$ showing the long term changes that

NOTE Confidence: 0.803226053714752

 $00:04:52.202 \rightarrow 00:04:55.016$ occur from chronic drug use in the

NOTE Confidence: 0.803226053714752

 $00:04:55.016 \rightarrow 00:04:57.554$ brain and connecting that then too.

NOTE Confidence: 0.803226053714752

 $00{:}04{:}57{.}560 \dashrightarrow 00{:}04{:}59{.}989$ Unical outcomes one of the things that

NOTE Confidence: 0.803226053714752

 $00{:}04{:}59{.}989 \dashrightarrow 00{:}05{:}02{.}763$ I think has been really critical is

NOTE Confidence: 0.803226053714752

 $00:05:02.763 \rightarrow 00:05:05.259$ he's also pushed the envelope trying

NOTE Confidence: 0.803226053714752

 $00{:}05{:}05{.}332 \dashrightarrow 00{:}05{:}07{.}760$ to understand individual differences

NOTE Confidence: 0.803226053714752

00:05:07.760 --> 00:05:10.188 looking at genetic polymorphisms,

NOTE Confidence: 0.803226053714752

 $00{:}05{:}10.190 \dashrightarrow 00{:}05{:}12.410$ but also affect if personality

NOTE Confidence: 0.803226053714752

 $00:05:12.410 \longrightarrow 00:05:13.742$ environmental interactions that

 $00:05:13.742 \rightarrow 00:05:16.497$ are so important in affecting this.

NOTE Confidence: 0.803226053714752

00:05:16.500 --> 00:05:17.494 These alterations,

NOTE Confidence: 0.803226053714752

 $00:05:17.494 \rightarrow 00:05:19.979$ long-term alterations as a function

NOTE Confidence: 0.803226053714752

 $00:05:19.979 \longrightarrow 00:05:23.042$ of chronic drug use as a function

NOTE Confidence: 0.803226053714752

 $00:05:23.042 \longrightarrow 00:05:24.167$ of drug with drawal,

NOTE Confidence: 0.803226053714752

 $00{:}05{:}24.170 \dashrightarrow 00{:}05{:}26.636$ and more recently now into what

NOTE Confidence: 0.803226053714752

 $00{:}05{:}26.636 \dashrightarrow 00{:}05{:}29.190$ are the effects of treatment.

NOTE Confidence: 0.803226053714752

 $00:05:29.190 \longrightarrow 00:05:31.620$ And so he is plunged forward.

NOTE Confidence: 0.803226053714752

 $00:05:31.620 \dashrightarrow 00:05:34.412$ An has been looking at how we can

NOTE Confidence: 0.803226053714752

 $00:05:34.412 \rightarrow 00:05:35.604$ develop efficacious strategies

NOTE Confidence: 0.803226053714752

 $00:05:35.604 \rightarrow 00:05:37.714$ for treating and reversing these

NOTE Confidence: 0.803226053714752

 $00{:}05{:}37{.}714 \dashrightarrow 00{:}05{:}40{.}130$ long term effects of addiction.

NOTE Confidence: 0.803226053714752

 $00{:}05{:}40{.}130 \dashrightarrow 00{:}05{:}42{.}554$ He has authored more than 250

NOTE Confidence: 0.803226053714752

00:05:42.554 --> 00:05:43.766 original research papers,

NOTE Confidence: 0.803226053714752

 $00:05:43.770 \longrightarrow 00:05:45.362$ reviews and book chapters.

NOTE Confidence: 0.803226053714752

 $00:05:45.362 \rightarrow 00:05:47.750$ He's been cited more than 17,000

- NOTE Confidence: 0.803226053714752
- $00:05:47.820 \longrightarrow 00:05:49.440$ times in the literature.
- NOTE Confidence: 0.872125327587128
- $00:05:49.440 \dashrightarrow 00:05:53.085$ About half of that in the last five years.
- NOTE Confidence: 0.872125327587128
- $00:05:53.090 \longrightarrow 00:05:55.508$ So really continuing to have a
- NOTE Confidence: 0.872125327587128
- $00:05:55.508 \rightarrow 00:05:57.950$ major current impact on the field.
- NOTE Confidence: 0.872125327587128
- $00:05:57.950 \dashrightarrow 00:06:00.440$ And so it's my real pleasure.
- NOTE Confidence: 0.872125327587128
- $00:06:00.440 \longrightarrow 00:06:02.897$ To give you doctor Elliot Stein and
- NOTE Confidence: 0.872125327587128
- $00:06:02.897 \rightarrow 00:06:05.748$ he's going to be speaking about state,
- NOTE Confidence: 0.872125327587128
- $00:06:05.750 \longrightarrow 00:06:07.162$ trait and subtype consideration
- NOTE Confidence: 0.872125327587128
- $00{:}06{:}07{.}162 \dashrightarrow 00{:}06{:}08{.}927$ and substance use disorders of
- NOTE Confidence: 0.872125327587128
- $00:06:08.927 \longrightarrow 00:06:10.668$ you from nicotine dependence.
- NOTE Confidence: 0.850576758384705
- 00:06:11.350 --> 00:06:13.730 Well, thanks for Gina,
- NOTE Confidence: 0.850576758384705
- $00:06:13.730 \longrightarrow 00:06:16.705$ thanks for that very kind,
- NOTE Confidence: 0.850576758384705
- 00:06:16.710 --> 00:06:17.919 overly kind introduction.
- NOTE Confidence: 0.850576758384705
- $00{:}06{:}17{.}919 \dashrightarrow 00{:}06{:}19{.}934$ Thanks for every one for attending
- NOTE Confidence: 0.850576758384705
- $00:06:19.934 \rightarrow 00:06:22.137$ today in this rather awkward talking
- NOTE Confidence: 0.850576758384705

 $00:06:22.137 \longrightarrow 00:06:24.499$ to screen that we that we've been

NOTE Confidence: 0.850576758384705

 $00{:}06{:}24.499 \dashrightarrow 00{:}06{:}26.627$ doing for the last couple of months.

NOTE Confidence: 0.850576758384705

 $00{:}06{:}26{.}630 \dashrightarrow 00{:}06{:}29{.}366$ So what I'm going to try to do today

NOTE Confidence: 0.850576758384705

00:06:29.366 --> 00:06:32.039 is give you a bit of an overview

NOTE Confidence: 0.850576758384705

 $00:06:32.039 \longrightarrow 00:06:34.739$ not going to be able to touch on

NOTE Confidence: 0.850576758384705

 $00{:}06{:}34.739 \dashrightarrow 00{:}06{:}36.704$ all of the things that Regina

NOTE Confidence: 0.850576758384705

00:06:36.704 --> 00:06:38.000 mentioned in her introduction,

NOTE Confidence: 0.850576758384705

 $00{:}06{:}38{.}000 \dashrightarrow 00{:}06{:}40{.}328$ but a bit of an overview of our

NOTE Confidence: 0.850576758384705

 $00:06:40.328 \rightarrow 00:06:42.740$ thinking the last few years on how

NOTE Confidence: 0.850576758384705

 $00:06:42.740 \longrightarrow 00:06:44.495$ we are approaching a substance,

NOTE Confidence: 0.850576758384705

 $00:06:44.500 \rightarrow 00:06:46.708$ use disorder and maybe some insights

NOTE Confidence: 0.850576758384705

 $00:06:46.708 \rightarrow 00:06:48.810$ and maybe some controversies as to why.

NOTE Confidence: 0.850576758384705

 $00{:}06{:}48.810 \dashrightarrow 00{:}06{:}52.620$ Our treatment outcomes are still not

NOTE Confidence: 0.850576758384705

 $00:06:52.620 \rightarrow 00:06:54.525$ particularly particularly favorable.

NOTE Confidence: 0.850576758384705

 $00{:}06{:}54{.}530 \dashrightarrow 00{:}07{:}00{.}140$ So let's see if this works.

NOTE Confidence: 0.850576758384705

 $00{:}07{:}00{.}140 \dashrightarrow 00{:}07{:}03{.}700$ Ah. OK, there we go.

 $00:07:03.700 \longrightarrow 00:07:06.290$ OK well smoking is bad so if

NOTE Confidence: 0.850576758384705

 $00:07:06.290 \longrightarrow 00:07:08.633$ smoking is bad then abstinence

NOTE Confidence: 0.850576758384705

 $00{:}07{:}08.633 \dashrightarrow 00{:}07{:}10.925$ abstinence must be good.

NOTE Confidence: 0.850576758384705

 $00:07:10.930 \longrightarrow 00:07:13.636$ Well, most of the move my.

NOTE Confidence: 0.882061958312988

00:07:16.010 --> 00:07:17.810 Pictures of you guys to another

NOTE Confidence: 0.882061958312988

00:07:17.810 - 00:07:20.210 part of the screen. There we go OK.

NOTE Confidence: 0.901125013828278

 $00:07:23.010 \rightarrow 00:07:26.142$ That's better OK, so most of the folks in

NOTE Confidence: 0.901125013828278

 $00:07:26.142 \dashrightarrow 00:07:29.356$ the in America have gotten that message.

NOTE Confidence: 0.901125013828278

 $00{:}07{:}29{.}360 \dashrightarrow 00{:}07{:}32{.}936$ Went down to about 17 or 18% of the

NOTE Confidence: 0.901125013828278

 $00:07:32.936 \rightarrow 00:07:34.613$ country still smoking, unfortunately.

NOTE Confidence: 0.901125013828278

 $00:07:34.613 \rightarrow 00:07:37.994$ We're still doing very poorly in treatment

NOTE Confidence: 0.901125013828278

00:07:37.994 --> 00:07:41.358 outcomes with at least 50% of the of those

NOTE Confidence: 0.901125013828278

 $00{:}07{:}41.358 \dashrightarrow 00{:}07{:}44.153$ who want to quit returning to active

NOTE Confidence: 0.901125013828278

 $00{:}07{:}44.153 \dashrightarrow 00{:}07{:}47.233$ smoking within about a month or so.

NOTE Confidence: 0.901125013828278

 $00:07:47.240 \longrightarrow 00:07:48.524$ So what's going on?

 $00:07:48.524 \rightarrow 00:07:51.420$ What are the bad things that are happening

NOTE Confidence: 0.901125013828278

 $00:07:51.420 \longrightarrow 00:07:54.126$ during abstinence and the basic message?

NOTE Confidence: 0.901125013828278

 $00{:}07{:}54.130 \dashrightarrow 00{:}07{:}56.050$ Here is, it's the nicotine

NOTE Confidence: 0.901125013828278

00:07:56.050 --> 00:07:56.818 withdrawal syndrome.

NOTE Confidence: 0.901125013828278

 $00{:}07{:}56.820 \dashrightarrow 00{:}07{:}59.106$ And as mariela dibiase has said,

NOTE Confidence: 0.901125013828278

 $00{:}07{:}59{.}110 \dashrightarrow 00{:}08{:}01{.}150$ we get we precipitate both somatic

NOTE Confidence: 0.901125013828278

 $00:08:01.150 \longrightarrow 00:08:03.444$ and affect if symptoms of withdrawal

NOTE Confidence: 0.901125013828278

 $00:08:03.444 \rightarrow 00:08:05.619$ during acute during acute abstinence,

NOTE Confidence: 0.901125013828278

 $00:08:05.620 \rightarrow 00:08:07.156$ including things like craving,

NOTE Confidence: 0.901125013828278

00:08:07.156 --> 00:08:08.344 irritability, anxiety, loss,

NOTE Confidence: 0.901125013828278

 $00{:}08{:}08{.}344 \dashrightarrow 00{:}08{:}11{.}158$ we've all been around folks who just

NOTE Confidence: 0.901125013828278

 $00:08:11.158 \rightarrow 00:08:13.328$ quit smoking and then particularly

NOTE Confidence: 0.901125013828278

 $00{:}08{:}13.328 \dashrightarrow 00{:}08{:}15.016$ fun to be around.

NOTE Confidence: 0.901125013828278

 $00:08:15.020 \rightarrow 00:08:17.974$ But it's those negative affect of symptoms

NOTE Confidence: 0.901125013828278

 $00:08:17.974 \rightarrow 00:08:20.959$ that account for can you see my pointer?

NOTE Confidence: 0.901125013828278

 $00:08:20.960 \longrightarrow 00:08:22.148$ Is that possible?

00:08:22.148 --> 00:08:25.412 Yeah, OK, so it's the negative affect of

NOTE Confidence: 0.901125013828278

 $00:08:25.412 \rightarrow 00:08:28.088$ symptoms that account for most of this.

NOTE Confidence: 0.901125013828278

00:08:28.090 --> 00:08:29.790 This failure in treatment,

NOTE Confidence: 0.901125013828278

 $00:08:29.790 \longrightarrow 00:08:31.490$ so negative reinforcement and

NOTE Confidence: 0.901125013828278

 $00:08:31.490 \rightarrow 00:08:33.629$ accidents really are not good friends.

NOTE Confidence: 0.901125013828278

00:08:33.630 --> 00:08:35.178 But you know,

NOTE Confidence: 0.901125013828278

 $00:08:35.178 \longrightarrow 00:08:38.790$ we've known that for quite some time.

NOTE Confidence: 0.901125013828278

 $00:08:38.790 \longrightarrow 00:08:39.672$ So given this,

NOTE Confidence: 0.901125013828278

 $00:08:39.672 \longrightarrow 00:08:41.730$ why are we still so bad at

NOTE Confidence: 0.901125013828278

 $00:08:41.803 \rightarrow 00:08:44.167$ treatment and treatment outcomes?

NOTE Confidence: 0.901125013828278

 $00:08:44.170 \rightarrow 00:08:46.697$ And so the position that I'm going

NOTE Confidence: 0.901125013828278

 $00:08:46.697 \longrightarrow 00:08:49.455$ to layout for you today is that

NOTE Confidence: 0.901125013828278

 $00{:}08{:}49{.}455 \dashrightarrow 00{:}08{:}51{.}849$ that really a brain based approach.

NOTE Confidence: 0.901125013828278

00:08:51.850 --> 00:08:54.209 A systems based approach may be what

NOTE Confidence: 0.901125013828278

 $00:08:54.209 \rightarrow 00:08:55.768$ it's been missing traditionally

 $00:08:55.768 \rightarrow 00:08:57.220$ and without this,

NOTE Confidence: 0.901125013828278

 $00{:}08{:}57{.}220$ --> $00{:}08{:}59{.}140$ without these validated and I

NOTE Confidence: 0.901125013828278

00:08:59.140 --> 00:09:01.060 see and I emphasize validated,

NOTE Confidence: 0.901125013828278

 $00:09:01.060 \rightarrow 00:09:02.215$ clinically validated biomarkers,

NOTE Confidence: 0.901125013828278

 $00:09:02.215 \longrightarrow 00:09:03.370$ we really can't.

NOTE Confidence: 0.901125013828278

 $00{:}09{:}03.370 \dashrightarrow 00{:}09{:}06.058$ That this is sort of my coals

NOTE Confidence: 0.901125013828278

 $00{:}09{:}06{.}058 \dashrightarrow 00{:}09{:}07{.}210$ to Newcastle slide.

NOTE Confidence: 0.901125013828278

 $00:09:07.210 \rightarrow 00:09:09.140$ We can't really objectively assess.

NOTE Confidence: 0.901125013828278

 $00:09:09.140 \longrightarrow 00:09:11.513$ The severity of the level of dependence

NOTE Confidence: 0.901125013828278

 $00:09:11.513 \dashrightarrow 00:09:13.409$ we can fractionate the phenotype.

NOTE Confidence: 0.901125013828278

00:09:13.410 --> 00:09:15.100 We can't do individual differences

NOTE Confidence: 0.901125013828278

 $00:09:15.100 \rightarrow 00:09:16.790$ or personalized medicine were not

NOTE Confidence: 0.901125013828278

 $00{:}09{:}16.846 \dashrightarrow 00{:}09{:}19.054$ able to assess drug development in

NOTE Confidence: 0.901125013828278

 $00:09:19.054 \rightarrow 00:09:20.526$ treatment interventions of objectively,

NOTE Confidence: 0.901125013828278

 $00:09:20.530 \rightarrow 00:09:22.770$ we can't really look at the efficacy

NOTE Confidence: 0.901125013828278

 $00{:}09{:}22.770 \dashrightarrow 00{:}09{:}25.366$ of a treatment until it's too late

- NOTE Confidence: 0.901125013828278
- 00:09:25.366 00:09:26.934 until the individual relapses.
- NOTE Confidence: 0.901125013828278
- 00:09:26.940 --> 00:09:29.076 So I would posit to you,
- NOTE Confidence: 0.901125013828278
- $00:09:29.080 \rightarrow 00:09:32.608$ if you can't measure it, how we really fix.
- NOTE Confidence: 0.901125013828278
- 00:09:32.608 --> 00:09:35.676 And so Matt said, Wanna a former postdoc?
- NOTE Confidence: 0.901125013828278
- $00:09:35.676 \dashrightarrow 00:09:38.220$ And I wrote an opinion piece on this.
- NOTE Confidence: 0.901125013828278
- 00:09:38.220 --> 00:09:40.375 And if you're interested was
- NOTE Confidence: 0.901125013828278
- $00:09:40.375 \longrightarrow 00:09:42.530$ less came out last year.
- NOTE Confidence: 0.901125013828278
- 00:09:42.530 00:09:45.407 So This is why where I may,
- NOTE Confidence: 0.901125013828278
- $00{:}09{:}45{.}410 \dashrightarrow 00{:}09{:}47{.}870$ I may upset a few people.
- NOTE Confidence: 0.901125013828278
- $00:09:47.870 \longrightarrow 00:09:50.126$ What is it that we currently
- NOTE Confidence: 0.901125013828278
- $00:09:50.126 \rightarrow 00:09:53.467$ doing an I took this this quote I
- NOTE Confidence: 0.901125013828278
- $00{:}09{:}53.467 \dashrightarrow 00{:}09{:}56.083$ can't remember which paper it is.
- NOTE Confidence: 0.901125013828278
- $00:09:56.090 \rightarrow 00:09:58.680$ It doesn't matter because we all really
- NOTE Confidence: 0.901125013828278
- $00:09:58.680 \dashrightarrow 00:10:02.260$ say this in the first paragraph about papers,
- NOTE Confidence: 0.901125013828278
- $00{:}10{:}02{.}260 \dashrightarrow 00{:}10{:}04{.}315$ prominent theories of addiction posit
- NOTE Confidence: 0.901125013828278

 $00:10:04.315 \rightarrow 00:10:06.370$ that deficits in prefrontal mode,

NOTE Confidence: 0.901125013828278

 $00{:}10{:}06{.}370 \dashrightarrow 00{:}10{:}07{.}190$ cortical function,

NOTE Confidence: 0.901125013828278

 $00:10:07.190 \longrightarrow 00:10:08.420$ impaired cognitive control,

NOTE Confidence: 0.901125013828278

 $00:10:08.420 \rightarrow 00:10:09.653$ inhibitory prepotent behaviors,

NOTE Confidence: 0.901125013828278

 $00{:}10{:}09{.}653 \dashrightarrow 00{:}10{:}11{.}297$ biasing towards into receptor

NOTE Confidence: 0.901125013828278

00:10:11.297 --> 00:10:12.530 signals and craving.

NOTE Confidence: 0.901125013828278

 $00{:}10{:}12{.}530 \dashrightarrow 00{:}10{:}13{.}226$ It's complicated.

NOTE Confidence: 0.901125013828278

00:10:13.226 --> 00:10:13.574 Right,

NOTE Confidence: 0.901125013828278

 $00:10:13.574 \rightarrow 00:10:16.740$ we all say this in our first paragraph,

NOTE Confidence: 0.901125013828278

 $00:10:16.740 \rightarrow 00:10:19.684$ but when we tried to develop new treatments,

NOTE Confidence: 0.901125013828278

 $00{:}10{:}19.690 \dashrightarrow 00{:}10{:}21.500$ are basic working hypothesis is

NOTE Confidence: 0.901125013828278

 $00:10:21.500 \longrightarrow 00:10:23.310$ something like this better pharmaco

NOTE Confidence: 0.901125013828278

 $00{:}10{:}23.370 \dashrightarrow 00{:}10{:}25.395$ the rapies require more specific and

NOTE Confidence: 0.901125013828278

 $00{:}10{:}25{.}395 \dashrightarrow 00{:}10{:}27{.}015$ selective receptor based agents

NOTE Confidence: 0.901125013828278

00:10:27.015 --> 00:10:28.888 abetter silver bullet if you will,

NOTE Confidence: 0.901125013828278

 $00{:}10{:}28.890 \dashrightarrow 00{:}10{:}30.855$ to engage with these specific

- NOTE Confidence: 0.901125013828278
- 00:10:30.855 --> 00:10:32.820 receptor based system which will
- NOTE Confidence: 0.901125013828278
- 00:10:32.885 --> 00:10:34.657 further prevent drug taking.
- NOTE Confidence: 0.901125013828278
- $00{:}10{:}34.660 \dashrightarrow 00{:}10{:}35.172$ Indeed,
- NOTE Confidence: 0.901125013828278
- $00:10:35.172 \longrightarrow 00:10:37.220$ perhaps universe eviction and
- NOTE Confidence: 0.901125013828278
- $00{:}10{:}37.220 \dashrightarrow 00{:}10{:}39.780$ this treatment based hypothesis is
- NOTE Confidence: 0.901125013828278
- $00{:}10{:}39.854 \dashrightarrow 00{:}10{:}41.914$ coming from the really tremendous
- NOTE Confidence: 0.901125013828278
- $00:10:41.914 \longrightarrow 00:10:43.974$ progress that we made in
- NOTE Confidence: 0.847423493862152
- $00{:}10{:}44.052 \dashrightarrow 00{:}10{:}46.566$ a cellular and molecular basis in
- NOTE Confidence: 0.847423493862152
- $00{:}10{:}46.566 \dashrightarrow 00{:}10{:}50.058$ preclinical work over the last decade or so.
- NOTE Confidence: 0.847423493862152
- 00:10:50.058 --> 00:10:53.229 But as you know, of course this
- NOTE Confidence: 0.847423493862152
- $00:10:53.229 \rightarrow 00:10:54.588$ monotherapy approaches fail.
- NOTE Confidence: 0.847423493862152
- 00:10:54.590 --> 00:10:55.949 Recidivism remains just
- NOTE Confidence: 0.847423493862152
- $00:10:55.949 \rightarrow 00:10:58.214$ unacceptably high for our patients.
- NOTE Confidence: 0.847423493862152
- $00{:}10{:}58.220 \dashrightarrow 00{:}11{:}00.028$ Neither agonist or antagonist
- NOTE Confidence: 0.847423493862152
- $00:11:00.028 \rightarrow 00:11:01.836$ therapy really is fixed.
- NOTE Confidence: 0.847423493862152

- 00:11:01.840 --> 00:11:03.660 The disease. Of course,
- NOTE Confidence: 0.847423493862152
- $00{:}11{:}03.660 \dashrightarrow 00{:}11{:}05.935$ some agonists and partial agonist.
- NOTE Confidence: 0.847423493862152
- $00{:}11{:}05{.}940 \dashrightarrow 00{:}11{:}07{.}980$ Can maintain some individuals.
- NOTE Confidence: 0.847423493862152
- 00:11:07.980 --> 00:11:10.530 Offer some periods of time,
- NOTE Confidence: 0.847423493862152
- $00{:}11{:}10.530 \dashrightarrow 00{:}11{:}13.590$ some for extended periods of time,
- NOTE Confidence: 0.847423493862152
- $00:11:13.590 \rightarrow 00:11:16.140$ for example methadone across people,
- NOTE Confidence: 0.847423493862152
- $00{:}11{:}16{.}140 \dashrightarrow 00{:}11{:}16{.}659$ morphine.
- NOTE Confidence: 0.847423493862152
- 00:11:16.659 --> 00:11:19.254 Our team for anything purpose
- NOTE Confidence: 0.847423493862152
- 00:11:19.254 --> 00:11:22.440 smoking but but really in general
- NOTE Confidence: 0.847423493862152
- $00:11:22.440 \rightarrow 00:11:24.995$ these this agonist approach doesn't
- NOTE Confidence: 0.847423493862152
- 00:11:24.995 --> 00:11:27.869 really lead to sustain accent.
- NOTE Confidence: 0.847423493862152
- $00:11:27.870 \longrightarrow 00:11:29.946$ And then, even if it did,
- NOTE Confidence: 0.847423493862152
- $00:11:29.950 \rightarrow 00:11:32.372$ is is reducing drug intake and reversing
- NOTE Confidence: 0.847423493862152
- $00:11:32.372 \rightarrow 00:11:34.099$ addiction really the same thing?
- NOTE Confidence: 0.847423493862152
- $00:11:34.100 \longrightarrow 00:11:37.088$ Can we treat them with the
- NOTE Confidence: 0.847423493862152
- $00:11:37.088 \rightarrow 00:11:38.582$ same single intervention?

- NOTE Confidence: 0.847423493862152
- 00:11:38.590 --> 00:11:39.508 So of course,
- NOTE Confidence: 0.847423493862152
- $00:11:39.508 \rightarrow 00:11:41.650$ this hypothesis assumes that the absence of
- NOTE Confidence: 0.847423493862152
- $00:11:41.710 \longrightarrow 00:11:44.125$ behavior reflects the absence of the disease,
- NOTE Confidence: 0.847423493862152
- $00:11:44.130 \longrightarrow 00:11:44.848$ and again,
- NOTE Confidence: 0.847423493862152
- $00:11:44.848 \rightarrow 00:11:47.361$ this group knows that that's not not
- NOTE Confidence: 0.847423493862152
- $00{:}11{:}47{.}361 \dashrightarrow 00{:}11{:}49{.}859$ even close to the imagery sentence.
- NOTE Confidence: 0.847423493862152
- $00:11:49.860 \rightarrow 00:11:52.709$ So what might an alternative hypothesis be?
- NOTE Confidence: 0.847423493862152
- $00:11:52.710 \rightarrow 00:11:53.124$ Well,
- NOTE Confidence: 0.847423493862152
- $00{:}11{:}53{.}124 \dashrightarrow 00{:}11{:}55{.}608$ since indeed substance use disorder is
- NOTE Confidence: 0.847423493862152
- $00:11:55.608 \rightarrow 00:11:58.599$ a complex in a psychiatric disorder,
- NOTE Confidence: 0.847423493862152
- 00:11:58.600 --> 00:12:00.007 high psychiatric comorbidity,
- NOTE Confidence: 0.847423493862152
- $00{:}12{:}00{.}007 \dashrightarrow 00{:}12{:}02{.}352$ dys regulated multiple systems or cognitive
- NOTE Confidence: 0.847423493862152
- 00:12:02.352 --> 00:12:04.488 affective personality systems reward systems.
- NOTE Confidence: 0.847423493862152
- $00{:}12{:}04{.}490 \dashrightarrow 00{:}12{:}06{.}750$ As I'll show you later.
- NOTE Confidence: 0.847423493862152
- $00{:}12{:}06.750 \dashrightarrow 00{:}12{:}09.459$ Maybe rather than or at least in
- NOTE Confidence: 0.847423493862152

 $00:12:09.459 \rightarrow 00:12:12.640$ addition to a better molecular level.

NOTE Confidence: 0.847423493862152

 $00:12:12.640 \longrightarrow 00:12:13.402$ Medicinal chemistry,

NOTE Confidence: 0.847423493862152

 $00{:}12{:}13.402 \dashrightarrow 00{:}12{:}16.450$ we really need to think about a systems

NOTE Confidence: 0.847423493862152

 $00:12:16.516 \longrightarrow 00:12:18.472$ level neuro biological treatment

NOTE Confidence: 0.847423493862152

 $00:12:18.472 \rightarrow 00:12:20.917$ strategy that takes into consideration

NOTE Confidence: 0.847423493862152

 $00{:}12{:}20{.}917 \dashrightarrow 00{:}12{:}23{.}569$ these multiple other prediction phases.

NOTE Confidence: 0.847423493862152

00:12:23.570 --> 00:12:24.224 Not George,

NOTE Confidence: 0.847423493862152

00:12:24.224 --> 00:12:26.186 proven Orville cast have come up

NOTE Confidence: 0.847423493862152

 $00{:}12{:}26.186 \dashrightarrow 00{:}12{:}28.453$ with a cartoon reminding us that

NOTE Confidence: 0.847423493862152

 $00{:}12{:}28.453 \dashrightarrow 00{:}12{:}30.763$ addiction is not a static disease,

NOTE Confidence: 0.847423493862152

 $00{:}12{:}30{.}770 \dashrightarrow 00{:}12{:}32{.}230$ but rather a cyclotron.

