

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 --> 00:00:05.305 to welcome doctor Elliot Stein

NOTE Confidence: 0.847765982151031

00:00:05.305 --> 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 --> 00:00:13.291 neuroimaging research branch and chief

NOTE Confidence: 0.847765982151031

00:00:13.291 --> 00:00:15.716 of cognitive and affective neuroscience

NOTE Confidence: 0.847765982151031

00:00:15.716 --> 00:00:18.538 of addiction section at the National

NOTE Confidence: 0.847765982151031

00:00:18.538 --> 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 --> 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 --> 00:00:34.489 his post high school education here

NOTE Confidence: 0.847765982151031

00:00:34.489 --> 00:00:37.513 in Connecticut and got his bachelors

NOTE Confidence: 0.847765982151031  
00:00:37.513 --> 00:00:40.049 at Quinnipiac University in Biology  
NOTE Confidence: 0.847765982151031  
00:00:40.049 --> 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 --> 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 --> 00:00:54.089 Caltech with doctor James Olds who.  
NOTE Confidence: 0.847765982151031  
00:00:54.090 --> 00:00:57.586 Many of you may recall was famous for  
NOTE Confidence: 0.847765982151031  
00:00:57.586 --> 00:00:59.851 discovering what would got labeled  
NOTE Confidence: 0.847765982151031  
00:00:59.851 --> 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 --> 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 --> 00:01:11.289 processes like human motivation,  
NOTE Confidence: 0.847765982151031  
00:01:11.290 --> 00:01:14.377 which he was very interested in studying,  
NOTE Confidence: 0.847765982151031  
00:01:14.380 --> 00:01:16.580 and made big contributions on,  
NOTE Confidence: 0.847765982151031

00:01:16.580 --> 00:01:17.024 needed,  
NOTE Confidence: 0.847765982151031

00:01:17.024 --> 00:01:19.688 needed study of the central nervous  
NOTE Confidence: 0.847765982151031

00:01:19.688 --> 00:01:21.869 system and and the brain.  
NOTE Confidence: 0.847765982151031

00:01:21.870 --> 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 --> 00:01:30.642 think that this time has really  
NOTE Confidence: 0.847765982151031

00:01:30.642 --> 00:01:33.660 epitomized that sort of spirit and  
NOTE Confidence: 0.847765982151031

00:01:33.660 --> 00:01:36.916 goal in the work that he has done.  
NOTE Confidence: 0.847765982151031

00:01:36.920 --> 00:01:39.075 After getting if completing his  
NOTE Confidence: 0.847765982151031

00:01:39.075 --> 00:01:41.736 post doc with Doctor Olds that  
NOTE Confidence: 0.847765982151031

00:01:41.736 --> 00:01:43.876 this time moved to Wisconsin,  
NOTE Confidence: 0.847765982151031

00:01:43.880 --> 00:01:46.778 he was on the faculty at Marquette  
NOTE Confidence: 0.847765982151031

00:01:46.778 --> 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 --> 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 --> 00:02:00.850 professor. He was there for  
NOTE Confidence: 0.803226053714752  
00:02:00.850 --> 00:02:04.585 a long time and then in 2002 he joined  
NOTE Confidence: 0.803226053714752  
00:02:04.585 --> 00:02:08.255 the naida IRP as chief of the newly.  
NOTE Confidence: 0.803226053714752  
00:02:08.260 --> 00:02:10.956 Created neuroimaging research branch.  
NOTE Confidence: 0.803226053714752  
00:02:10.956 --> 00:02:15.633 This is really important because I think  
NOTE Confidence: 0.803226053714752  
00:02:15.633 --> 00:02:18.837 one of the real major contributions  
NOTE Confidence: 0.803226053714752  
00:02:18.837 --> 00:02:22.329 of doctor Stein is that he used  
NOTE Confidence: 0.803226053714752  
00:02:22.329 --> 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 --> 00:02:31.785 specially looking also at white  
NOTE Confidence: 0.803226053714752  
00:02:31.785 --> 00:02:34.691 matter tracks using diffusion tensor  
NOTE Confidence: 0.803226053714752  
00:02:34.691 --> 00:02:37.516 imaging and of course positive  
NOTE Confidence: 0.803226053714752  
00:02:37.516 --> 00:02:39.590 positive emission tomography pet.  
NOTE Confidence: 0.803226053714752

00:02:39.590 --> 00:02:40.928 Studies as well,  
NOTE Confidence: 0.803226053714752

00:02:40.928 --> 00:02:42.266 and most importantly,  
NOTE Confidence: 0.803226053714752

00:02:42.270 --> 00:02:45.830 doing this both in humans and in animals,  
NOTE Confidence: 0.803226053714752

00:02:45.830 --> 00:02:47.322 which you can do.  
NOTE Confidence: 0.803226053714752

00:02:47.322 --> 00:02:50.163 I think at using the naida IRP  
NOTE Confidence: 0.803226053714752

00:02:50.163 --> 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 --> 00:02:58.320 your scientists and this allowed  
NOTE Confidence: 0.803226053714752

00:02:58.320 --> 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 --> 00:03:06.798 but also then translate that,  
NOTE Confidence: 0.803226053714752

00:03:06.800 --> 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 --> 00:03:16.390 and I think that we benefited a lot from that  
NOTE Confidence: 0.803226053714752

00:03:16.481 --> 00:03:20.275 kind of Translational back and forth work.

NOTE Confidence: 0.803226053714752  
00:03:20.280 --> 00:03:23.549 The other thing that that he has,  
NOTE Confidence: 0.803226053714752  
00:03:23.550 --> 00:03:25.806 I think pioneered has been what  
NOTE Confidence: 0.803226053714752  
00:03:25.806 --> 00:03:28.061 he identifies as event related  
NOTE Confidence: 0.803226053714752  
00:03:28.061 --> 00:03:30.098 cognitive neuroscience designs,  
NOTE Confidence: 0.803226053714752  
00:03:30.100 --> 00:03:32.440 which allowed us to look  
NOTE Confidence: 0.803226053714752  
00:03:32.440 --> 00:03:33.844 at functional neuroimaging,  
NOTE Confidence: 0.803226053714752  
00:03:33.850 --> 00:03:35.254 meaning essentially understanding  
NOTE Confidence: 0.803226053714752  
00:03:35.254 --> 00:03:36.658 different brain functions,  
NOTE Confidence: 0.803226053714752  
00:03:36.660 --> 00:03:38.552 an understanding the circuits  
NOTE Confidence: 0.803226053714752  
00:03:38.552 --> 00:03:40.444 from a systems science.  
NOTE Confidence: 0.803226053714752  
00:03:40.450 --> 00:03:42.580 And understanding different networks that  
NOTE Confidence: 0.803226053714752  
00:03:42.580 --> 00:03:44.710 contribute to those different functions.  
NOTE Confidence: 0.803226053714752  
00:03:44.710 --> 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 --> 00:03:54.506 based on findings that he had,  
NOTE Confidence: 0.803226053714752

00:03:54.510 --> 00:03:56.964 which showed the chronic drug use  
NOTE Confidence: 0.803226053714752

00:03:56.964 --> 00:03:59.190 alters this executive control network.  
NOTE Confidence: 0.803226053714752

00:03:59.190 --> 00:04:01.746 In addition to that he has.  
NOTE Confidence: 0.803226053714752

00:04:01.750 --> 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 --> 00:04:08.984 the role of the insula,  
NOTE Confidence: 0.803226053714752

00:04:08.990 --> 00:04:11.180 which is an int receptive.  
NOTE Confidence: 0.803226053714752

00:04:11.180 --> 00:04:15.698 Hub in the brain for feelings in the body.  
NOTE Confidence: 0.803226053714752

00:04:15.700 --> 00:04:18.430 Signals that coming from inside of  
NOTE Confidence: 0.803226053714752

00:04:18.430 --> 00:04:21.655 the body and his work has really  
NOTE Confidence: 0.803226053714752

00:04:21.655 --> 00:04:24.714 sort of move the field forward in  
NOTE Confidence: 0.803226053714752

00:04:24.809 --> 00:04:26.951 addiction around understanding  
NOTE Confidence: 0.803226053714752

00:04:26.951 --> 00:04:29.807 insulin networks as well.  
NOTE Confidence: 0.803226053714752

00:04:29.810 --> 00:04:32.778 I think the since 2002 if we think  
NOTE Confidence: 0.803226053714752

00:04:32.778 --> 00:04:35.600 back the last two decades there has  
NOTE Confidence: 0.803226053714752

00:04:35.600 --> 00:04:38.651 been a lot of signs showing sort

NOTE Confidence: 0.803226053714752  
00:04:38.651 --> 00:04:41.567 of addiction as a brain disease,  
NOTE Confidence: 0.803226053714752  
00:04:41.570 --> 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 --> 00:04:47.322 that home with translating the  
NOTE Confidence: 0.803226053714752  
00:04:47.322 --> 00:04:49.687 work from animal experiments to  
NOTE Confidence: 0.803226053714752  
00:04:49.687 --> 00:04:52.202 showing the long term changes that  
NOTE Confidence: 0.803226053714752  
00:04:52.202 --> 00:04:55.016 occur from chronic drug use in the  
NOTE Confidence: 0.803226053714752  
00:04:55.016 --> 00:04:57.554 brain and connecting that then too.  
NOTE Confidence: 0.803226053714752  
00:04:57.560 --> 00:04:59.989 Unical outcomes one of the things that  
NOTE Confidence: 0.803226053714752  
00:04:59.989 --> 00:05:02.763 I think has been really critical is  
NOTE Confidence: 0.803226053714752  
00:05:02.763 --> 00:05:05.259 he's also pushed the envelope trying  
NOTE Confidence: 0.803226053714752  
00:05:05.332 --> 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 --> 00:05:12.410 but also affect if personality  
NOTE Confidence: 0.803226053714752  
00:05:12.410 --> 00:05:13.742 environmental interactions that  
NOTE Confidence: 0.803226053714752



00:05:13.742 --> 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 --> 00:05:19.979 long-term alterations as a function  
NOTE Confidence: 0.803226053714752

00:05:19.979 --> 00:05:23.042 of chronic drug use as a function  
NOTE Confidence: 0.803226053714752

00:05:23.042 --> 00:05:24.167 of drug withdrawal,  
NOTE Confidence: 0.803226053714752

00:05:24.170 --> 00:05:26.636 and more recently now into what  
NOTE Confidence: 0.803226053714752

00:05:26.636 --> 00:05:29.190 are the effects of treatment.  
NOTE Confidence: 0.803226053714752

00:05:29.190 --> 00:05:31.620 And so he is plunged forward.  
NOTE Confidence: 0.803226053714752

00:05:31.620 --> 00:05:34.412 An has been looking at how we can  
NOTE Confidence: 0.803226053714752

00:05:34.412 --> 00:05:35.604 develop efficacious strategies  
NOTE Confidence: 0.803226053714752

00:05:35.604 --> 00:05:37.714 for treating and reversing these  
NOTE Confidence: 0.803226053714752

00:05:37.714 --> 00:05:40.130 long term effects of addiction.  
NOTE Confidence: 0.803226053714752

00:05:40.130 --> 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 --> 00:05:45.362 reviews and book chapters.  
NOTE Confidence: 0.803226053714752

00:05:45.362 --> 00:05:47.750 He's been cited more than 17,000

NOTE Confidence: 0.803226053714752  
00:05:47.820 --> 00:05:49.440 times in the literature.  
NOTE Confidence: 0.872125327587128  
00:05:49.440 --> 00:05:53.085 About half of that in the last five years.  
NOTE Confidence: 0.872125327587128  
00:05:53.090 --> 00:05:55.508 So really continuing to have a  
NOTE Confidence: 0.872125327587128  
00:05:55.508 --> 00:05:57.950 major current impact on the field.  
NOTE Confidence: 0.872125327587128  
00:05:57.950 --> 00:06:00.440 And so it's my real pleasure.  
NOTE Confidence: 0.872125327587128  
00:06:00.440 --> 00:06:02.897 To give you doctor Elliot Stein and  
NOTE Confidence: 0.872125327587128  
00:06:02.897 --> 00:06:05.748 he's going to be speaking about state,  
NOTE Confidence: 0.872125327587128  
00:06:05.750 --> 00:06:07.162 trait and subtype consideration  
NOTE Confidence: 0.872125327587128  
00:06:07.162 --> 00:06:08.927 and substance use disorders of  
NOTE Confidence: 0.872125327587128  
00:06:08.927 --> 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 --> 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 --> 00:06:19.934 Thanks for everyone for attending  
NOTE Confidence: 0.850576758384705  
00:06:19.934 --> 00:06:22.137 today in this rather awkward talking  
NOTE Confidence: 0.850576758384705

00:06:22.137 --> 00:06:24.499 to screen that we that we've been  
NOTE Confidence: 0.850576758384705

00:06:24.499 --> 00:06:26.627 doing for the last couple of months.  
NOTE Confidence: 0.850576758384705

00:06:26.630 --> 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 --> 00:06:34.739 not going to be able to touch on  
NOTE Confidence: 0.850576758384705

00:06:34.739 --> 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 --> 00:06:40.328 but a bit of an overview of our  
NOTE Confidence: 0.850576758384705

00:06:40.328 --> 00:06:42.740 thinking the last few years on how  
NOTE Confidence: 0.850576758384705

00:06:42.740 --> 00:06:44.495 we are approaching a substance,  
NOTE Confidence: 0.850576758384705

00:06:44.500 --> 00:06:46.708 use disorder and maybe some insights  
NOTE Confidence: 0.850576758384705

00:06:46.708 --> 00:06:48.810 and maybe some controversies as to why.  
NOTE Confidence: 0.850576758384705

00:06:48.810 --> 00:06:52.620 Our treatment outcomes are still not  
NOTE Confidence: 0.850576758384705

00:06:52.620 --> 00:06:54.525 particularly particularly favorable.  
NOTE Confidence: 0.850576758384705

00:06:54.530 --> 00:07:00.140 So let's see if this works.  
NOTE Confidence: 0.850576758384705

00:07:00.140 --> 00:07:03.700 Ah. OK, there we go.

NOTE Confidence: 0.850576758384705  
00:07:03.700 --> 00:07:06.290 OK well smoking is bad so if  
NOTE Confidence: 0.850576758384705  
00:07:06.290 --> 00:07:08.633 smoking is bad then abstinence  
NOTE Confidence: 0.850576758384705  
00:07:08.633 --> 00:07:10.925 abstinence must be good.  
NOTE Confidence: 0.850576758384705  
00:07:10.930 --> 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 --> 00:07:26.142 That's better OK, so most of the folks in  
NOTE Confidence: 0.901125013828278  
00:07:26.142 --> 00:07:29.356 the in America have gotten that message.  
NOTE Confidence: 0.901125013828278  
00:07:29.360 --> 00:07:32.936 Went down to about 17 or 18% of the  
NOTE Confidence: 0.901125013828278  
00:07:32.936 --> 00:07:34.613 country still smoking, unfortunately.  
NOTE Confidence: 0.901125013828278  
00:07:34.613 --> 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 --> 00:07:44.153 who want to quit returning to active  
NOTE Confidence: 0.901125013828278  
00:07:44.153 --> 00:07:47.233 smoking within about a month or so.  
NOTE Confidence: 0.901125013828278  
00:07:47.240 --> 00:07:48.524 So what's going on?  
NOTE Confidence: 0.901125013828278

00:07:48.524 --> 00:07:51.420 What are the bad things that are happening

NOTE Confidence: 0.901125013828278

00:07:51.420 --> 00:07:54.126 during abstinence and the basic message?