NOTE Confidence: 0.847423493862152

 $00:12:32.230 \rightarrow 00:12:34.055$ And while there's some potentially

NOTE Confidence: 0.847423493862152

 $00:12:34.055 \rightarrow 00:12:35.810$ some issues with this model,

NOTE Confidence: 0.847423493862152

 $00{:}12{:}35{.}810 \dashrightarrow 00{:}12{:}38{.}690$ I think it's a good one for touristically.

NOTE Confidence: 0.847423493862152

 $00:12:38.690 \rightarrow 00:12:42.036$ Think about what we're what we're actually

NOTE Confidence: 0.847423493862152

 $00:12:42.036 \rightarrow 00:12:46.336$ doing when a patient presents in front of us.

- NOTE Confidence: 0.847423493862152
- $00:12:46.340 \longrightarrow 00:12:47.872$ And this binge intoxication phase,
- NOTE Confidence: 0.847423493862152
- $00:12:47.872 \longrightarrow 00:12:49.930$ the phase that we think about it,
- NOTE Confidence: 0.847423493862152
- $00:12:49.930 \longrightarrow 00:12:51.897$ certainly with our animal models of increases
- NOTE Confidence: 0.847423493862152
- $00:12:51.897 \rightarrow 00:12:53.818$ in dopamine in the nucleus accumbens,
- NOTE Confidence: 0.847423493862152
- $00:12:53.820 \longrightarrow 00:12:54.416$ is really,
- NOTE Confidence: 0.847423493862152
- $00:12:54.416 \longrightarrow 00:12:55.906$ if you think about it,
- NOTE Confidence: 0.847423493862152
- $00{:}12{:}55{.}910 \dashrightarrow 00{:}12{:}57{.}098$ is not a treatment.
- NOTE Confidence: 0.840475976467133
- 00:13:07.570 --> 00:13:09.670 If you will has mode,
- NOTE Confidence: 0.840475976467133
- $00{:}13{:}09{.}670 \dashrightarrow 00{:}13{:}12{.}414$ it doesn't live in the new basic
- NOTE Confidence: 0.840475976467133
- 00:13:12.414 --> 00:13:14.710 comments anymore due to plasticity.
- NOTE Confidence: 0.840475976467133
- $00{:}13{:}14.710 \dashrightarrow 00{:}13{:}17.230$ It's now in a number of
- NOTE Confidence: 0.840475976467133
- $00{:}13{:}17{.}230 \dashrightarrow 00{:}13{:}18{.}490$ other distributed systems.
- NOTE Confidence: 0.840475976467133
- 00:13:18.490 --> 00:13:20.910 Many synapses removed and differentially
- NOTE Confidence: 0.840475976467133
- $00{:}13{:}20{.}910 \dashrightarrow 00{:}13{:}23{.}330$ manifest across these affected systems.
- NOTE Confidence: 0.840475976467133
- 00:13:23.330 --> 00:13:26.338 So you know, I would ask you how?
- NOTE Confidence: 0.840475976467133

 $00:13:26.340 \rightarrow 00:13:27.992$ How could pharmacologic blockade

NOTE Confidence: 0.840475976467133

 $00{:}13{:}27{.}992 \dashrightarrow 00{:}13{:}30{.}470$ or or agonist replacement of a

NOTE Confidence: 0.840475976467133

 $00:13:30.541 \rightarrow 00:13:32.801$ sneeze or critical limbic dopamine

NOTE Confidence: 0.840475976467133

 $00:13:32.801 \rightarrow 00:13:35.061$ system really reverse the disease?

NOTE Confidence: 0.840475976467133

 $00:13:35.070 \rightarrow 00:13:37.850$ So you know the theme today is going to be.

NOTE Confidence: 0.840475976467133

00:13:37.850 - 00:13:39.235 Maybe we don't really need

NOTE Confidence: 0.840475976467133

 $00:13:39.235 \longrightarrow 00:13:40.343$ a better silver bullet.

NOTE Confidence: 0.840475976467133

 $00:13:40.350 \longrightarrow 00:13:42.630$ Maybe what we need is a

NOTE Confidence: 0.840475976467133

00:13:42.630 --> 00:13:43.770 silver buckshot approach.

NOTE Confidence: 0.840475976467133

 $00:13:43.770 \longrightarrow 00:13:46.276$ And maybe we need to take into

NOTE Confidence: 0.840475976467133

00:13:46.276 --> 00:13:48.955 account both the acute state of the

NOTE Confidence: 0.840475976467133

 $00{:}13{:}48.955 \dashrightarrow 00{:}13{:}51.804$ individual as well as the trait of

NOTE Confidence: 0.840475976467133

 $00{:}13{:}51{.}804 \dashrightarrow 00{:}13{:}54{.}219$ addiction that they presented with.

NOTE Confidence: 0.840475976467133

 $00:13:54.220 \longrightarrow 00:13:56.767$ So the rest of the talk is going to

NOTE Confidence: 0.840475976467133

 $00{:}13{:}56{.}767 \dashrightarrow 00{:}13{:}59{.}222$ be organized around that theme of

NOTE Confidence: 0.840475976467133

 $00:13:59.222 \rightarrow 00:14:02.359$ looking at both the trait of addiction.

- NOTE Confidence: 0.840475976467133
- 00:14:02.360 --> 00:14:03.386 If you will,
- NOTE Confidence: 0.840475976467133
- $00:14:03.386 \rightarrow 00:14:05.438$ the severity of addiction as well
- NOTE Confidence: 0.840475976467133
- $00{:}14{:}05{.}438 \dashrightarrow 00{:}14{:}07{.}417$ as the acute transition traits
- NOTE Confidence: 0.840475976467133
- $00:14:07.417 \longrightarrow 00:14:09.763$ that we see during acute and
- NOTE Confidence: 0.840475976467133
- $00:14:09.834 \rightarrow 00:14:11.928$ long-term long-term accidents.
- NOTE Confidence: 0.840475976467133
- $00:14:11.930 \longrightarrow 00:14:14.254$ And so I would posit that more
- NOTE Confidence: 0.840475976467133
- $00:14:14.254 \rightarrow 00:14:16.189$ treatment outcomes may be related to,
- NOTE Confidence: 0.840475976467133
- $00:14:16.190 \longrightarrow 00:14:17.410$ at least in part,
- NOTE Confidence: 0.840475976467133
- $00:14:17.410 \rightarrow 00:14:19.240$ to focus on the results alleviating
- NOTE Confidence: 0.840475976467133
- $00:14:19.297 \rightarrow 00:14:20.677$ withdrawal rather than focusing
- NOTE Confidence: 0.840475976467133
- $00:14:20.677 \longrightarrow 00:14:22.747$ on the cause of the problem.
- NOTE Confidence: 0.840475976467133
- 00:14:22.750 --> 00:14:25.350 This drug induced neuroplasticity.
- NOTE Confidence: 0.840475976467133
- $00{:}14{:}25{.}350 \dashrightarrow 00{:}14{:}27{.}126$ And so we went into this a number
- NOTE Confidence: 0.840475976467133
- $00{:}14{:}27.126 \dashrightarrow 00{:}14{:}28.891$ of years ago with the hypothesis
- NOTE Confidence: 0.840475976467133
- $00{:}14{:}28{.}891 \dashrightarrow 00{:}14{:}30{.}476$ that addiction severity is linked
- NOTE Confidence: 0.840475976467133

 $00:14:30.476 \rightarrow 00:14:32.433$ to activity within and between the

NOTE Confidence: 0.840475976467133

 $00:14:32.433 \rightarrow 00:14:34.940$ anterior singular and one of its players.

NOTE Confidence: 0.840475976467133

 $00:14:34.940 \rightarrow 00:14:37.298$ This trail. Well, why the singular?

NOTE Confidence: 0.840475976467133

 $00:14:37.298 \longrightarrow 00:14:38.928$ Where did that come from?

NOTE Confidence: 0.840475976467133

 $00{:}14{:}38{.}930 \dashrightarrow 00{:}14{:}41{.}247$ And there's a number of pieces of

NOTE Confidence: 0.840475976467133

 $00:14:41.247 \rightarrow 00:14:43.315$ literature that I'm putting up here NOTE Confidence: 0.840475976467133

 $00:14:43.315 \longrightarrow 00:14:45.674$ that justified for us time that single NOTE Confidence: 0.840475976467133

 $00:14:45.741 \rightarrow 00:14:48.133$ it might in fact be a common target

NOTE Confidence: 0.840475976467133

00:14:48.133 --> 00:14:49.908 for nicotine and other abuse drugs,

NOTE Confidence: 0.840475976467133

00:14:49.908 --> 00:14:51.660 and maybe a convergent region that's

NOTE Confidence: 0.840475976467133

00:14:51.716 --> 00:14:53.646 pivotal for nicotine's diverse effects.

NOTE Confidence: 0.840475976467133

 $00:14:53.650 \rightarrow 00:14:55.939$ And when we get going in this,

NOTE Confidence: 0.840475976467133

 $00{:}14{:}55{.}940 \dashrightarrow 00{:}14{:}57{.}775$ this was before any knowledge

NOTE Confidence: 0.840475976467133

 $00{:}14{:}57{.}775 \dashrightarrow 00{:}15{:}00{.}029$ of large scale networks and the

NOTE Confidence: 0.840475976467133

 $00:15:00.029 \rightarrow 00:15:01.769$ salience network that I'll be

NOTE Confidence: 0.840475976467133

 $00:15:01.769 \longrightarrow 00:15:03.809$ talking to you about later on.

- NOTE Confidence: 0.840475976467133
- $00{:}15{:}03{.}810 \dashrightarrow 00{:}15{:}06{.}210$ So let me put this into a bit of a
- NOTE Confidence: 0.840475976467133
- $00{:}15{:}06{.}283 \dashrightarrow 00{:}15{:}09{.}097$ perspective and a figure that I adopted
- NOTE Confidence: 0.840475976467133
- 00:15:09.097 --> 00:15:11.440 from adapted from Suzanne Habren,
- NOTE Confidence: 0.840475976467133
- 00:15:11.440 --> 00:15:13.528 Brian Knutson a few years ago,
- NOTE Confidence: 0.840475976467133
- $00{:}15{:}13.530 \dashrightarrow 00{:}15{:}15.552$ just to emphasize that these cortical
- NOTE Confidence: 0.840475976467133
- $00{:}15{:}15{.}552 \dashrightarrow 00{:}15{:}17{.}307$ striatal loops that Suzanne is
- NOTE Confidence: 0.840475976467133
- $00:15:17.307 \longrightarrow 00:15:19.077$ beautifully elucidated over the years,
- NOTE Confidence: 0.840475976467133
- $00{:}15{:}19{.}080 \dashrightarrow 00{:}15{:}21{.}824$ let me put some function on top of
- NOTE Confidence: 0.840475976467133
- $00:15:21.824 \dashrightarrow 00:15:24.626$ that when we think about the VM Pfc,
- NOTE Confidence: 0.840475976467133
- $00:15:24.630 \longrightarrow 00:15:26.370$ we think about value, reward,
- NOTE Confidence: 0.840475976467133
- $00:15:26.370 \rightarrow 00:15:28.446$ and decision making in the OSC,
- NOTE Confidence: 0.840475976467133
- $00{:}15{:}28{.}450 \dashrightarrow 00{:}15{:}29{.}410$ the Dorsal ACC.
- NOTE Confidence: 0.840475976467133
- $00{:}15{:}29{.}410$ --> $00{:}15{:}32{.}116$ Then I'm going to be talking about now
- NOTE Confidence: 0.840475976467133
- $00{:}15{:}32{.}116 \dashrightarrow 00{:}15{:}34{.}528$ and ever monitoring and every detection.
- NOTE Confidence: 0.840475976467133
- $00:15:34.530 \longrightarrow 00:15:36.300$ Executive control in the DL,
- NOTE Confidence: 0.840475976467133

00:15:36.300 --> 00:15:38.406 Pfc and just to be complete,

NOTE Confidence: 0.840475976467133

 $00:15:38.410 \rightarrow 00:15:41.587$ I think we have to only talk about addiction.

NOTE Confidence: 0.840475976467133

 $00{:}15{:}41.590 \dashrightarrow 00{:}15{:}42.652$ Think about attention.

NOTE Confidence: 0.840475976467133

 $00:15:42.652 \rightarrow 00:15:43.360$ Intentional processing.

NOTE Confidence: 0.840475976467133

 $00{:}15{:}43.360 \dashrightarrow 00{:}15{:}45.265$ Basically in the posterior parietal

NOTE Confidence: 0.840475976467133

 $00{:}15{:}45{.}265 \dashrightarrow 00{:}15{:}48{.}203$ cortex and one of the things that we've

NOTE Confidence: 0.840475976467133

 $00:15:48.203 \rightarrow 00:15:51.120$ now had a over the last number of years.

NOTE Confidence: 0.840475976467133

00:15:51.120 --> 00:15:53.196 Kind of a Super Ordinal organization

NOTE Confidence: 0.840475976467133

 $00{:}15{:}53{.}196 \dashrightarrow 00{:}15{:}55{.}769$ on top of these regions in these

NOTE Confidence: 0.840475976467133

 $00{:}15{:}55{.}769 \dashrightarrow 00{:}15{:}57{.}634$ large scale brain networks that

NOTE Confidence: 0.840475976467133

 $00{:}15{:}57.634 \dashrightarrow 00{:}16{:}00.402$ seem to be able to explain a lot

NOTE Confidence: 0.840475976467133

 $00:16:00.402 \longrightarrow 00:16:02.062$ of the nurse psychiatric symptoms

NOTE Confidence: 0.840475976467133

 $00:16:02.062 \rightarrow 00:16:04.174$ that that will be talking about,

NOTE Confidence: 0.840475976467133

 $00{:}16{:}04{.}180 \dashrightarrow 00{:}16{:}06{.}478$ at least from the perspective of.

NOTE Confidence: 0.840475976467133

 $00{:}16{:}06{.}480 \dashrightarrow 00{:}16{:}08{.}530$ Of addiction and the other

NOTE Confidence: 0.840475976467133

 $00:16:08.530 \longrightarrow 00:16:10.580$ thing I wanted to point

 $00:16:10.662 \rightarrow 00:16:13.448$ out is that many of these players,

NOTE Confidence: 0.84111076593399

 $00:16:13.450 \longrightarrow 00:16:15.526$ most of these players that I've

NOTE Confidence: 0.84111076593399

 $00:16:15.526 \rightarrow 00:16:17.453$ just highlighted are just ripe

NOTE Confidence: 0.84111076593399

 $00{:}16{:}17{.}453 \dashrightarrow 00{:}16{:}19{.}345$ with nicotinic receptor receptors

NOTE Confidence: 0.84111076593399

 $00{:}16{:}19{.}345 \dashrightarrow 00{:}16{:}21{.}237$ and various receptors subtypes.

NOTE Confidence: 0.84111076593399

 $00{:}16{:}21{.}240 \dashrightarrow 00{:}16{:}23{.}568$ And it's not surprising therefore that

NOTE Confidence: 0.84111076593399

 $00:16:23.568 \rightarrow 00:16:26.896$ a lot of what we're seeing with to bacco

NOTE Confidence: 0.84111076593399

 $00:16:26.896 \rightarrow 00:16:30.047$ use disorder is being biased by many

NOTE Confidence: 0.84111076593399

 $00{:}16{:}30.047 \dashrightarrow 00{:}16{:}32.657$ many systems throughout the Neuraxis.

NOTE Confidence: 0.84111076593399

 $00{:}16{:}32{.}660 \dashrightarrow 00{:}16{:}35{.}873$ OK, so with that introduction we began

NOTE Confidence: 0.84111076593399

 $00{:}16{:}35{.}873 \dashrightarrow 00{:}16{:}39{.}770$ this sort of adventure 10 is h years ago.

NOTE Confidence: 0.84111076593399

 $00{:}16{:}39{.}770 \dashrightarrow 00{:}16{:}42{.}392$ Now with this hypothesis that the

NOTE Confidence: 0.84111076593399

 $00{:}16{:}42.392 \dashrightarrow 00{:}16{:}44.980$ singular was involved in addiction,

NOTE Confidence: 0.84111076593399

 $00:16:44.980 \longrightarrow 00:16:48.298$ and So what we did very simply,

NOTE Confidence: 0.84111076593399

 $00:16:48.300 \longrightarrow 00:16:50.248$ this is, I believe,

 $00:16:50.248 \rightarrow 00:16:53.520$ the first wrestling state study done in,

NOTE Confidence: 0.84111076593399

 $00{:}16{:}53{.}520 \dashrightarrow 00{:}16{:}55{.}734$ and certainly nicotine a number of

NOTE Confidence: 0.84111076593399

 $00{:}16{:}55{.}734 \dashrightarrow 00{:}16{:}59{.}124$ years ago was we divided the singular

NOTE Confidence: 0.84111076593399

 $00:16:59.124 \rightarrow 00:17:01.568$ into its cytoarchitectonic components.

NOTE Confidence: 0.84111076593399

00:17:01.570 --> 00:17:02.638 7 seven areas.

NOTE Confidence: 0.84111076593399

 $00{:}17{:}02.638 \dashrightarrow 00{:}17{:}05.130$ Answer if you Post Area 1 middle

NOTE Confidence: 0.84111076593399

 $00:17:05.215 \rightarrow 00:17:07.189$ singular area bilaterally,

NOTE Confidence: 0.84111076593399

 $00:17:07.190 \longrightarrow 00:17:09.818$ so 14 areas each was a seed and we

NOTE Confidence: 0.84111076593399

 $00{:}17{:}09{.}818 \dashrightarrow 00{:}17{:}12{.}690$ did a whole brain regression against

NOTE Confidence: 0.84111076593399

 $00{:}17{:}12.690 \dashrightarrow 00{:}17{:}15.190$ the level of nicotine dependence

NOTE Confidence: 0.84111076593399

00:17:15.268 --> 00:17:17.944 against the practice from index and

NOTE Confidence: 0.84111076593399

 $00:17:17.944 \dashrightarrow 00:17:20.948$ what we identified was a single area.

NOTE Confidence: 0.84111076593399

 $00{:}17{:}20{.}948 \dashrightarrow 00{:}17{:}22{.}978$ Within the the ventral stratum,

NOTE Confidence: 0.84111076593399

 $00{:}17{:}22{.}980 \dashrightarrow 00{:}17{:}24{.}972$ what was interesting when we looked

NOTE Confidence: 0.84111076593399

 $00{:}17{:}24{.}972 \dashrightarrow 00{:}17{:}28{.}038$ at this data is that the that the

NOTE Confidence: 0.84111076593399

 $00:17:28.038 \rightarrow 00:17:30.123$ strength of this circuit negatively

- NOTE Confidence: 0.84111076593399
- $00{:}17{:}30{.}123 \dashrightarrow 00{:}17{:}32{.}344$ correlated with with the nicotine
- NOTE Confidence: 0.84111076593399
- $00:17:32.344 \rightarrow 00:17:34.514$ addiction severity of the individual.
- NOTE Confidence: 0.84111076593399
- 00:17:34.520 --> 00:17:37.306 But most importantly in this first study,
- NOTE Confidence: 0.84111076593399
- $00:17:37.310 \longrightarrow 00:17:39.235$ when we scan these individuals
- NOTE Confidence: 0.84111076593399
- $00{:}17{:}39{.}235 \dashrightarrow 00{:}17{:}41{.}690$ on an off a nicotine Patch,
- NOTE Confidence: 0.84111076593399
- $00{:}17{:}41.690 \dashrightarrow 00{:}17{:}45.263$ there was no change to the to the circuit.
- NOTE Confidence: 0.84111076593399
- $00:17:45.270 \rightarrow 00:17:47.395$ These dime diamonds and triangles
- NOTE Confidence: 0.84111076593399
- $00{:}17{:}47{.}395 \dashrightarrow 00{:}17{:}50{.}369$ indicate a single subject scan on two
- NOTE Confidence: 0.84111076593399
- $00{:}17{:}50{.}369 \dashrightarrow 00{:}17{:}52{.}715$ different occasions on and off nicotine
- NOTE Confidence: 0.84111076593399
- $00{:}17{:}52.715 \dashrightarrow 00{:}17{:}54.900$ off nicotine on and off nicotine.
- NOTE Confidence: 0.84111076593399
- $00{:}17{:}54{.}900 \dashrightarrow 00{:}17{:}57{.}329$ And so this circuit appeared to be
- NOTE Confidence: 0.84111076593399
- $00{:}17{:}57{.}329 \dashrightarrow 00{:}17{:}59{.}746$ reflective of that rate of addiction and
- NOTE Confidence: 0.84111076593399
- $00{:}17{:}59{.}746$ --> $00{:}18{:}02{.}500$ not the current state of the individual.
- NOTE Confidence: 0.885979473590851
- 00:18:04.710 --> 00:18:07.130 About this time, Mr.
- NOTE Confidence: 0.885979473590851
- $00{:}18{:}07{.}130 \dashrightarrow 00{:}18{:}10{.}760$ Big the opera 5 polymorphism was
- NOTE Confidence: 0.885979473590851

 $00:18:10.878 \rightarrow 00:18:14.988$ becoming recognized as an important.

NOTE Confidence: 0.885979473590851

 $00{:}18{:}14.990 \dashrightarrow 00{:}18{:}16.614$ Determinant in nicotine addiction.

NOTE Confidence: 0.885979473590851

00:18:16.614 --> 00:18:20.216 And so we wanted to see if you want to

NOTE Confidence: 0.885979473590851

 $00{:}18{:}20{.}216 \dashrightarrow 00{:}18{:}22{.}669$ see what its role was in this circuit

NOTE Confidence: 0.885979473590851

 $00{:}18{:}22.669 \dashrightarrow 00{:}18{:}25.266$ and so the next year together with

NOTE Confidence: 0.885979473590851

00:18:25.266 --> 00:18:28.125 David Goldman at the NI AAA it hung. NOTE Confidence: 0.885979473590851

 $00:18:28.130 \rightarrow 00:18:30.260$ We did essentially the same experiment.

NOTE Confidence: 0.885979473590851

 $00:18:30.260 \rightarrow 00:18:32.703$ Now starting only the dorsal ACC because

NOTE Confidence: 0.885979473590851

 $00{:}18{:}32{.}703 \dashrightarrow 00{:}18{:}35{.}484$ we knew that was sort of the answer and

NOTE Confidence: 0.885979473590851

 $00{:}18{:}35{.}484 \dashrightarrow 00{:}18{:}37{.}954$ now did a whole brain regression not

NOTE Confidence: 0.885979473590851

00:18:37.954 --> 00:18:40.546 against the phenotype of Fagot Strong,

NOTE Confidence: 0.885979473590851

00:18:40.550 - 00:18:42.590 but against the genotype of this

NOTE Confidence: 0.885979473590851

00:18:42.590 --> 00:18:43.950 A5 polymorphism and basically

NOTE Confidence: 0.885979473590851

 $00{:}18{:}44.012 \dashrightarrow 00{:}18{:}45.548$ identified the same circuit.

NOTE Confidence: 0.885979473590851

 $00:18:45.550 \rightarrow 00:18:48.854$ With the same relationship once one now with

NOTE Confidence: 0.885979473590851

 $00:18:48.854 \rightarrow 00:18:51.819$ the phenotype and one against the genotype.

 $00{:}18{:}51{.}820 \dashrightarrow 00{:}18{:}54{.}524$ And we thought these early data supported a

NOTE Confidence: 0.885979473590851

 $00{:}18{:}54{.}524 \dashrightarrow 00{:}18{:}57{.}619$ role for the dorsal ACC and Strydom in trade,

NOTE Confidence: 0.885979473590851

 $00:18:57.620 \longrightarrow 00:18:59.424$ but not state dependence.

NOTE Confidence: 0.885979473590851

 $00:18:59.424 \rightarrow 00:19:02.515$ So the next logical question was, well,

NOTE Confidence: 0.885979473590851

 $00{:}19{:}02{.}515 \dashrightarrow 00{:}19{:}04{.}825$ are there pre dispositional differences in

NOTE Confidence: 0.885979473590851

 $00:19:04.825 \rightarrow 00:19:07.169$ these circuits that potentiates smoking?

NOTE Confidence: 0.885979473590851

 $00{:}19{:}07{.}170 \dashrightarrow 00{:}19{:}10{.}159$ Or does the smoking behavior over the

NOTE Confidence: 0.885979473590851

 $00:19:10.159 \rightarrow 00:19:13.667$ over period of time change these service?

NOTE Confidence: 0.885979473590851

 $00{:}19{:}13.670 \dashrightarrow 00{:}19{:}15.534$ Well, it's difficult to do in humans to

NOTE Confidence: 0.885979473590851

 $00:19:15.534 \rightarrow 00:19:17.559$ do these long-term longitudinal studies,

NOTE Confidence: 0.885979473590851

 $00:19:17.560 \longrightarrow 00:19:19.954$ and it may be that Abcd in a few

NOTE Confidence: 0.885979473590851

 $00:19:19.954 \rightarrow 00:19:22.040$ years will give us this answer,

NOTE Confidence: 0.885979473590851

 $00{:}19{:}22.040 \dashrightarrow 00{:}19{:}24.304$ but an approach that we took at the

NOTE Confidence: 0.885979473590851

 $00{:}19{:}24{.}304 \dashrightarrow 00{:}19{:}26{.}489$ time was at a conference back to

NOTE Confidence: 0.885979473590851

 $00{:}19{:}26{.}489 \dashrightarrow 00{:}19{:}28{.}976$ remember when we used to be able to

 $00:19:28.976 \rightarrow 00:19:31.006$ go to conferences and I was having

NOTE Confidence: 0.885979473590851

 $00{:}19{:}31.010 \dashrightarrow 00{:}19{:}32.550$ a conversation with Rachel Tyne dale

NOTE Confidence: 0.885979473590851

 $00{:}19{:}32{.}550 \dashrightarrow 00{:}19{:}34{.}700$ and she was telling me about the

NOTE Confidence: 0.885979473590851

00:19:34.700 --> 00:19:35.800 sith to ASICS enzyme,

NOTE Confidence: 0.885979473590851

 $00:19:35.800 \rightarrow 00:19:37.886$ which is a cytochrome p-450 liver enzyme.

NOTE Confidence: 0.885979473590851

 $00{:}19{:}37{.}890 \dashrightarrow 00{:}19{:}39{.}744$ And it's the main enzyme that

NOTE Confidence: 0.885979473590851

 $00:19:39.744 \longrightarrow 00:19:41.180$ metabolizes nicotine for coating it.

NOTE Confidence: 0.885979473590851

00:19:41.180 --> 00:19:42.670 I didn't think that was

NOTE Confidence: 0.885979473590851

00:19:42.670 --> 00:19:43.266 particularly interesting,

NOTE Confidence: 0.885979473590851

 $00:19:43.270 \rightarrow 00:19:45.076$ 'cause I'm not a little guy.

NOTE Confidence: 0.885979473590851

 $00{:}19{:}45{.}080 \dashrightarrow 00{:}19{:}48{.}280$ But until I started to take a look that a

NOTE Confidence: 0.885979473590851

 $00:19:48.367 \rightarrow 00:19:51.415$ the same time is genetically regulated,

NOTE Confidence: 0.885979473590851

 $00:19:51.420 \longrightarrow 00:19:53.395$ is 26 different isozymes or

NOTE Confidence: 0.885979473590851

 $00:19:53.395 \rightarrow 00:19:54.975$ so and and Rachel,

NOTE Confidence: 0.885979473590851

 $00:19:54.980 \rightarrow 00:19:58.373$ it's lab has been able to provide people or

NOTE Confidence: 0.885979473590851

 $00:19:58.373 \rightarrow 00:20:00.919$ categorize people into those with normal,

- NOTE Confidence: 0.885979473590851
- $00{:}20{:}00{.}920 \dashrightarrow 00{:}20{:}02{.}732$ intermediate and slow metabolic
- NOTE Confidence: 0.885979473590851
- $00:20:02.732 \rightarrow 00:20:05.450$ systems or nicotine and what became
- NOTE Confidence: 0.885979473590851
- $00:20:05.518 \rightarrow 00:20:07.597$ interesting to me as a brain guy
- NOTE Confidence: 0.885979473590851
- $00:20:07.597 \longrightarrow 00:20:10.285$ is it looks like these that this
- NOTE Confidence: 0.885979473590851
- $00:20:10.285 \rightarrow 00:20:12.009$ liver enzyme changes behavior.
- NOTE Confidence: 0.885979473590851
- $00:20:12.010 \longrightarrow 00:20:13.590$ Individuals that were better
- NOTE Confidence: 0.885979473590851
- $00{:}20{:}13.590 \dashrightarrow 00{:}20{:}15.565$ slow metabolizers have lower fat.
- NOTE Confidence: 0.885979473590851
- 00:20:15.570 --> 00:20:17.206 Astronomy smoke, fewer cigarettes.
- NOTE Confidence: 0.885979473590851
- $00{:}20{:}17.206 \dashrightarrow 00{:}20{:}19.950$ And it can predict treatment matching out,
- NOTE Confidence: 0.885979473590851
- $00:20:19.950 \rightarrow 00:20:21.540$ so this became rather interesting
- NOTE Confidence: 0.885979473590851
- $00:20:21.540 \longrightarrow 00:20:24.302$ and so we want to know if this
- NOTE Confidence: 0.885979473590851
- 00:20:24.302 --> 00:20:26.142 situation it's Gina type actually
- NOTE Confidence: 0.885979473590851
- $00:20:26.142 \longrightarrow 00:20:27.855$ shapes brain circuits differentially
- NOTE Confidence: 0.885979473590851
- $00{:}20{:}27.855 \dashrightarrow 00{:}20{:}30.130$ in smokers and non smokers.
- NOTE Confidence: 0.885979473590851
- $00{:}20{:}30{.}130 \dashrightarrow 00{:}20{:}32{.}596$ And would it offer alter brain
- NOTE Confidence: 0.885979473590851

 $00:20:32.596 \longrightarrow 00:20:35.652$ connectivity and so we did that that

NOTE Confidence: 0.885979473590851

 $00:20:35.652 \rightarrow 00:20:38.304$ study together with Rachel and Supinely

NOTE Confidence: 0.885979473590851

00:20:38.304 --> 00:20:41.623 who is a postdoc in the lab at the time.

NOTE Confidence: 0.885979473590851

 $00{:}20{:}41.630 \dashrightarrow 00{:}20{:}44.372$ And perhaps the most important and

NOTE Confidence: 0.885979473590851

 $00{:}20{:}44.372 \dashrightarrow 00{:}20{:}46.580$ interesting contrasts that we did

NOTE Confidence: 0.885979473590851

 $00{:}20{:}46{.}580 \dashrightarrow 00{:}20{:}49{.}280$ looking at this data was a gene by was

NOTE Confidence: 0.885979473590851

 $00:20:49.356 \rightarrow 00:20:51.856$ it gene by environment interaction?

NOTE Confidence: 0.885979473590851

 $00:20:51.860 \rightarrow 00:20:53.900$ So three genotyped by smoking

NOTE Confidence: 0.885979473590851

 $00:20:53.900 \longrightarrow 00:20:55.124$ versus non smoking.

NOTE Confidence: 0.885979473590851

 $00{:}20{:}55{.}130 \dashrightarrow 00{:}20{:}58{.}050$ And in this analysis we didn't want to

NOTE Confidence: 0.885979473590851

 $00{:}20{:}58.050 \dashrightarrow 00{:}21{:}01.097$ have a hypothesis of looking under the

NOTE Confidence: 0.885979473590851

 $00:21:01.097 \rightarrow 00:21:04.960$ same lamppost and so we used a data driven.

NOTE Confidence: 0.885979473590851

00:21:04.960 --> 00:21:07.300 Metric graph theory metrical

NOTE Confidence: 0.885979473590851

 $00:21:07.300 \longrightarrow 00:21:09.640$ functional connectivity strength and

NOTE Confidence: 0.885979473590851

 $00{:}21{:}09.640 \dashrightarrow 00{:}21{:}12.073$ basically this analysis allows you

NOTE Confidence: 0.885979473590851

 $00:21:12.073 \rightarrow 00:21:14.838$ to identify the hubs in the brain.

- NOTE Confidence: 0.885979473590851
- $00:21:14.840 \longrightarrow 00:21:17.310$ The areas of highest ugliness
- NOTE Confidence: 0.885979473590851
- $00{:}21{:}17{.}310 \dashrightarrow 00{:}21{:}19{.}286$ that interconnect rain errors,
- NOTE Confidence: 0.797232389450073
- $00{:}21{:}19{.}290 \dashrightarrow 00{:}21{:}23{.}727$ and when we did that whole brain data driven,
- NOTE Confidence: 0.797232389450073
- $00:21:23.730 \longrightarrow 00:21:26.845$ we identified two areas defense
- NOTE Confidence: 0.797232389450073
- $00:21:26.845 \longrightarrow 00:21:29.960$ Australian in the dorsal ACC.
- NOTE Confidence: 0.797232389450073
- $00{:}21{:}29{.}960 \dashrightarrow 00{:}21{:}31{.}994$ We extracted those data and plotted
- NOTE Confidence: 0.797232389450073
- $00{:}21{:}31{.}994 \dashrightarrow 00{:}21{:}34{.}543$ them to see what was driving this
- NOTE Confidence: 0.797232389450073
- $00{:}21{:}34{.}543 \dashrightarrow 00{:}21{:}36{.}418$ relationship and what it was.
- NOTE Confidence: 0.797232389450073
- $00{:}21{:}36{.}420 \dashrightarrow 00{:}21{:}38{.}844$ What was driving the relationship was
- NOTE Confidence: 0.797232389450073
- $00:21:38.844 \longrightarrow 00:21:41.117$ the slow metabolizers in smokers that
- NOTE Confidence: 0.797232389450073
- 00:21:41.117 --> 00:21:43.915 we saw a less hub enis, if you will.
- NOTE Confidence: 0.797232389450073
- 00:21:43.915 --> 00:21:46.330 In both of these areas in this
- NOTE Confidence: 0.797232389450073
- 00:21:46.412 --> 00:21:48.897 genotype group in smokers only.
- NOTE Confidence: 0.797232389450073
- $00{:}21{:}48{.}900 \dashrightarrow 00{:}21{:}51{.}825$ And interesting enough that SES
- NOTE Confidence: 0.797232389450073
- $00:21:51.825 \longrightarrow 00:21:54.750$ level that happiness level also
- NOTE Confidence: 0.797232389450073
$00:21:54.846 \rightarrow 00:21:57.866$ predicted or correlated very nicely

NOTE Confidence: 0.797232389450073

 $00{:}21{:}57.866 \dashrightarrow 00{:}22{:}01.685$ with the individuals level of trade

NOTE Confidence: 0.797232389450073

 $00:22:01.685 \rightarrow 00:22:04.509$ dependence severity very consistent

NOTE Confidence: 0.797232389450073

 $00:22:04.509 \rightarrow 00:22:08.866$ with something from the literature of.

NOTE Confidence: 0.797232389450073

00:22:08.866 --> 00:22:10.518 Smoking behavior.

NOTE Confidence: 0.797232389450073

 $00{:}22{:}10.520 \dashrightarrow 00{:}22{:}14.144$ So, OK, we've identified a couple of hubs.

NOTE Confidence: 0.797232389450073

 $00:22:14.150 \longrightarrow 00:22:15.860$ The next question was, well,

NOTE Confidence: 0.797232389450073

 $00:22:15.860 \longrightarrow 00:22:17.912$ what are the tracks into these

NOTE Confidence: 0.797232389450073

 $00:22:17.912 \longrightarrow 00:22:18.596$ train stations?

NOTE Confidence: 0.797232389450073

 $00{:}22{:}18.600 \dashrightarrow 00{:}22{:}21.365$ What are the circus that might be

NOTE Confidence: 0.797232389450073

 $00{:}22{:}21{.}365 \dashrightarrow 00{:}22{:}23{.}254$ potentially biasing these hearts and

NOTE Confidence: 0.797232389450073

 $00:22:23.254 \rightarrow 00:22:25.774$ one way to approach that was then to

NOTE Confidence: 0.797232389450073

 $00{:}22{:}25.842 \dashrightarrow 00{:}22{:}28.250$ take each of these two areas and use

NOTE Confidence: 0.797232389450073

 $00{:}22{:}28{.}250 \dashrightarrow 00{:}22{:}30{.}798$ each one is a seed into a separate

NOTE Confidence: 0.797232389450073

00:22:30.798 --> 00:22:32.620 standard resting state connectivity analysis.

NOTE Confidence: 0.797232389450073

 $00:22:32.620 \longrightarrow 00:22:34.330$ And when we did that,

 $00:22:34.330 \rightarrow 00:22:37.058$ we identify from the dorsal ACC the insula,

NOTE Confidence: 0.797232389450073

 $00{:}22{:}37.060 \dashrightarrow 00{:}22{:}39.508$ as well as the ACC and from the bench

NOTE Confidence: 0.797232389450073

 $00{:}22{:}39{.}508 \dashrightarrow 00{:}22{:}41{.}966$ and stratum the insular and as as

NOTE Confidence: 0.797232389450073

 $00:22:41.966 \rightarrow 00:22:44.310$ Regina mentioned in the introduction.

NOTE Confidence: 0.797232389450073

 $00:22:44.310 \longrightarrow 00:22:46.417$ This is become one of the main

NOTE Confidence: 0.797232389450073

 $00:22:46.417 \longrightarrow 00:22:47.750$ foci in the labs,

NOTE Confidence: 0.797232389450073

 $00{:}22{:}47.750 \dashrightarrow 00{:}22{:}50.306$ and I emphasize insulin here because

NOTE Confidence: 0.797232389450073

 $00{:}22{:}50{.}306 \dashrightarrow 00{:}22{:}53{.}554$ I'm going to come back to this in a

NOTE Confidence: 0.797232389450073

 $00:22:53.554 \rightarrow 00:22:56.280$ few more times in a few more stage.

NOTE Confidence: 0.797232389450073

00:22:56.280 --> 00:22:56.602 OK,

NOTE Confidence: 0.797232389450073

 $00:22:56.602 \rightarrow 00:22:58.856$ so this is pretty cool that that

NOTE Confidence: 0.797232389450073

 $00{:}22{:}58.856 \dashrightarrow 00{:}23{:}00{.}277$ salience network components look

NOTE Confidence: 0.797232389450073

00:23:00.277 --> 00:23:02.425 like they may reflect your bias

NOTE Confidence: 0.797232389450073

 $00:23:02.425 \longrightarrow 00:23:04.239$ that traded diction severity.

NOTE Confidence: 0.797232389450073

 $00:23:04.240 \longrightarrow 00:23:06.774$ Well, that was nice, but who cares?

 $00:23:06.780 \longrightarrow 00:23:09.006$ Are there any functional consequences to

NOTE Confidence: 0.797232389450073

 $00{:}23{:}09{.}006 \dashrightarrow 00{:}23{:}11.478$ having changed in Hoppiness in these smokers?

NOTE Confidence: 0.797232389450073

 $00:23:11.480 \longrightarrow 00:23:13.936$ So the way one way we approach that

NOTE Confidence: 0.797232389450073

 $00:23:13.936 \rightarrow 00:23:16.744$ was we needed to probe both eventual

NOTE Confidence: 0.797232389450073

 $00:23:16.744 \longrightarrow 00:23:19.450$ stratum and the door sellers to see,

NOTE Confidence: 0.797232389450073

 $00:23:19.450 \longrightarrow 00:23:21.676$ and perhaps the best way to

NOTE Confidence: 0.797232389450073

 $00{:}23{:}21.676 \dashrightarrow 00{:}23{:}23.430$ approach the ventral stratum Mr.

NOTE Confidence: 0.797232389450073

00:23:23.430 --> 00:23:24.534 User reward task.

NOTE Confidence: 0.797232389450073

 $00{:}23{:}24{.}534 \dashrightarrow 00{:}23{:}26{.}742$ In this case the The Famous.

NOTE Confidence: 0.797232389450073

00:23:26.750 - 00:23:28.370 Monetary incentive delay cast.

NOTE Confidence: 0.797232389450073

 $00:23:28.370 \longrightarrow 00:23:30.395$ Where we analyzed this data,

NOTE Confidence: 0.797232389450073

 $00:23:30.400 \rightarrow 00:23:32.818$ just simply a simple contrast gains

NOTE Confidence: 0.797232389450073

 $00{:}23{:}32{.}818 \dashrightarrow 00{:}23{:}35{.}144$ greater than neutral and we didn't

NOTE Confidence: 0.797232389450073

 $00:23:35.144 \longrightarrow 00:23:37.076$ have enough subjects to look at

NOTE Confidence: 0.797232389450073

 $00:23:37.076 \dashrightarrow 00:23:39.340$ it and intermediate phenotype.

NOTE Confidence: 0.797232389450073

 $00:23:39.340 \rightarrow 00:23:42.580$ So only the normal and the slow metabolizers.

 $00:23:42.580 \longrightarrow 00:23:45.016$ And when we plotted these data,

NOTE Confidence: 0.797232389450073

 $00{:}23{:}45{.}020 \dashrightarrow 00{:}23{:}47{.}420$ we notice that when individuals

NOTE Confidence: 0.797232389450073

 $00{:}23{:}47{.}420 \dashrightarrow 00{:}23{:}48{.}380$ were accident.

NOTE Confidence: 0.797232389450073

 $00:23:48.380 \longrightarrow 00:23:50.320$ This slow metabolizers just

NOTE Confidence: 0.797232389450073

 $00{:}23{:}50{.}320 \dashrightarrow 00{:}23{:}52{.}745$ couldn't couldn't create enough of

NOTE Confidence: 0.797232389450073

 $00{:}23{:}52{.}745 \dashrightarrow 00{:}23{:}55{.}659$ a signal in the ventral striatum.

NOTE Confidence: 0.797232389450073

 $00:23:55.660 \rightarrow 00:23:59.540$ However, when we gave them a nicotine Patch,

NOTE Confidence: 0.797232389450073

 $00{:}23{:}59{.}540 \dashrightarrow 00{:}24{:}02{.}648$ both the slow metabolizers as well as

NOTE Confidence: 0.797232389450073

 $00{:}24{:}02.648 \dashrightarrow 00{:}24{:}05.620$ frankly the slow metabolizers and non

NOTE Confidence: 0.797232389450073

 $00{:}24{:}05{.}620 \dashrightarrow 00{:}24{:}09{.}246$ smokers were able to increase their there.

NOTE Confidence: 0.797232389450073

00:24:09.250 --> 00:24:10.810 Interest rate or signal while

NOTE Confidence: 0.797232389450073

 $00{:}24{:}10.810 \dashrightarrow 00{:}24{:}12.370$ they're performing a reward chest,

NOTE Confidence: 0.797232389450073

 $00{:}24{:}12{.}370 \dashrightarrow 00{:}24{:}13{.}542$ not a particular surprise.

NOTE Confidence: 0.797232389450073

00:24:13.542 --> 00:24:15.688 We know that we know that nicotine

NOTE Confidence: 0.797232389450073

 $00{:}24{:}15.688 \dashrightarrow 00{:}24{:}17.668$ is in fact a cognitive enhancer,

 $00:24:17.670 \longrightarrow 00:24:20.078$ and I'll show you some data in that

NOTE Confidence: 0.797232389450073

 $00:24:20.078 \rightarrow 00:24:22.975$ in non smokers as well as we go along.

NOTE Confidence: 0.797232389450073

 $00{:}24{:}22{.}980 \dashrightarrow 00{:}24{:}25{.}157$ Or what about probing the dorsal ACC?

NOTE Confidence: 0.797232389450073

 $00:24:25.160 \rightarrow 00:24:28.280$ A great way to do that is with a go.

NOTE Confidence: 0.797232389450073

 $00{:}24{:}28{.}280 \dashrightarrow 00{:}24{:}30{.}830$ No go type of the task and when we did

NOTE Confidence: 0.797232389450073

 $00{:}24{:}30{.}897 \dashrightarrow 00{:}24{:}33{.}102$ that we saw exactly the same answer

NOTE Confidence: 0.797232389450073

 $00:24:33.102 \longrightarrow 00:24:35.459$ both in non smokers and smokers.

NOTE Confidence: 0.797232389450073

 $00:24:35.460 \longrightarrow 00:24:37.644$ And again when we gave them an

NOTE Confidence: 0.797232389450073

00:24:37.644 --> 00:24:38.580 acute nicotine Patch

NOTE Confidence: 0.820130944252014

 $00:24:38.641 \longrightarrow 00:24:39.619$ we reverse this.

NOTE Confidence: 0.820130944252014

00:24:39.620 --> 00:24:41.984 Deficit if you will,

NOTE Confidence: 0.820130944252014

 $00:24:41.984 \longrightarrow 00:24:44.348$ in nicotine absolute state.

NOTE Confidence: 0.820130944252014

 $00:24:44.350 \longrightarrow 00:24:46.306$ So these circuits and hugs and

NOTE Confidence: 0.820130944252014

00:24:46.306 --> 00:24:48.011 modified only in smokers suggesting

NOTE Confidence: 0.820130944252014

00:24:48.011 -> 00:24:50.377 a change in in putatively a change

NOTE Confidence: 0.820130944252014

 $00{:}24{:}50{.}377 \dashrightarrow 00{:}24{:}52{.}361$ in nicotine concentrations in the

 $00:24:52.361 \rightarrow 00:24:54.436$ brain so slow metabolizers presumably

NOTE Confidence: 0.820130944252014

 $00{:}24{:}54{.}436 \dashrightarrow 00{:}24{:}56{.}682$ would have more nicotine off for

NOTE Confidence: 0.820130944252014

 $00{:}24{:}56.682 \dashrightarrow 00{:}24{:}59.270$ longer periods of time in their brain,

NOTE Confidence: 0.820130944252014

 $00:24:59.270 \rightarrow 00:25:01.460$ and this induced these circuit changes.

NOTE Confidence: 0.820130944252014

 $00{:}25{:}01{.}460 \dashrightarrow 00{:}25{:}03{.}734$ That's the hypothesis coming in from

NOTE Confidence: 0.820130944252014

 $00{:}25{:}03.734 \dashrightarrow 00{:}25{:}06.341$ this study and the same circuit seem

NOTE Confidence: 0.820130944252014

 $00:25:06.341 \longrightarrow 00:25:08.707$ to change both at rest and when

NOTE Confidence: 0.820130944252014

 $00:25:08.779 \longrightarrow 00:25:10.915$ the individual is doing a task,

NOTE Confidence: 0.820130944252014

 $00:25:10.920 \longrightarrow 00:25:12.380$ suggesting that this is

NOTE Confidence: 0.820130944252014

00:25:12.380 --> 00:25:13.110 functionally significant,

NOTE Confidence: 0.820130944252014

 $00{:}25{:}13.110 \dashrightarrow 00{:}25{:}15.276$ and it looks like slower smokers

NOTE Confidence: 0.820130944252014

00:25:15.276 -> 00:25:17.180 with these slower Gina types.

NOTE Confidence: 0.820130944252014

 $00{:}25{:}17.180 \dashrightarrow 00{:}25{:}20.378$ Are less responsive than to the

NOTE Confidence: 0.820130944252014

 $00{:}25{:}20{.}378 \dashrightarrow 00{:}25{:}23{.}889$ anticipation of veins less responsive to.

NOTE Confidence: 0.820130944252014

 $00:25:23.890 \longrightarrow 00:25:25.342$ To to to errors,

 $00:25:25.342 \rightarrow 00:25:27.520$ and this certainly seems to make

NOTE Confidence: 0.820130944252014

00:25:27.603 --> 00:25:30.183 sense when we think about it

NOTE Confidence: 0.820130944252014

 $00{:}25{:}30{.}183 \dashrightarrow 00{:}25{:}31{.}903$ from a treatment perspective.

NOTE Confidence: 0.820130944252014

00:25:31.910 --> 00:25:32.348 Well,

NOTE Confidence: 0.820130944252014

 $00{:}25{:}32{.}348 \dashrightarrow 00{:}25{:}35{.}414$ another way we can see if these

NOTE Confidence: 0.820130944252014

 $00{:}25{:}35{.}414 \dashrightarrow 00{:}25{:}38{.}198$ circuits are pre dispositional is to

NOTE Confidence: 0.820130944252014

 $00:25:38.198 \longrightarrow 00:25:41.460$ induce them to try to change them.

NOTE Confidence: 0.820130944252014

00:25:41.460 --> 00:25:43.310 And so, with animal models,

NOTE Confidence: 0.820130944252014

 $00:25:43.310 \rightarrow 00:25:45.900$ preclinical models are very good at this,

NOTE Confidence: 0.820130944252014

 $00:25:45.900 \rightarrow 00:25:48.860$ and this was a challenge that Robin Healey,

NOTE Confidence: 0.820130944252014

 $00{:}25{:}48.860 \dashrightarrow 00{:}25{:}50.710$ a postdoc in the lab,

NOTE Confidence: 0.820130944252014

 $00:25:50.710 \longrightarrow 00:25:51.982$ took on just recently,

NOTE Confidence: 0.820130944252014

 $00{:}25{:}51{.}982 \dashrightarrow 00{:}25{:}54{.}595$ and what she did was she made a

NOTE Confidence: 0.820130944252014

 $00:25:54.595 \rightarrow 00:25:56.503$ group of ratchet or three groups

NOTE Confidence: 0.820130944252014

 $00:25:56.503 \rightarrow 00:25:58.588$ of rats dependent two different

NOTE Confidence: 0.820130944252014

 $00:25:58.588 \rightarrow 00:26:01.348$ doses and doses Saline and implanted

00:26:01.348 --> 00:26:03.294 osmotic Minipump's for two weeks,

NOTE Confidence: 0.820130944252014

 $00:26:03.294 \rightarrow 00:26:05.880$ and then let the pumps run out.

NOTE Confidence: 0.820130944252014

00:26:05.880 --> 00:26:08.470 And they were in another two weeks

NOTE Confidence: 0.820130944252014

 $00{:}26{:}08{.}470 \dashrightarrow 00{:}26{:}09{.}580$ of Force Absolutes.

NOTE Confidence: 0.820130944252014

 $00:26:09.580 \longrightarrow 00:26:11.524$ We determined how dependent they were

NOTE Confidence: 0.820130944252014

 $00:26:11.524 \rightarrow 00:26:14.409$ by giving them an injection of Mecamylamine.

NOTE Confidence: 0.820130944252014

 $00{:}26{:}14.410 \dashrightarrow 00{:}26{:}16.115$ IP and then measuring a

NOTE Confidence: 0.820130944252014

 $00:26:16.115 \longrightarrow 00:26:17.479$ number of somatic signs.

NOTE Confidence: 0.820130944252014

 $00{:}26{:}17{.}480 \dashrightarrow 00{:}26{:}19{.}185$ And this dependent score that

NOTE Confidence: 0.820130944252014

00:26:19.185 --> 00:26:20.549 I'm showing you here.

NOTE Confidence: 0.820130944252014

 $00:26:20.550 \longrightarrow 00:26:23.638$ We're going to use as as our

NOTE Confidence: 0.820130944252014

 $00{:}26{:}23.638 \dashrightarrow 00{:}26{:}26.478$ surrogate for the Fagots Room in use.

NOTE Confidence: 0.820130944252014

00:26:26.480 --> 00:26:27.214 So OK,

NOTE Confidence: 0.820130944252014

 $00{:}26{:}27{.}214 \dashrightarrow 00{:}26{:}29{.}783$ so now we have to go back.

NOTE Confidence: 0.820130944252014

 $00{:}26{:}29{.}790 \dashrightarrow 00{:}26{:}31{.}910$ So now we have a model to look

 $00:26:31.910 \longrightarrow 00:26:34.464$ at this if we could recapitulate

NOTE Confidence: 0.820130944252014

 $00:26:34.464 \rightarrow 00:26:36.416$ this singular striatal circuit.

NOTE Confidence: 0.820130944252014

 $00:26:36.420 \longrightarrow 00:26:38.622$ But what's the homologous region in

NOTE Confidence: 0.820130944252014

 $00:26:38.622 \rightarrow 00:26:42.298$ the rat in the rent of the human dorsal ACC?

NOTE Confidence: 0.820130944252014

 $00{:}26{:}42.300 \dashrightarrow 00{:}26{:}45.495$ So we didn't know and we don't want to

NOTE Confidence: 0.820130944252014

 $00{:}26{:}45{.}495 \dashrightarrow 00{:}26{:}48{.}078$ just look at the anatomic descriptors

NOTE Confidence: 0.820130944252014

 $00{:}26{:}48.078 \dashrightarrow 00{:}26{:}51.299$ in the Atlas and So what we did.

NOTE Confidence: 0.820130944252014

00:26:51.300 --> 00:26:52.032 It was,

NOTE Confidence: 0.820130944252014

 $00{:}26{:}52.032 \dashrightarrow 00{:}26{:}54.228$ it was another analytic trick or

NOTE Confidence: 0.820130944252014

 $00:26:54.228 \rightarrow 00:26:56.149$ the modularity analysis where we

NOTE Confidence: 0.820130944252014

 $00:26:56.149 \longrightarrow 00:26:58.014$ simply took the entire frontal

NOTE Confidence: 0.820130944252014

 $00{:}26{:}58.014 \dashrightarrow 00{:}27{:}00.657$ lobe of the rat and submitted it

NOTE Confidence: 0.820130944252014

 $00:27:00.657 \longrightarrow 00:27:02.487$ to this modularity approach to

NOTE Confidence: 0.820130944252014

 $00:27:02.490 \longrightarrow 00:27:04.734$ allow the computer to tell us

NOTE Confidence: 0.820130944252014

00:27:04.734 --> 00:27:06.969 how many divisions do you have?

NOTE Confidence: 0.820130944252014

00:27:06.970 --> 00:27:08.830 How many modules you have?

- NOTE Confidence: 0.820130944252014
- 00:27:08.830 --> 00:27:09.877 Do you have,
- NOTE Confidence: 0.820130944252014
- $00{:}27{:}09{.}877 \dashrightarrow 00{:}27{:}11{.}971$ and the computer came back with
- NOTE Confidence: 0.820130944252014
- $00{:}27{:}11{.}971 \dashrightarrow 00{:}27{:}14{.}634$ five and we use each of these five
- NOTE Confidence: 0.820130944252014
- $00:27:14.634 \rightarrow 00:27:16.974$ modules that we gave names simply
- NOTE Confidence: 0.820130944252014
- $00:27:16.974 \rightarrow 00:27:19.144$ because they overlaid onto some
- NOTE Confidence: 0.820130944252014
- $00:27:19.144 \rightarrow 00:27:21.648$ major Atlas regions and we use.
- NOTE Confidence: 0.820130944252014
- 00:27:21.648 --> 00:27:24.534 Each of these five modules, it seeds,
- NOTE Confidence: 0.820130944252014
- 00:27:24.534 --> 00:27:27.066 and only one of those modules,
- NOTE Confidence: 0.820130944252014
- $00{:}27{:}27{.}070 \dashrightarrow 00{:}27{:}30{.}326$ the what we call the ACC middle region
- NOTE Confidence: 0.820130944252014
- $00:27:30.326 \longrightarrow 00:27:34.259$ and only a circuit from there into the.
- NOTE Confidence: 0.820130944252014
- $00:27:34.260 \longrightarrow 00:27:37.151$ In this case in the dorsal stratum
- NOTE Confidence: 0.820130944252014
- $00{:}27{:}37{.}151 \dashrightarrow 00{:}27{:}38{.}885$ negatively correlated with the
- NOTE Confidence: 0.820130944252014
- $00{:}27{:}38.885 \dashrightarrow 00{:}27{:}41.025$ dependent scores of these animals.
- NOTE Confidence: 0.820130944252014
- 00:27:41.030 --> 00:27:44.264 Very, very similar to the three
- NOTE Confidence: 0.820130944252014
- $00:27:44.264 \rightarrow 00:27:47.689$ studies that I just showed you.
- NOTE Confidence: 0.820130944252014

00:27:47.690 - 00:27:49.616 This is a very complicated slide.

NOTE Confidence: 0.820130944252014

00:27:49.620 --> 00:27:51.755 You only want to give you 1

NOTE Confidence: 0.820130944252014

 $00:27:51.755 \longrightarrow 00:27:53.150$ message from this paper.

NOTE Confidence: 0.820130944252014

 $00:27:53.150 \rightarrow 00:27:54.762$ Just came out recently.

NOTE Confidence: 0.820130944252014

 $00:27:54.762 \longrightarrow 00:27:56.777$ And the question then was,

NOTE Confidence: 0.839934170246124

 $00{:}27{:}56{.}780 \dashrightarrow 00{:}27{:}59{.}993$ are there in fact since I can

NOTE Confidence: 0.839934170246124

 $00:27:59.993 \rightarrow 00:28:02.189$ induce these circuits in rats?

NOTE Confidence: 0.839934170246124

 $00{:}28{:}02{.}190 \dashrightarrow 00{:}28{:}04{.}910$ Are their baseline circuits pre

NOTE Confidence: 0.839934170246124

 $00{:}28{:}04{.}910 \dashrightarrow 00{:}28{:}07{.}086$ dispositional circuits that might

NOTE Confidence: 0.839934170246124

 $00:28:07.086 \longrightarrow 00:28:09.713$ modify or moderate the ability of

NOTE Confidence: 0.839934170246124

 $00{:}28{:}09{.}713 \dashrightarrow 00{:}28{:}12.630$ nicotine to cause to cause dependence?