NOTE Confidence: 0.901125013828278

00:07:54.130 --> 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 --> 00:07:59.106 And as mariela dibiase has said,

NOTE Confidence: 0.901125013828278

00:07:59.110 --> 00:08:01.150 we get we precipitate both somatic

NOTE Confidence: 0.901125013828278

00:08:01.150 --> 00:08:03.444 and affect if symptoms of withdrawal

NOTE Confidence: 0.901125013828278

00:08:03.444 --> 00:08:05.619 during acute during acute abstinence,

NOTE Confidence: 0.901125013828278

00:08:05.620 --> 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 --> 00:08:11.158 we've all been around folks who just

NOTE Confidence: 0.901125013828278

00:08:11.158 --> 00:08:13.328 quit smoking and then particularly

NOTE Confidence: 0.901125013828278

00:08:13.328 --> 00:08:15.016 fun to be around.

NOTE Confidence: 0.901125013828278

00:08:15.020 --> 00:08:17.974 But it's those negative affect of symptoms

NOTE Confidence: 0.901125013828278

00:08:17.974 --> 00:08:20.959 that account for can you see my pointer?

NOTE Confidence: 0.901125013828278

00:08:20.960 --> 00:08:22.148 Is that possible?

NOTE Confidence: 0.901125013828278  
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 --> 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 --> 00:08:31.490 so negative reinforcement and  
NOTE Confidence: 0.901125013828278  
00:08:31.490 --> 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 --> 00:08:38.790 we've known that for quite some time.  
NOTE Confidence: 0.901125013828278  
00:08:38.790 --> 00:08:39.672 So given this,  
NOTE Confidence: 0.901125013828278  
00:08:39.672 --> 00:08:41.730 why are we still so bad at  
NOTE Confidence: 0.901125013828278  
00:08:41.803 --> 00:08:44.167 treatment and treatment outcomes?  
NOTE Confidence: 0.901125013828278  
00:08:44.170 --> 00:08:46.697 And so the position that I'm going  
NOTE Confidence: 0.901125013828278  
00:08:46.697 --> 00:08:49.455 to layout for you today is that  
NOTE Confidence: 0.901125013828278  
00:08:49.455 --> 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 --> 00:08:55.768 it's been missing traditionally  
NOTE Confidence: 0.901125013828278

00:08:55.768 --> 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 --> 00:09:02.215 clinically validated biomarkers,  
NOTE Confidence: 0.901125013828278

00:09:02.215 --> 00:09:03.370 we really can't.  
NOTE Confidence: 0.901125013828278

00:09:03.370 --> 00:09:06.058 That this is sort of my coals  
NOTE Confidence: 0.901125013828278

00:09:06.058 --> 00:09:07.210 to Newcastle slide.  
NOTE Confidence: 0.901125013828278

00:09:07.210 --> 00:09:09.140 We can't really objectively assess.  
NOTE Confidence: 0.901125013828278

00:09:09.140 --> 00:09:11.513 The severity of the level of dependence  
NOTE Confidence: 0.901125013828278

00:09:11.513 --> 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 --> 00:09:16.790 or personalized medicine were not  
NOTE Confidence: 0.901125013828278

00:09:16.846 --> 00:09:19.054 able to assess drug development in  
NOTE Confidence: 0.901125013828278

00:09:19.054 --> 00:09:20.526 treatment interventions of objectively,  
NOTE Confidence: 0.901125013828278

00:09:20.530 --> 00:09:22.770 we can't really look at the efficacy  
NOTE Confidence: 0.901125013828278

00:09:22.770 --> 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 --> 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 --> 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 --> 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 --> 00:09:47.870 I may upset a few people.  
NOTE Confidence: 0.901125013828278  
00:09:47.870 --> 00:09:50.126 What is it that we currently  
NOTE Confidence: 0.901125013828278  
00:09:50.126 --> 00:09:53.467 doing an I took this this quote I  
NOTE Confidence: 0.901125013828278  
00:09:53.467 --> 00:09:56.083 can't remember which paper it is.  
NOTE Confidence: 0.901125013828278  
00:09:56.090 --> 00:09:58.680 It doesn't matter because we all really  
NOTE Confidence: 0.901125013828278  
00:09:58.680 --> 00:10:02.260 say this in the first paragraph about papers,  
NOTE Confidence: 0.901125013828278  
00:10:02.260 --> 00:10:04.315 prominent theories of addiction posit  
NOTE Confidence: 0.901125013828278



00:10:04.315 --> 00:10:06.370 that deficits in prefrontal mode,  
NOTE Confidence: 0.901125013828278

00:10:06.370 --> 00:10:07.190 cortical function,  
NOTE Confidence: 0.901125013828278

00:10:07.190 --> 00:10:08.420 impaired cognitive control,  
NOTE Confidence: 0.901125013828278

00:10:08.420 --> 00:10:09.653 inhibitory prepotent behaviors,  
NOTE Confidence: 0.901125013828278

00:10:09.653 --> 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 --> 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 --> 00:10:16.740 we all say this in our first paragraph,  
NOTE Confidence: 0.901125013828278

00:10:16.740 --> 00:10:19.684 but when we tried to develop new treatments,  
NOTE Confidence: 0.901125013828278

00:10:19.690 --> 00:10:21.500 are basic working hypothesis is  
NOTE Confidence: 0.901125013828278

00:10:21.500 --> 00:10:23.310 something like this better pharmaco  
NOTE Confidence: 0.901125013828278

00:10:23.370 --> 00:10:25.395 therapies require more specific and  
NOTE Confidence: 0.901125013828278

00:10:25.395 --> 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 --> 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 --> 00:10:35.172 Indeed,  
NOTE Confidence: 0.901125013828278  
00:10:35.172 --> 00:10:37.220 perhaps universe eviction and  
NOTE Confidence: 0.901125013828278  
00:10:37.220 --> 00:10:39.780 this treatment based hypothesis is  
NOTE Confidence: 0.901125013828278  
00:10:39.854 --> 00:10:41.914 coming from the really tremendous  
NOTE Confidence: 0.901125013828278  
00:10:41.914 --> 00:10:43.974 progress that we made in  
NOTE Confidence: 0.847423493862152  
00:10:44.052 --> 00:10:46.566 a cellular and molecular basis in  
NOTE Confidence: 0.847423493862152  
00:10:46.566 --> 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 --> 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 --> 00:10:58.214 unacceptably high for our patients.  
NOTE Confidence: 0.847423493862152  
00:10:58.220 --> 00:11:00.028 Neither agonist or antagonist  
NOTE Confidence: 0.847423493862152  
00:11:00.028 --> 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 --> 00:11:05.935 some agonists and partial agonist.  
NOTE Confidence: 0.847423493862152

00:11:05.940 --> 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 --> 00:11:13.590 some for extended periods of time,  
NOTE Confidence: 0.847423493862152

00:11:13.590 --> 00:11:16.140 for example methadone across people,  
NOTE Confidence: 0.847423493862152

00:11:16.140 --> 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 --> 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 --> 00:11:29.946 And then, even if it did,  
NOTE Confidence: 0.847423493862152

00:11:29.950 --> 00:11:32.372 is is reducing drug intake and reversing  
NOTE Confidence: 0.847423493862152

00:11:32.372 --> 00:11:34.099 addiction really the same thing?  
NOTE Confidence: 0.847423493862152

00:11:34.100 --> 00:11:37.088 Can we treat them with the  
NOTE Confidence: 0.847423493862152

00:11:37.088 --> 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 --> 00:11:41.650 this hypothesis assumes that the absence of  
NOTE Confidence: 0.847423493862152  
00:11:41.710 --> 00:11:44.125 behavior reflects the absence of the disease,  
NOTE Confidence: 0.847423493862152  
00:11:44.130 --> 00:11:44.848 and again,  
NOTE Confidence: 0.847423493862152  
00:11:44.848 --> 00:11:47.361 this group knows that that's not not  
NOTE Confidence: 0.847423493862152  
00:11:47.361 --> 00:11:49.859 even close to the imagery sentence.  
NOTE Confidence: 0.847423493862152  
00:11:49.860 --> 00:11:52.709 So what might an alternative hypothesis be?  
NOTE Confidence: 0.847423493862152  
00:11:52.710 --> 00:11:53.124 Well,  
NOTE Confidence: 0.847423493862152  
00:11:53.124 --> 00:11:55.608 since indeed substance use disorder is  
NOTE Confidence: 0.847423493862152  
00:11:55.608 --> 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 --> 00:12:02.352 dysregulated 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 --> 00:12:06.750 As I'll show you later.  
NOTE Confidence: 0.847423493862152  
00:12:06.750 --> 00:12:09.459 Maybe rather than or at least in  
NOTE Confidence: 0.847423493862152

00:12:09.459 --> 00:12:12.640 addition to a better molecular level.  
NOTE Confidence: 0.847423493862152

00:12:12.640 --> 00:12:13.402 Medicinal chemistry,  
NOTE Confidence: 0.847423493862152

00:12:13.402 --> 00:12:16.450 we really need to think about a systems  
NOTE Confidence: 0.847423493862152

00:12:16.516 --> 00:12:18.472 level neuro biological treatment  
NOTE Confidence: 0.847423493862152

00:12:18.472 --> 00:12:20.917 strategy that takes into consideration  
NOTE Confidence: 0.847423493862152

00:12:20.917 --> 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 --> 00:12:28.453 with a cartoon reminding us that  
NOTE Confidence: 0.847423493862152

00:12:28.453 --> 00:12:30.763 addiction is not a static disease,  
NOTE Confidence: 0.847423493862152

00:12:30.770 --> 00:12:32.230 but rather a cyclotron.  
NOTE Confidence: 0.847423493862152

00:12:32.230 --> 00:12:34.055 And while there's some potentially  
NOTE Confidence: 0.847423493862152

00:12:34.055 --> 00:12:35.810 some issues with this model,  
NOTE Confidence: 0.847423493862152

00:12:35.810 --> 00:12:38.690 I think it's a good one for touristically.  
NOTE Confidence: 0.847423493862152

00:12:38.690 --> 00:12:42.036 Think about what we're what we're actually  
NOTE Confidence: 0.847423493862152

00:12:42.036 --> 00:12:46.336 doing when a patient presents in front of us.

NOTE Confidence: 0.847423493862152

00:12:46.340 --> 00:12:47.872 And this binge intoxication phase,

NOTE Confidence: 0.847423493862152

00:12:47.872 --> 00:12:49.930 the phase that we think about it,

NOTE Confidence: 0.847423493862152

00:12:49.930 --> 00:12:51.897 certainly with our animal models of increases

NOTE Confidence: 0.847423493862152

00:12:51.897 --> 00:12:53.818 in dopamine in the nucleus accumbens,

NOTE Confidence: 0.847423493862152

00:12:53.820 --> 00:12:54.416 is really,

NOTE Confidence: 0.847423493862152

00:12:54.416 --> 00:12:55.906 if you think about it,

NOTE Confidence: 0.847423493862152

00:12:55.910 --> 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 --> 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 --> 00:13:17.230 It's now in a number of

NOTE Confidence: 0.840475976467133

00:13:17.230 --> 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 --> 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 --> 00:13:27.992 How could pharmacologic blockade  
NOTE Confidence: 0.840475976467133

00:13:27.992 --> 00:13:30.470 or or agonist replacement of a  
NOTE Confidence: 0.840475976467133

00:13:30.541 --> 00:13:32.801 sneeze or critical limbic dopamine  
NOTE Confidence: 0.840475976467133

00:13:32.801 --> 00:13:35.061 system really reverse the disease?  
NOTE Confidence: 0.840475976467133

00:13:35.070 --> 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 --> 00:13:40.343 a better silver bullet.  
NOTE Confidence: 0.840475976467133

00:13:40.350 --> 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 --> 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 --> 00:13:51.804 individual as well as the trait of  
NOTE Confidence: 0.840475976467133

00:13:51.804 --> 00:13:54.219 addiction that they presented with.  
NOTE Confidence: 0.840475976467133

00:13:54.220 --> 00:13:56.767 So the rest of the talk is going to  
NOTE Confidence: 0.840475976467133

00:13:56.767 --> 00:13:59.222 be organized around that theme of  
NOTE Confidence: 0.840475976467133

00:13:59.222 --> 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 --> 00:14:05.438 the severity of addiction as well  
NOTE Confidence: 0.840475976467133  
00:14:05.438 --> 00:14:07.417 as the acute transition traits  
NOTE Confidence: 0.840475976467133  
00:14:07.417 --> 00:14:09.763 that we see during acute and  
NOTE Confidence: 0.840475976467133  
00:14:09.834 --> 00:14:11.928 long-term long-term accidents.  
NOTE Confidence: 0.840475976467133  
00:14:11.930 --> 00:14:14.254 And so I would posit that more  
NOTE Confidence: 0.840475976467133  
00:14:14.254 --> 00:14:16.189 treatment outcomes may be related to,  
NOTE Confidence: 0.840475976467133  
00:14:16.190 --> 00:14:17.410 at least in part,  
NOTE Confidence: 0.840475976467133  
00:14:17.410 --> 00:14:19.240 to focus on the results alleviating  
NOTE Confidence: 0.840475976467133  
00:14:19.297 --> 00:14:20.677 withdrawal rather than focusing  
NOTE Confidence: 0.840475976467133  
00:14:20.677 --> 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 --> 00:14:27.126 And so we went into this a number  
NOTE Confidence: 0.840475976467133  
00:14:27.126 --> 00:14:28.891 of years ago with the hypothesis  
NOTE Confidence: 0.840475976467133  
00:14:28.891 --> 00:14:30.476 that addiction severity is linked  
NOTE Confidence: 0.840475976467133



00:14:30.476 --> 00:14:32.433 to activity within and between the  
NOTE Confidence: 0.840475976467133

00:14:32.433 --> 00:14:34.940 anterior singular and one of its players.  
NOTE Confidence: 0.840475976467133

00:14:34.940 --> 00:14:37.298 This trail. Well, why the singular?  
NOTE Confidence: 0.840475976467133

00:14:37.298 --> 00:14:38.928 Where did that come from?  
NOTE Confidence: 0.840475976467133

00:14:38.930 --> 00:14:41.247 And there's a number of pieces of  
NOTE Confidence: 0.840475976467133

00:14:41.247 --> 00:14:43.315 literature that I'm putting up here  
NOTE Confidence: 0.840475976467133

00:14:43.315 --> 00:14:45.674 that justified for us time that single  
NOTE Confidence: 0.840475976467133

00:14:45.741 --> 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 --> 00:14:55.939 And when we get going in this,  
NOTE Confidence: 0.840475976467133

00:14:55.940 --> 00:14:57.775 this was before any knowledge  
NOTE Confidence: 0.840475976467133

00:14:57.775 --> 00:15:00.029 of large scale networks and the  
NOTE Confidence: 0.840475976467133

00:15:00.029 --> 00:15:01.769 salience network that I'll be  
NOTE Confidence: 0.840475976467133

00:15:01.769 --> 00:15:03.809 talking to you about later on.