NOTE Confidence: 0.839934170246124

 $00:28:12.630 \longrightarrow 00:28:15.115$ And in a very complicated

NOTE Confidence: 0.839934170246124

00:28:15.115 --> 00:28:16.109 moderation analysis,

NOTE Confidence: 0.839934170246124

 $00:28:16.110 \rightarrow 00:28:19.694$ I just want to highlight that two circuits

NOTE Confidence: 0.839934170246124

 $00:28:19.694 \rightarrow 00:28:23.349$ an insula frontal circuit shown up here

NOTE Confidence: 0.839934170246124

 $00:28:23.349 \rightarrow 00:28:26.540$ and insula striatal circuit down here,

- NOTE Confidence: 0.839934170246124
- $00:28:26.540 \longrightarrow 00:28:29.978$ fully moderated the relationship between the
- NOTE Confidence: 0.839934170246124
- $00{:}28{:}29{.}978 \dashrightarrow 00{:}28{:}34{.}039$ ACC ventral stratum and nicotine dependence.
- NOTE Confidence: 0.839934170246124
- $00:28:34.040 \rightarrow 00:28:36.808$ More details on how we got to these
- NOTE Confidence: 0.839934170246124
- $00{:}28{:}36{.}808 \dashrightarrow 00{:}28{:}38{.}846$ these intrinsic circuits are on this
- NOTE Confidence: 0.839934170246124
- $00:28:38.846 \rightarrow 00:28:41.608$ paper that came out just a few months
- NOTE Confidence: 0.839934170246124
- 00:28:41.608 --> 00:28:43.948 ago in the Journal of neuroscience,
- NOTE Confidence: 0.839934170246124
- $00:28:43.950 \longrightarrow 00:28:46.056$ but it looks like again the
- NOTE Confidence: 0.839934170246124
- $00:28:46.056 \longrightarrow 00:28:47.870$ conclusion would be that this.
- NOTE Confidence: 0.839934170246124
- $00{:}28{:}47.870 \dashrightarrow 00{:}28{:}50.425$ ACC striatal circuit seems to
- NOTE Confidence: 0.839934170246124
- 00:28:50.425 --> 00:28:52.980 track it became dependent severity.
- NOTE Confidence: 0.839934170246124
- $00:28:52.980 \rightarrow 00:28:55.540$ It's moderated by individual differences,
- NOTE Confidence: 0.839934170246124
- $00{:}28{:}55{.}540 \dashrightarrow 00{:}28{:}57{.}070$ even individual differences
- NOTE Confidence: 0.839934170246124
- $00:28:57.070 \longrightarrow 00:28:59.620$ in rats in from insula,
- NOTE Confidence: 0.839934170246124
- $00{:}28{:}59{.}620 \dashrightarrow 00{:}29{:}01{.}664$ frontal and executive insula.
- NOTE Confidence: 0.839934170246124
- 00:29:01.664 --> 00:29:03.197 Striatal circuits trap.
- NOTE Confidence: 0.861091077327728

00:29:05.660 --> 00:29:09.321 OK, so let's move on from nicotine

NOTE Confidence: 0.861091077327728

00:29:09.321 --> 00:29:12.785 trade trade circuits to looking at

NOTE Confidence: 0.861091077327728

 $00:29:12.785 \longrightarrow 00:29:15.780$ the consequences of acute nicotine

NOTE Confidence: 0.861091077327728

 $00:29:15.780 \rightarrow 00:29:19.360$ withdrawal and state related circuitry.

NOTE Confidence: 0.861091077327728

 $00{:}29{:}19{.}360 \dashrightarrow 00{:}29{:}22{.}592$ And as I said at the Abbey on

NOTE Confidence: 0.861091077327728

 $00{:}29{:}22{.}592 \dashrightarrow 00{:}29{:}24{.}999$ said nicotine with drawal is A,

NOTE Confidence: 0.861091077327728

00:29:25.000 --> 00:29:27.170 is it random, nasty syndrome,

NOTE Confidence: 0.861091077327728

00:29:27.170 --> 00:29:29.154 high anxiety, irritability, craving,

NOTE Confidence: 0.861091077327728

 $00{:}29{:}29{.}154 \dashrightarrow 00{:}29{:}32{.}130$ lots of negative negative affect as

NOTE Confidence: 0.861091077327728

 $00:29:32.201 \rightarrow 00:29:34.816$ well as executive control impairments.

NOTE Confidence: 0.861091077327728

 $00{:}29{:}34.820 \dashrightarrow 00{:}29{:}36.730$ When we give nicotine replacement,

NOTE Confidence: 0.861091077327728

 $00:29:36.730 \longrightarrow 00:29:39.390$ at least to it, to some extent,

NOTE Confidence: 0.861091077327728

 $00:29:39.390 \longrightarrow 00:29:41.295$ it were those incorrectly we

NOTE Confidence: 0.861091077327728

00:29:41.295 - 00:29:43.200 can reduce at least partially.

NOTE Confidence: 0.861091077327728

 $00{:}29{:}43.200 \dashrightarrow 00{:}29{:}46.596$ Many of these acute with drawal symptoms.

NOTE Confidence: 0.861091077327728

 $00:29:46.600 \rightarrow 00:29:49.127$ And so our hypothesis going into this

- NOTE Confidence: 0.861091077327728
- $00:29:49.127 \rightarrow 00:29:51.198$ series of experiments was that state,
- NOTE Confidence: 0.861091077327728
- 00:29:51.200 --> 00:29:51.910 like withdrawal,
- NOTE Confidence: 0.861091077327728
- $00:29:51.910 \longrightarrow 00:29:54.040$ is centered on the insulin and
- NOTE Confidence: 0.861091077327728
- $00:29:54.040 \rightarrow 00:29:55.843$ its associated circuitry and may
- NOTE Confidence: 0.861091077327728
- $00{:}29{:}55{.}843 \dashrightarrow 00{:}29{:}57{.}563$ ultimately serve as as Rajeev
- NOTE Confidence: 0.861091077327728
- $00{:}29{:}57{.}563 \dashrightarrow 00{:}29{:}59{.}340$ Dimension as a frequent target.
- NOTE Confidence: 0.795346319675446
- 00:30:01.710 --> 00:30:04.370 Well, OK, just like I said with
- NOTE Confidence: 0.795346319675446
- $00:30:04.370 \longrightarrow 00:30:06.550$ the singular why the insulin?
- NOTE Confidence: 0.795346319675446
- $00:30:06.550 \longrightarrow 00:30:08.560$ Where did this come from?
- NOTE Confidence: 0.795346319675446
- 00:30:08.560 --> 00:30:11.152 And really it has to go back to
- NOTE Confidence: 0.795346319675446
- $00:30:11.152 \rightarrow 00:30:13.617$ this seminal paper by Nafion and
- NOTE Confidence: 0.795346319675446
- 00:30:13.617 $\operatorname{-->}$ 00:30:15.792 Antoine Beshara and science within
- NOTE Confidence: 0.795346319675446
- $00{:}30{:}15{.}792 \dashrightarrow 00{:}30{:}18{.}471$ they noted that individuals who had
- NOTE Confidence: 0.795346319675446
- $00{:}30{:}18{.}471 \dashrightarrow 00{:}30{:}21{.}053$ strokes that were limited to or
- NOTE Confidence: 0.795346319675446
- $00:30:21.053 \rightarrow 00:30:23.068$ incorporated regions in the insula,
- NOTE Confidence: 0.795346319675446

 $00:30:23.070 \rightarrow 00:30:25.482$ if they were smokers before before

NOTE Confidence: 0.795346319675446

 $00{:}30{:}25{.}482 \dashrightarrow 00{:}30{:}27{.}499$ the stroke, they spontaneously stopped

NOTE Confidence: 0.795346319675446

 $00:30:27.499 \longrightarrow 00:30:30.320$ smoking after the smoke at the stroke.

NOTE Confidence: 0.795346319675446

 $00:30:30.320 \longrightarrow 00:30:31.592$ At least many did.

NOTE Confidence: 0.795346319675446

 $00:30:31.592 \rightarrow 00:30:34.240$ And probably the best sentence in this paper.

NOTE Confidence: 0.795346319675446

 $00:30:34.240 \rightarrow 00:30:36.408$ If you haven't read it when they ask

NOTE Confidence: 0.795346319675446

 $00:30:36.408 \rightarrow 00:30:38.158$ them individual why they stop smoking.

NOTE Confidence: 0.795346319675446

00:30:38.160 -> 00:30:39.840 The person said, well, it was.

NOTE Confidence: 0.795346319675446

 $00:30:39.840 \longrightarrow 00:30:42.108$ If my body forgot that I was a smoker

NOTE Confidence: 0.795346319675446

 $00:30:42.108 \rightarrow 00:30:43.894$ and that really says everything

NOTE Confidence: 0.795346319675446

 $00:30:43.894 \dashrightarrow 00:30:46.102$ about what the insular is doing.

NOTE Confidence: 0.795346319675446

00:30:46.110 --> 00:30:47.163 In our lab,

NOTE Confidence: 0.795346319675446

 $00:30:47.163 \rightarrow 00:30:49.269$ we've also seen differences in Gray

NOTE Confidence: 0.795346319675446

00:30:49.269 --> 00:30:51.219 matter greater Gray matter density

NOTE Confidence: 0.795346319675446

 $00{:}30{:}51{.}219 \dashrightarrow 00{:}30{:}53{.}962$ in the insula in smokers versus non

NOTE Confidence: 0.795346319675446

 $00:30:53.962 \rightarrow 00:30:56.573$ smokers that very nicely relates to Alexa.

 $00:30:56.580 \dashrightarrow 00:30:59.254$ Find me up in these individuals in

NOTE Confidence: 0.795346319675446

 $00{:}30{:}59{.}254 \dashrightarrow 00{:}31{:}01{.}780$ these non Alexa find individuals.

NOTE Confidence: 0.795346319675446

 $00{:}31{:}01{.}780 \dashrightarrow 00{:}31{:}04{.}498$ I also want to point out and in the

NOTE Confidence: 0.795346319675446

00:31:04.498 --> 00:31:07.068 scheme of the George Group is proposed

NOTE Confidence: 0.795346319675446

 $00:31:07.068 \rightarrow 00:31:10.407$ in his three cycles that two of those cycles.

NOTE Confidence: 0.795346319675446

00:31:10.410 --> 00:31:11.790 Two of those aspects,

NOTE Confidence: 0.795346319675446

00:31:11.790 --> 00:31:13.170 both withdrawal and negative,

NOTE Confidence: 0.795346319675446

 $00{:}31{:}13{.}170 \dashrightarrow 00{:}31{:}15{.}876$ affect as well as the anticipation

NOTE Confidence: 0.795346319675446

00:31:15.876 --> 00:31:18.180 preoccupation phase do include do

NOTE Confidence: 0.795346319675446

 $00:31:18.180 \longrightarrow 00:31:20.736$ include the installer in these circuits.

NOTE Confidence: 0.795346319675446

 $00:31:20.740 \rightarrow 00:31:24.124$ Our data that I showed you a moment ago,

NOTE Confidence: 0.795346319675446

00:31:24.130 --> 00:31:25.754 a few moments ago,

NOTE Confidence: 0.795346319675446

 $00{:}31{:}25{.}754 \dashrightarrow 00{:}31{:}27{.}784$ also implicated installer as biasing

NOTE Confidence: 0.795346319675446

 $00{:}31{:}27.784 \dashrightarrow 00{:}31{:}30.327$ these trait related in solicitations.

NOTE Confidence: 0.795346319675446

 $00{:}31{:}30{.}330 \dashrightarrow 00{:}31{:}32{.}760$ Let me summarize to other studies

 $00:31:32.760 \longrightarrow 00:31:35.791$ in the lab that have gotten us

NOTE Confidence: 0.795346319675446

 $00{:}31{:}35{.}791 \dashrightarrow 00{:}31{:}38{.}437$ into this into this insular mode.

NOTE Confidence: 0.795346319675446

00:31:38.440 - 00:31:41.856 Max subtle in a number of years ago,

NOTE Confidence: 0.795346319675446

 $00:31:41.860 \rightarrow 00:31:43.875$ identified the amygdala using the

NOTE Confidence: 0.795346319675446

 $00{:}31{:}43.875 \dashrightarrow 00{:}31{:}46.412$ Hariri basis task is being sensitive

NOTE Confidence: 0.795346319675446

 $00:31:46.412 \rightarrow 00:31:49.118$ to state related changes in nicotine.

NOTE Confidence: 0.795346319675446

 $00:31:49.120 \longrightarrow 00:31:52.042$ He then used the amygdala that

NOTE Confidence: 0.795346319675446

 $00:31:52.042 \longrightarrow 00:31:53.503$ he identified functionally.

NOTE Confidence: 0.795346319675446

 $00:31:53.510 \longrightarrow 00:31:58.340$ As you seen and identified.

NOTE Confidence: 0.795346319675446

 $00:31:58.340 \longrightarrow 00:32:00.080$ Insula circuit continuing to

NOTE Confidence: 0.795346319675446

 $00{:}32{:}00{.}080 \dashrightarrow 00{:}32{:}01{.}385$ walk this circuit.

NOTE Confidence: 0.795346319675446

 $00{:}32{:}01{.}390 \dashrightarrow 00{:}32{:}04{.}891$ He now used the insular as a seed and

NOTE Confidence: 0.795346319675446

 $00:32:04.891 \rightarrow 00:32:07.477$ identify the default mode network.

NOTE Confidence: 0.795346319675446

 $00:32:07.480 \longrightarrow 00:32:09.655$ The full network that we

NOTE Confidence: 0.795346319675446

 $00{:}32{:}09.655 \dashrightarrow 00{:}32{:}10.960$ now know classically.

NOTE Confidence: 0.795346319675446

00:32:10.960 --> 00:32:11.394 PCC,

- NOTE Confidence: 0.795346319675446
- 00:32:11.394 --> 00:32:13.130 eventual medial Pfc power,
- NOTE Confidence: 0.795346319675446
- $00:32:13.130 \longrightarrow 00:32:14.870$ hippocampal gyrus and interesting
- NOTE Confidence: 0.795346319675446
- $00:32:14.870 \longrightarrow 00:32:16.175$ Lee and importantly,
- NOTE Confidence: 0.795346319675446
- $00:32:16.180 \longrightarrow 00:32:18.772$ this circuit does not change in
- NOTE Confidence: 0.795346319675446
- $00{:}32{:}18.772 \dashrightarrow 00{:}32{:}21.625$ non smokers but is enhanced when
- NOTE Confidence: 0.795346319675446
- $00:32:21.625 \longrightarrow 00:32:24.215$ the individual is in absent.
- NOTE Confidence: 0.795346319675446
- $00:32:24.220 \longrightarrow 00:32:26.400$ Matt also identified that this
- NOTE Confidence: 0.795346319675446
- 00:32:26.400 --> 00:32:29.182 insula VM Pfc circuit fully mediated
- NOTE Confidence: 0.795346319675446
- $00{:}32{:}29{.}182 \dashrightarrow 00{:}32{:}31{.}286$ the relationship between trait
- NOTE Confidence: 0.795346319675446
- 00:32:31.286 --> 00:32:33.916 Alexa Pinya and stayed crated,
- NOTE Confidence: 0.795346319675446
- $00:32:33.920 \rightarrow 00:32:37.264$ so we had enough evidence now going in
- NOTE Confidence: 0.795346319675446
- $00:32:37.264 \longrightarrow 00:32:40.802$ that the incident was likely involved
- NOTE Confidence: 0.795346319675446
- $00:32:40.802 \rightarrow 00:32:44.062$ in this nicotine withdrawal syndrome.
- NOTE Confidence: 0.795346319675446
- $00{:}32{:}44.070 \dashrightarrow 00{:}32{:}45.740$ So the installation we all
- NOTE Confidence: 0.795346319675446
- $00:32:45.740 \longrightarrow 00:32:47.410$ took neuroanatomy buried in the
- NOTE Confidence: 0.795346319675446

 $00:32:47.469 \longrightarrow 00:32:49.139$ middle of this temporal lobe,

NOTE Confidence: 0.795346319675446

 $00{:}32{:}49{.}140 \dashrightarrow 00{:}32{:}51{.}499$ yet to kind of crank open the

NOTE Confidence: 0.795346319675446

 $00:32:51.499 \longrightarrow 00:32:53.528$ brain and see it in there.

NOTE Confidence: 0.795346319675446

 $00:32:53.530 \rightarrow 00:32:55.798$ Probably the best review paper and

NOTE Confidence: 0.795346319675446

 $00{:}32{:}55{.}798 \dashrightarrow 00{:}32{:}57{.}659$ the breast best theoretical paper

NOTE Confidence: 0.795346319675446

 $00{:}32{:}57.659 \dashrightarrow 00{:}32{:}59.626$ that that I came across and

NOTE Confidence: 0.795346319675446

 $00:32:59.626 \dashrightarrow 00:33:01.275$ I would really encourage those

NOTE Confidence: 0.795346319675446

 $00:33:01.275 \rightarrow 00:33:03.669$ of you who might be interested in

NOTE Confidence: 0.795346319675446

 $00{:}33{:}03{.}670 \dashrightarrow 00{:}33{:}04{.}684$ the insular regions.

NOTE Confidence: 0.795346319675446

00:33:04.684 --> 00:33:06.912 Bud Craig's paper, about 10 years ago,

NOTE Confidence: 0.795346319675446

 $00:33:06.912 \longrightarrow 00:33:08.730$ where he emphasized that the insula

NOTE Confidence: 0.795346319675446

00:33:08.793 --> 00:33:10.647 really has a gradient of processing

NOTE Confidence: 0.795346319675446

 $00:33:10.647 \longrightarrow 00:33:12.382$ from post theory and anterior

NOTE Confidence: 0.795346319675446

00:33:12.382 --> 00:33:14.146 insula from from interoceptive,

NOTE Confidence: 0.795346319675446

 $00:33:14.150 \rightarrow 00:33:15.718$ processing homeostatic processing with.

NOTE Confidence: 0.795346319675446

 $00:33:15.718 \rightarrow 00:33:17.286$ Amygdala and hypothalamic inputs.

 $00:33:17.290 \rightarrow 00:33:20.730$ And as one goes more rostral, more anterija.

NOTE Confidence: 0.795346319675446

 $00:33:20.730 \dashrightarrow 00:33:22.450$ This information is integrated

NOTE Confidence: 0.795346319675446

 $00{:}33{:}22{.}450 \dashrightarrow 00{:}33{:}24{.}170$ and kick more forward,

NOTE Confidence: 0.814464807510376

 $00{:}33{:}24.170 \dashrightarrow 00{:}33{:}26.972$ integrated, and kick more anteriorly where

NOTE Confidence: 0.814464807510376

 $00:33:26.972 \longrightarrow 00:33:30.457$ the most anterior regions of the of the

NOTE Confidence: 0.814464807510376

 $00{:}33{:}30{.}457 \dashrightarrow 00{:}33{:}32{.}767$ insula are involved in hedonic processing.

NOTE Confidence: 0.814464807510376

 $00:33:32.770 \longrightarrow 00:33:34.408$ Motivational cognitive processing

NOTE Confidence: 0.814464807510376

 $00:33:34.408 \longrightarrow 00:33:37.684$ with inputs from areas that we

NOTE Confidence: 0.814464807510376

 $00:33:37.684 \longrightarrow 00:33:40.190$ think are players in the bank.

NOTE Confidence: 0.814464807510376

 $00:33:40.190 \rightarrow 00:33:42.926$ And this review article by Craig

NOTE Confidence: 0.814464807510376

 $00:33:42.926 \rightarrow 00:33:46.186$ LED us to hypothesize a number of

NOTE Confidence: 0.814464807510376

 $00:33:46.186 \dashrightarrow 00:33:48.886$ years ago that the salience network,

NOTE Confidence: 0.814464807510376

 $00{:}33{:}48.890 \dashrightarrow 00{:}33{:}52.054$ the ACC and anterior insular served as

NOTE Confidence: 0.814464807510376

 $00{:}33{:}52.054 \dashrightarrow 00{:}33{:}55.760$ sort of the pivot of a Teeter Totter.

NOTE Confidence: 0.814464807510376

 $00:33:55.760 \dashrightarrow 00:33:58.966$ And when an individual was in accidents,

 $00:33:58.970 \longrightarrow 00:34:01.390$ this salience network bias the

NOTE Confidence: 0.814464807510376

 $00{:}34{:}01{.}390 \dashrightarrow 00{:}34{:}03{.}810$ individual to pay more attention

NOTE Confidence: 0.814464807510376

 $00:34:03.890 \rightarrow 00:34:06.380$ to internal states to pay attention

NOTE Confidence: 0.814464807510376

 $00:34:06.380 \longrightarrow 00:34:09.040$ to that craving to that hunger.

NOTE Confidence: 0.814464807510376

 $00:34:09.040 \longrightarrow 00:34:11.390$ When the individual is sated.

NOTE Confidence: 0.814464807510376

 $00{:}34{:}11{.}390 \dashrightarrow 00{:}34{:}14{.}198$ This bias system encourage the individual

NOTE Confidence: 0.814464807510376

 $00{:}34{:}14.198 \dashrightarrow 00{:}34{:}17.448$ to spend more time in executive mode

NOTE Confidence: 0.814464807510376

 $00:34:17.448 \longrightarrow 00:34:20.046$ to be able to concentrate focus.

NOTE Confidence: 0.814464807510376

 $00{:}34{:}20.050 \dashrightarrow 00{:}34{:}23.154$ It also allowed us to start to look

NOTE Confidence: 0.814464807510376

 $00{:}34{:}23.154 \dashrightarrow 00{:}34{:}26.583$ at the fact that the insula has been

NOTE Confidence: 0.814464807510376

 $00{:}34{:}26{.}583 \dashrightarrow 00{:}34{:}29{.}940$ divided into a number of different areas,

NOTE Confidence: 0.814464807510376

 $00{:}34{:}29{.}940 \dashrightarrow 00{:}34{:}32{.}245$ whether it's by using functional

NOTE Confidence: 0.814464807510376

00:34:32.245 --> 00:34:33.628 connectivity or Cytoarchitectonic's

NOTE Confidence: 0.814464807510376

 $00:34:33.628 \rightarrow 00:34:35.529$ or behavior for that matter,

NOTE Confidence: 0.814464807510376

 $00:34:35.530 \longrightarrow 00:34:37.210$ on this list, divide,

NOTE Confidence: 0.814464807510376

 $00:34:37.210 \longrightarrow 00:34:40.260$ then divide into three major three major,

- NOTE Confidence: 0.814464807510376
- $00:34:40.260 \longrightarrow 00:34:40.924$ with subdivisions.
- NOTE Confidence: 0.814464807510376
- $00{:}34{:}40{.}924 \dashrightarrow 00{:}34{:}43{.}580$ And so the question we next had was
- NOTE Confidence: 0.814464807510376
- $00{:}34{:}43.649 \dashrightarrow 00{:}34{:}45.889$ how did these circuits from each of
- NOTE Confidence: 0.814464807510376
- $00:34:45.889 \rightarrow 00:34:48.124$ these regions of the insulin different
- NOTE Confidence: 0.814464807510376
- $00:34:48.124 \rightarrow 00:34:50.542$ as a function of nicotine withdrawal?
- NOTE Confidence: 0.814464807510376
- $00{:}34{:}50{.}550 \dashrightarrow 00{:}34{:}53{.}485$ And do these circuits have
- NOTE Confidence: 0.814464807510376
- $00:34:53.485 \longrightarrow 00:34:54.659$ behavioral consequences?
- NOTE Confidence: 0.814464807510376
- $00{:}34{:}54{.}660 \dashrightarrow 00{:}34{:}57{.}260$ So this is the work of John Kadota
- NOTE Confidence: 0.814464807510376
- $00:34:57.260 \longrightarrow 00:34:59.470$ and his research assistant,
- NOTE Confidence: 0.814464807510376
- 00:34:59.470 00:35:02.251 and what he did was he took of these
- NOTE Confidence: 0.814464807510376
- $00:35:02.251 \rightarrow 00:35:04.033$ three divisions and hypothesis
- NOTE Confidence: 0.814464807510376
- $00{:}35{:}04{.}033 \dashrightarrow 00{:}35{:}06{.}817$ driven fashion use each of these
- NOTE Confidence: 0.814464807510376
- $00:35:06.817 \rightarrow 00:35:09.496$ three regions of the insular seeds,
- NOTE Confidence: 0.814464807510376
- $00{:}35{:}09{.}500 \dashrightarrow 00{:}35{:}12{.}223$ and had each of these three large
- NOTE Confidence: 0.814464807510376
- $00:35:12.223 \rightarrow 00:35:14.310$ scale networks as as targets,
- NOTE Confidence: 0.814464807510376

 $00:35:14.310 \longrightarrow 00:35:16.752$ and what he identified with three

NOTE Confidence: 0.814464807510376

 $00:35:16.752 \longrightarrow 00:35:19.210$ circuits that were biased as a

NOTE Confidence: 0.814464807510376

 $00{:}35{:}19{.}210$ --> $00{:}35{:}20{.}726$ function of acute accidents.

NOTE Confidence: 0.814464807510376

 $00:35:20.730 \longrightarrow 00:35:22.730$ This was 48 hour accents,

NOTE Confidence: 0.814464807510376

 $00:35:22.730 \dashrightarrow 00:35:25.166$ one from the ventral insula too.

NOTE Confidence: 0.814464807510376

 $00{:}35{:}25{.}170 \dashrightarrow 00{:}35{:}26{.}858$ Piece of the DL.

NOTE Confidence: 0.814464807510376

 $00:35:26.858 \rightarrow 00:35:30.139$ Pfc from the posterior insula into the ACC,

NOTE Confidence: 0.814464807510376

 $00:35:30.140 \dashrightarrow 00:35:34.084$ and from the dorsal insula into the DNA.

NOTE Confidence: 0.814464807510376

 $00:35:34.090 \rightarrow 00:35:36.820$ And what was interesting is that they

NOTE Confidence: 0.814464807510376

 $00:35:36.820 \dashrightarrow 00:35:38.950$ also had behavioral consequences.

NOTE Confidence: 0.814464807510376

 $00{:}35{:}38{.}950 \dashrightarrow 00{:}35{:}41{.}596$ At least two of them did,

NOTE Confidence: 0.814464807510376

 $00:35:41.600 \longrightarrow 00:35:43.064$ and that with this,

NOTE Confidence: 0.814464807510376

 $00:35:43.064 \rightarrow 00:35:45.260$ this first circuit negatively is very

NOTE Confidence: 0.814464807510376

00:35:45.333 --> 00:35:48.228 strongly negatively correlating with craving,

NOTE Confidence: 0.814464807510376

 $00{:}35{:}48{.}230 \dashrightarrow 00{:}35{:}50{.}410$ and this salience network

NOTE Confidence: 0.814464807510376

 $00:35:50.410 \longrightarrow 00:35:52.045$ circuit correlating with.

00:35:52.050 --> 00:35:53.568 The WS WS,

NOTE Confidence: 0.814464807510376

 $00:35:53.568 \rightarrow 00:35:55.086$ sadness and anger.

NOTE Confidence: 0.814464807510376

 $00{:}35{:}55{.}090 \dashrightarrow 00{:}35{:}57{.}625$ There was no relationship with

NOTE Confidence: 0.814464807510376

 $00:35:57.625 \rightarrow 00:35:58.639$ cognitive performance.

NOTE Confidence: 0.814464807510376

 $00:35:58.640 \rightarrow 00:36:03.368$ During looking at these insular circuits.

NOTE Confidence: 0.814464807510376

00:36:03.370 - > 00:36:05.288 And so we've we've sort of think

NOTE Confidence: 0.814464807510376

 $00{:}36{:}05{.}288 \dashrightarrow 00{:}36{:}06{.}660$ about these three circuits.

NOTE Confidence: 0.814464807510376

 $00:36:06.660 \rightarrow 00:36:08.746$ Is 1 related to affect want interception?

NOTE Confidence: 0.814464807510376

00:36:08.750 --> 00:36:10.103 Want to cognition?

NOTE Confidence: 0.814464807510376

 $00{:}36{:}10.103 \dashrightarrow 00{:}36{:}13.260$ And when we looked at the state

NOTE Confidence: 0.814464807510376

 $00:36:13.354 \rightarrow 00:36:15.429$ of a little bit closer,

NOTE Confidence: 0.814464807510376

 $00{:}36{:}15{.}430 \dashrightarrow 00{:}36{:}18{.}862$ we kind of looked at this this terminal

NOTE Confidence: 0.814464807510376

 $00{:}36{:}18.862 \dashrightarrow 00{:}36{:}22.199$ region if you will and the DL Pfc and

NOTE Confidence: 0.814464807510376

 $00{:}36{:}22.199 \dashrightarrow 00{:}36{:}25.070$ it's Mac on where this cross hairs on

NOTE Confidence: 0.814464807510376

00:36:25.070 --> 00:36:28.109 to where the F three 1020 placement

 $00:36:28.109 \rightarrow 00:36:31.790$ is where we give TMS at the DL Pfc.

NOTE Confidence: 0.814464807510376

 $00:36:31.790 \dashrightarrow 00:36:34.250$ So perhaps what we've identified

NOTE Confidence: 0.814464807510376

 $00:36:34.250 \longrightarrow 00:36:36.218$ serendipitously would be a

NOTE Confidence: 0.814464807510376

 $00:36:36.218 \longrightarrow 00:36:39.081$ location that we might be able to

NOTE Confidence: 0.814464807510376

 $00:36:39.081 \rightarrow 00:36:40.980$ target and justify targeting our.

NOTE Confidence: 0.814464807510376

 $00{:}36{:}40{.}980 \dashrightarrow 00{:}36{:}45{.}432$ TMS treatments to modify these circuits and

NOTE Confidence: 0.814464807510376

 $00:36:45.432 \rightarrow 00:36:50.150$ involved in the negative consequences of.

NOTE Confidence: 0.814464807510376

 $00:36:50.150 \rightarrow 00:36:56.598$ The nicotine withdrawal syndrome.

NOTE Confidence: 0.814464807510376

00:36:56.598 --> 00:36:58.210 OK.

NOTE Confidence: 0.814464807510376

 $00:36:58.210 \rightarrow 00:37:00.000$ Tell me how we're doing.

NOTE Confidence: 0.814464807510376

 $00{:}37{:}00{.}000 \dashrightarrow 00{:}37{:}02{.}247$ I've got a couple of more studies

NOTE Confidence: 0.814464807510376

 $00{:}37{:}02{.}247 \dashrightarrow 00{:}37{:}04{.}640$ I'd like to quickly go through.

NOTE Confidence: 0.814464807510376

00:37:04.640 --> 00:37:07.138 Trish, Trish, are you have some time?

NOTE Confidence: 0.814464807510376

00:37:07.140 --> 00:37:07.520 OK,

NOTE Confidence: 0.814464807510376

 $00:37:07.520 \longrightarrow 00:37:07.900$ great.

NOTE Confidence: 0.814464807510376

00:37:07.900 - 00:37:10.940 Just just I can't see you so wave

00:37:11.033 - 00:37:12.845 at me or shut me off.

NOTE Confidence: 0.827893912792206

 $00{:}37{:}12.850 \dashrightarrow 00{:}37{:}14.946$ OK so we want to start to look

NOTE Confidence: 0.827893912792206

 $00{:}37{:}14.946 \dashrightarrow 00{:}37{:}17.133$ now at these state trade aspects

NOTE Confidence: 0.827893912792206

 $00:37:17.133 \dashrightarrow 00:37:19.985$ in decision making and then an in

NOTE Confidence: 0.827893912792206

 $00{:}37{:}19{.}985 \dashrightarrow 00{:}37{:}21{.}573$ reward learning very important

NOTE Confidence: 0.827893912792206

 $00:37:21.573 \rightarrow 00:37:24.600$ process as you know in in substance

NOTE Confidence: 0.827893912792206

 $00:37:24.600 \dashrightarrow 00:37:26.680$ use development and maintenance.

NOTE Confidence: 0.827893912792206

 $00:37:26.680 \longrightarrow 00:37:29.024$ And we began to look about at a

NOTE Confidence: 0.827893912792206

 $00:37:29.024 \rightarrow 00:37:31.233$ test that hasn't been used very

NOTE Confidence: 0.827893912792206

 $00{:}37{:}31{.}233 \dashrightarrow 00{:}37{:}33{.}549$ much in addiction are called the

NOTE Confidence: 0.827893912792206

00:37:33.629 --> 00:37:36.277 probabilistic reversal learning task,

NOTE Confidence: 0.827893912792206

 $00{:}37{:}36{.}280 \dashrightarrow 00{:}37{:}38{.}280$ and we like this task.

NOTE Confidence: 0.827893912792206

 $00:37:38.280 \longrightarrow 00:37:40.240$ We suppressive captures two different

NOTE Confidence: 0.827893912792206

 $00{:}37{:}40{.}240 \dashrightarrow 00{:}37{:}41{.}808$ constructs that are important

NOTE Confidence: 0.827893912792206

00:37:41.808 --> 00:37:43.880 in reward based decision making,

00:37:43.880 --> 00:37:45.880 reward sensitivity and cognitive flexibility.

NOTE Confidence: 0.827893912792206

 $00:37:45.880 \rightarrow 00:37:48.064$ How an individual changes one's behavior

NOTE Confidence: 0.827893912792206

 $00:37:48.064 \rightarrow 00:37:50.628$ in the face of negative outcomes

NOTE Confidence: 0.827893912792206

 $00:37:50.628 \rightarrow 00:37:53.228$ versus maintaining a previous choice.

NOTE Confidence: 0.827893912792206

 $00{:}37{:}53{.}230 \dashrightarrow 00{:}37{:}55{.}925$ And this task has been used because

NOTE Confidence: 0.827893912792206

 $00{:}37{:}55{.}925 \dashrightarrow 00{:}37{:}59{.}007$ we used it because it relies on

NOTE Confidence: 0.827893912792206

 $00:37:59.007 \longrightarrow 00:38:01.767$ NCL circuitry and we've shown that

NOTE Confidence: 0.827893912792206

00:38:01.858 --> 00:38:04.908 this circuitry is changed with

NOTE Confidence: 0.827893912792206

 $00:38:04.908 \longrightarrow 00:38:06.128$ nicotine dependence.

NOTE Confidence: 0.827893912792206

00:38:06.130 --> 00:38:07.566 But how it's been,

NOTE Confidence: 0.827893912792206

 $00{:}38{:}07{.}566 \dashrightarrow 00{:}38{:}10{.}252$ how it is involved in smoking in

NOTE Confidence: 0.827893912792206

 $00:38:10.252 \rightarrow 00:38:13.395$ the state or trade at ameliorated by

NOTE Confidence: 0.827893912792206

00:38:13.395 --> 00:38:15.500 Pharmacotherapies is really unknown.

NOTE Confidence: 0.827893912792206

 $00:38:15.500 \dashrightarrow 00:38:17.636$ So this is work of at least Lesage

NOTE Confidence: 0.827893912792206

 $00{:}38{:}17.636 \dashrightarrow 00{:}38{:}19.887$ post dot dot in the lab and it's a

NOTE Confidence: 0.827893912792206

 $00:38:19.887 \longrightarrow 00:38:22.399$ task that we modify based on one that

00:38:22.399 --> 00:38:25.028 Roshan cools published a number of years ago,

NOTE Confidence: 0.827893912792206

 $00{:}38{:}25{.}028 \dashrightarrow 00{:}38{:}27{.}438$ and again I would encourage people to think

NOTE Confidence: 0.827893912792206

 $00:38:27.438 \longrightarrow 00:38:29.895$ about this task is not used an awful lot,

NOTE Confidence: 0.827893912792206

 $00:38:29.900 \rightarrow 00:38:32.098$ and certainly not in addiction and we

NOTE Confidence: 0.827893912792206

 $00:38:32.098 \rightarrow 00:38:34.800$ really like it a lot and I'll show you why.

NOTE Confidence: 0.827893912792206

 $00:38:34.800 \dashrightarrow 00:38:37.096$ It's a very simple task for the subject.

NOTE Confidence: 0.827893912792206

00:38:37.100 - 00:38:38.588 They see two fractals and they

NOTE Confidence: 0.827893912792206

 $00:38:38.588 \longrightarrow 00:38:40.270$ have to pick one arbitrarily.

NOTE Confidence: 0.827893912792206

 $00:38:40.270 \longrightarrow 00:38:41.705$ The computer has decided what

NOTE Confidence: 0.827893912792206

 $00:38:41.705 \longrightarrow 00:38:42.853$ the right answer is.

NOTE Confidence: 0.827893912792206

 $00:38:42.860 \dashrightarrow 00:38:44.558$ That's over here are the individual

NOTE Confidence: 0.827893912792206

 $00{:}38{:}44{.}558 \dashrightarrow 00{:}38{:}46{.}390$ doesn't know and they get feedback.

NOTE Confidence: 0.827893912792206

 $00{:}38{:}46{.}390 \dashrightarrow 00{:}38{:}49{.}406$ It's a probabilistic pass, so they get true.

NOTE Confidence: 0.827893912792206

00:38:49.410 --> 00:38:52.373 A true answer about 75% of the time,

NOTE Confidence: 0.827893912792206

 $00{:}38{:}52{.}373 \dashrightarrow 00{:}38{:}54{.}900$ and they can make a decision to

 $00:38:54.988 \rightarrow 00:38:57.697$ either stay when they make a win.

NOTE Confidence: 0.827893912792206

 $00{:}38{:}57{.}700 \dashrightarrow 00{:}39{:}00{.}828$ All or if they lose their inside to

NOTE Confidence: 0.827893912792206

 $00:39:00.828 \longrightarrow 00:39:04.336$ stay or they can ship when they make.

NOTE Confidence: 0.827893912792206

 $00:39:04.340 \longrightarrow 00:39:07.360$ When they lose so Wednesday, Lucia.

NOTE Confidence: 0.827893912792206

 $00{:}39{:}07{.}360 \dashrightarrow 00{:}39{:}11{.}120$ A type of behavior.

NOTE Confidence: 0.827893912792206

 $00{:}39{:}11{.}120 \dashrightarrow 00{:}39{:}13.656$ We did this task in both smokers and

NOTE Confidence: 0.827893912792206

 $00:39:13.656 \rightarrow 00:39:15.676$ non smokers in a very complicated

NOTE Confidence: 0.827893912792206

 $00:39:15.676 \rightarrow 00:39:18.120$ fashion that you know we can do it.

NOTE Confidence: 0.827893912792206

 $00:39:18.120 \longrightarrow 00:39:19.324$ The at the IRP.

NOTE Confidence: 0.827893912792206

 $00:39{:}19.324 \dashrightarrow 00{:}39{:}20.829$ We stand individual six times

NOTE Confidence: 0.827893912792206

 $00:39:20.829 \longrightarrow 00:39:22.890$ on and off and nicotine Patch.

NOTE Confidence: 0.827893912792206

 $00{:}39{:}22{.}890 \dashrightarrow 00{:}39{:}25{.}394$ Two of those times was with a chronic

NOTE Confidence: 0.827893912792206

 $00:39:25.394 \longrightarrow 00:39:27.557$ of Renick Ling Pill and two of

NOTE Confidence: 0.827893912792206

 $00{:}39{:}27{.}557 \dashrightarrow 00{:}39{:}30{.}093$ those times was with uh with it's a

NOTE Confidence: 0.827893912792206

 $00:39:30.093 \rightarrow 00:39:32.091$ placebo pill because we wanted to

NOTE Confidence: 0.827893912792206

 $00:39:32.091 \rightarrow 00:39:34.020$ look at this drug drug interaction.

00:39:34.020 --> 00:39:35.934 As you know varenna clean is

NOTE Confidence: 0.827893912792206

 $00:39:35.934 \rightarrow 00:39:37.577$ generally given clinically while the

NOTE Confidence: 0.827893912792206

00:39:37.577 --> 00:39:39.419 individual is still is still smoking.

NOTE Confidence: 0.827893912792206

00:39:39.420 --> 00:39:41.876 So how would you analyze it past like

NOTE Confidence: 0.827893912792206

 $00:39:41.876 \rightarrow 00:39:44.190$ this behavior you can't look at accuracy,

NOTE Confidence: 0.827893912792206

00:39:44.190 - 00:39:45.910 you can trigger reaction time.

NOTE Confidence: 0.827893912792206

 $00:39:45.910 \longrightarrow 00:39:48.830$ And was at least did she use the

NOTE Confidence: 0.827893912792206

 $00:39:48.830 \longrightarrow 00:39:50.433$ computational model something called

NOTE Confidence: 0.827893912792206

 $00{:}39{:}50{.}433 \dashrightarrow 00{:}39{:}53{.}233$ The Hidden Markov model and she did

NOTE Confidence: 0.827893912792206

 $00:39:53.233 \rightarrow 00:39:55.814$ this as a function of group smokers

NOTE Confidence: 0.827893912792206

 $00:39:55.814 \dashrightarrow 00:39:57.569$ and non smokers and treatment.

NOTE Confidence: 0.827893912792206

 $00{:}39{:}57{.}569 \dashrightarrow 00{:}40{:}00{.}361$ And as you can see there were no

NOTE Confidence: 0.827893912792206

 $00{:}40{:}00{.}361 \dashrightarrow 00{:}40{:}02{.}140$ effects of pharma cotherapy choose

NOTE Confidence: 0.827893912792206

00:40:02.140 --> 00:40:04.852 me in nonsmokers but since we're

NOTE Confidence: 0.827893912792206

 $00{:}40{:}04{.}852 \dashrightarrow 00{:}40{:}07{.}267$ getting a little short on time I'm

 $00:40:07.267 \longrightarrow 00:40:09.676$ not going to detail with this bias

NOTE Confidence: 0.827893912792206

 $00:40:09.676 \longrightarrow 00:40:11.586$ this day or inverse temperature

NOTE Confidence: 0.827893912792206

 $00:40:11.586 \longrightarrow 00:40:13.842$ means but basically it tells us

NOTE Confidence: 0.827893912792206

 $00:40:13.842 \longrightarrow 00:40:15.972$ that in the absolute state and

NOTE Confidence: 0.818055510520935

 $00:40:16.041 \longrightarrow 00:40:18.123$ that's here. In in orange,

NOTE Confidence: 0.818055510520935

 $00:40:18.123 \longrightarrow 00:40:20.649$ in the absolute state and smokers,

NOTE Confidence: 0.818055510520935

 $00:40:20.650 \rightarrow 00:40:22.750$ these individuals were more impulsive.

NOTE Confidence: 0.818055510520935

 $00:40:22.750 \longrightarrow 00:40:25.368$ In this task they made more rash

NOTE Confidence: 0.818055510520935

 $00:40:25.368 \rightarrow 00:40:27.810$ decisions when facing negative outcomes.

NOTE Confidence: 0.818055510520935

 $00{:}40{:}27.810 \dashrightarrow 00{:}40{:}31.247$ And Moreover this deficit if you will

NOTE Confidence: 0.818055510520935

 $00{:}40{:}31{.}247 \dashrightarrow 00{:}40{:}34{.}907$ was reversed both when they put on a

NOTE Confidence: 0.818055510520935

 $00:40:34.907 \rightarrow 00:40:38.350$ nicotine Patch and when they had on parent.

NOTE Confidence: 0.818055510520935

00:40:38.350 --> 00:40:40.606 So it's a really nice computational

NOTE Confidence: 0.818055510520935

 $00:40:40.606 \longrightarrow 00:40:43.506$ way to look at real world kind

NOTE Confidence: 0.818055510520935

 $00:40:43.506 \rightarrow 00:40:45.266$ of decision making basis.

NOTE Confidence: 0.818055510520935

00:40:45.270 - 00:40:47.867 How about when we bring this this

 $00:40:47.867 \rightarrow 00:40:50.560$ task into the brain very quickly?

NOTE Confidence: 0.818055510520935

 $00{:}40{:}50{.}560 \dashrightarrow 00{:}40{:}53{.}360$ When we look at reward greater than

NOTE Confidence: 0.818055510520935

 $00{:}40{:}53.360 \dashrightarrow 00{:}40{:}55.439$ punishment is whole brain Maps.

NOTE Confidence: 0.818055510520935

 $00:40:55.440 \rightarrow 00:40:58.510$ We see the very nice DMM map map as you

NOTE Confidence: 0.818055510520935

 $00{:}40{:}58{.}592 \dashrightarrow 00{:}41{:}01{.}864$ see when we look at what punishment does

NOTE Confidence: 0.818055510520935

 $00:41:01.864 \rightarrow 00:41:05.207$ very nicely activates the salience network.

NOTE Confidence: 0.818055510520935

 $00:41:05.210 \rightarrow 00:41:08.857$ The dorsal ACC and eventual straight up.

NOTE Confidence: 0.818055510520935

 $00:41:08.860 \rightarrow 00:41:11.956$ However, when we look at cognitive

NOTE Confidence: 0.818055510520935

 $00:41:11.956 \rightarrow 00:41:14.020$ flexibility that we operationally

NOTE Confidence: 0.818055510520935

00:41:14.105 --> 00:41:17.066 define as loose shift minus loose stay,

NOTE Confidence: 0.818055510520935

00:41:17.070 --> 00:41:20.446 it's all about the salience network, right?

NOTE Confidence: 0.818055510520935

00:41:20.446 --> 00:41:22.826 There's negative outcomes activates activate

NOTE Confidence: 0.818055510520935

 $00:41:22.826 \rightarrow 00:41:25.280$ beautifully on the salience network.

NOTE Confidence: 0.818055510520935

 $00{:}41{:}25{.}280 \dashrightarrow 00{:}41{:}28{.}178$ Well, how about as a function

NOTE Confidence: 0.818055510520935

 $00:41:28.178 \rightarrow 00:41:30.110$ of state and trade?

 $00:41:30.110 \longrightarrow 00:41:33.505$ Well when we look at rewards sensitivity.

NOTE Confidence: 0.818055510520935

00:41:33.510 --> 00:41:35.830 S
mokers present with a

NOTE Confidence: 0.818055510520935

00:41:35.830 --> 00:41:37.570 hypoactive bilateral striatum.

NOTE Confidence: 0.818055510520935

00:41:37.570 --> 00:41:40.910 I hypoactive dorsal ACC similar

NOTE Confidence: 0.818055510520935

 $00{:}41{:}40{.}910 \dashrightarrow 00{:}41{:}44{.}250$ to perform ance feedback that I'm

NOTE Confidence: 0.818055510520935

00:41:44.356 --> 00:41:48.004 going to show you in just a moment,

NOTE Confidence: 0.818055510520935

 $00{:}41{:}48.010 \dashrightarrow 00{:}41{:}52.408$ and these impairments are not not

NOTE Confidence: 0.818055510520935

 $00:41:52.408 \rightarrow 00:41:55.340$ modulated by nicotinic agonists.

NOTE Confidence: 0.818055510520935

00:41:55.340 --> 00:41:56.092 However,

NOTE Confidence: 0.818055510520935

 $00:41:56.092 \rightarrow 00:42:01.356$ they are yet again another paradigm another.

NOTE Confidence: 0.818055510520935

 $00:42:01.360 \longrightarrow 00:42:03.580$ Way of looking at this,

NOTE Confidence: 0.818055510520935

 $00:42:03.580 \rightarrow 00:42:05.880$ they deficits are also proportional

NOTE Confidence: 0.818055510520935

 $00{:}42{:}05{.}880 \dashrightarrow 00{:}42{:}08{.}812$ to the level of nicotine dependence

NOTE Confidence: 0.818055510520935

 $00:42:08.812 \longrightarrow 00:42:10.477$ of the individual.

NOTE Confidence: 0.818055510520935

00:42:10.480 --> 00:42:12.598 However, in contrast,

NOTE Confidence: 0.818055510520935

 $00:42:12.598 \longrightarrow 00:42:15.422$ the cognitive flexibility contrast

 $00:42:15.422 \longrightarrow 00:42:19.674$ showed us a state related different

NOTE Confidence: 0.818055510520935

 $00:42:19.674 \rightarrow 00:42:23.724$ such that in in smokers during

NOTE Confidence: 0.818055510520935

 $00:42:23.724 \rightarrow 00:42:26.998$ abstinence they perform much worse.

NOTE Confidence: 0.818055510520935

 $00:42:27.000 \longrightarrow 00:42:29.904$ And this activation is reversed in

NOTE Confidence: 0.818055510520935

 $00:42:29.904 \rightarrow 00:42:32.709$ the presence of acute of acute.

NOTE Confidence: 0.818055510520935

00:42:32.710 --> 00:42:36.643 So what did I just show you very quickly?

NOTE Confidence: 0.818055510520935

00:42:36.650 --> 00:42:37.424 I apologize.

NOTE Confidence: 0.818055510520935

 $00:42:37.424 \rightarrow 00:42:40.133$ The study is published that acute absence

NOTE Confidence: 0.818055510520935

 $00{:}42{:}40{.}133 \dashrightarrow 00{:}42{:}43{.}217$ that state smokers were excessively flexible.

NOTE Confidence: 0.818055510520935

00:42:43.220 --> 00:42:46.258 They will bias to shift their choices

NOTE Confidence: 0.818055510520935

 $00{:}42{:}46.258 \dashrightarrow 00{:}42{:}48.941$ with neural activity in the dopamine

NOTE Confidence: 0.818055510520935

 $00{:}42{:}48{.}941 \dashrightarrow 00{:}42{:}51{.}539$ systems and in the salience network.

NOTE Confidence: 0.818055510520935

00:42:51.540 --> 00:42:52.103 Areas.

NOTE Confidence: 0.818055510520935

 $00{:}42{:}52.103 \dashrightarrow 00{:}42{:}54.918$ Reduced before this behavioral shift.

NOTE Confidence: 0.818055510520935

 $00{:}42{:}54{.}920 \dashrightarrow 00{:}42{:}56{.}540$ Acute administration of nicotinic

 $00:42:56.540 \longrightarrow 00:42:57.755$ receptor agonist restored.

NOTE Confidence: 0.818055510520935

 $00{:}42{:}57.760 \dashrightarrow 00{:}42{:}59.940$ These both behavioral and neural

NOTE Confidence: 0.818055510520935

 $00{:}42{:}59{.}940 \dashrightarrow 00{:}43{:}02{.}120$ processes comparable to that in

NOTE Confidence: 0.818055510520935

 $00:43:02.188 \longrightarrow 00:43:04.228$ non smokers and what was really

NOTE Confidence: 0.818055510520935

 $00{:}43{:}04{.}228 \dashrightarrow 00{:}43{:}06{.}989$ cool in this study and I love

NOTE Confidence: 0.818055510520935

 $00{:}43{:}06{.}989 \dashrightarrow 00{:}43{:}08{.}315$ doubled Association studies.

NOTE Confidence: 0.818055510520935

 $00:43:08.320 \longrightarrow 00:43:10.686$ What we saw in this case though

NOTE Confidence: 0.818055510520935

 $00:43:10.686 \rightarrow 00:43:13.424$ is that in trade of smoking we

NOTE Confidence: 0.818055510520935

 $00:43:13.424 \longrightarrow 00:43:15.884$ saw a lowest sensitivity in the

NOTE Confidence: 0.818055510520935

 $00{:}43{:}15{.}973 \dashrightarrow 00{:}43{:}18{.}468$ dorsal striatum and dorsal ACC.

NOTE Confidence: 0.818055510520935

 $00:43:18.470 \rightarrow 00:43:21.305$ The same players that we've been seeing,

NOTE Confidence: 0.818055510520935

 $00:43:21.310 \rightarrow 00:43:23.812$ which was not alleviated by nicotinic

NOTE Confidence: 0.818055510520935

 $00{:}43{:}23.812 \dashrightarrow 00{:}43{:}25.850$ stimulation but was associated with.

NOTE Confidence: 0.818055510520935

 $00:43:25.850 \rightarrow 00:43:27.760$ And consistent with the message

NOTE Confidence: 0.818055510520935

00:43:27.760 --> 00:43:30.509 I'm trying to leave you with today,

NOTE Confidence: 0.818055510520935

 $00{:}43{:}30{.}510 \dashrightarrow 00{:}43{:}32{.}618$ that different constructs different

 $00:43:32.618 \longrightarrow 00:43:35.253$ computations exist in the brain

NOTE Confidence: 0.818055510520935

00:43:35.253 --> 00:43:37.287 depending upon how you probe it

NOTE Confidence: 0.818055510520935

 $00{:}43{:}37{.}287 \dashrightarrow 00{:}43{:}39{.}550$ and the state of the individual.

NOTE Confidence: 0.818055510520935

 $00:43:39.550 \longrightarrow 00:43:42.178$ So further evidence that maybe we

NOTE Confidence: 0.818055510520935

00:43:42.178 --> 00:43:44.956 need a multimodal type of approach

NOTE Confidence: 0.818055510520935

 $00{:}43{:}44{.}956 \dashrightarrow 00{:}43{:}47{.}306$ rather than a monotherapy approach

NOTE Confidence: 0.818055510520935

 $00:43:47.306 \longrightarrow 00:43:50.048$ when we think about as you do.

NOTE Confidence: 0.818055510520935

00:43:50.050 --> 00:43:52.468 OK, one more very quick study.

NOTE Confidence: 0.818055510520935

00:43:52.470 --> 00:43:55.390 It's A kind of cool study that just

NOTE Confidence: 0.818055510520935

 $00:43:55.390 \longrightarrow 00:43:58.594$ came out a few months ago and it's

NOTE Confidence: 0.818055510520935

 $00{:}43{:}58{.}594 \dashrightarrow 00{:}44{:}01{.}566$ about the Habenula and the reason we

NOTE Confidence: 0.818055510520935

 $00:44:01.566 \rightarrow 00:44:04.583$ wanted to go into the habenula stress.

NOTE Confidence: 0.818055510520935

 $00:44:04.590 \longrightarrow 00:44:06.564$ This is an area that really

NOTE Confidence: 0.818055510520935

 $00{:}44{:}06{.}564 \dashrightarrow 00{:}44{:}07{.}880$ thinks about really is

NOTE Confidence: 0.795257210731506

 $00:44:07.949 \rightarrow 00:44:10.649$ involved in negative aversive processing.
$00:44:10.650 \rightarrow 00:44:12.705$ It's hypothesize be hyperactive and

NOTE Confidence: 0.795257210731506

 $00:44:12.705 \rightarrow 00:44:15.100$ nicotine withdrawal and anhedonia and pull.

NOTE Confidence: 0.795257210731506

00:44:15.100 --> 00:44:17.120 Kenny is shown very nicely.

NOTE Confidence: 0.795257210731506

00:44:17.120 --> 00:44:18.980 A5 nicotinic receptor modulations

NOTE Confidence: 0.795257210731506

 $00:44:18.980 \longrightarrow 00:44:21.305$ within the within the Habenula.

NOTE Confidence: 0.795257210731506

 $00{:}44{:}21{.}310 \dashrightarrow 00{:}44{:}23{.}900$ So this is a study that that started in the

NOTE Confidence: 0.795257210731506

 $00:44:23.961 \rightarrow 00:44:26.306$ lab when when that southerns was there,

NOTE Confidence: 0.795257210731506

 $00:44:26.310 \longrightarrow 00:44:27.219$ like many things,

NOTE Confidence: 0.795257210731506

 $00:44:27.219 \rightarrow 00:44:29.771$ life gets in the way we were finally

NOTE Confidence: 0.795257210731506

 $00:44:29.771 \rightarrow 00:44:32.305$ able to publish this few months ago.

NOTE Confidence: 0.795257210731506

 $00{:}44{:}32{.}310 \dashrightarrow 00{:}44{:}36{.}046$ But the venue is a really small areas,

NOTE Confidence: 0.795257210731506

 $00:44:36.050 \rightarrow 00:44:38.846$ maybe 5 boxes big in humans.

NOTE Confidence: 0.795257210731506

 $00:44:38.850 \longrightarrow 00:44:40.369$ You know how do we activate it?

NOTE Confidence: 0.795257210731506

00:44:40.370 - 00:44:42.400 How do we know we're really there?

NOTE Confidence: 0.795257210731506

 $00:44:42.400 \longrightarrow 00:44:44.254$ And this is another very novel

NOTE Confidence: 0.795257210731506

 $00:44:44.254 \rightarrow 00:44:46.659$ task that I do not understand why

- NOTE Confidence: 0.795257210731506
- $00:44:46.659 \longrightarrow 00:44:48.855$ it's never been used to that.
- NOTE Confidence: 0.795257210731506
- $00{:}44{:}48.860 \dashrightarrow 00{:}44{:}51.920$ Well, I do understand it's a very long test.
- NOTE Confidence: 0.795257210731506
- $00{:}44{:}51{.}920 \dashrightarrow 00{:}44{:}54{.}167$ Takes about 30 minutes in the Mac
- NOTE Confidence: 0.795257210731506
- $00:44:54.167 \longrightarrow 00:44:56.949$ and this is a task that is burger
- NOTE Confidence: 0.795257210731506
- $00{:}44{:}56{.}949 \dashrightarrow 00{:}44{:}59{.}060$ published a number of years ago.
- NOTE Confidence: 0.795257210731506
- $00:44:59.060 \longrightarrow 00:44:59.676$ Simple text,
- NOTE Confidence: 0.795257210731506
- $00{:}44{:}59.676 \dashrightarrow 00{:}45{:}02.140$ 2 balls appear on a screen of different
- NOTE Confidence: 0.795257210731506
- $00{:}45{:}02.208 \dashrightarrow 00{:}45{:}04.532$ positions and they start to move at
- NOTE Confidence: 0.795257210731506
- $00{:}45{:}04{.}532 \dashrightarrow 00{:}45{:}06{.}701$ different speeds and the the participant
- NOTE Confidence: 0.795257210731506
- $00:45:06.701 \rightarrow 00:45:08.915$ only sees them for 100 milliseconds.
- NOTE Confidence: 0.795257210731506
- $00:45:08.920 \longrightarrow 00:45:11.712$ They go off and then they have to
- NOTE Confidence: 0.795257210731506
- $00:45:11.712 \longrightarrow 00:45:14.040$ guess which ball would have hit.
- NOTE Confidence: 0.795257210731506
- $00{:}45{:}14.040 \dashrightarrow 00{:}45{:}15.870$ Would have hit the end
- NOTE Confidence: 0.795257210731506
- $00{:}45{:}15.870 \dashrightarrow 00{:}45{:}17.700$ if there was enough time.
- NOTE Confidence: 0.795257210731506
- $00{:}45{:}17.700 \dashrightarrow 00{:}45{:}20.256$ And the individual is given feedback,
- NOTE Confidence: 0.795257210731506

00:45:20.260 --> 00:45:21.544 either informative feedback,

NOTE Confidence: 0.795257210731506

 $00{:}45{:}21{.}544 \dashrightarrow 00{:}45{:}24{.}104$ a :) that they were correct,

NOTE Confidence: 0.795257210731506

00:45:24.104 --> 00:45:26.668 frowny face, if they were incorrect,

NOTE Confidence: 0.795257210731506

 $00:45:26.668 \rightarrow 00:45:28.376$ to get enough jitter,

NOTE Confidence: 0.795257210731506

 $00:45:28.380 \longrightarrow 00:45:30.530$ we give them occasional non.