NOTE Confidence: 0.840475976467133  
00:15:03.810 --> 00:15:06.210 So let me put this into a bit of a  
NOTE Confidence: 0.840475976467133  
00:15:06.283 --> 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 --> 00:15:15.552 just to emphasize that these cortical  
NOTE Confidence: 0.840475976467133  
00:15:15.552 --> 00:15:17.307 striatal loops that Suzanne is  
NOTE Confidence: 0.840475976467133  
00:15:17.307 --> 00:15:19.077 beautifully elucidated over the years,  
NOTE Confidence: 0.840475976467133  
00:15:19.080 --> 00:15:21.824 let me put some function on top of  
NOTE Confidence: 0.840475976467133  
00:15:21.824 --> 00:15:24.626 that when we think about the VM Pfc,  
NOTE Confidence: 0.840475976467133  
00:15:24.630 --> 00:15:26.370 we think about value, reward,  
NOTE Confidence: 0.840475976467133  
00:15:26.370 --> 00:15:28.446 and decision making in the OSC,  
NOTE Confidence: 0.840475976467133  
00:15:28.450 --> 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 --> 00:15:34.528 and ever monitoring and every detection.  
NOTE Confidence: 0.840475976467133  
00:15:34.530 --> 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 --> 00:15:41.587 I think we have to only talk about addiction.  
NOTE Confidence: 0.840475976467133

00:15:41.590 --> 00:15:42.652 Think about attention.  
NOTE Confidence: 0.840475976467133

00:15:42.652 --> 00:15:43.360 Intentional processing.  
NOTE Confidence: 0.840475976467133

00:15:43.360 --> 00:15:45.265 Basically in the posterior parietal  
NOTE Confidence: 0.840475976467133

00:15:45.265 --> 00:15:48.203 cortex and one of the things that we've  
NOTE Confidence: 0.840475976467133

00:15:48.203 --> 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 --> 00:15:55.769 on top of these regions in these  
NOTE Confidence: 0.840475976467133

00:15:55.769 --> 00:15:57.634 large scale brain networks that  
NOTE Confidence: 0.840475976467133

00:15:57.634 --> 00:16:00.402 seem to be able to explain a lot  
NOTE Confidence: 0.840475976467133

00:16:00.402 --> 00:16:02.062 of the nurse psychiatric symptoms  
NOTE Confidence: 0.840475976467133

00:16:02.062 --> 00:16:04.174 that that will be talking about,  
NOTE Confidence: 0.840475976467133

00:16:04.180 --> 00:16:06.478 at least from the perspective of.  
NOTE Confidence: 0.840475976467133

00:16:06.480 --> 00:16:08.530 Of addiction and the other  
NOTE Confidence: 0.840475976467133

00:16:08.530 --> 00:16:10.580 thing I wanted to point

NOTE Confidence: 0.84111076593399

00:16:10.662 --> 00:16:13.448 out is that many of these players,

NOTE Confidence: 0.84111076593399

00:16:13.450 --> 00:16:15.526 most of these players that I've

NOTE Confidence: 0.84111076593399

00:16:15.526 --> 00:16:17.453 just highlighted are just ripe

NOTE Confidence: 0.84111076593399

00:16:17.453 --> 00:16:19.345 with nicotinic receptor receptors

NOTE Confidence: 0.84111076593399

00:16:19.345 --> 00:16:21.237 and various receptors subtypes.

NOTE Confidence: 0.84111076593399

00:16:21.240 --> 00:16:23.568 And it's not surprising therefore that

NOTE Confidence: 0.84111076593399

00:16:23.568 --> 00:16:26.896 a lot of what we're seeing with tobacco

NOTE Confidence: 0.84111076593399

00:16:26.896 --> 00:16:30.047 use disorder is being biased by many

NOTE Confidence: 0.84111076593399

00:16:30.047 --> 00:16:32.657 many systems throughout the Neuraxis.

NOTE Confidence: 0.84111076593399

00:16:32.660 --> 00:16:35.873 OK, so with that introduction we began

NOTE Confidence: 0.84111076593399

00:16:35.873 --> 00:16:39.770 this sort of adventure 10 ish years ago.

NOTE Confidence: 0.84111076593399

00:16:39.770 --> 00:16:42.392 Now with this hypothesis that the

NOTE Confidence: 0.84111076593399

00:16:42.392 --> 00:16:44.980 singular was involved in addiction,

NOTE Confidence: 0.84111076593399

00:16:44.980 --> 00:16:48.298 and So what we did very simply,

NOTE Confidence: 0.84111076593399

00:16:48.300 --> 00:16:50.248 this is, I believe,

NOTE Confidence: 0.84111076593399

00:16:50.248 --> 00:16:53.520 the first wrestling state study done in,  
NOTE Confidence: 0.84111076593399

00:16:53.520 --> 00:16:55.734 and certainly nicotine a number of  
NOTE Confidence: 0.84111076593399

00:16:55.734 --> 00:16:59.124 years ago was we divided the singular  
NOTE Confidence: 0.84111076593399

00:16:59.124 --> 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 --> 00:17:05.130 Answer if you Post Area 1 middle  
NOTE Confidence: 0.84111076593399

00:17:05.215 --> 00:17:07.189 singular area bilaterally,  
NOTE Confidence: 0.84111076593399

00:17:07.190 --> 00:17:09.818 so 14 areas each was a seed and we  
NOTE Confidence: 0.84111076593399

00:17:09.818 --> 00:17:12.690 did a whole brain regression against  
NOTE Confidence: 0.84111076593399

00:17:12.690 --> 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 --> 00:17:20.948 what we identified was a single area.  
NOTE Confidence: 0.84111076593399

00:17:20.948 --> 00:17:22.978 Within the the ventral stratum,  
NOTE Confidence: 0.84111076593399

00:17:22.980 --> 00:17:24.972 what was interesting when we looked  
NOTE Confidence: 0.84111076593399

00:17:24.972 --> 00:17:28.038 at this data is that the that the  
NOTE Confidence: 0.84111076593399

00:17:28.038 --> 00:17:30.123 strength of this circuit negatively

NOTE Confidence: 0.84111076593399

00:17:30.123 --> 00:17:32.344 correlated with with the nicotine

NOTE Confidence: 0.84111076593399

00:17:32.344 --> 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 --> 00:17:39.235 when we scan these individuals

NOTE Confidence: 0.84111076593399

00:17:39.235 --> 00:17:41.690 on an off a nicotine Patch,

NOTE Confidence: 0.84111076593399

00:17:41.690 --> 00:17:45.263 there was no change to the to the circuit.

NOTE Confidence: 0.84111076593399

00:17:45.270 --> 00:17:47.395 These dime diamonds and triangles

NOTE Confidence: 0.84111076593399

00:17:47.395 --> 00:17:50.369 indicate a single subject scan on two

NOTE Confidence: 0.84111076593399

00:17:50.369 --> 00:17:52.715 different occasions on and off nicotine

NOTE Confidence: 0.84111076593399

00:17:52.715 --> 00:17:54.900 off nicotine on and off nicotine.

NOTE Confidence: 0.84111076593399

00:17:54.900 --> 00:17:57.329 And so this circuit appeared to be

NOTE Confidence: 0.84111076593399

00:17:57.329 --> 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 --> 00:18:10.760 Big the opera 5 polymorphism was

NOTE Confidence: 0.885979473590851

00:18:10.878 --> 00:18:14.988 becoming recognized as an important.  
NOTE Confidence: 0.885979473590851

00:18:14.990 --> 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 --> 00:18:22.669 see what its role was in this circuit  
NOTE Confidence: 0.885979473590851

00:18:22.669 --> 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 --> 00:18:30.260 We did essentially the same experiment.  
NOTE Confidence: 0.885979473590851

00:18:30.260 --> 00:18:32.703 Now starting only the dorsal ACC because  
NOTE Confidence: 0.885979473590851

00:18:32.703 --> 00:18:35.484 we knew that was sort of the answer and  
NOTE Confidence: 0.885979473590851

00:18:35.484 --> 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 --> 00:18:45.548 identified the same circuit.  
NOTE Confidence: 0.885979473590851

00:18:45.550 --> 00:18:48.854 With the same relationship once one now with  
NOTE Confidence: 0.885979473590851

00:18:48.854 --> 00:18:51.819 the phenotype and one against the genotype.

NOTE Confidence: 0.885979473590851

00:18:51.820 --> 00:18:54.524 And we thought these early data supported a

NOTE Confidence: 0.885979473590851

00:18:54.524 --> 00:18:57.619 role for the dorsal ACC and Striatum in trade,

NOTE Confidence: 0.885979473590851

00:18:57.620 --> 00:18:59.424 but not state dependence.

NOTE Confidence: 0.885979473590851

00:18:59.424 --> 00:19:02.515 So the next logical question was, well,

NOTE Confidence: 0.885979473590851

00:19:02.515 --> 00:19:04.825 are there pre dispositional differences in

NOTE Confidence: 0.885979473590851

00:19:04.825 --> 00:19:07.169 these circuits that potentiates smoking?

NOTE Confidence: 0.885979473590851

00:19:07.170 --> 00:19:10.159 Or does the smoking behavior over the

NOTE Confidence: 0.885979473590851

00:19:10.159 --> 00:19:13.667 over period of time change these service?

NOTE Confidence: 0.885979473590851

00:19:13.670 --> 00:19:15.534 Well, it's difficult to do in humans to

NOTE Confidence: 0.885979473590851

00:19:15.534 --> 00:19:17.559 do these long-term longitudinal studies,

NOTE Confidence: 0.885979473590851

00:19:17.560 --> 00:19:19.954 and it may be that Abcd in a few

NOTE Confidence: 0.885979473590851

00:19:19.954 --> 00:19:22.040 years will give us this answer,

NOTE Confidence: 0.885979473590851

00:19:22.040 --> 00:19:24.304 but an approach that we took at the

NOTE Confidence: 0.885979473590851

00:19:24.304 --> 00:19:26.489 time was at a conference back to

NOTE Confidence: 0.885979473590851

00:19:26.489 --> 00:19:28.976 remember when we used to be able to

NOTE Confidence: 0.885979473590851



00:19:28.976 --> 00:19:31.006 go to conferences and I was having  
NOTE Confidence: 0.885979473590851

00:19:31.010 --> 00:19:32.550 a conversation with Rachel Tynedale  
NOTE Confidence: 0.885979473590851

00:19:32.550 --> 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 --> 00:19:37.886 which is a cytochrome p-450 liver enzyme.  
NOTE Confidence: 0.885979473590851

00:19:37.890 --> 00:19:39.744 And it's the main enzyme that  
NOTE Confidence: 0.885979473590851

00:19:39.744 --> 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 --> 00:19:45.076 'cause I'm not a little guy.  
NOTE Confidence: 0.885979473590851

00:19:45.080 --> 00:19:48.280 But until I started to take a look that a  
NOTE Confidence: 0.885979473590851

00:19:48.367 --> 00:19:51.415 the same time is genetically regulated,  
NOTE Confidence: 0.885979473590851

00:19:51.420 --> 00:19:53.395 is 26 different isozymes or  
NOTE Confidence: 0.885979473590851

00:19:53.395 --> 00:19:54.975 so and and Rachel,  
NOTE Confidence: 0.885979473590851

00:19:54.980 --> 00:19:58.373 it's lab has been able to provide people or  
NOTE Confidence: 0.885979473590851

00:19:58.373 --> 00:20:00.919 categorize people into those with normal,

NOTE Confidence: 0.885979473590851  
00:20:00.920 --> 00:20:02.732 intermediate and slow metabolic  
NOTE Confidence: 0.885979473590851  
00:20:02.732 --> 00:20:05.450 systems or nicotine and what became  
NOTE Confidence: 0.885979473590851  
00:20:05.518 --> 00:20:07.597 interesting to me as a brain guy  
NOTE Confidence: 0.885979473590851  
00:20:07.597 --> 00:20:10.285 is it looks like these that this  
NOTE Confidence: 0.885979473590851  
00:20:10.285 --> 00:20:12.009 liver enzyme changes behavior.  
NOTE Confidence: 0.885979473590851  
00:20:12.010 --> 00:20:13.590 Individuals that were better  
NOTE Confidence: 0.885979473590851  
00:20:13.590 --> 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 --> 00:20:19.950 And it can predict treatment matching out,  
NOTE Confidence: 0.885979473590851  
00:20:19.950 --> 00:20:21.540 so this became rather interesting  
NOTE Confidence: 0.885979473590851  
00:20:21.540 --> 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 --> 00:20:27.855 shapes brain circuits differentially  
NOTE Confidence: 0.885979473590851  
00:20:27.855 --> 00:20:30.130 in smokers and non smokers.  
NOTE Confidence: 0.885979473590851  
00:20:30.130 --> 00:20:32.596 And would it offer alter brain  
NOTE Confidence: 0.885979473590851

00:20:32.596 --> 00:20:35.652 connectivity and so we did that that  
NOTE Confidence: 0.885979473590851

00:20:35.652 --> 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 --> 00:20:44.372 And perhaps the most important and  
NOTE Confidence: 0.885979473590851

00:20:44.372 --> 00:20:46.580 interesting contrasts that we did  
NOTE Confidence: 0.885979473590851

00:20:46.580 --> 00:20:49.280 looking at this data was a gene by was  
NOTE Confidence: 0.885979473590851

00:20:49.356 --> 00:20:51.856 it gene by environment interaction?  
NOTE Confidence: 0.885979473590851

00:20:51.860 --> 00:20:53.900 So three genotyped by smoking  
NOTE Confidence: 0.885979473590851

00:20:53.900 --> 00:20:55.124 versus non smoking.  
NOTE Confidence: 0.885979473590851

00:20:55.130 --> 00:20:58.050 And in this analysis we didn't want to  
NOTE Confidence: 0.885979473590851

00:20:58.050 --> 00:21:01.097 have a hypothesis of looking under the  
NOTE Confidence: 0.885979473590851

00:21:01.097 --> 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 --> 00:21:09.640 functional connectivity strength and  
NOTE Confidence: 0.885979473590851

00:21:09.640 --> 00:21:12.073 basically this analysis allows you  
NOTE Confidence: 0.885979473590851

00:21:12.073 --> 00:21:14.838 to identify the hubs in the brain.