NOTE Confidence: 0.795257210731506

 $00{:}45{:}30{.}530$ --> $00{:}45{:}33{.}800$ Informative information and then often

NOTE Confidence: 0.795257210731506

 $00{:}45{:}33{.}800 \dashrightarrow 00{:}45{:}36{.}416$ a noninformative feedback whether

NOTE Confidence: 0.795257210731506

 $00{:}45{:}36{.}416 \dashrightarrow 00{:}45{:}39{.}368$ they were correct or incorrect.

NOTE Confidence: 0.795257210731506

 $00{:}45{:}39{.}370 \dashrightarrow 00{:}45{:}41{.}813$ So because of time these were the

NOTE Confidence: 0.795257210731506

 $00{:}45{:}41.813 \dashrightarrow 00{:}45{:}43.769$ same individuals that we scanned

NOTE Confidence: 0.795257210731506

 $00:45:43.769 \dashrightarrow 00:45:45.754$ on multiple occasions. Task worked.

NOTE Confidence: 0.795257210731506

 $00{:}45{:}45{.}754 \dashrightarrow 00{:}45{:}47{.}926$ It's biased like most of these

NOTE Confidence: 0.795257210731506

 $00:45:47.926 \longrightarrow 00:45:50.658$ kind of reward tasks or people are

NOTE Confidence: 0.795257210731506

 $00{:}45{:}50{.}658 \dashrightarrow 00{:}45{:}52{.}561$ correct 65% of the time.

NOTE Confidence: 0.795257210731506

 $00{:}45{:}52{.}561 \dashrightarrow 00{:}45{:}54{.}823$ There faster when they are correct.

NOTE Confidence: 0.795257210731506

 $00:45:54.830 \rightarrow 00:45:58.600$ So the task did what it was supposed to do.

- NOTE Confidence: 0.795257210731506
- 00:45:58.600 --> 00:46:00.355 But interesting Lee in smokers
- NOTE Confidence: 0.795257210731506
- $00:46:00.355 \rightarrow 00:46:02.740$ there were more errors of omission,
- NOTE Confidence: 0.795257210731506
- $00:46:02.740 \longrightarrow 00:46:05.393$ number of no responses and these errors
- NOTE Confidence: 0.795257210731506
- $00:46:05.393 \rightarrow 00:46:07.719$ of omission were improved when we
- NOTE Confidence: 0.795257210731506
- $00{:}46{:}07{.}719 \dashrightarrow 00{:}46{:}10{.}323$ scan them up with either parent eccle.
- NOTE Confidence: 0.795257210731506
- 00:46:10.330 --> 00:46:11.126 Or nicotine.
- NOTE Confidence: 0.795257210731506
- $00:46:11.126 \rightarrow 00:46:13.912$ They also got better than non smokers,
- NOTE Confidence: 0.795257210731506
- $00:46:13.920 \longrightarrow 00:46:16.320$ got better with nicotine as well.
- NOTE Confidence: 0.795257210731506
- $00:46:16.320 \longrightarrow 00:46:17.912$ Again not a surprise.
- NOTE Confidence: 0.795257210731506
- $00:46:17.912 \longrightarrow 00:46:19.902$ So did the task work.
- NOTE Confidence: 0.795257210731506
- $00:46:19.910 \longrightarrow 00:46:21.574$ The answer is yes.
- NOTE Confidence: 0.795257210731506
- $00:46:21.574 \rightarrow 00:46:24.070$ I'm outlining the habenula for you
- NOTE Confidence: 0.795257210731506
- $00{:}46{:}24.156 \dashrightarrow 00{:}46{:}26.826$ over here and these white circles.
- NOTE Confidence: 0.795257210731506
- $00:46:26.830 \longrightarrow 00:46:29.350$ When the individual made an error,
- NOTE Confidence: 0.795257210731506
- $00{:}46{:}29{.}350 \dashrightarrow 00{:}46{:}31{.}450$ the habenula starts to scream
- NOTE Confidence: 0.795257210731506

00:46:31.450 --> 00:46:32.290 increased activity.

NOTE Confidence: 0.795257210731506

00:46:32.290 --> 00:46:33.595 Insulet increased activity.

NOTE Confidence: 0.795257210731506

00:46:33.595 --> 00:46:35.770 The Strydom shows an increase

NOTE Confidence: 0.795257210731506

 $00:46:35.770 \rightarrow 00:46:38.290$ activity when the individual gets is

NOTE Confidence: 0.795257210731506

 $00:46:38.290 \longrightarrow 00:46:40.265$ correct and gets positive feedback.

NOTE Confidence: 0.795257210731506

 $00:46:40.270 \longrightarrow 00:46:43.357$ So exactly what you would expect a NOTE Confidence: 0.795257210731506

 $00{:}46{:}43.357 \dashrightarrow 00{:}46{:}46.158$ task like this to do? Interesting Lee.

NOTE Confidence: 0.795257210731506

 $00:46:46.158 \longrightarrow 00:46:47.854$ The relationship between the

NOTE Confidence: 0.795257210731506

 $00{:}46{:}47.854 \dashrightarrow 00{:}46{:}50.010$ insula screaming and the habenula

NOTE Confidence: 0.795257210731506

 $00:46:50.010 \rightarrow 00:46:51.606$ screaming is almost one,

NOTE Confidence: 0.795257210731506

 $00{:}46{:}51{.}610 \dashrightarrow 00{:}46{:}54{.}148$ and so these two structures are

NOTE Confidence: 0.795257210731506

 $00{:}46{:}54{.}148 \dashrightarrow 00{:}46{:}56{.}230$ integrating their their processing very,

NOTE Confidence: 0.795257210731506

 $00:46:56.230 \longrightarrow 00:46:57.248$ very closely.

NOTE Confidence: 0.795257210731506

 $00:46:57.248 \rightarrow 00:47:00.811$ So very quickly then when we re

NOTE Confidence: 0.795257210731506

 $00{:}47{:}00{.}811 \dashrightarrow 00{:}47{:}03{.}420$ analyze this data with contrast

NOTE Confidence: 0.795257210731506

 $00:47:03.420 \longrightarrow 00:47:05.925$ as a function of group,

- NOTE Confidence: 0.795257210731506
- $00{:}47{:}05{.}930 \dashrightarrow 00{:}47{:}09{.}227$ what we found was that when we
- NOTE Confidence: 0.795257210731506
- $00{:}47{:}09{.}227 \dashrightarrow 00{:}47{:}12{.}738$ look at errors minus correct that.
- NOTE Confidence: 0.795257210731506
- $00:47:12.740 \longrightarrow 00:47:15.734$ On that non smokers very nicely
- NOTE Confidence: 0.795257210731506
- $00:47:15.734 \longrightarrow 00:47:18.790$ were able to process their error
- NOTE Confidence: 0.795257210731506
- $00{:}47{:}18.790 \dashrightarrow 00{:}47{:}22.150$ response but in the in the stratum
- NOTE Confidence: 0.795257210731506
- $00:47:22.150 \longrightarrow 00:47:24.359$ but smokers were not.
- NOTE Confidence: 0.795257210731506
- $00:47:24.360 \longrightarrow 00:47:24.747$ Conversely,
- NOTE Confidence: 0.795257210731506
- $00:47:24.747 \longrightarrow 00:47:27.069$ on the initial response in smokers,
- NOTE Confidence: 0.795257210731506
- $00:47:27.070 \longrightarrow 00:47:30.010$ or was much greater when they
- NOTE Confidence: 0.795257210731506
- $00:47:30.010 \longrightarrow 00:47:31.970$ made errors than it
- NOTE Confidence: 0.827910244464874
- $00:47:32.077 \rightarrow 00:47:34.730$ was in non smokers. Does this
- NOTE Confidence: 0.827910244464874
- $00:47:34.730 \longrightarrow 00:47:37.355$ change is a function of acute state?
- NOTE Confidence: 0.827910244464874
- 00:47:37.360 -> 00:47:39.978 The answer is yes, that in smokers,
- NOTE Confidence: 0.827910244464874
- $00{:}47{:}39{.}980 \dashrightarrow 00{:}47{:}42{.}465$ but none but not non smokers when
- NOTE Confidence: 0.827910244464874
- $00{:}47{:}42.465 \dashrightarrow 00{:}47{:}44.393$ the individuals are absent the
- NOTE Confidence: 0.827910244464874

 $00:47:44.393 \rightarrow 00:47:46.358$ Habenula was screaming the VM.

NOTE Confidence: 0.827910244464874

00:47:46.360 --> 00:47:48.670 Pfc is screaming much more

NOTE Confidence: 0.827910244464874

 $00{:}47{:}48.670 \dashrightarrow 00{:}47{:}51.660$ than in the state and state.

NOTE Confidence: 0.827910244464874

00:47:51.660 - 00:47:53.994 We did a very quick anatomic

NOTE Confidence: 0.827910244464874

 $00:47:53.994 \longrightarrow 00:47:55.550$ Lorelei to demonstrate that,

NOTE Confidence: 0.827910244464874

 $00:47:55.550 \longrightarrow 00:47:58.266$ in fact, this really is true insula.

NOTE Confidence: 0.827910244464874

 $00{:}47{:}58{.}270$ --> $00{:}48{:}02{.}810$ I'm trying to have Angela and not. And

NOTE Confidence: 0.567303992807865

 $00{:}48{:}02{.}810 \dashrightarrow 00{:}48{:}05{.}630$ another. He and she.

NOTE Confidence: 0.930347204208374

00:48:07.290 --> 00:48:08.070 I'm sorry.

NOTE Confidence: 0.815314650535584

00:48:10.790 --> 00:48:12.990 Keep going someones my commuted

NOTE Confidence: 0.815314650535584

00:48:12.990 --> 00:48:14.310 your OK. OK

NOTE Confidence: 0.815314650535584

00:48:14.310 --> 00:48:17.523 So what did I just show you too quickly

NOTE Confidence: 0.815314650535584

 $00{:}48{:}17.523 \dashrightarrow 00{:}48{:}20.151$ that we see a differential pattern

NOTE Confidence: 0.815314650535584

 $00{:}48{:}20{.}151 \dashrightarrow 00{:}48{:}22{.}977$ of brain activity in the Habenula

NOTE Confidence: 0.815314650535584

 $00{:}48{:}22.977 \dashrightarrow 00{:}48{:}25.747$ the insula ACC eventual stratum,

NOTE Confidence: 0.815314650535584

 $00:48:25.750 \rightarrow 00:48:27.950$ following positive and negative feedback,

 $00{:}48{:}27{.}950 \dashrightarrow 00{:}48{:}31{.}134$ and we see again again at the Association

NOTE Confidence: 0.815314650535584

 $00{:}48{:}31{.}134 \dashrightarrow 00{:}48{:}33{.}780$ between trait life addiction and state

NOTE Confidence: 0.815314650535584

00:48:33.780 --> 00:48:36.972 like with drawal in that smokers show a

NOTE Confidence: 0.815314650535584

 $00:48:36.972 \rightarrow 00:48:39.756$ reduced right or responsibility to positive

NOTE Confidence: 0.815314650535584

 $00:48:39.756 \rightarrow 00:48:42.806$ feedback which was not ameliorated by.

NOTE Confidence: 0.815314650535584

 $00{:}48{:}42.806 \dashrightarrow 00{:}48{:}45.014$ Nicotinic agonists was correlated

NOTE Confidence: 0.815314650535584

 $00:48:45.014 \rightarrow 00:48:47.540$ with severity of addiction,

NOTE Confidence: 0.815314650535584

00:48:47.540 --> 00:48:51.025 and Conversely habenula activity following

NOTE Confidence: 0.815314650535584

 $00:48:51.025 \rightarrow 00:48:55.159$ positive feedback was reversed by an RT.

NOTE Confidence: 0.815314650535584

 $00:48:55.160 \rightarrow 00:48:56.720$ Which was correlated with with craving,

NOTE Confidence: 0.815314650535584

 $00:48:56.720 \longrightarrow 00:49:00.428$ which I didn't have a chance to show you.

NOTE Confidence: 0.815314650535584

 $00{:}49{:}00{.}430 \dashrightarrow 00{:}49{:}03{.}314$ So this novel evidence again seems to

NOTE Confidence: 0.815314650535584

 $00:49:03.314 \rightarrow 00:49:05.721$ suggest that why these monotherapies

NOTE Confidence: 0.815314650535584

 $00:49:05.721 \longrightarrow 00:49:08.446$ might not be overly effective.

NOTE Confidence: 0.815314650535584

 $00{:}49{:}08{.}450 \dashrightarrow 00{:}49{:}11{.}516$ Alright, I'm going to skip the with

 $00:49:11.516 \longrightarrow 00:49:14.462$ the summary and one tickle only

NOTE Confidence: 0.815314650535584

00:49:14.462 --> 00:49:16.007 Becaus
w Regina said.

NOTE Confidence: 0.815314650535584

00:49:16.010 --> 00:49:18.970 We're moving into treatment.

NOTE Confidence: 0.815314650535584

 $00:49:18.970 \longrightarrow 00:49:22.306$ This is a study that just came out.

NOTE Confidence: 0.815314650535584

 $00{:}49{:}22{.}310 \dashrightarrow 00{:}49{:}24{.}806$ MD, PhD screen in the lab of wanted

NOTE Confidence: 0.815314650535584

 $00{:}49{:}24.806 \dashrightarrow 00{:}49{:}27.922$ to see theoretically if PVCS at least

NOTE Confidence: 0.815314650535584

 $00:49:27.922 \longrightarrow 00:49:30.800$ acutely could modify these service and

NOTE Confidence: 0.815314650535584

 $00{:}49{:}30{.}800 \dashrightarrow 00{:}49{:}33{.}502$ with Sarah did was taking the hypothesis

NOTE Confidence: 0.815314650535584

 $00{:}49{:}33.502 \dashrightarrow 00{:}49{:}37.380$ of this three network key to tar.

NOTE Confidence: 0.815314650535584

 $00:49:37.380 \longrightarrow 00:49:39.204$ And using this hypothesis,

NOTE Confidence: 0.815314650535584

 $00{:}49{:}39{.}204 \dashrightarrow 00{:}49{:}43{.}949$ put Anodal T DCS let me show you where it is.

NOTE Confidence: 0.815314650535584

00:49:43.950 --> 00:49:46.140 Put TCS over the VM,

NOTE Confidence: 0.815314650535584

 $00{:}49{:}46{.}140 \dashrightarrow 00{:}49{:}49{.}234$ Pfc and the DL Pfc and switch

NOTE Confidence: 0.815314650535584

 $00:49:49.234 \longrightarrow 00:49:51.400$ polarities with an oral DL,

NOTE Confidence: 0.815314650535584

00:49:51.400 --> 00:49:54.240 Pfc or cat photo DL Pfc to try

NOTE Confidence: 0.815314650535584

 $00:49:54.240 \longrightarrow 00:49:57.104$ to modify this three large scale

- NOTE Confidence: 0.815314650535584
- $00{:}49{:}57{.}104 \dashrightarrow 00{:}50{:}00{.}194$ networks again using the same power
- NOTE Confidence: 0.815314650535584
- $00:50:00.287 \longrightarrow 00:50:03.220$ line we've been using in the lab.
- NOTE Confidence: 0.815314650535584
- $00{:}50{:}03{.}220 \dashrightarrow 00{:}50{:}05{.}878$ We scan smokers on and off
- NOTE Confidence: 0.815314650535584
- $00:50:05.878 \longrightarrow 00:50:07.650$ and nicotine Patch with.
- NOTE Confidence: 0.815314650535584
- $00{:}50{:}07.650 \dashrightarrow 00{:}50{:}09.555$ See the sham stimulation or
- NOTE Confidence: 0.815314650535584
- $00{:}50{:}09{.}555 \dashrightarrow 00{:}50{:}11.079$ an Ola Catholic stimulation.
- NOTE Confidence: 0.815314650535584
- $00:50:11.080 \longrightarrow 00:50:13.530$ We did the same thing and non
- NOTE Confidence: 0.815314650535584
- $00:50:13.530 \rightarrow 00:50:16.030$ smokers but only scanned them once.
- NOTE Confidence: 0.815314650535584
- $00:50:16.030 \longrightarrow 00:50:17.935$ No drugs for these folks
- NOTE Confidence: 0.815314650535584
- $00:50:17.935 \longrightarrow 00:50:19.459$ and importantly we scanned.
- NOTE Confidence: 0.815314650535584
- $00:50:19.460 \rightarrow 00:50:22.808$ We presented T DCS in the magnet so we
- NOTE Confidence: 0.815314650535584
- $00:50:22.808 \rightarrow 00:50:25.704$ were doing this online in real time
- NOTE Confidence: 0.815314650535584
- $00:50:25.704 \rightarrow 00:50:28.950$ to watch how the brain is changing
- NOTE Confidence: 0.815314650535584
- $00{:}50{:}28{.}950 \dashrightarrow 00{:}50{:}32{.}004$ as a function of this intervention.
- NOTE Confidence: 0.815314650535584
- 00:50:32.010 --> 00:50:33.666 Because Sarah wanted to be a
- NOTE Confidence: 0.815314650535584

 $00:50:33.666 \longrightarrow 00:50:35.260$ measure and not a mapper.

NOTE Confidence: 0.815314650535584

 $00:50:35.260 \rightarrow 00:50:37.906$ We use tasks that we well knew what they,

NOTE Confidence: 0.815314650535584

 $00:50:37.910 \longrightarrow 00:50:40.270$ what they did. So she had a priority.

NOTE Confidence: 0.815314650535584

00:50:40.270 --> 00:50:42.090 Regions of interest to look

NOTE Confidence: 0.815314650535584

 $00:50:42.090 \longrightarrow 00:50:43.910$ at the effects of PVCS.

NOTE Confidence: 0.815314650535584

 $00{:}50{:}43{.}910 \dashrightarrow 00{:}50{:}46{.}556$ She used the parametric flanker task

NOTE Confidence: 0.815314650535584

 $00:50:46.556 \rightarrow 00:50:50.266$ that we developed in the lab that very

NOTE Confidence: 0.815314650535584

 $00:50:50.266 \rightarrow 00:50:52.591$ nicely distinguishes smokers from non

NOTE Confidence: 0.815314650535584

 $00{:}50{:}52{.}591 \dashrightarrow 00{:}50{:}55{.}084$ from non smokers and I don't have

NOTE Confidence: 0.815314650535584

 $00:50:55.084 \rightarrow 00:50:58.265$ time to to go into that and perhaps I

NOTE Confidence: 0.815314650535584

 $00{:}50{:}58.265 \dashrightarrow 00{:}51{:}01.087$ won't tell you simply that the tasks

NOTE Confidence: 0.815314650535584

 $00:51:01.087 \longrightarrow 00:51:03.697$ were parametric flanker task work and

NOTE Confidence: 0.815314650535584

 $00:51:03.697 \dashrightarrow 00:51:06.368$ people did worse smokers be worse.

NOTE Confidence: 0.815314650535584

 $00:51:06.370 \rightarrow 00:51:09.874$ They did worse when they were in abstinence

NOTE Confidence: 0.815314650535584

 $00{:}51{:}09{.}874 \dashrightarrow 00{:}51{:}12{.}313$ but importantly for this piece of

NOTE Confidence: 0.815314650535584

 $00:51:12.313 \rightarrow 00:51:15.140$ the presentation and a single 30 minute.

- NOTE Confidence: 0.815314650535584
- 00:51:15.140 --> 00:51:22.434 2 million add auto TVCS increase the.
- NOTE Confidence: 0.815314650535584
- $00{:}51{:}22{.}440 \dashrightarrow 00{:}51{:}26{.}276$ The rush or ACC activity when the
- NOTE Confidence: 0.815314650535584
- $00{:}51{:}26{.}276 \dashrightarrow 00{:}51{:}29{.}672$ individual is doing a conflict ask
- NOTE Confidence: 0.815314650535584
- $00:51:29.672 \rightarrow 00:51:32.960$ the effect was bigger and smokers
- NOTE Confidence: 0.815314650535584
- $00{:}51{:}32{.}960 \dashrightarrow 00{:}51{:}36{.}665$ than nonsmokers for the N back
- NOTE Confidence: 0.815314650535584
- $00{:}51{:}36.665 \dashrightarrow 00{:}51{:}39.715$ task again behaviourally the task
- NOTE Confidence: 0.815314650535584
- 00:51:39.720 --> 00:51:43.188 worked and again acute T DCS.
- NOTE Confidence: 0.815314650535584
- $00:51:43.190 \longrightarrow 00:51:45.872$ To the DLP FC enhanced the
- NOTE Confidence: 0.815314650535584
- 00:51:45.872 --> 00:51:48.730 deactivation on a 3 backpacks,
- NOTE Confidence: 0.815314650535584
- $00:51:48.730 \rightarrow 00:51:52.994$ allowing that performance to be to be better.
- NOTE Confidence: 0.815314650535584
- $00{:}51{:}53{.}000 \dashrightarrow 00{:}51{:}54{.}248$ And it did so.
- NOTE Confidence: 0.815314650535584
- $00:51:54.248 \longrightarrow 00:51:56.120$ And this was the main point.
- NOTE Confidence: 0.815314650535584
- $00{:}51{:}56{.}120 \dashrightarrow 00{:}51{:}58{.}297$ I want to leave you with it.
- NOTE Confidence: 0.798081696033478
- $00{:}51{:}58{.}300 \dashrightarrow 00{:}52{:}00{.}514$ Did so better in the savant
- NOTE Confidence: 0.798081696033478
- 00:52:00.514 --> 00:52:02.463 nicotine Satan state than in
- NOTE Confidence: 0.798081696033478

 $00:52:02.463 \longrightarrow 00:52:04.438$ the nicotine withdraw in state.

NOTE Confidence: 0.798081696033478

 $00{:}52{:}04{.}440 \dashrightarrow 00{:}52{:}07{.}640$ So that suggests to us.

NOTE Confidence: 0.798081696033478

00:52:07.640 --> 00:52:10.748 Let me skip the E field mapping.

NOTE Confidence: 0.798081696033478

 $00:52:10.750 \rightarrow 00:52:13.258$ This suggested to us that smokers

NOTE Confidence: 0.798081696033478

00:52:13.258 --> 00:52:15.830 would since they were more sensitive

NOTE Confidence: 0.798081696033478

 $00:52:15.830 \longrightarrow 00:52:18.700$ when they were sated than that and NOTE Confidence: 0.798081696033478

 $00:52:18.700 \rightarrow 00:52:21.398$ when they were cognitively engage.

NOTE Confidence: 0.798081696033478

 $00{:}52{:}21{.}400 \dashrightarrow 00{:}52{:}24{.}320$ It may be that this Admiral TV

NOTE Confidence: 0.798081696033478

 $00:52:24.320 \longrightarrow 00:52:28.067$ CS might be a useful ad on the rapy

NOTE Confidence: 0.798081696033478

 $00:52:28.067 \rightarrow 00:52:29.534$ alongside nicotine replacement

NOTE Confidence: 0.798081696033478

 $00{:}52{:}29{.}534 \dashrightarrow 00{:}52{:}32{.}350$ to perhaps increase the gain

NOTE Confidence: 0.798081696033478

 $00:52:32.350 \longrightarrow 00:52:34.590$ of modifying these circuits.

NOTE Confidence: 0.798081696033478

 $00:52:34.590 \longrightarrow 00:52:36.198$ So I apologize for these last

NOTE Confidence: 0.798081696033478

00:52:36.198 --> 00:52:38.044 last few minutes of kind of

NOTE Confidence: 0.798081696033478

 $00:52:38.044 \rightarrow 00:52:39.468$ rushing rushing through things.

NOTE Confidence: 0.798081696033478

 $00:52:39.470 \longrightarrow 00:52:42.233$ I just want to end with thanking the folks

 $00:52:42.233 \longrightarrow 00:52:45.264$ in the lab who really did all of the work,

NOTE Confidence: 0.798081696033478

 $00{:}52{:}45{.}270 \dashrightarrow 00{:}52{:}47{.}166$ and I think I've mentioned those

NOTE Confidence: 0.798081696033478

 $00:52:47.166 \longrightarrow 00:52:48.930$ that were involved along the way.

NOTE Confidence: 0.798081696033478

 $00:52:48.930 \longrightarrow 00:52:50.856$ Some of my outside collaborators that

NOTE Confidence: 0.798081696033478

 $00:52:50.856 \rightarrow 00:52:52.590$ I've also highlighted along the way.

NOTE Confidence: 0.798081696033478

00:52:52.590 --> 00:52:55.326 I want to thank my to for ITS support,

NOTE Confidence: 0.798081696033478

 $00:52:55.330 \longrightarrow 00:52:57.498$ and I want to thank you for your

NOTE Confidence: 0.798081696033478

00:52:57.498 --> 00:52:58.989 indulgence in your attention,

NOTE Confidence: 0.798081696033478

 $00:52:58.990 \longrightarrow 00:52:59.300$ thanks.

NOTE Confidence: 0.830803871154785

00:53:01.560 --> 00:53:03.560 Thank you so much, Elliott.

NOTE Confidence: 0.830803871154785

00:53:03.560 - 00:53:05.560 That was just beautiful Ann.

NOTE Confidence: 0.830803871154785

00:53:05.560 --> 00:53:08.344 Really, such a such a Tour de force

NOTE Confidence: 0.830803871154785

 $00:53:08.344 \longrightarrow 00:53:10.753$ with with all of these details

NOTE Confidence: 0.830803871154785

 $00:53:10.753 \dashrightarrow 00:53:13.207$ I mean functional mapping of the

NOTE Confidence: 0.830803871154785

 $00{:}53{:}13.293 \dashrightarrow 00{:}53{:}16.296$ brain in the context of smoking in

 $00:53:16.296 \rightarrow 00:53:18.360$ different state and trait effects.

NOTE Confidence: 0.830803871154785

 $00{:}53{:}18{.}360 \dashrightarrow 00{:}53{:}20{.}360$ We're just we're just gorgeous.

NOTE Confidence: 0.830803871154785

 $00:53:20.360 \longrightarrow 00:53:23.424$ Let me just open this up now for

NOTE Confidence: 0.830803871154785

 $00:53:23.424 \rightarrow 00:53:26.357$ questions and comments from all of you.

NOTE Confidence: 0.830803871154785

 $00:53:26.360 \longrightarrow 00:53:29.041$ I also want to just point out

NOTE Confidence: 0.830803871154785

 $00{:}53{:}29{.}041 \dashrightarrow 00{:}53{:}31{.}568$ that in fact the CME links.

NOTE Confidence: 0.830803871154785

 $00{:}53{:}31{.}570 \dashrightarrow 00{:}53{:}33{.}120$ Are in the chat box.

NOTE Confidence: 0.830803871154785

00:53:33.120 --> 00:53:35.600 If you need to get for CME credit,

NOTE Confidence: 0.830803871154785

00:53:35.600 --> 00:53:37.770 so please make sure and get that,

NOTE Confidence: 0.830803871154785

 $00:53:37.770 \rightarrow 00:53:39.940$ but I'm opening it up to questions.

NOTE Confidence: 0.896728515625

00:53:42.180 --> 00:53:44.445 You can use the chat

NOTE Confidence: 0.896728515625

 $00:53:44.445 \longrightarrow 00:53:46.710$ function or raise your hand.

NOTE Confidence: 0.896728515625

 $00:53:46.710 \longrightarrow 00:53:48.772$ Let me start actually Elliot.

NOTE Confidence: 0.896728515625

 $00:53:48.772 \rightarrow 00:53:51.720$ That was really gorgeous an it's just

NOTE Confidence: 0.896728515625

 $00{:}53{:}51{.}720 \dashrightarrow 00{:}53{:}54{.}108$ beautiful how you use different tasks

NOTE Confidence: 0.896728515625

 $00{:}53{:}54{.}108 \dashrightarrow 00{:}53{:}56{.}946$ that focus in on different aspects of

- NOTE Confidence: 0.896728515625
- $00{:}53{:}56{.}946 \dashrightarrow 00{:}53{:}59{.}706$ function to sort of dissect the brain
- NOTE Confidence: 0.896728515625
- $00{:}53{:}59{.}706 \dashrightarrow 00{:}54{:}02{.}539$ under under a different drug related states.
- NOTE Confidence: 0.896728515625
- $00:54:02.540 \rightarrow 00:54:05.389$ The question I have is actually twofold.
- NOTE Confidence: 0.896728515625
- $00:54:05.390 \rightarrow 00:54:07.903$ One is there's a lot of blunting
- NOTE Confidence: 0.896728515625
- $00{:}54{:}07{.}903 \dashrightarrow 00{:}54{:}09{.}850$ under these acute with drawal.
- NOTE Confidence: 0.896728515625
- 00:54:09.850 --> 00:54:11.880 Sort of chronic drug use
- NOTE Confidence: 0.896728515625
- $00:54:11.880 \longrightarrow 00:54:13.504$ states that you showed.
- NOTE Confidence: 0.896728515625
- $00{:}54{:}13.510 \dashrightarrow 00{:}54{:}15.958$ It made me start to think
- NOTE Confidence: 0.896728515625
- $00:54:15.958 \longrightarrow 00:54:17.590$ of whether that's tolerance.
- NOTE Confidence: 0.896728515625
- $00:54:17.590 \rightarrow 00:54:22.054$ Or just a lower level of functioning and?
- NOTE Confidence: 0.896728515625
- $00:54:22.060 \rightarrow 00:54:23.745$ Anan therefore you know the
- NOTE Confidence: 0.896728515625
- $00{:}54{:}23.745 \dashrightarrow 00{:}54{:}25.430$ flip side would be there.
- NOTE Confidence: 0.896728515625
- $00{:}54{:}25{.}430 \dashrightarrow 00{:}54{:}27{.}758$ Is there sort of you know you're in
- NOTE Confidence: 0.896728515625
- $00:54:27.758 \rightarrow 00:54:30.268$ the trap where if you try to reverse
- NOTE Confidence: 0.896728515625
- $00:54:30.268 \dashrightarrow 00:54:32.510$ that you might have sensitization.
- NOTE Confidence: 0.896728515625

 $00:54:32.510 \longrightarrow 00:54:34.556$ So what was sort of worried

NOTE Confidence: 0.896728515625

 $00{:}54{:}34{.}556 \dashrightarrow 00{:}54{:}36{.}210$ about that piece of it?

NOTE Confidence: 0.896728515625

00:54:36.210 --> 00:54:38.569 So how do you think about that?

NOTE Confidence: 0.896728515625

 $00:54:38.570 \longrightarrow 00:54:40.316$ But the second thing you know

NOTE Confidence: 0.896728515625

 $00:54:40.316 \longrightarrow 00:54:42.253$ I'm going back to your silver

NOTE Confidence: 0.896728515625

 $00{:}54{:}42{.}253 \dashrightarrow 00{:}54{:}44{.}371$ bucks hot and the notion that even NOTE Confidence: 0.896728515625

00:54:44.371 -> 00:54:46.910 in studying this it because so many

NOTE Confidence: 0.896728515625

00:54:46.910 - 00:54:48.675 regions an networks are affected,

NOTE Confidence: 0.896728515625

 $00{:}54{:}48.680 \dashrightarrow 00{:}54{:}50.036$ different networks are affected.

NOTE Confidence: 0.896728515625

 $00{:}54{:}50{.}036 \dashrightarrow 00{:}54{:}52{.}461$ If we wanted to reverse this sort

NOTE Confidence: 0.896728515625

 $00:54:52.461 \longrightarrow 00:54:54.126$ of like your brain stimulation.

NOTE Confidence: 0.896728515625

00:54:54.130 --> 00:54:56.937 Approach even in studying it do need

NOTE Confidence: 0.896728515625

 $00{:}54{:}56{.}937 \dashrightarrow 00{:}55{:}00{.}038$ tasks that are not so focused in fact,

NOTE Confidence: 0.896728515625

 $00:55:00.040 \longrightarrow 00:55:02.404$ that I'm not just focused on

NOTE Confidence: 0.896728515625

 $00:55:02.404 \longrightarrow 00:55:03.980$ a uni dimensional aspect,

NOTE Confidence: 0.896728515625

 $00:55:03.980 \dashrightarrow 00:55:06.735$ but rather because drugs of abuse are

 $00:55:06.735 \rightarrow 00:55:09.500$ affecting so many regions that we need.

NOTE Confidence: 0.896728515625

 $00{:}55{:}09{.}500 \dashrightarrow 00{:}55{:}12{.}251$ Some things that are more wides pread in

NOTE Confidence: 0.896728515625

 $00:55:12.251 \rightarrow 00:55:14.619$ their effects of activating the brain.

NOTE Confidence: 0.872581660747528

 $00:55:15.520 \longrightarrow 00:55:17.844$ Yeah yeah. So let me take that.

NOTE Confidence: 0.872581660747528

 $00:55:17.850 \longrightarrow 00:55:19.182$ That second question first

NOTE Confidence: 0.872581660747528

 $00{:}55{:}19{.}182 \dashrightarrow 00{:}55{:}20{.}847$ 'cause I can remember it.

NOTE Confidence: 0.872581660747528

 $00{:}55{:}20.850 \dashrightarrow 00{:}55{:}23.754$ So you know when we think about so

NOTE Confidence: 0.872581660747528

00:55:23.754 --> 00:55:26.386 why would DL Pfc TMS work right?

NOTE Confidence: 0.872581660747528

 $00:55:26.390 \rightarrow 00:55:28.700$ Why? Why does it seem to be

NOTE Confidence: 0.872581660747528

 $00:55:28.700 \rightarrow 00:55:30.440$ reasonably efficacious in depression?

NOTE Confidence: 0.872581660747528

 $00:55:30.440 \longrightarrow 00:55:31.968$ Maybe in another nurse?

NOTE Confidence: 0.872581660747528

 $00{:}55{:}31{.}968 \dashrightarrow 00{:}55{:}33{.}878$ Psychiatric disorders OC D is

NOTE Confidence: 0.872581660747528

 $00{:}55{:}33.878 \dashrightarrow 00{:}55{:}35.930$ going to prove this, you know.

NOTE Confidence: 0.872581660747528

 $00{:}55{:}35{.}930 \dashrightarrow 00{:}55{:}39{.}730$ What is it about the DL Pfc it happens to?

NOTE Confidence: 0.872581660747528

 $00{:}55{:}39{.}730 \dashrightarrow 00{:}55{:}41{.}330$ Of course be something accessible

 $00:55:41.330 \rightarrow 00:55:43.550$ by TMS which doesn't go very deep,

NOTE Confidence: 0.872581660747528

 $00:55:43.550 \longrightarrow 00:55:45.320$ but when you think about the

NOTE Confidence: 0.872581660747528

 $00:55:45.320 \rightarrow 00:55:47.476$ circuitry in one of the one pieces

NOTE Confidence: 0.872581660747528

 $00:55:47.476 \rightarrow 00:55:49.590$ that I showed you in bed circuitry

NOTE Confidence: 0.872581660747528

 $00:55:49.653 \rightarrow 00:55:51.807$ between there and the insula right,

NOTE Confidence: 0.872581660747528

 $00:55:51.810 \longrightarrow 00:55:53.954$ maybe we can think of this as being NOTE Confidence: 0.872581660747528

 $00:55:53.954 \rightarrow 00:55:56.384$ sort of top of funnel that what we're

NOTE Confidence: 0.872581660747528

 $00:55:56.384 \rightarrow 00:55:58.794$ what we're doing is we're accessing a

NOTE Confidence: 0.872581660747528

 $00:55:58.794 \rightarrow 00:56:01.038$ lodging network from this from this.

NOTE Confidence: 0.872581660747528

 $00{:}56{:}01{.}040 \dashrightarrow 00{:}56{:}03{.}768$ Or maybe it's an inverse funnel than that

NOTE Confidence: 0.872581660747528

 $00{:}56{:}03.768 \dashrightarrow 00{:}56{:}06.434$ I'm accessing it from this point that I mean,

NOTE Confidence: 0.872581660747528

 $00:56:06.440 \longrightarrow 00:56:08.729$ the DL Pfc is a sketch pad.

NOTE Confidence: 0.872581660747528

 $00{:}56{:}08{.}730 \dashrightarrow 00{:}56{:}10{.}210$ This is where we are.

NOTE Confidence: 0.872581660747528

 $00{:}56{:}10.210 \dashrightarrow 00{:}56{:}12.023$ Lots of things are going in and

NOTE Confidence: 0.872581660747528

 $00:56:12.023 \rightarrow 00:56:13.749$ out of brain for processing.

NOTE Confidence: 0.872581660747528

 $00:56:13.750 \longrightarrow 00:56:14.396$ You know,

 $00:56:14.396 \longrightarrow 00:56:15.688$ executive function talking to

NOTE Confidence: 0.872581660747528

 $00{:}56{:}15.688 \dashrightarrow 00{:}56{:}17.640$ a lot of downstream components.

NOTE Confidence: 0.872581660747528

 $00:56:17.640 \longrightarrow 00:56:21.344$ And so it may be that these multifaceted

NOTE Confidence: 0.872581660747528

 $00:56:21.344 \rightarrow 00:56:24.868$ aspects of Sud that we all acknowledge

NOTE Confidence: 0.872581660747528

 $00{:}56{:}24.868 \dashrightarrow 00{:}56{:}27.959$ with come together in these large

NOTE Confidence: 0.872581660747528

 $00:56:27.959 \rightarrow 00:56:30.959$ scale logical networks that may be

NOTE Confidence: 0.872581660747528

 $00{:}56{:}30{.}959 \dashrightarrow 00{:}56{:}35{.}780$ amenable to to an intervention like that.

NOTE Confidence: 0.872581660747528

 $00{:}56{:}35{.}780 \dashrightarrow 00{:}56{:}37{.}440$ It's uh.

NOTE Confidence: 0.872581660747528

00:56:37.440 --> 00:56:40.020 You know the you're right there,

NOTE Confidence: 0.872581660747528

 $00:56:40.020 \longrightarrow 00:56:42.090$ there's some of the things

NOTE Confidence: 0.872581660747528

 $00:56:42.090 \longrightarrow 00:56:44.750$ that are that we wonder about.

NOTE Confidence: 0.872581660747528

 $00:56:44.750 \longrightarrow 00:56:47.330$ From the one hand going on,

NOTE Confidence: 0.872581660747528

 $00{:}56{:}47{.}330 \dashrightarrow 00{:}56{:}49{.}030$ uh, thinking about specificity,

NOTE Confidence: 0.872581660747528

 $00{:}56{:}49{.}030 \dashrightarrow 00{:}56{:}51{.}580$ event of an atomy and specificity of

NOTE Confidence: 0.872581660747528

 $00{:}56{:}51{.}650 \dashrightarrow 00{:}56{:}53{.}794$ the receptor target, versus perhaps,

- 00:56:53.794 --> 00:56:54.668 you know,
- NOTE Confidence: 0.872581660747528
- $00{:}56{:}54{.}668 \dashrightarrow 00{:}56{:}57{.}290$ the most efficacious treatment we have
- NOTE Confidence: 0.872581660747528
- $00:56:57.361 \rightarrow 00:57:00.224$ in psychiatry today is the least specific,
- NOTE Confidence: 0.872581660747528
- 00:57:00.230 --> 00:57:00.660 right.
- NOTE Confidence: 0.872581660747528
- $00{:}57{:}00{.}660 \dashrightarrow 00{:}57{:}04{.}550$ So ECT works on, you know, 70% is h of.
- NOTE Confidence: 0.872581660747528
- $00{:}57{:}04{.}550 \dashrightarrow 00{:}57{:}06{.}428$ Medication resistant depression.
- NOTE Confidence: 0.872581660747528
- $00:57:06.428 \longrightarrow 00:57:08.306$ And there's no,
- NOTE Confidence: 0.872581660747528
- $00{:}57{:}08{.}310 \dashrightarrow 00{:}57{:}10{.}346$ there's no localization there.
- NOTE Confidence: 0.872581660747528
- $00:57:10.346 \rightarrow 00:57:14.650$ So you know the other thing I would point
- NOTE Confidence: 0.872581660747528
- $00{:}57{:}14.650 \dashrightarrow 00{:}57{:}17.997$ out is if we look carefully at Suzanne
- NOTE Confidence: 0.872581660747528
- 00:57:17.997 --> 00:57:21.309 Hager's work and the loop structure,
- NOTE Confidence: 0.872581660747528
- $00:57:21.310 \longrightarrow 00:57:23.878$ and again if you get beyond
- NOTE Confidence: 0.872581660747528
- $00:57:23.878 \longrightarrow 00:57:25.590$ the cortical stried piece,
- NOTE Confidence: 0.872581660747528
- $00:57:25.590 \rightarrow 00:57:29.014$ but the pieces that are talking into this,
- NOTE Confidence: 0.872581660747528
- $00:57:29.020 \longrightarrow 00:57:31.570$ that what we're doing is we're
- NOTE Confidence: 0.872581660747528
- 00:57:31.570 00:57:33.730 really bringing into into play.

- NOTE Confidence: 0.872581660747528
- 00:57:33.730 --> 00:57:35.745 You know many many downstream
- NOTE Confidence: 0.872581660747528
- $00:57:35.745 \rightarrow 00:57:38.430$ structures in both in the disease,
- NOTE Confidence: 0.872581660747528
- $00{:}57{:}38{.}430 \dashrightarrow 00{:}57{:}40{.}570$ and perhaps in this intervention.
- NOTE Confidence: 0.872581660747528
- $00:57:40.570 \longrightarrow 00:57:43.470$ Now to your first question.
- NOTE Confidence: 0.872581660747528
- 00:57:43.470 00:57:46.926 What's going on during this acute
- NOTE Confidence: 0.872581660747528
- $00:57:46.926 \rightarrow 00:57:50.274$ accidents versus versus satiety, right so?
- NOTE Confidence: 0.872581660747528
- 00:57:50.274 --> 00:57:51.318 Is it?
- NOTE Confidence: 0.872581660747528
- $00:57:51.318 \rightarrow 00:57:55.220$ Is it simply a matter of well,
- NOTE Confidence: 0.872581660747528
- $00:57:55.220 \longrightarrow 00:57:57.605$ so you talked about tolerance
- NOTE Confidence: 0.872581660747528
- $00:57:57.605 \rightarrow 00:57:59.513$ and sensitization right when?
- NOTE Confidence: 0.872581660747528
- $00:57:59.520 \rightarrow 00:58:02.960$ When an acutely abstinent smoker?
- NOTE Confidence: 0.872581660747528
- $00{:}58{:}02{.}960 \dashrightarrow 00{:}58{:}06{.}300$ Smokes or gets a Patch.
- NOTE Confidence: 0.872581660747528
- 00:58:06.300 00:58:08.575 They're not gonna smoke then
- NOTE Confidence: 0.872581660747528
- 00:58:08.575 --> 00:58:11.739 not going on a on a bench.
- NOTE Confidence: 0.872581660747528
- $00:58:11.740 \longrightarrow 00:58:12.646$ They're not,
- NOTE Confidence: 0.872581660747528

 $00:58:12.646 \rightarrow 00:58:15.364$ they're not trying to to overcome.

NOTE Confidence: 0.872581660747528

00:58:15.370 --> 00:58:17.230 Some deficit state beyond an

NOTE Confidence: 0.872581660747528

00:58:17.230 --> 00:58:18.355 equilibrium point, right?

NOTE Confidence: 0.872581660747528

 $00:58:18.355 \rightarrow 00:58:19.480$ They seem to,

NOTE Confidence: 0.872581660747528

 $00{:}58{:}19{.}480 \dashrightarrow 00{:}58{:}22{.}205$ and in fact there is almost no

NOTE Confidence: 0.872581660747528

 $00{:}58{:}22.205 \dashrightarrow 00{:}58{:}24.551$ tolerance to smoking people that smoke

NOTE Confidence: 0.872581660747528

 $00{:}58{:}24{.}551 \dashrightarrow 00{:}58{:}27{.}821$ a pack a day smoker pack a day and

NOTE Confidence: 0.872581660747528

 $00:58:27.821 \rightarrow 00:58:31.040$ for 20 years they smoke a pack a day.

NOTE Confidence: 0.872581660747528

 $00:58:31.040 \longrightarrow 00:58:33.200$ That's very different than the profile

NOTE Confidence: 0.872581660747528

 $00:58:33.200 \rightarrow 00:58:35.509$ to see with opioids with alcohol.

NOTE Confidence: 0.872581660747528

00:58:35.510 --> 00:58:37.380 So it's a very different,

NOTE Confidence: 0.872581660747528

 $00:58:37.380 \longrightarrow 00:58:38.487$ very different drug.

NOTE Confidence: 0.872581660747528

00:58:38.487 --> 00:58:40.701 And So what we're thinking is

NOTE Confidence: 0.872581660747528

00:58:40.701 - 00:58:42.496 happening is there really isn't

NOTE Confidence: 0.872581660747528

 $00{:}58{:}42.496 \dashrightarrow 00{:}58{:}44.530$ a cute an acute deprivation state

NOTE Confidence: 0.848867356777191

 $00:58:44.592 \rightarrow 00:58:46.380$ that's that's simply reverse.

- NOTE Confidence: 0.848867356777191
- $00:58:46.380 \rightarrow 00:58:48.385$ Ameliorated by the replacement of
- NOTE Confidence: 0.848867356777191
- $00:58:48.385 \longrightarrow 00:58:50.398$ nicotine, and that's an that's
- NOTE Confidence: 0.848867356777191
- $00:58:50.398 \longrightarrow 00:58:52.408$ shown cognitively as well as
- NOTE Confidence: 0.820339739322662
- $00:58:52.410 \longrightarrow 00:58:54.018$ in these circuits, right?
- NOTE Confidence: 0.820339739322662
- 00:58:54.018 --> 00:58:56.024 Right? Thank you. That's great.
- NOTE Confidence: 0.820339739322662
- $00:58:56.024 \dashrightarrow 00:58:59.239$ We have a question in the chat box.
- NOTE Confidence: 0.820339739322662
- $00:58:59.240 \rightarrow 00:59:01.658$ How well do would behavioral interventions?
- NOTE Confidence: 0.820339739322662
- 00:59:01.660 --> 00:59:03.268 Hypnotherapy versus more Pfc
- NOTE Confidence: 0.820339739322662
- $00{:}59{:}03.268 \dashrightarrow 00{:}59{:}05.680$ based ones like CBT effect these
- NOTE Confidence: 0.828417216028486
- $00:59:05.680 \rightarrow 00:59:08.608$ networks? I think all interventions are
- NOTE Confidence: 0.828417216028486
- $00:59:08.608 \rightarrow 00:59:12.419$ going to change if you change the brain.
- NOTE Confidence: 0.828417216028486
- $00:59:12.420 \rightarrow 00:59:14.975$ You're going to change the networks and
- NOTE Confidence: 0.828417216028486
- $00:59:14.975 \rightarrow 00:59:17.619$ whether we change them pharmacologically.
- NOTE Confidence: 0.828417216028486
- $00{:}59{:}17.620 \dashrightarrow 00{:}59{:}19.096$ Using noninvasive brain stimulation.
- NOTE Confidence: 0.828417216028486
- $00:59:19.096 \longrightarrow 00:59:21.310$ Whether we use CBT or other
- NOTE Confidence: 0.828417216028486

 $00{:}59{:}21.368 \dashrightarrow 00{:}59{:}22.810$ behavioral interventions.

NOTE Confidence: 0.828417216028486

 $00:59:22.810 \longrightarrow 00:59:24.850$ Of course, these circuits

NOTE Confidence: 0.828417216028486

00:59:24.850 --> 00:59:27.202 will change absolutely. My my.

NOTE Confidence: 0.828417216028486

 $00:59:27.202 \rightarrow 00:59:30.079$ My long-term hope is that it's going

NOTE Confidence: 0.828417216028486

 $00{:}59{:}30{.}079 \dashrightarrow 00{:}59{:}33{.}203$ to be a combination the rapy and you

NOTE Confidence: 0.828417216028486

 $00{:}59{:}33{.}203 \dashrightarrow 00{:}59{:}36{.}337$ and I would talk about this over

NOTE Confidence: 0.828417216028486

 $00:59:36.337 \rightarrow 00:59:39.340$ the years that it's going to be.

NOTE Confidence: 0.828417216028486

 $00:59:39.340 \rightarrow 00:59:41.064$ You know, supportive pharmacotherapy,

NOTE Confidence: 0.828417216028486

 $00:59:41.064 \rightarrow 00:59:42.357$ interventional behavioral interventions,

NOTE Confidence: 0.828417216028486

 $00:59:42.360 \rightarrow 00:59:44.520$ and with potentially neural modulation,

NOTE Confidence: 0.828417216028486

 $00:59:44.520 \longrightarrow 00:59:46.680$ then that might enhance these

NOTE Confidence: 0.828417216028486

 $00:59:46.680 \longrightarrow 00:59:47.976$ these these approaches.

NOTE Confidence: 0.919082959493001

00:59:48.720 --> 00:59:55.020 Yeah. Any other thoughts and comments?

NOTE Confidence: 0.84974867105484

00:59:56.680 --> 00:59:58.765 Hi if it's OK, I don't

NOTE Confidence: 0.84974867105484

 $00:59:58.765 \longrightarrow 01:00:00.500$ really have a question just

NOTE Confidence: 0.84974867105484

 $01:00:00.500 \rightarrow 01:00:03.274$ like a feel good moment for a second.

- NOTE Confidence: 0.84974867105484
- 01:00:03.274 --> 01:00:05.008 My name is Justin Morales,
- NOTE Confidence: 0.84974867105484
- $01{:}00{:}05{.}008 \dashrightarrow 01{:}00{:}06{.}744$ I'm actually a fourth year
- NOTE Confidence: 0.84974867105484
- $01{:}00{:}06.744 \dashrightarrow 01{:}00{:}08.132$ medical student at Howard.
- NOTE Confidence: 0.84974867105484
- $01:00:08.132 \longrightarrow 01:00:09.518$ Fortunate to join this
- NOTE Confidence: 0.84974867105484
- 01:00:09.520 --> 01:00:10.558 call to Doctor
- NOTE Confidence: 0.84974867105484
- $01{:}00{:}10.560 \dashrightarrow 01{:}00{:}12.636$ Schottenfeld who passed it along and
- NOTE Confidence: 0.84974867105484
- $01:00:12.640 \longrightarrow 01:00:14.374$ really I joined the call.
- NOTE Confidence: 0.84974867105484
- 01:00:14.374 --> 01:00:15.068 Doctor Stein.
- NOTE Confidence: 0.84974867105484
- $01:00:15.070 \longrightarrow 01:00:16.810$ You might not recall this.
- NOTE Confidence: 0.84974867105484
- 01:00:16.810 --> 01:00:19.237 I worked in your lab 10 years
- NOTE Confidence: 0.84974867105484
- $01:00:19.237 \longrightarrow 01:00:21.315$ ago as a high school student.
- NOTE Confidence: 0.84974867105484
- $01{:}00{:}21.315 \dashrightarrow 01{:}00{:}23.745$ Now in my 4th year medical school.
- NOTE Confidence: 0.84974867105484
- 01:00:23.745 -> 01:00:26.518 So very proud and happy to be able
- NOTE Confidence: 0.84974867105484
- $01{:}00{:}26.518 \dashrightarrow 01{:}00{:}28.594$ to join a list ening to everything
- NOTE Confidence: 0.84974867105484
- $01{:}00{:}28.600 \dashrightarrow 01{:}00{:}31.370$ that you've done over these past 10 years.
- NOTE Confidence: 0.84974867105484

- 01:00:31.370 --> 01:00:32.702 Continuing to, you know,
- NOTE Confidence: 0.84974867105484
- $01{:}00{:}32.702 \dashrightarrow 01{:}00{:}33.950$ pursue science and medicine,
- NOTE Confidence: 0.84974867105484
- $01{:}00{:}33.950 \dashrightarrow 01{:}00{:}35.523$ and I think it's great.
- NOTE Confidence: 0.84974867105484
- 01:00:35.523 --> 01:00:38.339 So I just wanted to join it and just
- NOTE Confidence: 0.846236169338226
- $01{:}00{:}38{.}340 \dashrightarrow 01{:}00{:}40{.}836$ kind of say hi blast from the past.
- NOTE Confidence: 0.846236169338226
- 01:00:40.840 --> 01:00:41.466 Justin thanks.
- NOTE Confidence: 0.846236169338226
- 01:00:41.466 --> 01:00:42.718 Thanks for introducing yourself.
- NOTE Confidence: 0.846236169338226
- $01{:}00{:}42.720 \dashrightarrow 01{:}00{:}46.160$ I will say one of the best parts of this job.
- NOTE Confidence: 0.846236169338226
- $01{:}00{:}46.160 \dashrightarrow 01{:}00{:}48.344$ The absolute best parts of this job.
- NOTE Confidence: 0.846236169338226
- $01:00:48.350 \rightarrow 01:00:50.228$ Other students working in the lab,
- NOTE Confidence: 0.846236169338226
- $01:00:50.230 \rightarrow 01:00:51.482$ whether they're they're coming
- NOTE Confidence: 0.846236169338226
- 01:00:51.482 --> 01:00:53.360 through in high school or college,
- NOTE Confidence: 0.846236169338226
- $01:00:53.360 \longrightarrow 01:00:55.670$ we have a number of programs at
- NOTE Confidence: 0.846236169338226
- $01{:}00{:}55{.}670 \dashrightarrow 01{:}00{:}57{.}292$ the intramural program and we
- NOTE Confidence: 0.846236169338226
- $01:00:57.292 \rightarrow 01:00:58.990$ get students in at all levels,
- NOTE Confidence: 0.846236169338226
- $01:00:58.990 \rightarrow 01:01:01.566$ and it's it's absolutely the best part of.

- NOTE Confidence: 0.846236169338226
- 01:01:01.570 --> 01:01:02.728 Doing science, I
- NOTE Confidence: 0.777802288532257
- $01:01:02.730 \longrightarrow 01:01:03.500$ think wonderful.
- NOTE Confidence: 0.777802288532257
- $01{:}01{:}03.500 \dashrightarrow 01{:}01{:}05.040$ Well, thank you Justin.
- NOTE Confidence: 0.777802288532257
- $01{:}01{:}05{.}040 \dashrightarrow 01{:}01{:}08{.}028$ I hope we can interact you over to Yale
- NOTE Confidence: 0.777802288532257
- $01:01:08.028 \longrightarrow 01:01:10.827$ for your post medical school years.
- NOTE Confidence: 0.777802288532257
- $01:01:10.830 \longrightarrow 01:01:12.374$ We have two questions,
- NOTE Confidence: 0.777802288532257
- 01:01:12.374 --> 01:01:14.518 one from Shelly Ament, Shelly.
- NOTE Confidence: 0.777802288532257
- 01:01:14.518 --> 01:01:17.940 Go ahead and then Suchitra. Hey
- NOTE Confidence: 0.864145636558533
- 01:01:17.940 --> 01:01:20.550 Elliot, wonderful to see you again.
- NOTE Confidence: 0.864145636558533
- 01:01:20.550 --> 01:01:22.720 Also, one of your previous
- NOTE Confidence: 0.864145636558533
- $01{:}01{:}22.720 \dashrightarrow 01{:}01{:}25.325$ MD PhD students in your lab.
- NOTE Confidence: 0.864145636558533
- 01:01:25.325 --> 01:01:27.675 I have a question since more
- NOTE Confidence: 0.864145636558533
- 01:01:27.675 --> 01:01:29.590 more lately I'm focused on
- NOTE Confidence: 0.864145636558533
- 01:01:29.662 --> 01:01:31.830 ambiguity and decision making.
- NOTE Confidence: 0.864145636558533
- 01:01:31.830 --> 01:01:34.002 I'm wondering in your habenula
- NOTE Confidence: 0.864145636558533

 $01:01:34.002 \rightarrow 01:01:37.039$ study when you had the error made

NOTE Confidence: 0.864145636558533

 $01{:}01{:}37{.}040 \dashrightarrow 01{:}01{:}39{.}854$ and you gave the feedback of the

NOTE Confidence: 0.864145636558533

 $01:01:39.854 \rightarrow 01:01:42.076$ negative frowny phase versus the

NOTE Confidence: 0.864145636558533

 $01:01:42.076 \rightarrow 01:01:44.416$ error made an ambiguous feedback.