NOTE Confidence: 0.885979473590851  
00:21:14.840 --> 00:21:17.310 The areas of highest ugliness  
NOTE Confidence: 0.885979473590851  
00:21:17.310 --> 00:21:19.286 that interconnect rain errors,  
NOTE Confidence: 0.797232389450073  
00:21:19.290 --> 00:21:23.727 and when we did that whole brain data driven,  
NOTE Confidence: 0.797232389450073  
00:21:23.730 --> 00:21:26.845 we identified two areas defense  
NOTE Confidence: 0.797232389450073  
00:21:26.845 --> 00:21:29.960 Australian in the dorsal ACC.  
NOTE Confidence: 0.797232389450073  
00:21:29.960 --> 00:21:31.994 We extracted those data and plotted  
NOTE Confidence: 0.797232389450073  
00:21:31.994 --> 00:21:34.543 them to see what was driving this  
NOTE Confidence: 0.797232389450073  
00:21:34.543 --> 00:21:36.418 relationship and what it was.  
NOTE Confidence: 0.797232389450073  
00:21:36.420 --> 00:21:38.844 What was driving the relationship was  
NOTE Confidence: 0.797232389450073  
00:21:38.844 --> 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 --> 00:21:51.825 And interesting enough that SES  
NOTE Confidence: 0.797232389450073  
00:21:51.825 --> 00:21:54.750 level that happiness level also  
NOTE Confidence: 0.797232389450073

00:21:54.846 --> 00:21:57.866 predicted or correlated very nicely  
NOTE Confidence: 0.797232389450073

00:21:57.866 --> 00:22:01.685 with the individuals level of trade  
NOTE Confidence: 0.797232389450073

00:22:01.685 --> 00:22:04.509 dependence severity very consistent  
NOTE Confidence: 0.797232389450073

00:22:04.509 --> 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 --> 00:22:14.144 So, OK, we've identified a couple of hubs.  
NOTE Confidence: 0.797232389450073

00:22:14.150 --> 00:22:15.860 The next question was, well,  
NOTE Confidence: 0.797232389450073

00:22:15.860 --> 00:22:17.912 what are the tracks into these  
NOTE Confidence: 0.797232389450073

00:22:17.912 --> 00:22:18.596 train stations?  
NOTE Confidence: 0.797232389450073

00:22:18.600 --> 00:22:21.365 What are the circus that might be  
NOTE Confidence: 0.797232389450073

00:22:21.365 --> 00:22:23.254 potentially biasing these hearts and  
NOTE Confidence: 0.797232389450073

00:22:23.254 --> 00:22:25.774 one way to approach that was then to  
NOTE Confidence: 0.797232389450073

00:22:25.842 --> 00:22:28.250 take each of these two areas and use  
NOTE Confidence: 0.797232389450073

00:22:28.250 --> 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 --> 00:22:34.330 And when we did that,

NOTE Confidence: 0.797232389450073  
00:22:34.330 --> 00:22:37.058 we identify from the dorsal ACC the insula,  
NOTE Confidence: 0.797232389450073  
00:22:37.060 --> 00:22:39.508 as well as the ACC and from the bench  
NOTE Confidence: 0.797232389450073  
00:22:39.508 --> 00:22:41.966 and stratum the insular and as as  
NOTE Confidence: 0.797232389450073  
00:22:41.966 --> 00:22:44.310 Regina mentioned in the introduction.  
NOTE Confidence: 0.797232389450073  
00:22:44.310 --> 00:22:46.417 This is become one of the main  
NOTE Confidence: 0.797232389450073  
00:22:46.417 --> 00:22:47.750 foci in the labs,  
NOTE Confidence: 0.797232389450073  
00:22:47.750 --> 00:22:50.306 and I emphasize insulin here because  
NOTE Confidence: 0.797232389450073  
00:22:50.306 --> 00:22:53.554 I'm going to come back to this in a  
NOTE Confidence: 0.797232389450073  
00:22:53.554 --> 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 --> 00:22:58.856 so this is pretty cool that that  
NOTE Confidence: 0.797232389450073  
00:22:58.856 --> 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 --> 00:23:04.239 that traded diction severity.  
NOTE Confidence: 0.797232389450073  
00:23:04.240 --> 00:23:06.774 Well, that was nice, but who cares?  
NOTE Confidence: 0.797232389450073

00:23:06.780 --> 00:23:09.006 Are there any functional consequences to  
NOTE Confidence: 0.797232389450073

00:23:09.006 --> 00:23:11.478 having changed in Hoppiness in these smokers?  
NOTE Confidence: 0.797232389450073

00:23:11.480 --> 00:23:13.936 So the way one way we approach that  
NOTE Confidence: 0.797232389450073

00:23:13.936 --> 00:23:16.744 was we needed to probe both eventual  
NOTE Confidence: 0.797232389450073

00:23:16.744 --> 00:23:19.450 stratum and the door sellers to see,  
NOTE Confidence: 0.797232389450073

00:23:19.450 --> 00:23:21.676 and perhaps the best way to  
NOTE Confidence: 0.797232389450073

00:23:21.676 --> 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 --> 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 --> 00:23:30.395 Where we analyzed this data,  
NOTE Confidence: 0.797232389450073

00:23:30.400 --> 00:23:32.818 just simply a simple contrast gains  
NOTE Confidence: 0.797232389450073

00:23:32.818 --> 00:23:35.144 greater than neutral and we didn't  
NOTE Confidence: 0.797232389450073

00:23:35.144 --> 00:23:37.076 have enough subjects to look at  
NOTE Confidence: 0.797232389450073

00:23:37.076 --> 00:23:39.340 it and intermediate phenotype.  
NOTE Confidence: 0.797232389450073

00:23:39.340 --> 00:23:42.580 So only the normal and the slow metabolizers.

NOTE Confidence: 0.797232389450073

00:23:42.580 --> 00:23:45.016 And when we plotted these data,

NOTE Confidence: 0.797232389450073

00:23:45.020 --> 00:23:47.420 we notice that when individuals

NOTE Confidence: 0.797232389450073

00:23:47.420 --> 00:23:48.380 were accident.

NOTE Confidence: 0.797232389450073

00:23:48.380 --> 00:23:50.320 This slow metabolizers just

NOTE Confidence: 0.797232389450073

00:23:50.320 --> 00:23:52.745 couldn't couldn't create enough of

NOTE Confidence: 0.797232389450073

00:23:52.745 --> 00:23:55.659 a signal in the ventral striatum.

NOTE Confidence: 0.797232389450073

00:23:55.660 --> 00:23:59.540 However, when we gave them a nicotine Patch,

NOTE Confidence: 0.797232389450073

00:23:59.540 --> 00:24:02.648 both the slow metabolizers as well as

NOTE Confidence: 0.797232389450073

00:24:02.648 --> 00:24:05.620 frankly the slow metabolizers and non

NOTE Confidence: 0.797232389450073

00:24:05.620 --> 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 --> 00:24:12.370 they're performing a reward chest,

NOTE Confidence: 0.797232389450073

00:24:12.370 --> 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 --> 00:24:17.668 is in fact a cognitive enhancer,

NOTE Confidence: 0.797232389450073



00:24:17.670 --> 00:24:20.078 and I'll show you some data in that  
NOTE Confidence: 0.797232389450073

00:24:20.078 --> 00:24:22.975 in non smokers as well as we go along.  
NOTE Confidence: 0.797232389450073

00:24:22.980 --> 00:24:25.157 Or what about probing the dorsal ACC?  
NOTE Confidence: 0.797232389450073

00:24:25.160 --> 00:24:28.280 A great way to do that is with a go.  
NOTE Confidence: 0.797232389450073

00:24:28.280 --> 00:24:30.830 No go type of the task and when we did  
NOTE Confidence: 0.797232389450073

00:24:30.897 --> 00:24:33.102 that we saw exactly the same answer  
NOTE Confidence: 0.797232389450073

00:24:33.102 --> 00:24:35.459 both in non smokers and smokers.  
NOTE Confidence: 0.797232389450073

00:24:35.460 --> 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 --> 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 --> 00:24:44.348 in nicotine absolute state.  
NOTE Confidence: 0.820130944252014

00:24:44.350 --> 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 --> 00:24:52.361 in nicotine concentrations in the

NOTE Confidence: 0.820130944252014

00:24:52.361 --> 00:24:54.436 brain so slow metabolizers presumably

NOTE Confidence: 0.820130944252014

00:24:54.436 --> 00:24:56.682 would have more nicotine off for

NOTE Confidence: 0.820130944252014

00:24:56.682 --> 00:24:59.270 longer periods of time in their brain,

NOTE Confidence: 0.820130944252014

00:24:59.270 --> 00:25:01.460 and this induced these circuit changes.

NOTE Confidence: 0.820130944252014

00:25:01.460 --> 00:25:03.734 That's the hypothesis coming in from

NOTE Confidence: 0.820130944252014

00:25:03.734 --> 00:25:06.341 this study and the same circuit seem

NOTE Confidence: 0.820130944252014

00:25:06.341 --> 00:25:08.707 to change both at rest and when

NOTE Confidence: 0.820130944252014

00:25:08.779 --> 00:25:10.915 the individual is doing a task,

NOTE Confidence: 0.820130944252014

00:25:10.920 --> 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 --> 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 --> 00:25:20.378 Are less responsive than to the

NOTE Confidence: 0.820130944252014

00:25:20.378 --> 00:25:23.889 anticipation of veins less responsive to.

NOTE Confidence: 0.820130944252014

00:25:23.890 --> 00:25:25.342 To to to errors,

NOTE Confidence: 0.820130944252014

00:25:25.342 --> 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 --> 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 --> 00:25:35.414 another way we can see if these  
NOTE Confidence: 0.820130944252014

00:25:35.414 --> 00:25:38.198 circuits are pre dispositional is to  
NOTE Confidence: 0.820130944252014

00:25:38.198 --> 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 --> 00:25:45.900 preclinical models are very good at this,  
NOTE Confidence: 0.820130944252014

00:25:45.900 --> 00:25:48.860 and this was a challenge that Robin Healey,  
NOTE Confidence: 0.820130944252014

00:25:48.860 --> 00:25:50.710 a postdoc in the lab,  
NOTE Confidence: 0.820130944252014

00:25:50.710 --> 00:25:51.982 took on just recently,  
NOTE Confidence: 0.820130944252014

00:25:51.982 --> 00:25:54.595 and what she did was she made a  
NOTE Confidence: 0.820130944252014

00:25:54.595 --> 00:25:56.503 group of ratchet or three groups  
NOTE Confidence: 0.820130944252014

00:25:56.503 --> 00:25:58.588 of rats dependent two different  
NOTE Confidence: 0.820130944252014

00:25:58.588 --> 00:26:01.348 doses and doses Saline and implanted

NOTE Confidence: 0.820130944252014  
00:26:01.348 --> 00:26:03.294 osmotic Minipump's for two weeks,  
NOTE Confidence: 0.820130944252014  
00:26:03.294 --> 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 --> 00:26:09.580 of Force Absolutes.  
NOTE Confidence: 0.820130944252014  
00:26:09.580 --> 00:26:11.524 We determined how dependent they were  
NOTE Confidence: 0.820130944252014  
00:26:11.524 --> 00:26:14.409 by giving them an injection of Mecamylamine.  
NOTE Confidence: 0.820130944252014  
00:26:14.410 --> 00:26:16.115 IP and then measuring a  
NOTE Confidence: 0.820130944252014  
00:26:16.115 --> 00:26:17.479 number of somatic signs.  
NOTE Confidence: 0.820130944252014  
00:26:17.480 --> 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 --> 00:26:23.638 We're going to use as as as our  
NOTE Confidence: 0.820130944252014  
00:26:23.638 --> 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 --> 00:26:29.783 so now we have to go back.  
NOTE Confidence: 0.820130944252014  
00:26:29.790 --> 00:26:31.910 So now we have a model to look  
NOTE Confidence: 0.820130944252014

00:26:31.910 --> 00:26:34.464 at this if we could recapitulate  
NOTE Confidence: 0.820130944252014

00:26:34.464 --> 00:26:36.416 this singular striatal circuit.  
NOTE Confidence: 0.820130944252014

00:26:36.420 --> 00:26:38.622 But what's the homologous region in  
NOTE Confidence: 0.820130944252014

00:26:38.622 --> 00:26:42.298 the rat in the vent of the human dorsal ACC?  
NOTE Confidence: 0.820130944252014

00:26:42.300 --> 00:26:45.495 So we didn't know and we don't want to  
NOTE Confidence: 0.820130944252014

00:26:45.495 --> 00:26:48.078 just look at the anatomic descriptors  
NOTE Confidence: 0.820130944252014

00:26:48.078 --> 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 --> 00:26:54.228 it was another analytic trick or  
NOTE Confidence: 0.820130944252014

00:26:54.228 --> 00:26:56.149 the modularity analysis where we  
NOTE Confidence: 0.820130944252014

00:26:56.149 --> 00:26:58.014 simply took the entire frontal  
NOTE Confidence: 0.820130944252014

00:26:58.014 --> 00:27:00.657 lobe of the rat and submitted it  
NOTE Confidence: 0.820130944252014

00:27:00.657 --> 00:27:02.487 to this modularity approach to  
NOTE Confidence: 0.820130944252014

00:27:02.490 --> 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 --> 00:27:11.971 and the computer came back with  
NOTE Confidence: 0.820130944252014  
00:27:11.971 --> 00:27:14.634 five and we use each of these five  
NOTE Confidence: 0.820130944252014  
00:27:14.634 --> 00:27:16.974 modules that we gave names simply  
NOTE Confidence: 0.820130944252014  
00:27:16.974 --> 00:27:19.144 because they overlaid onto some  
NOTE Confidence: 0.820130944252014  
00:27:19.144 --> 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 --> 00:27:30.326 the what we call the ACC middle region  
NOTE Confidence: 0.820130944252014  
00:27:30.326 --> 00:27:34.259 and only a circuit from there into into the.  
NOTE Confidence: 0.820130944252014  
00:27:34.260 --> 00:27:37.151 In this case in the dorsal stratum  
NOTE Confidence: 0.820130944252014  
00:27:37.151 --> 00:27:38.885 negatively correlated with the  
NOTE Confidence: 0.820130944252014  
00:27:38.885 --> 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 --> 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 --> 00:27:53.150 message from this paper.  
NOTE Confidence: 0.820130944252014

00:27:53.150 --> 00:27:54.762 Just came out recently.  
NOTE Confidence: 0.820130944252014

00:27:54.762 --> 00:27:56.777 And the question then was,  
NOTE Confidence: 0.839934170246124

00:27:56.780 --> 00:27:59.993 are there in fact since I can  
NOTE Confidence: 0.839934170246124

00:27:59.993 --> 00:28:02.189 induce these circuits in rats?  
NOTE Confidence: 0.839934170246124

00:28:02.190 --> 00:28:04.910 Are their baseline circuits pre  
NOTE Confidence: 0.839934170246124

00:28:04.910 --> 00:28:07.086 dispositional circuits that might  
NOTE Confidence: 0.839934170246124

00:28:07.086 --> 00:28:09.713 modify or moderate the ability of  
NOTE Confidence: 0.839934170246124

00:28:09.713 --> 00:28:12.630 nicotine to cause to cause dependence?  
NOTE Confidence: 0.839934170246124

00:28:12.630 --> 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 --> 00:28:19.694 I just want to highlight that two circuits  
NOTE Confidence: 0.839934170246124

00:28:19.694 --> 00:28:23.349 an insula frontal circuit shown up here  
NOTE Confidence: 0.839934170246124

00:28:23.349 --> 00:28:26.540 and insula striatal circuit down here,

NOTE Confidence: 0.839934170246124  
00:28:26.540 --> 00:28:29.978 fully moderated the relationship between the  
NOTE Confidence: 0.839934170246124  
00:28:29.978 --> 00:28:34.039 ACC ventral stratum and nicotine dependence.  
NOTE Confidence: 0.839934170246124  
00:28:34.040 --> 00:28:36.808 More details on how we got to these  
NOTE Confidence: 0.839934170246124  
00:28:36.808 --> 00:28:38.846 these intrinsic circuits are on this  
NOTE Confidence: 0.839934170246124  
00:28:38.846 --> 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 --> 00:28:46.056 but it looks like again the  
NOTE Confidence: 0.839934170246124  
00:28:46.056 --> 00:28:47.870 conclusion would be that this.  
NOTE Confidence: 0.839934170246124  
00:28:47.870 --> 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 --> 00:28:55.540 It's moderated by individual differences,  
NOTE Confidence: 0.839934170246124  
00:28:55.540 --> 00:28:57.070 even individual differences  
NOTE Confidence: 0.839934170246124  
00:28:57.070 --> 00:28:59.620 in rats in from insula,  
NOTE Confidence: 0.839934170246124  
00:28:59.620 --> 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 --> 00:29:15.780 the consequences of acute nicotine  
NOTE Confidence: 0.861091077327728

00:29:15.780 --> 00:29:19.360 withdrawal and state related circuitry.  
NOTE Confidence: 0.861091077327728

00:29:19.360 --> 00:29:22.592 And as I said at the Abbey on  
NOTE Confidence: 0.861091077327728

00:29:22.592 --> 00:29:24.999 said nicotine withdrawal 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 --> 00:29:32.130 lots of negative negative affect as  
NOTE Confidence: 0.861091077327728

00:29:32.201 --> 00:29:34.816 well as executive control impairments.  
NOTE Confidence: 0.861091077327728

00:29:34.820 --> 00:29:36.730 When we give nicotine replacement,  
NOTE Confidence: 0.861091077327728

00:29:36.730 --> 00:29:39.390 at least to it, to some extent,  
NOTE Confidence: 0.861091077327728

00:29:39.390 --> 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 --> 00:29:46.596 Many of these acute withdrawal symptoms.  
NOTE Confidence: 0.861091077327728

00:29:46.600 --> 00:29:49.127 And so our hypothesis going into this

NOTE Confidence: 0.861091077327728

00:29:49.127 --> 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 --> 00:29:54.040 is centered on the insulin and

NOTE Confidence: 0.861091077327728

00:29:54.040 --> 00:29:55.843 its associated circuitry and may

NOTE Confidence: 0.861091077327728

00:29:55.843 --> 00:29:57.563 ultimately serve as as Rajeev

NOTE Confidence: 0.861091077327728

00:29:57.563 --> 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 --> 00:30:06.550 the singular why the insulin?

NOTE Confidence: 0.795346319675446

00:30:06.550 --> 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 --> 00:30:13.617 this seminal paper by Nafion and

NOTE Confidence: 0.795346319675446

00:30:13.617 --> 00:30:15.792 Antoine Beshara and science within

NOTE Confidence: 0.795346319675446

00:30:15.792 --> 00:30:18.471 they noted that individuals who had

NOTE Confidence: 0.795346319675446

00:30:18.471 --> 00:30:21.053 strokes that were limited to or

NOTE Confidence: 0.795346319675446

00:30:21.053 --> 00:30:23.068 incorporated regions in the insula,

NOTE Confidence: 0.795346319675446

00:30:23.070 --> 00:30:25.482 if they were smokers before before  
NOTE Confidence: 0.795346319675446

00:30:25.482 --> 00:30:27.499 the stroke, they spontaneously stopped  
NOTE Confidence: 0.795346319675446

00:30:27.499 --> 00:30:30.320 smoking after the smoke at the stroke.  
NOTE Confidence: 0.795346319675446

00:30:30.320 --> 00:30:31.592 At least many did.  
NOTE Confidence: 0.795346319675446

00:30:31.592 --> 00:30:34.240 And probably the best sentence in this paper.  
NOTE Confidence: 0.795346319675446

00:30:34.240 --> 00:30:36.408 If you haven't read it when they ask  
NOTE Confidence: 0.795346319675446

00:30:36.408 --> 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 --> 00:30:42.108 If my body forgot that I was a smoker  
NOTE Confidence: 0.795346319675446

00:30:42.108 --> 00:30:43.894 and that really says everything  
NOTE Confidence: 0.795346319675446

00:30:43.894 --> 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 --> 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 --> 00:30:53.962 in the insula in smokers versus non  
NOTE Confidence: 0.795346319675446

00:30:53.962 --> 00:30:56.573 smokers that very nicely relates to Alexa.

NOTE Confidence: 0.795346319675446  
00:30:56.580 --> 00:30:59.254 Find me up in these individuals in  
NOTE Confidence: 0.795346319675446  
00:30:59.254 --> 00:31:01.780 these non Alexa find individuals.  
NOTE Confidence: 0.795346319675446  
00:31:01.780 --> 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 --> 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 --> 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 --> 00:31:20.736 include the installer in these circuits.  
NOTE Confidence: 0.795346319675446  
00:31:20.740 --> 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 --> 00:31:27.784 also implicated installer as biasing  
NOTE Confidence: 0.795346319675446  
00:31:27.784 --> 00:31:30.327 these trait related in solicitations.  
NOTE Confidence: 0.795346319675446  
00:31:30.330 --> 00:31:32.760 Let me summarize to other studies  
NOTE Confidence: 0.795346319675446

00:31:32.760 --> 00:31:35.791 in the lab that have gotten us  
NOTE Confidence: 0.795346319675446

00:31:35.791 --> 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 --> 00:31:43.875 identified the amygdala using the  
NOTE Confidence: 0.795346319675446

00:31:43.875 --> 00:31:46.412 Hariri basis task is being sensitive  
NOTE Confidence: 0.795346319675446

00:31:46.412 --> 00:31:49.118 to state related changes in nicotine.  
NOTE Confidence: 0.795346319675446

00:31:49.120 --> 00:31:52.042 He then used the amygdala that  
NOTE Confidence: 0.795346319675446

00:31:52.042 --> 00:31:53.503 he identified functionally.  
NOTE Confidence: 0.795346319675446

00:31:53.510 --> 00:31:58.340 As you seen and identified.  
NOTE Confidence: 0.795346319675446

00:31:58.340 --> 00:32:00.080 Insula circuit continuing to  
NOTE Confidence: 0.795346319675446

00:32:00.080 --> 00:32:01.385 walk this circuit.  
NOTE Confidence: 0.795346319675446

00:32:01.390 --> 00:32:04.891 He now used the insular as a seed and  
NOTE Confidence: 0.795346319675446

00:32:04.891 --> 00:32:07.477 identify the default mode network.  
NOTE Confidence: 0.795346319675446

00:32:07.480 --> 00:32:09.655 The full network that we  
NOTE Confidence: 0.795346319675446

00:32:09.655 --> 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 --> 00:32:14.870 hippocampal gyrus and interesting  
NOTE Confidence: 0.795346319675446  
00:32:14.870 --> 00:32:16.175 Lee and importantly,  
NOTE Confidence: 0.795346319675446  
00:32:16.180 --> 00:32:18.772 this circuit does not change in  
NOTE Confidence: 0.795346319675446  
00:32:18.772 --> 00:32:21.625 non smokers but is enhanced when  
NOTE Confidence: 0.795346319675446  
00:32:21.625 --> 00:32:24.215 the individual is in absent.  
NOTE Confidence: 0.795346319675446  
00:32:24.220 --> 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 --> 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 --> 00:32:37.264 so we had enough evidence now going in  
NOTE Confidence: 0.795346319675446  
00:32:37.264 --> 00:32:40.802 that the incident was likely involved  
NOTE Confidence: 0.795346319675446  
00:32:40.802 --> 00:32:44.062 in this nicotine withdrawal syndrome.  
NOTE Confidence: 0.795346319675446  
00:32:44.070 --> 00:32:45.740 So the installation we all  
NOTE Confidence: 0.795346319675446  
00:32:45.740 --> 00:32:47.410 took neuroanatomy buried in the  
NOTE Confidence: 0.795346319675446

00:32:47.469 --> 00:32:49.139 middle of this temporal lobe,  
NOTE Confidence: 0.795346319675446

00:32:49.140 --> 00:32:51.499 yet to kind of crank open the  
NOTE Confidence: 0.795346319675446

00:32:51.499 --> 00:32:53.528 brain and see it in there.  
NOTE Confidence: 0.795346319675446

00:32:53.530 --> 00:32:55.798 Probably the best review paper and  
NOTE Confidence: 0.795346319675446

00:32:55.798 --> 00:32:57.659 the breast best theoretical paper  
NOTE Confidence: 0.795346319675446

00:32:57.659 --> 00:32:59.626 that that that I came across and  
NOTE Confidence: 0.795346319675446

00:32:59.626 --> 00:33:01.275 I would really encourage those  
NOTE Confidence: 0.795346319675446

00:33:01.275 --> 00:33:03.669 of you who might be interested in  
NOTE Confidence: 0.795346319675446

00:33:03.670 --> 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 --> 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 --> 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 --> 00:33:15.718 processing homeostatic processing with.  
NOTE Confidence: 0.795346319675446

00:33:15.718 --> 00:33:17.286 Amygdala and hypothalamic inputs.

NOTE Confidence: 0.795346319675446

00:33:17.290 --> 00:33:20.730 And as one goes more rostral, more anteriorly.

NOTE Confidence: 0.795346319675446

00:33:20.730 --> 00:33:22.450 This information is integrated

NOTE Confidence: 0.795346319675446

00:33:22.450 --> 00:33:24.170 and kick more forward,

NOTE Confidence: 0.814464807510376

00:33:24.170 --> 00:33:26.972 integrated, and kick more anteriorly where

NOTE Confidence: 0.814464807510376

00:33:26.972 --> 00:33:30.457 the most anterior regions of the of the

NOTE Confidence: 0.814464807510376

00:33:30.457 --> 00:33:32.767 insula are involved in hedonic processing.

NOTE Confidence: 0.814464807510376

00:33:32.770 --> 00:33:34.408 Motivational cognitive processing

NOTE Confidence: 0.814464807510376

00:33:34.408 --> 00:33:37.684 with inputs from areas that we

NOTE Confidence: 0.814464807510376

00:33:37.684 --> 00:33:40.190 think are players in the bank.

NOTE Confidence: 0.814464807510376

00:33:40.190 --> 00:33:42.926 And this review article by Craig

NOTE Confidence: 0.814464807510376

00:33:42.926 --> 00:33:46.186 LED us to hypothesize a number of

NOTE Confidence: 0.814464807510376

00:33:46.186 --> 00:33:48.886 years ago that the salience network,

NOTE Confidence: 0.814464807510376

00:33:48.890 --> 00:33:52.054 the ACC and anterior insular served as

NOTE Confidence: 0.814464807510376

00:33:52.054 --> 00:33:55.760 sort of the pivot of a Teeter Totter.

NOTE Confidence: 0.814464807510376

00:33:55.760 --> 00:33:58.966 And when an individual was in accidents,

NOTE Confidence: 0.814464807510376



00:33:58.970 --> 00:34:01.390 this salience network bias the  
NOTE Confidence: 0.814464807510376

00:34:01.390 --> 00:34:03.810 individual to pay more attention  
NOTE Confidence: 0.814464807510376

00:34:03.890 --> 00:34:06.380 to internal states to pay attention  
NOTE Confidence: 0.814464807510376

00:34:06.380 --> 00:34:09.040 to that craving to that hunger.  
NOTE Confidence: 0.814464807510376

00:34:09.040 --> 00:34:11.390 When the individual is sated.  
NOTE Confidence: 0.814464807510376

00:34:11.390 --> 00:34:14.198 This bias system encourage the individual  
NOTE Confidence: 0.814464807510376

00:34:14.198 --> 00:34:17.448 to spend more time in executive mode  
NOTE Confidence: 0.814464807510376

00:34:17.448 --> 00:34:20.046 to be able to concentrate focus.  
NOTE Confidence: 0.814464807510376

00:34:20.050 --> 00:34:23.154 It also allowed us to start to look  
NOTE Confidence: 0.814464807510376

00:34:23.154 --> 00:34:26.583 at the fact that the insula has been  
NOTE Confidence: 0.814464807510376

00:34:26.583 --> 00:34:29.940 divided into a number of different areas,  
NOTE Confidence: 0.814464807510376

00:34:29.940 --> 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 --> 00:34:35.529 or behavior for that matter,  
NOTE Confidence: 0.814464807510376

00:34:35.530 --> 00:34:37.210 on this list, divide,  
NOTE Confidence: 0.814464807510376

00:34:37.210 --> 00:34:40.260 then divide into three major three major,

NOTE Confidence: 0.814464807510376

00:34:40.260 --> 00:34:40.924 with subdivisions.

NOTE Confidence: 0.814464807510376

00:34:40.924 --> 00:34:43.580 And so the question we next had was

NOTE Confidence: 0.814464807510376

00:34:43.649 --> 00:34:45.889 how did these circuits from each of

NOTE Confidence: 0.814464807510376

00:34:45.889 --> 00:34:48.124 these regions of the insulin different

NOTE Confidence: 0.814464807510376

00:34:48.124 --> 00:34:50.542 as a function of nicotine withdrawal?

NOTE Confidence: 0.814464807510376

00:34:50.550 --> 00:34:53.485 And do these circuits have

NOTE Confidence: 0.814464807510376

00:34:53.485 --> 00:34:54.659 behavioral consequences?

NOTE Confidence: 0.814464807510376

00:34:54.660 --> 00:34:57.260 So this is the work of John Kadota

NOTE Confidence: 0.814464807510376

00:34:57.260 --> 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 --> 00:35:04.033 three divisions and hypothesis

NOTE Confidence: 0.814464807510376

00:35:04.033 --> 00:35:06.817 driven fashion use each of these

NOTE Confidence: 0.814464807510376

00:35:06.817 --> 00:35:09.496 three regions of the insular seeds,

NOTE Confidence: 0.814464807510376

00:35:09.500 --> 00:35:12.223 and had each of these three large

NOTE Confidence: 0.814464807510376

00:35:12.223 --> 00:35:14.310 scale networks as as targets,

NOTE Confidence: 0.814464807510376

00:35:14.310 --> 00:35:16.752 and what he identified with three  
NOTE Confidence: 0.814464807510376

00:35:16.752 --> 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 --> 00:35:22.730 This was 48 hour accents,  
NOTE Confidence: 0.814464807510376

00:35:22.730 --> 00:35:25.166 one from the ventral insula too.  
NOTE Confidence: 0.814464807510376

00:35:25.170 --> 00:35:26.858 Piece of the DL.  
NOTE Confidence: 0.814464807510376

00:35:26.858 --> 00:35:30.139 Pfc from the posterior insula into the ACC,  
NOTE Confidence: 0.814464807510376

00:35:30.140 --> 00:35:34.084 and from the dorsal insula into the DNA.  
NOTE Confidence: 0.814464807510376

00:35:34.090 --> 00:35:36.820 And what was interesting is that they  
NOTE Confidence: 0.814464807510376

00:35:36.820 --> 00:35:38.950 also had behavioral consequences.  
NOTE Confidence: 0.814464807510376

00:35:38.950 --> 00:35:41.596 At least two of them did,  
NOTE Confidence: 0.814464807510376

00:35:41.600 --> 00:35:43.064 and that with this,  
NOTE Confidence: 0.814464807510376

00:35:43.064 --> 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 --> 00:35:50.410 and this salience network  
NOTE Confidence: 0.814464807510376

00:35:50.410 --> 00:35:52.045 circuit correlating with.