NOTE Confidence: 0.864145636558533

 $01:01:44.420 \longrightarrow 01:01:47.556$ Did you look at that to see what

NOTE Confidence: 0.864145636558533

01:01:47.556 --> 01:01:49.630 the ambiguous feedback would

NOTE Confidence: 0.878468342125416

 $01:01:49.630 \longrightarrow 01:01:54.134$ activate? We we, we did and and I.

NOTE Confidence: 0.878468342125416

01:01:54.140 --> 01:01:55.316 Yet again, apologize for

NOTE Confidence: 0.878468342125416

 $01{:}01{:}55{.}316 \dashrightarrow 01{:}01{:}57{.}080$ the speed that I that I.

NOTE Confidence: 0.878468342125416

 $01:01:57.080 \rightarrow 01:01:58.838$ I thought the study was cool,

NOTE Confidence: 0.878468342125416

01:01:58.840 --> 01:02:00.976 so I just wanted to just came out

NOTE Confidence: 0.878468342125416

 $01:02:00.976 \longrightarrow 01:02:03.550$ so I wanted to tease you with it.

NOTE Confidence: 0.878468342125416

 $01{:}02{:}03.550 \dashrightarrow 01{:}02{:}05.020$ Yeah there were two bars.

NOTE Confidence: 0.878468342125416

 $01:02:05.020 \longrightarrow 01:02:07.036$ If you can think of the slide there

NOTE Confidence: 0.878468342125416

 $01:02:07.036 \longrightarrow 01:02:09.077$ are two bars to the right that

NOTE Confidence: 0.878468342125416

 $01{:}02{:}09{.}077 \dashrightarrow 01{:}02{:}10{.}929$ we're both yellow and those were

- NOTE Confidence: 0.878468342125416
- $01{:}02{:}10{.}929 \dashrightarrow 01{:}02{:}12{.}867$ the those were the non informative
- NOTE Confidence: 0.878468342125416
- $01{:}02{:}12.867 \dashrightarrow 01{:}02{:}15.016$ feedback and it was sort of a
- NOTE Confidence: 0.878468342125416
- $01:02:15.016 \longrightarrow 01:02:15.898$ neutral activity activation.
- NOTE Confidence: 0.76599109172821
- $01:02:18.140 \rightarrow 01:02:20.720$ They don't wanna separate Unity Center.
- NOTE Confidence: 0.76599109172821
- 01:02:20.720 --> 01:02:23.300 You didn't pull out a separate
- NOTE Confidence: 0.76599109172821
- 01:02:23.300 --> 01:02:25.450 like locus of ambiguity. OK,
- NOTE Confidence: 0.76599109172821
- 01:02:25.450 --> 01:02:27.600 thank you, it's really interesting.
- NOTE Confidence: 0.323649793863297
- 01:02:29.470 --> 01:02:30.410 Suchitra
- NOTE Confidence: 0.859870076179504
- $01{:}02{:}33.640 \dashrightarrow 01{:}02{:}35.710$ Sorry I'm trying to unmute myself
- NOTE Confidence: 0.859870076179504
- $01:02:35.710 \longrightarrow 01:02:37.780$ later. That was a wonderful talk.
- NOTE Confidence: 0.859870076179504
- 01:02:37.780 --> 01:02:39.808 Thank you so much. It's it's.
- NOTE Confidence: 0.859870076179504
- 01:02:39.808 --> 01:02:42.076 It's great to see such a nice
- NOTE Confidence: 0.859870076179504
- $01{:}02{:}42.076 \dashrightarrow 01{:}02{:}44.199$ series of studies that you know
- NOTE Confidence: 0.859870076179504
- $01{:}02{:}44.199 \dashrightarrow 01{:}02{:}46.410$ are all connect and makes sense.
- NOTE Confidence: 0.859870076179504
- $01{:}02{:}46.410 \dashrightarrow 01{:}02{:}49.470$ I wish we were also lucky to have results
- NOTE Confidence: 0.859870076179504

 $01:02:49.470 \longrightarrow 01:02:52.270$ which kind of all fit together so well.

NOTE Confidence: 0.859870076179504

 $01{:}02{:}52{.}270 \dashrightarrow 01{:}02{:}54{.}000$ So thank you for that.

NOTE Confidence: 0.859870076179504

 $01:02:54.000 \rightarrow 01:02:57.450$ I guess my question is more of a general one,

NOTE Confidence: 0.859870076179504

 $01:02:57.450 \rightarrow 01:03:00.501$ which is a lot of the studies that you

NOTE Confidence: 0.859870076179504

 $01{:}03{:}00.501 \dashrightarrow 01{:}03{:}02.620$ presented were in the adult brain.

NOTE Confidence: 0.859870076179504

 $01:03:02.620 \rightarrow 01:03:04.004$ If I understand correctly.

NOTE Confidence: 0.859870076179504

 $01{:}03{:}04{.}004 \dashrightarrow 01{:}03{:}06{.}451$ You know now we are in the

NOTE Confidence: 0.859870076179504

 $01{:}03{:}06{.}451 \dashrightarrow 01{:}03{:}08{.}209$ in the US and World Wide.

NOTE Confidence: 0.859870076179504

 $01:03:08.210 \longrightarrow 01:03:10.618$ We are facing this huge problem with

NOTE Confidence: 0.859870076179504

01:03:10.618 --> 01:03:12.290 nicotine use through E cigarettes

NOTE Confidence: 0.859870076179504

 $01{:}03{:}12.290 \dashrightarrow 01{:}03{:}14.602$ in youth and have you know I would.

NOTE Confidence: 0.859870076179504

 $01:03:14.610 \rightarrow 01:03:16.584$ I would think knowing little bit that

NOTE Confidence: 0.859870076179504

 $01{:}03{:}16.584 \dashrightarrow 01{:}03{:}19.026$ I do about the youth brain that you

NOTE Confidence: 0.859870076179504

 $01{:}03{:}19{.}026 \dashrightarrow 01{:}03{:}21{.}335$ would anticipate that a lot of the

NOTE Confidence: 0.859870076179504

 $01:03:21.335 \rightarrow 01:03:22.771$ flexibility or inflexibility that

NOTE Confidence: 0.859870076179504

 $01{:}03{:}22.771 \dashrightarrow 01{:}03{:}25.185$ you're seeing in the adult brain would

- NOTE Confidence: 0.859870076179504
- $01:03:25.185 \rightarrow 01:03:27.135$ reflect very differently in the youth
- NOTE Confidence: 0.859870076179504
- $01{:}03{:}27{.}135 \dashrightarrow 01{:}03{:}29{.}007$ brain is what my understanding is.
- NOTE Confidence: 0.859870076179504
- 01:03:29.010 $\operatorname{-->}$ 01:03:30.774 Could you may
be speak a little
- NOTE Confidence: 0.859870076179504
- $01:03:30.774 \rightarrow 01:03:32.850$ bit to what you would expect?
- NOTE Confidence: 0.859870076179504
- $01:03:32.850 \rightarrow 01:03:35.410$ How some of these processes would work there?
- NOTE Confidence: 0.90646356344223
- 01:03:36.710 --> 01:03:38.135 Yeah, that's right,
- NOTE Confidence: 0.90646356344223
- $01:03:38.135 \longrightarrow 01:03:40.035$ that's a great question.
- NOTE Confidence: 0.90646356344223
- $01:03:40.040 \rightarrow 01:03:42.328$ So we have studied only adults as you,
- NOTE Confidence: 0.90646356344223
- $01:03:42.330 \longrightarrow 01:03:44.895$ as you alluded to. 18 to 60 year olds.
- NOTE Confidence: 0.90646356344223
- $01:03:44.900 \longrightarrow 01:03:47.847$ I think our our in our studies.
- NOTE Confidence: 0.90646356344223
- 01:03:47.850 --> 01:03:52.106 Um? And we know certainly the case
- NOTE Confidence: 0.90646356344223
- $01:03:52.106 \longrightarrow 01:03:53.851$ of smoking that nobody thought
- NOTE Confidence: 0.90646356344223
- $01:03:53.851 \rightarrow 01:03:55.285$ smoking as an adult, right?
- NOTE Confidence: 0.90646356344223
- 01:03:55.285 --> 01:03:57.700 If you can get your kids through
- NOTE Confidence: 0.90646356344223
- $01:03:57.700 \longrightarrow 01:03:59.807$ high school and not be a smoker,
- NOTE Confidence: 0.90646356344223

- $01:03:59.810 \rightarrow 01:04:02.085$ the likelihood of them smoking is very,
- NOTE Confidence: 0.90646356344223
- $01:04:02.090 \longrightarrow 01:04:03.065$ very small, right?
- NOTE Confidence: 0.90646356344223
- 01:04:03.065 --> 01:04:04.690 Almost everybody starts at 13,
- NOTE Confidence: 0.90646356344223
- 01:04:04.690 --> 01:04:05.946 fourteen, 15 years old,
- NOTE Confidence: 0.90646356344223
- $01{:}04{:}05{.}946 \dashrightarrow 01{:}04{:}09{.}238$ and we know that you as you just alluded to,
- NOTE Confidence: 0.90646356344223
- $01:04:09.240 \longrightarrow 01:04:11.190$ that that's the time of greatest
- NOTE Confidence: 0.90646356344223
- $01:04:11.190 \longrightarrow 01:04:12.490$ flexibility in the brain,
- NOTE Confidence: 0.90646356344223
- $01{:}04{:}12{.}490 \dashrightarrow 01{:}04{:}13{.}624$ greatest developmental plasticity.
- NOTE Confidence: 0.90646356344223
- $01{:}04{:}13.624 \dashrightarrow 01{:}04{:}16.270$ And so we have two things going
- NOTE Confidence: 0.90646356344223
- $01:04:16.331 \longrightarrow 01:04:18.119$ on right with beating the brain
- NOTE Confidence: 0.90646356344223
- $01{:}04{:}18{.}119 \dashrightarrow 01{:}04{:}19{.}942$ up with this for eign substance at
- NOTE Confidence: 0.90646356344223
- $01:04:19.942 \longrightarrow 01:04:21.944$ the same time that the brain is.
- NOTE Confidence: 0.90646356344223
- $01:04:21.950 \longrightarrow 01:04:22.800$ Is maturing.
- NOTE Confidence: 0.90646356344223
- $01:04:22.800 \longrightarrow 01:04:25.350$ And so you would expect that
- NOTE Confidence: 0.90646356344223
- $01:04:25.350 \longrightarrow 01:04:28.417$ one of the reasons perhaps why,
- NOTE Confidence: 0.90646356344223
- $01:04:28.420 \longrightarrow 01:04:29.617$ as an adult,

- NOTE Confidence: 0.90646356344223
- $01:04:29.617 \rightarrow 01:04:32.011$ this is such an insidious disease
- NOTE Confidence: 0.90646356344223
- 01:04:32.011 --> 01:04:34.568 and failure rates are so high,
- NOTE Confidence: 0.90646356344223
- $01:04:34.570 \longrightarrow 01:04:36.620$ is that that plasticity is
- NOTE Confidence: 0.90646356344223
- $01:04:36.620 \longrightarrow 01:04:38.670$ well locked in right now.
- NOTE Confidence: 0.90646356344223
- $01:04:38.670 \rightarrow 01:04:41.556$ Which of those circuits potentially were
- NOTE Confidence: 0.90646356344223
- $01{:}04{:}41.556 \dashrightarrow 01{:}04{:}44.988$ affected the most at that at that time?
- NOTE Confidence: 0.90646356344223
- $01:04:44.990 \longrightarrow 01:04:48.280$ I do have data in my pocket
- NOTE Confidence: 0.90646356344223
- $01:04:48.280 \rightarrow 01:04:52.229$ that is not ready for primetime.
- NOTE Confidence: 0.90646356344223
- $01{:}04{:}52{.}230 \dashrightarrow 01{:}04{:}55{.}954$ The the animal studies that I showed
- NOTE Confidence: 0.90646356344223
- $01:04:55.954 \longrightarrow 01:04:59.469$ you that that Robin Keeley did.
- NOTE Confidence: 0.90646356344223
- $01:04:59.470 \dashrightarrow 01:05:02.806$ We repeated in in neonatal rats.
- NOTE Confidence: 0.90646356344223
- $01:05:02.810 \longrightarrow 01:05:08.130$ So we we started this at P.
- NOTE Confidence: 0.90646356344223
- $01{:}05{:}08{.}130 \dashrightarrow 01{:}05{:}11{.}786$ He 20 I think and we gave rats
- NOTE Confidence: 0.90646356344223
- 01:05:11.786 --> 01:05:14.650 different amounts of nicotine at
- NOTE Confidence: 0.90646356344223
- $01:05:14.650 \rightarrow 01:05:17.122$ different starting points along
- NOTE Confidence: 0.90646356344223

 $01:05:17.122 \rightarrow 01:05:20.079$ development and we allowed them

NOTE Confidence: 0.90646356344223

 $01{:}05{:}20.079 \dashrightarrow 01{:}05{:}23.073$ to grow up with the nicotine.

NOTE Confidence: 0.90646356344223

01:05:23.080 --> 01:05:25.528 Again, it I think chronic nicotine,

NOTE Confidence: 0.90646356344223

 $01:05:25.530 \rightarrow 01:05:28.393$ and then we scan them along the

NOTE Confidence: 0.90646356344223

01:05:28.393 --> 01:05:29.620 developmental trajectory right?

NOTE Confidence: 0.90646356344223

01:05:29.620 --> 01:05:30.751 And so again,

NOTE Confidence: 0.90646356344223

 $01:05:30.751 \longrightarrow 01:05:33.967$ one of the nice things we have in

NOTE Confidence: 0.90646356344223

 $01:05:33.967 \dashrightarrow 01:05:36.464$ animal magnet. We can do scanning.

NOTE Confidence: 0.90646356344223

 $01{:}05{:}36{.}464 \dashrightarrow 01{:}05{:}39{.}362$ I think we scan these these rats

NOTE Confidence: 0.90646356344223

 $01:05:39.362 \dashrightarrow 01:05:41.997$ four times across the development.

NOTE Confidence: 0.90646356344223

 $01{:}05{:}42.000 \dashrightarrow 01{:}05{:}47.928$ It's a humongous data set and we're just.

NOTE Confidence: 0.90646356344223

01:05:47.930 --> 01:05:49.002 Thinking We're wrapping our

NOTE Confidence: 0.90646356344223

 $01:05:49.002 \longrightarrow 01:05:49.806$ heads around itself,

NOTE Confidence: 0.90646356344223

 $01:05:49.810 \longrightarrow 01:05:52.033$ give me a call in a couple of months

NOTE Confidence: 0.90646356344223

 $01:05:52.033 \rightarrow 01:05:54.115$ an I'll have some data for you,

NOTE Confidence: 0.90646356344223

 $01{:}05{:}54{.}120 \dashrightarrow 01{:}05{:}55{.}992$ but it's a critical question that

 $01{:}05{:}55{.}992 \dashrightarrow 01{:}05{:}57{.}910$ we think that this really is.

NOTE Confidence: 0.90646356344223

 $01:05:57.910 \longrightarrow 01:06:00.410$ Something that that's very relevant

NOTE Confidence: 0.90646356344223

 $01:06:00.410 \rightarrow 01:06:02.910$ clinically to smoking use disorder.

NOTE Confidence: 0.890278100967407

01:06:03.770 --> 01:06:06.115 Thank you yeah my I was really

NOTE Confidence: 0.890278100967407

 $01:06:06.115 \rightarrow 01:06:08.591$ curious to know whether this process

NOTE Confidence: 0.890278100967407

 $01:06:08.591 \longrightarrow 01:06:10.921$ that is changing that you're

NOTE Confidence: 0.890278100967407

 $01{:}06{:}10.921 \dashrightarrow 01{:}06{:}13.309$ describing you know with nicotine.

NOTE Confidence: 0.890278100967407

 $01{:}06{:}13.310 \dashrightarrow 01{:}06{:}15.977$ The timeliness of that and how it

NOTE Confidence: 0.890278100967407

 $01{:}06{:}15.977 \dashrightarrow 01{:}06{:}18.598$ changes in younger populations will be

NOTE Confidence: 0.890278100967407

 $01:06:18.598 \rightarrow 01:06:20.938$ very interesting to examine because

NOTE Confidence: 0.890278100967407

 $01:06:20.938 \longrightarrow 01:06:24.007$ you know you don't get the same

NOTE Confidence: 0.890278100967407

 $01{:}06{:}24.007 \dashrightarrow 01{:}06{:}26.057$ profile of nicotine with drawal in

NOTE Confidence: 0.861741483211518

 $01:06:26.060 \longrightarrow 01:06:27.716$ younger populations too, so.

NOTE Confidence: 0.861741483211518

 $01{:}06{:}27.716 \dashrightarrow 01{:}06{:}30.200$ Really, I'm really glad you mentioned that.

NOTE Confidence: 0.861741483211518

 $01{:}06{:}30{.}200 \dashrightarrow 01{:}06{:}32{.}258$ So kids when they stop smoking do
$01:06:32.258 \rightarrow 01:06:34.937$ not have a very serious effective

NOTE Confidence: 0.861741483211518

 $01{:}06{:}34{.}937 \dashrightarrow 01{:}06{:}40{.}221$ with drawal syndrome. I. That that's.

NOTE Confidence: 0.861741483211518

 $01:06:40.221 \rightarrow 01:06:43.750$ Fascinating. Any other there

NOTE Confidence: 0.868219435214996

 $01:06:43.750 \longrightarrow 01:06:46.490$ is another question in chat.

NOTE Confidence: 0.868219435214996

 $01{:}06{:}46.490 \dashrightarrow 01{:}06{:}50.330$ Regina is there data on relation between

NOTE Confidence: 0.868219435214996

01:06:50.330 --> 01:06:53.070 forms of therapy, neuro modulation,

NOTE Confidence: 0.868219435214996

01:06:53.070 --> 01:06:55.262 behavioral intervention or pharmacology

NOTE Confidence: 0.868219435214996

 $01:06:55.262 \rightarrow 01:06:58.000$ age and or individual differences?

NOTE Confidence: 0.241660013794899

01:06:59.470 --> 01:07:08.178 Wow, Ahah. I don't know.

NOTE Confidence: 0.820001661777496

01:07:08.180 $\operatorname{-->}$ 01:07:12.041 I don't know. We don't and I sort of

NOTE Confidence: 0.820001661777496

01:07:12.041 --> 01:07:15.295 alluded to and I had had a slide at

NOTE Confidence: 0.820001661777496

 $01{:}07{:}15{.}295 \dashrightarrow 01{:}07{:}18{.}591$ the end that I didn't punish you with

NOTE Confidence: 0.820001661777496

 $01{:}07{:}18.591 \dashrightarrow 01{:}07{:}21.476$ to look at at fractionating as we're

NOTE Confidence: 0.820001661777496

 $01:07:21.476 \rightarrow 01:07:23.486$ beginning to fractionate the phenotype,

NOTE Confidence: 0.820001661777496

 $01:07:23.490 \longrightarrow 01:07:25.940$ so we're not doing a particularly good

NOTE Confidence: 0.820001661777496

 $01:07:25.940 \longrightarrow 01:07:28.418$ job at looking at individual differences

NOTE Confidence: 0.820001661777496

 $01:07:28.418 \rightarrow 01:07:31.142$ with with interventions of any sort,

NOTE Confidence: 0.820001661777496

 $01{:}07{:}31{.}150 \dashrightarrow 01{:}07{:}32{.}990$ there is the nicotine metabolism

NOTE Confidence: 0.820001661777496

 $01{:}07{:}32{.}990 \dashrightarrow 01{:}07{:}35{.}333$ ratio work that Karen Lerman has

NOTE Confidence: 0.820001661777496

 $01:07:35.333 \longrightarrow 01:07:37.073$ shown for individual differences

NOTE Confidence: 0.820001661777496

 $01{:}07{:}37{.}073 \dashrightarrow 01{:}07{:}39{.}248$ with slow versus fast metabolizers.

NOTE Confidence: 0.820001661777496

 $01{:}07{:}39{.}250 \dashrightarrow 01{:}07{:}42{.}118$ And we know that slow metabolizers

NOTE Confidence: 0.820001661777496

 $01:07:42.118 \longrightarrow 01:07:45.075$ seem to do better with, well,

NOTE Confidence: 0.820001661777496

01:07:45.075 --> 01:07:47.015 builtron fast metabolizers seem

NOTE Confidence: 0.820001661777496

 $01:07:47.015 \longrightarrow 01:07:49.440$ to do better with NRT.

NOTE Confidence: 0.820001661777496

 $01{:}07{:}49{.}440 \dashrightarrow 01{:}07{:}52{.}737$ That's one of the best examples I

NOTE Confidence: 0.820001661777496

 $01:07:52.737 \rightarrow 01:07:55.440$ know of fractionating the phenotype.

NOTE Confidence: 0.820001661777496

 $01{:}07{:}55{.}440 \dashrightarrow 01{:}07{:}56{.}800$ I would hope that.

NOTE Confidence: 0.820001661777496

 $01{:}07{:}56.800 \dashrightarrow 01{:}07{:}59.772$ If we all get to do this wonderful

NOTE Confidence: 0.820001661777496

01:07:59.772 $\operatorname{-->}$ 01:08:03.587 job for a few more years that we we

NOTE Confidence: 0.820001661777496

 $01{:}08{:}03{.}587 \dashrightarrow 01{:}08{:}06{.}809$ can get down the road to begin to do.

NOTE Confidence: 0.820001661777496

 $01:08:06.810 \rightarrow 01:08:08.485$ I think some pretreatment phenotyping

NOTE Confidence: 0.820001661777496

01:08:08.485 --> 01:08:11.134 to be able to say you are in

NOTE Confidence: 0.820001661777496

 $01:08:11.134 \rightarrow 01:08:12.654$ fact the well builton person,

NOTE Confidence: 0.820001661777496

01:08:12.660 --> 01:08:14.935 your NRT Europe or rent a clean.

NOTE Confidence: 0.820001661777496

 $01{:}08{:}14{.}940 \dashrightarrow 01{:}08{:}18{.}230$ I mean if you think about it.

NOTE Confidence: 0.820001661777496

 $01:08:18.230 \rightarrow 01:08:21.275$ NRT works in 1015% of the people.

NOTE Confidence: 0.820001661777496

 $01:08:21.280 \longrightarrow 01:08:23.450$ Well buitron, 20 ish percent.

NOTE Confidence: 0.820001661777496

01:08:23.450 --> 01:08:25.270 Varenna clean thirtyish percent

NOTE Confidence: 0.820001661777496

 $01{:}08{:}25{.}270 \dashrightarrow 01{:}08{:}28{.}670$ if you keep them on for a year.

NOTE Confidence: 0.820001661777496

01:08:28.670 --> 01:08:32.382 So if we can fix 60% of the

NOTE Confidence: 0.820001661777496

 $01:08:32.382 \longrightarrow 01:08:35.137$ people 100% of the time.

NOTE Confidence: 0.820001661777496

 $01:08:35.140 \longrightarrow 01:08:35.662$ We've done.

NOTE Confidence: 0.820001661777496

01:08:35.662 --> 01:08:36.967 I mean, this is great,

NOTE Confidence: 0.820001661777496

 $01:08:36.970 \rightarrow 01:08:39.319$ but we just don't know who they are right?

NOTE Confidence: 0.820001661777496

 $01:08:39.320 \rightarrow 01:08:41.091$ And we also don't know if they're

NOTE Confidence: 0.820001661777496

 $01:08:41.091 \longrightarrow 01:08:42.959$ the same people or if these are

- NOTE Confidence: 0.820001661777496
- $01:08:42.959 \longrightarrow 01:08:44.279$ in fact independent Co boards.
- NOTE Confidence: 0.820001661777496
- $01:08:44.280 \longrightarrow 01:08:45.580$ So it's a great question.
- NOTE Confidence: 0.820001661777496
- $01{:}08{:}45{.}580 \dashrightarrow 01{:}08{:}46{.}624$ We're not there yet.
- NOTE Confidence: 0.820001661777496
- $01:08:46.624 \longrightarrow 01:08:48.190$ It's sort of the Holy Grail,
- NOTE Confidence: 0.820001661777496
- $01{:}08{:}48{.}190 \dashrightarrow 01{:}08{:}49{.}202$ at least in my.
- NOTE Confidence: 0.820001661777496
- $01:08:49.202 \longrightarrow 01:08:50.720$ In my thinking that we can
- NOTE Confidence: 0.820001661777496
- $01:08:50.783 \longrightarrow 01:08:52.108$ do that at some point.
- NOTE Confidence: 0.826059877872467
- $01:08:56.650 \rightarrow 01:08:59.650$ Wonderful, we really engage the audience.
- NOTE Confidence: 0.826059877872467
- 01:08:59.650 --> 01:09:02.150 So beautiful. You've got some
- NOTE Confidence: 0.826059877872467
- $01:09:02.150 \longrightarrow 01:09:04.150$ wonderful questions and answers.
- NOTE Confidence: 0.826059877872467
- 01:09:04.150 --> 01:09:06.650 I think we are almost
- NOTE Confidence: 0.826059877872467
- 01:09:06.650 --> 01:09:08.150 more question Ridata.
- NOTE Confidence: 0.826059877872467
- 01:09:08.150 --> 01:09:11.273 OK, Pittenger has his hand raised.
- NOTE Confidence: 0.826059877872467
- 01:09:11.273 --> 01:09:12.890 Go ahead, Chris.
- NOTE Confidence: 0.826059877872467
- $01{:}09{:}12.890 \dashrightarrow 01{:}09{:}14.728$ That wasn't my hand raised.
- NOTE Confidence: 0.826059877872467

- $01:09:14.728 \longrightarrow 01:09:15.826$ That was me
- NOTE Confidence: 0.628543972969055
- $01{:}09{:}15.830 \dashrightarrow 01{:}09{:}18.026$ clapping. Oh, it was the clap.
- NOTE Confidence: 0.628543972969055
- 01:09:18.030 --> 01:09:19.930 Christmas planning. Do you
- NOTE Confidence: 0.666228652000427
- $01:09:19.930 \longrightarrow 01:09:23.789$ see any good options? Trisha. I
- NOTE Confidence: 0.867055237293243
- $01{:}09{:}23.790 \dashrightarrow 01{:}09{:}25.810$ think we are all set.
- NOTE Confidence: 0.867055237293243
- $01:09:25.810 \longrightarrow 01:09:28.244$ I don't see any other hands
- NOTE Confidence: 0.867055237293243
- $01{:}09{:}28{.}244 \dashrightarrow 01{:}09{:}30{.}668$ raised and nothing else in chat.
- NOTE Confidence: 0.867055237293243
- 01:09:30.670 --> 01:09:33.505 Yeah, well, Elliot that was just beautiful.
- NOTE Confidence: 0.867055237293243
- 01:09:33.510 --> 01:09:35.940 Thank you for such a wonderful,
- NOTE Confidence: 0.867055237293243
- $01:09:35.940 \longrightarrow 01:09:36.752$ stimulating talk.
- NOTE Confidence: 0.867055237293243
- $01:09:36.752 \dashrightarrow 01:09:39.594$ It's got everybody's juices going and we.
- NOTE Confidence: 0.867055237293243
- $01:09:39.600 \longrightarrow 01:09:41.822$ Now we will be following up on
- NOTE Confidence: 0.867055237293243
- $01:09:41.822 \rightarrow 01:09:43.730$ your papers and things like that.
- NOTE Confidence: 0.867055237293243
- $01{:}09{:}43.730 \dashrightarrow 01{:}09{:}44.588$ Thanks so much.
- NOTE Confidence: 0.867055237293243
- $01{:}09{:}44.588 \dashrightarrow 01{:}09{:}46.590$ I know it's really early where you
- NOTE Confidence: 0.867055237293243
- $01:09:46.654 \rightarrow 01:09:48.537$ are and you've taken the you woken

- NOTE Confidence: 0.867055237293243
- $01{:}09{:}48.537 \dashrightarrow 01{:}09{:}50.982$ up early and we couldn't tell any
- NOTE Confidence: 0.867055237293243
- 01:09:50.982 --> 01:09:52.952 difference about sleep sleep deprivation.
- NOTE Confidence: 0.867055237293243
- 01:09:52.960 --> 01:09:53.908 You would just
- NOTE Confidence: 0.882969558238983
- 01:09:53.910 --> 01:09:55.182 fantastic thanks so much.
- NOTE Confidence: 0.882969558238983
- $01:09:55.182 \rightarrow 01:09:56.480$ Thank you everyone, thanks.