NOTE Confidence: 0.814464807510376  
00:35:52.050 --> 00:35:53.568 The WS WS,  
NOTE Confidence: 0.814464807510376  
00:35:53.568 --> 00:35:55.086 sadness and anger.  
NOTE Confidence: 0.814464807510376  
00:35:55.090 --> 00:35:57.625 There was no relationship with  
NOTE Confidence: 0.814464807510376  
00:35:57.625 --> 00:35:58.639 cognitive performance.  
NOTE Confidence: 0.814464807510376  
00:35:58.640 --> 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 --> 00:36:06.660 about these three circuits.  
NOTE Confidence: 0.814464807510376  
00:36:06.660 --> 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 --> 00:36:13.260 And when we looked at the state  
NOTE Confidence: 0.814464807510376  
00:36:13.354 --> 00:36:15.429 of a little bit closer,  
NOTE Confidence: 0.814464807510376  
00:36:15.430 --> 00:36:18.862 we kind of looked at this this terminal  
NOTE Confidence: 0.814464807510376  
00:36:18.862 --> 00:36:22.199 region if you will and the DL Pfc and  
NOTE Confidence: 0.814464807510376  
00:36:22.199 --> 00:36:25.070 it's Mac on where this crosshairs on  
NOTE Confidence: 0.814464807510376  
00:36:25.070 --> 00:36:28.109 to where the F three 1020 placement  
NOTE Confidence: 0.814464807510376

00:36:28.109 --> 00:36:31.790 is where we give TMS at the DL Pfc.  
NOTE Confidence: 0.814464807510376

00:36:31.790 --> 00:36:34.250 So perhaps what we've identified  
NOTE Confidence: 0.814464807510376

00:36:34.250 --> 00:36:36.218 serendipitously would be a  
NOTE Confidence: 0.814464807510376

00:36:36.218 --> 00:36:39.081 location that we might be able to  
NOTE Confidence: 0.814464807510376

00:36:39.081 --> 00:36:40.980 target and justify targeting our.  
NOTE Confidence: 0.814464807510376

00:36:40.980 --> 00:36:45.432 TMS treatments to modify these circuits and  
NOTE Confidence: 0.814464807510376

00:36:45.432 --> 00:36:50.150 involved in the negative consequences of.  
NOTE Confidence: 0.814464807510376

00:36:50.150 --> 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 --> 00:37:00.000 Tell me how we're doing.  
NOTE Confidence: 0.814464807510376

00:37:00.000 --> 00:37:02.247 I've got a couple of more studies  
NOTE Confidence: 0.814464807510376

00:37:02.247 --> 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 --> 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

NOTE Confidence: 0.827893912792206

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

NOTE Confidence: 0.827893912792206

00:37:12.850 --> 00:37:14.946 OK so we want to start to look

NOTE Confidence: 0.827893912792206

00:37:14.946 --> 00:37:17.133 now at these state trade aspects

NOTE Confidence: 0.827893912792206

00:37:17.133 --> 00:37:19.985 in decision making and then an in

NOTE Confidence: 0.827893912792206

00:37:19.985 --> 00:37:21.573 reward learning very important

NOTE Confidence: 0.827893912792206

00:37:21.573 --> 00:37:24.600 process as you know in in substance

NOTE Confidence: 0.827893912792206

00:37:24.600 --> 00:37:26.680 use development and maintenance.

NOTE Confidence: 0.827893912792206

00:37:26.680 --> 00:37:29.024 And we began to look about at a

NOTE Confidence: 0.827893912792206

00:37:29.024 --> 00:37:31.233 test that hasn't been used very

NOTE Confidence: 0.827893912792206

00:37:31.233 --> 00:37:33.549 much in addition 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 --> 00:37:38.280 and we like this task.

NOTE Confidence: 0.827893912792206

00:37:38.280 --> 00:37:40.240 We suppressive captures two different

NOTE Confidence: 0.827893912792206

00:37:40.240 --> 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,

NOTE Confidence: 0.827893912792206

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

NOTE Confidence: 0.827893912792206

00:37:45.880 --> 00:37:48.064 How an individual changes one's behavior

NOTE Confidence: 0.827893912792206

00:37:48.064 --> 00:37:50.628 in the face of negative outcomes

NOTE Confidence: 0.827893912792206

00:37:50.628 --> 00:37:53.228 versus maintaining a previous choice.

NOTE Confidence: 0.827893912792206

00:37:53.230 --> 00:37:55.925 And this task has been used because

NOTE Confidence: 0.827893912792206

00:37:55.925 --> 00:37:59.007 we used it because it relies on

NOTE Confidence: 0.827893912792206

00:37:59.007 --> 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 --> 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 --> 00:38:10.252 how it is involved in smoking in

NOTE Confidence: 0.827893912792206

00:38:10.252 --> 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 --> 00:38:17.636 So this is work of at least Lesage

NOTE Confidence: 0.827893912792206

00:38:17.636 --> 00:38:19.887 post dot dot in the lab and it's a

NOTE Confidence: 0.827893912792206

00:38:19.887 --> 00:38:22.399 task that we modify based on one that

NOTE Confidence: 0.827893912792206  
00:38:22.399 --> 00:38:25.028 Roshan cools published a number of years ago,  
NOTE Confidence: 0.827893912792206  
00:38:25.028 --> 00:38:27.438 and again I would encourage people to think  
NOTE Confidence: 0.827893912792206  
00:38:27.438 --> 00:38:29.895 about this task is not used an awful lot,  
NOTE Confidence: 0.827893912792206  
00:38:29.900 --> 00:38:32.098 and certainly not in addiction and we  
NOTE Confidence: 0.827893912792206  
00:38:32.098 --> 00:38:34.800 really like it a lot and I'll show you why.  
NOTE Confidence: 0.827893912792206  
00:38:34.800 --> 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 --> 00:38:40.270 have to pick one arbitrarily.  
NOTE Confidence: 0.827893912792206  
00:38:40.270 --> 00:38:41.705 The computer has decided what  
NOTE Confidence: 0.827893912792206  
00:38:41.705 --> 00:38:42.853 the right answer is.  
NOTE Confidence: 0.827893912792206  
00:38:42.860 --> 00:38:44.558 That's over here are the individual  
NOTE Confidence: 0.827893912792206  
00:38:44.558 --> 00:38:46.390 doesn't know and they get feedback.  
NOTE Confidence: 0.827893912792206  
00:38:46.390 --> 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 --> 00:38:54.900 and they can make a decision to  
NOTE Confidence: 0.827893912792206



00:38:54.988 --> 00:38:57.697 either stay when they make a win.  
NOTE Confidence: 0.827893912792206

00:38:57.700 --> 00:39:00.828 All or if they lose their inside to  
NOTE Confidence: 0.827893912792206

00:39:00.828 --> 00:39:04.336 stay or they can ship when they make.  
NOTE Confidence: 0.827893912792206

00:39:04.340 --> 00:39:07.360 When they lose so Wednesday, Lucia.  
NOTE Confidence: 0.827893912792206

00:39:07.360 --> 00:39:11.120 A type of behavior.  
NOTE Confidence: 0.827893912792206

00:39:11.120 --> 00:39:13.656 We did this task in both smokers and  
NOTE Confidence: 0.827893912792206

00:39:13.656 --> 00:39:15.676 non smokers in a very complicated  
NOTE Confidence: 0.827893912792206

00:39:15.676 --> 00:39:18.120 fashion that you know we can do it.  
NOTE Confidence: 0.827893912792206

00:39:18.120 --> 00:39:19.324 The at the IRP.  
NOTE Confidence: 0.827893912792206

00:39:19.324 --> 00:39:20.829 We stand individual six times  
NOTE Confidence: 0.827893912792206

00:39:20.829 --> 00:39:22.890 on and off and nicotine Patch.  
NOTE Confidence: 0.827893912792206

00:39:22.890 --> 00:39:25.394 Two of those times was with a chronic  
NOTE Confidence: 0.827893912792206

00:39:25.394 --> 00:39:27.557 of Renick Ling Pill and two of  
NOTE Confidence: 0.827893912792206

00:39:27.557 --> 00:39:30.093 those times was with uh with it's a  
NOTE Confidence: 0.827893912792206

00:39:30.093 --> 00:39:32.091 placebo pill because we wanted to  
NOTE Confidence: 0.827893912792206

00:39:32.091 --> 00:39:34.020 look at this drug drug interaction.

NOTE Confidence: 0.827893912792206

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

NOTE Confidence: 0.827893912792206

00:39:35.934 --> 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 --> 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 --> 00:39:48.830 And was at least did she use the

NOTE Confidence: 0.827893912792206

00:39:48.830 --> 00:39:50.433 computational model something called

NOTE Confidence: 0.827893912792206

00:39:50.433 --> 00:39:53.233 The Hidden Markov model and she did

NOTE Confidence: 0.827893912792206

00:39:53.233 --> 00:39:55.814 this as a function of group smokers

NOTE Confidence: 0.827893912792206

00:39:55.814 --> 00:39:57.569 and non smokers and treatment.

NOTE Confidence: 0.827893912792206

00:39:57.569 --> 00:40:00.361 And as you can see there were no

NOTE Confidence: 0.827893912792206

00:40:00.361 --> 00:40:02.140 effects of pharmacotherapy 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 --> 00:40:07.267 getting a little short on time I'm

NOTE Confidence: 0.827893912792206

00:40:07.267 --> 00:40:09.676 not going to detail with this bias  
NOTE Confidence: 0.827893912792206

00:40:09.676 --> 00:40:11.586 this day or inverse temperature  
NOTE Confidence: 0.827893912792206

00:40:11.586 --> 00:40:13.842 means but basically it tells us  
NOTE Confidence: 0.827893912792206

00:40:13.842 --> 00:40:15.972 that in the absolute state and  
NOTE Confidence: 0.818055510520935

00:40:16.041 --> 00:40:18.123 that's here. In in orange,  
NOTE Confidence: 0.818055510520935

00:40:18.123 --> 00:40:20.649 in the absolute state and smokers,  
NOTE Confidence: 0.818055510520935

00:40:20.650 --> 00:40:22.750 these individuals were more impulsive.  
NOTE Confidence: 0.818055510520935

00:40:22.750 --> 00:40:25.368 In this task they made more rash  
NOTE Confidence: 0.818055510520935

00:40:25.368 --> 00:40:27.810 decisions when facing negative outcomes.  
NOTE Confidence: 0.818055510520935

00:40:27.810 --> 00:40:31.247 And Moreover this deficit if you will  
NOTE Confidence: 0.818055510520935

00:40:31.247 --> 00:40:34.907 was reversed both when they put on a  
NOTE Confidence: 0.818055510520935

00:40:34.907 --> 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 --> 00:40:43.506 way to look at real world kind  
NOTE Confidence: 0.818055510520935

00:40:43.506 --> 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

NOTE Confidence: 0.818055510520935

00:40:47.867 --> 00:40:50.560 task into the brain very quickly?

NOTE Confidence: 0.818055510520935

00:40:50.560 --> 00:40:53.360 When we look at reward greater than

NOTE Confidence: 0.818055510520935

00:40:53.360 --> 00:40:55.439 punishment is whole brain Maps.

NOTE Confidence: 0.818055510520935

00:40:55.440 --> 00:40:58.510 We see the very nice DMM map map as you

NOTE Confidence: 0.818055510520935

00:40:58.592 --> 00:41:01.864 see when we look at what punishment does

NOTE Confidence: 0.818055510520935

00:41:01.864 --> 00:41:05.207 very nicely activates the salience network.

NOTE Confidence: 0.818055510520935

00:41:05.210 --> 00:41:08.857 The dorsal ACC and eventual straight up.

NOTE Confidence: 0.818055510520935

00:41:08.860 --> 00:41:11.956 However, when we look at cognitive

NOTE Confidence: 0.818055510520935

00:41:11.956 --> 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 --> 00:41:25.280 beautifully on the salience network.

NOTE Confidence: 0.818055510520935

00:41:25.280 --> 00:41:28.178 Well, how about as a function

NOTE Confidence: 0.818055510520935

00:41:28.178 --> 00:41:30.110 of state and trade?

NOTE Confidence: 0.818055510520935

00:41:30.110 --> 00:41:33.505 Well when we look at rewards sensitivity.  
NOTE Confidence: 0.818055510520935

00:41:33.510 --> 00:41:35.830 Smokers 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 --> 00:41:44.250 to performance 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 --> 00:41:52.408 and these impairments are not not  
NOTE Confidence: 0.818055510520935

00:41:52.408 --> 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 --> 00:42:01.356 they are yet again another paradigm another.  
NOTE Confidence: 0.818055510520935

00:42:01.360 --> 00:42:03.580 Way of looking at this,  
NOTE Confidence: 0.818055510520935

00:42:03.580 --> 00:42:05.880 they deficits are also proportional  
NOTE Confidence: 0.818055510520935

00:42:05.880 --> 00:42:08.812 to the level of nicotine dependence  
NOTE Confidence: 0.818055510520935

00:42:08.812 --> 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 --> 00:42:15.422 the cognitive flexibility contrast

NOTE Confidence: 0.818055510520935  
00:42:15.422 --> 00:42:19.674 showed us a state related different  
NOTE Confidence: 0.818055510520935  
00:42:19.674 --> 00:42:23.724 such that in in smokers during  
NOTE Confidence: 0.818055510520935  
00:42:23.724 --> 00:42:26.998 abstinence they perform much worse.  
NOTE Confidence: 0.818055510520935  
00:42:27.000 --> 00:42:29.904 And this activation is reversed in  
NOTE Confidence: 0.818055510520935  
00:42:29.904 --> 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 --> 00:42:40.133 The study is published that acute absence  
NOTE Confidence: 0.818055510520935  
00:42:40.133 --> 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 --> 00:42:48.941 with neural activity in the dopamine  
NOTE Confidence: 0.818055510520935  
00:42:48.941 --> 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 --> 00:42:54.918 Reduced before this behavioral shift.  
NOTE Confidence: 0.818055510520935  
00:42:54.920 --> 00:42:56.540 Acute administration of nicotinic  
NOTE Confidence: 0.818055510520935

00:42:56.540 --> 00:42:57.755 receptor agonist restored.  
NOTE Confidence: 0.818055510520935

00:42:57.760 --> 00:42:59.940 These both behavioral and neural  
NOTE Confidence: 0.818055510520935

00:42:59.940 --> 00:43:02.120 processes comparable to that in  
NOTE Confidence: 0.818055510520935

00:43:02.188 --> 00:43:04.228 non smokers and what was really  
NOTE Confidence: 0.818055510520935

00:43:04.228 --> 00:43:06.989 cool in this study and I love  
NOTE Confidence: 0.818055510520935

00:43:06.989 --> 00:43:08.315 doubled Association studies.  
NOTE Confidence: 0.818055510520935

00:43:08.320 --> 00:43:10.686 What we saw in this case though  
NOTE Confidence: 0.818055510520935

00:43:10.686 --> 00:43:13.424 is that in trade of smoking we  
NOTE Confidence: 0.818055510520935

00:43:13.424 --> 00:43:15.884 saw a lowest sensitivity in the  
NOTE Confidence: 0.818055510520935

00:43:15.973 --> 00:43:18.468 dorsal striatum and dorsal ACC.  
NOTE Confidence: 0.818055510520935

00:43:18.470 --> 00:43:21.305 The same players that we've been seeing,  
NOTE Confidence: 0.818055510520935

00:43:21.310 --> 00:43:23.812 which was not alleviated by nicotinic  
NOTE Confidence: 0.818055510520935

00:43:23.812 --> 00:43:25.850 stimulation but was associated with.  
NOTE Confidence: 0.818055510520935

00:43:25.850 --> 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 --> 00:43:32.618 that different constructs different

NOTE Confidence: 0.818055510520935  
00:43:32.618 --> 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 --> 00:43:39.550 and the state of the individual.  
NOTE Confidence: 0.818055510520935  
00:43:39.550 --> 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 --> 00:43:47.306 rather than a monotherapy approach  
NOTE Confidence: 0.818055510520935  
00:43:47.306 --> 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 --> 00:43:58.594 came out a few months ago and it's  
NOTE Confidence: 0.818055510520935  
00:43:58.594 --> 00:44:01.566 about the Habenula and the reason we  
NOTE Confidence: 0.818055510520935  
00:44:01.566 --> 00:44:04.583 wanted to go into the habenula stress.  
NOTE Confidence: 0.818055510520935  
00:44:04.590 --> 00:44:06.564 This is an area that really  
NOTE Confidence: 0.818055510520935  
00:44:06.564 --> 00:44:07.880 thinks about really is  
NOTE Confidence: 0.795257210731506  
00:44:07.949 --> 00:44:10.649 involved in negative aversive processing.  
NOTE Confidence: 0.795257210731506



00:44:10.650 --> 00:44:12.705 It's hypothesize be hyperactive and  
NOTE Confidence: 0.795257210731506

00:44:12.705 --> 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 --> 00:44:21.305 within the within the Habenula.  
NOTE Confidence: 0.795257210731506

00:44:21.310 --> 00:44:23.900 So this is a study that that started in the  
NOTE Confidence: 0.795257210731506

00:44:23.961 --> 00:44:26.306 lab when when that southernns was there,  
NOTE Confidence: 0.795257210731506

00:44:26.310 --> 00:44:27.219 like many things,  
NOTE Confidence: 0.795257210731506

00:44:27.219 --> 00:44:29.771 life gets in the way we were finally  
NOTE Confidence: 0.795257210731506

00:44:29.771 --> 00:44:32.305 able to publish this few months ago.  
NOTE Confidence: 0.795257210731506

00:44:32.310 --> 00:44:36.046 But the venue is a really small areas,  
NOTE Confidence: 0.795257210731506

00:44:36.050 --> 00:44:38.846 maybe 5 boxes big in humans.  
NOTE Confidence: 0.795257210731506

00:44:38.850 --> 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 --> 00:44:44.254 And this is another very novel  
NOTE Confidence: 0.795257210731506

00:44:44.254 --> 00:44:46.659 task that I do not understand why

NOTE Confidence: 0.795257210731506  
00:44:46.659 --> 00:44:48.855 it's never been used to that.  
NOTE Confidence: 0.795257210731506  
00:44:48.860 --> 00:44:51.920 Well, I do understand it's a very long test.  
NOTE Confidence: 0.795257210731506  
00:44:51.920 --> 00:44:54.167 Takes about 30 minutes in the Mac  
NOTE Confidence: 0.795257210731506  
00:44:54.167 --> 00:44:56.949 and this is a task that is burger  
NOTE Confidence: 0.795257210731506  
00:44:56.949 --> 00:44:59.060 published a number of years ago.  
NOTE Confidence: 0.795257210731506  
00:44:59.060 --> 00:44:59.676 Simple text,  
NOTE Confidence: 0.795257210731506  
00:44:59.676 --> 00:45:02.140 2 balls appear on a screen of different  
NOTE Confidence: 0.795257210731506  
00:45:02.208 --> 00:45:04.532 positions and they start to move at  
NOTE Confidence: 0.795257210731506  
00:45:04.532 --> 00:45:06.701 different speeds and the the participant  
NOTE Confidence: 0.795257210731506  
00:45:06.701 --> 00:45:08.915 only sees them for 100 milliseconds.  
NOTE Confidence: 0.795257210731506  
00:45:08.920 --> 00:45:11.712 They go off and then they have to  
NOTE Confidence: 0.795257210731506  
00:45:11.712 --> 00:45:14.040 guess which ball would have hit.  
NOTE Confidence: 0.795257210731506  
00:45:14.040 --> 00:45:15.870 Would have hit the end  
NOTE Confidence: 0.795257210731506  
00:45:15.870 --> 00:45:17.700 if there was enough time.  
NOTE Confidence: 0.795257210731506  
00:45:17.700 --> 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 --> 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 --> 00:45:28.376 to get enough jitter,  
NOTE Confidence: 0.795257210731506

00:45:28.380 --> 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 --> 00:45:36.416 a noninformative feedback whether  
NOTE Confidence: 0.795257210731506

00:45:36.416 --> 00:45:39.368 they were correct or incorrect.  
NOTE Confidence: 0.795257210731506

00:45:39.370 --> 00:45:41.813 So because of time these were the  
NOTE Confidence: 0.795257210731506

00:45:41.813 --> 00:45:43.769 same individuals that we scanned  
NOTE Confidence: 0.795257210731506

00:45:43.769 --> 00:45:45.754 on multiple occasions. Task worked.  
NOTE Confidence: 0.795257210731506

00:45:45.754 --> 00:45:47.926 It's biased like most of these  
NOTE Confidence: 0.795257210731506

00:45:47.926 --> 00:45:50.658 kind of reward tasks or people are  
NOTE Confidence: 0.795257210731506

00:45:50.658 --> 00:45:52.561 correct 65% of the time.  
NOTE Confidence: 0.795257210731506

00:45:52.561 --> 00:45:54.823 There faster when they are correct.  
NOTE Confidence: 0.795257210731506

00:45:54.830 --> 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 --> 00:46:02.740 there were more errors of omission,  
NOTE Confidence: 0.795257210731506  
00:46:02.740 --> 00:46:05.393 number of no responses and these errors  
NOTE Confidence: 0.795257210731506  
00:46:05.393 --> 00:46:07.719 of omission were improved when we  
NOTE Confidence: 0.795257210731506  
00:46:07.719 --> 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 --> 00:46:13.912 They also got better than non smokers,  
NOTE Confidence: 0.795257210731506  
00:46:13.920 --> 00:46:16.320 got better with nicotine as well.  
NOTE Confidence: 0.795257210731506  
00:46:16.320 --> 00:46:17.912 Again not a surprise.  
NOTE Confidence: 0.795257210731506  
00:46:17.912 --> 00:46:19.902 So did the task work.  
NOTE Confidence: 0.795257210731506  
00:46:19.910 --> 00:46:21.574 The answer is yes.  
NOTE Confidence: 0.795257210731506  
00:46:21.574 --> 00:46:24.070 I'm outlining the habenula for you  
NOTE Confidence: 0.795257210731506  
00:46:24.156 --> 00:46:26.826 over here and these white circles.  
NOTE Confidence: 0.795257210731506  
00:46:26.830 --> 00:46:29.350 When the individual made an error,  
NOTE Confidence: 0.795257210731506  
00:46:29.350 --> 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 --> 00:46:38.290 activity when the individual gets is  
NOTE Confidence: 0.795257210731506

00:46:38.290 --> 00:46:40.265 correct and gets positive feedback.  
NOTE Confidence: 0.795257210731506

00:46:40.270 --> 00:46:43.357 So exactly what you would expect a  
NOTE Confidence: 0.795257210731506

00:46:43.357 --> 00:46:46.158 task like this to do? Interesting Lee.  
NOTE Confidence: 0.795257210731506

00:46:46.158 --> 00:46:47.854 The relationship between the  
NOTE Confidence: 0.795257210731506

00:46:47.854 --> 00:46:50.010 insula screaming and the habenula  
NOTE Confidence: 0.795257210731506

00:46:50.010 --> 00:46:51.606 screaming is almost one,  
NOTE Confidence: 0.795257210731506

00:46:51.610 --> 00:46:54.148 and so these two structures are  
NOTE Confidence: 0.795257210731506

00:46:54.148 --> 00:46:56.230 integrating their their processing very,  
NOTE Confidence: 0.795257210731506

00:46:56.230 --> 00:46:57.248 very closely.  
NOTE Confidence: 0.795257210731506

00:46:57.248 --> 00:47:00.811 So very quickly then when we re  
NOTE Confidence: 0.795257210731506

00:47:00.811 --> 00:47:03.420 analyze this data with contrast  
NOTE Confidence: 0.795257210731506

00:47:03.420 --> 00:47:05.925 as a function of group,

NOTE Confidence: 0.795257210731506

00:47:05.930 --> 00:47:09.227 what we found was that when we

NOTE Confidence: 0.795257210731506

00:47:09.227 --> 00:47:12.738 look at errors minus correct that.

NOTE Confidence: 0.795257210731506

00:47:12.740 --> 00:47:15.734 On that non smokers very nicely

NOTE Confidence: 0.795257210731506

00:47:15.734 --> 00:47:18.790 were able to process their error

NOTE Confidence: 0.795257210731506

00:47:18.790 --> 00:47:22.150 response but in the in the stratum

NOTE Confidence: 0.795257210731506

00:47:22.150 --> 00:47:24.359 but smokers were not.

NOTE Confidence: 0.795257210731506

00:47:24.360 --> 00:47:24.747 Conversely,

NOTE Confidence: 0.795257210731506

00:47:24.747 --> 00:47:27.069 on the initial response in smokers,

NOTE Confidence: 0.795257210731506

00:47:27.070 --> 00:47:30.010 or was much greater when they

NOTE Confidence: 0.795257210731506

00:47:30.010 --> 00:47:31.970 made errors than it

NOTE Confidence: 0.827910244464874

00:47:32.077 --> 00:47:34.730 was in non smokers. Does this

NOTE Confidence: 0.827910244464874

00:47:34.730 --> 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 --> 00:47:42.465 but none but not non smokers when

NOTE Confidence: 0.827910244464874

00:47:42.465 --> 00:47:44.393 the individuals are absent the

NOTE Confidence: 0.827910244464874

00:47:44.393 --> 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 --> 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 --> 00:47:55.550 Lorelei to demonstrate that,  
NOTE Confidence: 0.827910244464874

00:47:55.550 --> 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 --> 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 --> 00:48:20.151 that we see a differential pattern  
NOTE Confidence: 0.815314650535584

00:48:20.151 --> 00:48:22.977 of brain activity in the Habenula  
NOTE Confidence: 0.815314650535584

00:48:22.977 --> 00:48:25.747 the insula ACC eventual stratum,  
NOTE Confidence: 0.815314650535584

00:48:25.750 --> 00:48:27.950 following positive and negative feedback,

NOTE Confidence: 0.815314650535584  
00:48:27.950 --> 00:48:31.134 and we see again again at the Association  
NOTE Confidence: 0.815314650535584  
00:48:31.134 --> 00:48:33.780 between trait life addiction and state  
NOTE Confidence: 0.815314650535584  
00:48:33.780 --> 00:48:36.972 like withdrawal in that smokers show a  
NOTE Confidence: 0.815314650535584  
00:48:36.972 --> 00:48:39.756 reduced right or responsibility to positive  
NOTE Confidence: 0.815314650535584  
00:48:39.756 --> 00:48:42.806 feedback which was not ameliorated by.  
NOTE Confidence: 0.815314650535584  
00:48:42.806 --> 00:48:45.014 Nicotinic agonists was correlated  
NOTE Confidence: 0.815314650535584  
00:48:45.014 --> 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 --> 00:48:55.159 positive feedback was reversed by an RT.  
NOTE Confidence: 0.815314650535584  
00:48:55.160 --> 00:48:56.720 Which was correlated with with craving,  
NOTE Confidence: 0.815314650535584  
00:48:56.720 --> 00:49:00.428 which I didn't have a chance to show you.  
NOTE Confidence: 0.815314650535584  
00:49:00.430 --> 00:49:03.314 So this novel evidence again seems to  
NOTE Confidence: 0.815314650535584  
00:49:03.314 --> 00:49:05.721 suggest that why these monotherapies  
NOTE Confidence: 0.815314650535584  
00:49:05.721 --> 00:49:08.446 might not be overly effective.  
NOTE Confidence: 0.815314650535584  
00:49:08.450 --> 00:49:11.516 Alright, I'm going to skip the with  
NOTE Confidence: 0.815314650535584



00:49:11.516 --> 00:49:14.462 the summary and one tickle only  
NOTE Confidence: 0.815314650535584

00:49:14.462 --> 00:49:16.007 Because 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 --> 00:49:22.306 This is a study that just came out.  
NOTE Confidence: 0.815314650535584

00:49:22.310 --> 00:49:24.806 MD, PhD screen in the lab of wanted  
NOTE Confidence: 0.815314650535584

00:49:24.806 --> 00:49:27.922 to see theoretically if PVCS at least  
NOTE Confidence: 0.815314650535584

00:49:27.922 --> 00:49:30.800 acutely could modify these service and  
NOTE Confidence: 0.815314650535584

00:49:30.800 --> 00:49:33.502 with Sarah did was taking the hypothesis  
NOTE Confidence: 0.815314650535584

00:49:33.502 --> 00:49:37.380 of this three network key to tar.  
NOTE Confidence: 0.815314650535584

00:49:37.380 --> 00:49:39.204 And using this hypothesis,  
NOTE Confidence: 0.815314650535584

00:49:39.204 --> 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 --> 00:49:49.234 Pfc and the DL Pfc and switch  
NOTE Confidence: 0.815314650535584

00:49:49.234 --> 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 --> 00:49:57.104 to modify this three large scale

NOTE Confidence: 0.815314650535584  
00:49:57.104 --> 00:50:00.194 networks again using the same power  
NOTE Confidence: 0.815314650535584  
00:50:00.287 --> 00:50:03.220 line we've been using in the lab.  
NOTE Confidence: 0.815314650535584  
00:50:03.220 --> 00:50:05.878 We scan smokers on and off  
NOTE Confidence: 0.815314650535584  
00:50:05.878 --> 00:50:07.650 and nicotine Patch with.  
NOTE Confidence: 0.815314650535584  
00:50:07.650 --> 00:50:09.555 See the sham stimulation or  
NOTE Confidence: 0.815314650535584  
00:50:09.555 --> 00:50:11.079 an Ola Catholic stimulation.  
NOTE Confidence: 0.815314650535584  
00:50:11.080 --> 00:50:13.530 We did the same thing and non  
NOTE Confidence: 0.815314650535584  
00:50:13.530 --> 00:50:16.030 smokers but only scanned them once.  
NOTE Confidence: 0.815314650535584  
00:50:16.030 --> 00:50:17.935 No drugs for these folks  
NOTE Confidence: 0.815314650535584  
00:50:17.935 --> 00:50:19.459 and importantly we scanned.  
NOTE Confidence: 0.815314650535584  
00:50:19.460 --> 00:50:22.808 We presented T DCS in the magnet so we  
NOTE Confidence: 0.815314650535584  
00:50:22.808 --> 00:50:25.704 were doing this online in real time  
NOTE Confidence: 0.815314650535584  
00:50:25.704 --> 00:50:28.950 to watch how the brain is changing  
NOTE Confidence: 0.815314650535584  
00:50:28.950 --> 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 --> 00:50:35.260 measure and not a mapper.  
NOTE Confidence: 0.815314650535584

00:50:35.260 --> 00:50:37.906 We use tasks that we well knew what they,  
NOTE Confidence: 0.815314650535584

00:50:37.910 --> 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 --> 00:50:43.910 at the effects of PVCS.  
NOTE Confidence: 0.815314650535584

00:50:43.910 --> 00:50:46.556 She used the parametric flanker task  
NOTE Confidence: 0.815314650535584

00:50:46.556 --> 00:50:50.266 that we developed in the lab that very  
NOTE Confidence: 0.815314650535584

00:50:50.266 --> 00:50:52.591 nicely distinguishes smokers from non  
NOTE Confidence: 0.815314650535584

00:50:52.591 --> 00:50:55.084 from non smokers and I don't have  
NOTE Confidence: 0.815314650535584

00:50:55.084 --> 00:50:58.265 time to to go into that and perhaps I  
NOTE Confidence: 0.815314650535584

00:50:58.265 --> 00:51:01.087 won't tell you simply that the tasks  
NOTE Confidence: 0.815314650535584

00:51:01.087 --> 00:51:03.697 were parametric flanker task work and  
NOTE Confidence: 0.815314650535584

00:51:03.697 --> 00:51:06.368 people did worse smokers be worse.  
NOTE Confidence: 0.815314650535584

00:51:06.370 --> 00:51:09.874 They did worse when they were in abstinence  
NOTE Confidence: 0.815314650535584

00:51:09.874 --> 00:51:12.313 but importantly for this piece of  
NOTE Confidence: 0.815314650535584

00:51:12.313 --> 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 --> 00:51:26.276 The rush or ACC activity when the  
NOTE Confidence: 0.815314650535584  
00:51:26.276 --> 00:51:29.672 individual is doing a conflict ask  
NOTE Confidence: 0.815314650535584  
00:51:29.672 --> 00:51:32.960 the effect was bigger and smokers  
NOTE Confidence: 0.815314650535584  
00:51:32.960 --> 00:51:36.665 than nonsmokers for the N back  
NOTE Confidence: 0.815314650535584  
00:51:36.665 --> 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 --> 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 --> 00:51:52.994 allowing that performance to be to be better.  
NOTE Confidence: 0.815314650535584  
00:51:53.000 --> 00:51:54.248 And it did so.  
NOTE Confidence: 0.815314650535584  
00:51:54.248 --> 00:51:56.120 And this was the main point.  
NOTE Confidence: 0.815314650535584  
00:51:56.120 --> 00:51:58.297 I want to leave you with it.  
NOTE Confidence: 0.798081696033478  
00:51:58.300 --> 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 --> 00:52:04.438 the nicotine withdraw in state.  
NOTE Confidence: 0.798081696033478

00:52:04.440 --> 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 --> 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 --> 00:52:18.700 when they were sated than that and  
NOTE Confidence: 0.798081696033478

00:52:18.700 --> 00:52:21.398 when they were cognitively engage.  
NOTE Confidence: 0.798081696033478

00:52:21.400 --> 00:52:24.320 It may be that that this Admiral TV  
NOTE Confidence: 0.798081696033478

00:52:24.320 --> 00:52:28.067 CS might be a useful ad on therapy  
NOTE Confidence: 0.798081696033478

00:52:28.067 --> 00:52:29.534 alongside nicotine replacement  
NOTE Confidence: 0.798081696033478

00:52:29.534 --> 00:52:32.350 to perhaps increase the gain  
NOTE Confidence: 0.798081696033478

00:52:32.350 --> 00:52:34.590 of modifying these circuits.  
NOTE Confidence: 0.798081696033478

00:52:34.590 --> 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 --> 00:52:39.468 rushing rushing through things.  
NOTE Confidence: 0.798081696033478

00:52:39.470 --> 00:52:42.233 I just want to end with thanking the folks

NOTE Confidence: 0.798081696033478

00:52:42.233 --> 00:52:45.264 in the lab who really did all of the work,

NOTE Confidence: 0.798081696033478

00:52:45.270 --> 00:52:47.166 and I think I've mentioned those

NOTE Confidence: 0.798081696033478

00:52:47.166 --> 00:52:48.930 that were involved along the way.

NOTE Confidence: 0.798081696033478

00:52:48.930 --> 00:52:50.856 Some of my outside collaborators that

NOTE Confidence: 0.798081696033478

00:52:50.856 --> 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 --> 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 --> 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 --> 00:53:10.753 with with all of these details

NOTE Confidence: 0.830803871154785

00:53:10.753 --> 00:53:13.207 I mean functional mapping of the

NOTE Confidence: 0.830803871154785

00:53:13.293 --> 00:53:16.296 brain in the context of smoking in

NOTE Confidence: 0.830803871154785

00:53:16.296 --> 00:53:18.360 different state and trait effects.  
NOTE Confidence: 0.830803871154785

00:53:18.360 --> 00:53:20.360 We're just we're just gorgeous.  
NOTE Confidence: 0.830803871154785

00:53:20.360 --> 00:53:23.424 Let me just open this up now for  
NOTE Confidence: 0.830803871154785

00:53:23.424 --> 00:53:26.357 questions and comments from all of you.  
NOTE Confidence: 0.830803871154785

00:53:26.360 --> 00:53:29.041 I also want to just point out  
NOTE Confidence: 0.830803871154785

00:53:29.041 --> 00:53:31.568 that in fact the CME links.  
NOTE Confidence: 0.830803871154785

00:53:31.570 --> 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 --> 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 --> 00:53:46.710 function or raise your hand.  
NOTE Confidence: 0.896728515625

00:53:46.710 --> 00:53:48.772 Let me start actually Elliot.  
NOTE Confidence: 0.896728515625

00:53:48.772 --> 00:53:51.720 That was really gorgeous an it's just  
NOTE Confidence: 0.896728515625

00:53:51.720 --> 00:53:54.108 beautiful how you use different tasks  
NOTE Confidence: 0.896728515625

00:53:54.108 --> 00:53:56.946 that focus in on different aspects of

NOTE Confidence: 0.896728515625  
00:53:56.946 --> 00:53:59.706 function to sort of dissect the brain  
NOTE Confidence: 0.896728515625  
00:53:59.706 --> 00:54:02.539 under under a different drug related states.  
NOTE Confidence: 0.896728515625  
00:54:02.540 --> 00:54:05.389 The question I have is actually twofold.  
NOTE Confidence: 0.896728515625  
00:54:05.390 --> 00:54:07.903 One is there's a lot of blunting  
NOTE Confidence: 0.896728515625  
00:54:07.903 --> 00:54:09.850 under these acute withdrawal.  
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 --> 00:54:13.504 states that you showed.  
NOTE Confidence: 0.896728515625  
00:54:13.510 --> 00:54:15.958 It made me start to think  
NOTE Confidence: 0.896728515625  
00:54:15.958 --> 00:54:17.590 of whether that's tolerance.  
NOTE Confidence: 0.896728515625  
00:54:17.590 --> 00:54:22.054 Or just a lower level of functioning and?  
NOTE Confidence: 0.896728515625  
00:54:22.060 --> 00:54:23.745 Anan therefore you know the  
NOTE Confidence: 0.896728515625  
00:54:23.745 --> 00:54:25.430 flip side would be there.  
NOTE Confidence: 0.896728515625  
00:54:25.430 --> 00:54:27.758 Is there sort of you know you're in  
NOTE Confidence: 0.896728515625  
00:54:27.758 --> 00:54:30.268 the trap where if you try to reverse  
NOTE Confidence: 0.896728515625  
00:54:30.268 --> 00:54:32.510 that you might have sensitization.  
NOTE Confidence: 0.896728515625



00:54:32.510 --> 00:54:34.556 So what was sort of worried  
NOTE Confidence: 0.896728515625

00:54:34.556 --> 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 --> 00:54:40.316 But the second thing you know  
NOTE Confidence: 0.896728515625

00:54:40.316 --> 00:54:42.253 I'm going back to your silver  
NOTE Confidence: 0.896728515625

00:54:42.253 --> 00:54:44.371 buckshot 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 --> 00:54:50.036 different networks are affected.  
NOTE Confidence: 0.896728515625

00:54:50.036 --> 00:54:52.461 If we wanted to reverse this sort  
NOTE Confidence: 0.896728515625

00:54:52.461 --> 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 --> 00:55:00.038 tasks that are not so focused in fact,  
NOTE Confidence: 0.896728515625

00:55:00.040 --> 00:55:02.404 that I'm not just focused on  
NOTE Confidence: 0.896728515625

00:55:02.404 --> 00:55:03.980 a uni dimensional aspect,  
NOTE Confidence: 0.896728515625

00:55:03.980 --> 00:55:06.735 but rather because drugs of abuse are

NOTE Confidence: 0.896728515625

00:55:06.735 --> 00:55:09.500 affecting so many regions that we need.

NOTE Confidence: 0.896728515625

00:55:09.500 --> 00:55:12.251 Some things that are more widespread in

NOTE Confidence: 0.896728515625

00:55:12.251 --> 00:55:14.619 their effects of activating the brain.

NOTE Confidence: 0.872581660747528

00:55:15.520 --> 00:55:17.844 Yeah yeah. So let me take that.

NOTE Confidence: 0.872581660747528

00:55:17.850 --> 00:55:19.182 That second question first

NOTE Confidence: 0.872581660747528

00:55:19.182 --> 00:55:20.847 'cause I can remember it.

NOTE Confidence: 0.872581660747528

00:55:20.850 --> 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 --> 00:55:28.700 Why? Why does it seem to be

NOTE Confidence: 0.872581660747528

00:55:28.700 --> 00:55:30.440 reasonably efficacious in depression?

NOTE Confidence: 0.872581660747528

00:55:30.440 --> 00:55:31.968 Maybe in another nurse?

NOTE Confidence: 0.872581660747528

00:55:31.968 --> 00:55:33.878 Psychiatric disorders OC D is

NOTE Confidence: 0.872581660747528

00:55:33.878 --> 00:55:35.930 going to prove this, you know.

NOTE Confidence: 0.872581660747528

00:55:35.930 --> 00:55:39.730 What is it about the DL Pfc it happens to?

NOTE Confidence: 0.872581660747528

00:55:39.730 --> 00:55:41.330 Of course be something accessible

NOTE Confidence: 0.872581660747528

00:55:41.330 --> 00:55:43.550 by TMS which doesn't go very deep,  
NOTE Confidence: 0.872581660747528

00:55:43.550 --> 00:55:45.320 but when you think about the  
NOTE Confidence: 0.872581660747528

00:55:45.320 --> 00:55:47.476 circuitry in one of the one pieces  
NOTE Confidence: 0.872581660747528

00:55:47.476 --> 00:55:49.590 that I showed you in bed circuitry  
NOTE Confidence: 0.872581660747528

00:55:49.653 --> 00:55:51.807 between there and the insula right,  
NOTE Confidence: 0.872581660747528

00:55:51.810 --> 00:55:53.954 maybe we can think of this as being  
NOTE Confidence: 0.872581660747528

00:55:53.954 --> 00:55:56.384 sort of top of funnel that what we're  
NOTE Confidence: 0.872581660747528

00:55:56.384 --> 00:55:58.794 what we're doing is we're accessing a  
NOTE Confidence: 0.872581660747528

00:55:58.794 --> 00:56:01.038 lodging network from this from this.  
NOTE Confidence: 0.872581660747528

00:56:01.040 --> 00:56:03.768 Or maybe it's an inverse funnel than that  
NOTE Confidence: 0.872581660747528

00:56:03.768 --> 00:56:06.434 I'm accessing it from this point that I mean,  
NOTE Confidence: 0.872581660747528

00:56:06.440 --> 00:56:08.729 the DL Pfc is a sketch pad.  
NOTE Confidence: 0.872581660747528

00:56:08.730 --> 00:56:10.210 This is where we are.  
NOTE Confidence: 0.872581660747528

00:56:10.210 --> 00:56:12.023 Lots of things are going in and  
NOTE Confidence: 0.872581660747528

00:56:12.023 --> 00:56:13.749 out of brain for processing.  
NOTE Confidence: 0.872581660747528

00:56:13.750 --> 00:56:14.396 You know,

NOTE Confidence: 0.872581660747528  
00:56:14.396 --> 00:56:15.688 executive function talking to  
NOTE Confidence: 0.872581660747528  
00:56:15.688 --> 00:56:17.640 a lot of downstream components.  
NOTE Confidence: 0.872581660747528  
00:56:17.640 --> 00:56:21.344 And so it may be that these multifaceted  
NOTE Confidence: 0.872581660747528  
00:56:21.344 --> 00:56:24.868 aspects of Sud that we all acknowledge  
NOTE Confidence: 0.872581660747528  
00:56:24.868 --> 00:56:27.959 with come together in these large  
NOTE Confidence: 0.872581660747528  
00:56:27.959 --> 00:56:30.959 scale logical networks that may be  
NOTE Confidence: 0.872581660747528  
00:56:30.959 --> 00:56:35.780 amenable to to an intervention like that.  
NOTE Confidence: 0.872581660747528  
00:56:35.780 --> 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 --> 00:56:42.090 there's some of the things  
NOTE Confidence: 0.872581660747528  
00:56:42.090 --> 00:56:44.750 that are that we wonder about.  
NOTE Confidence: 0.872581660747528  
00:56:44.750 --> 00:56:47.330 From the one hand going on,  
NOTE Confidence: 0.872581660747528  
00:56:47.330 --> 00:56:49.030 uh, thinking about specificity,  
NOTE Confidence: 0.872581660747528  
00:56:49.030 --> 00:56:51.580 event of anatomy and specificity of  
NOTE Confidence: 0.872581660747528  
00:56:51.650 --> 00:56:53.794 the receptor target, versus perhaps,  
NOTE Confidence: 0.872581660747528

00:56:53.794 --> 00:56:54.668 you know,  
NOTE Confidence: 0.872581660747528

00:56:54.668 --> 00:56:57.290 the most efficacious treatment we have  
NOTE Confidence: 0.872581660747528

00:56:57.361 --> 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 --> 00:57:04.550 So ECT works on, you know, 70% ish of.  
NOTE Confidence: 0.872581660747528

00:57:04.550 --> 00:57:06.428 Medication resistant depression.  
NOTE Confidence: 0.872581660747528

00:57:06.428 --> 00:57:08.306 And there's no,  
NOTE Confidence: 0.872581660747528

00:57:08.310 --> 00:57:10.346 there's no localization there.  
NOTE Confidence: 0.872581660747528

00:57:10.346 --> 00:57:14.650 So you know the other thing I would point  
NOTE Confidence: 0.872581660747528

00:57:14.650 --> 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 --> 00:57:23.878 and again if you get beyond  
NOTE Confidence: 0.872581660747528

00:57:23.878 --> 00:57:25.590 the cortical striated piece,  
NOTE Confidence: 0.872581660747528

00:57:25.590 --> 00:57:29.014 but the pieces that are talking into this,  
NOTE Confidence: 0.872581660747528

00:57:29.020 --> 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 --> 00:57:38.430 structures in both in the disease,  
NOTE Confidence: 0.872581660747528  
00:57:38.430 --> 00:57:40.570 and perhaps in this intervention.  
NOTE Confidence: 0.872581660747528  
00:57:40.570 --> 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 --> 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 --> 00:57:55.220 Is it simply a matter of well,  
NOTE Confidence: 0.872581660747528  
00:57:55.220 --> 00:57:57.605 so you talked about tolerance  
NOTE Confidence: 0.872581660747528  
00:57:57.605 --> 00:57:59.513 and sensitization right when?  
NOTE Confidence: 0.872581660747528  
00:57:59.520 --> 00:58:02.960 When an acutely abstinent smoker?  
NOTE Confidence: 0.872581660747528  
00:58:02.960 --> 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 --> 00:58:12.646 They're not,  
NOTE Confidence: 0.872581660747528

00:58:12.646 --> 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 --> 00:58:19.480 They seem to,  
NOTE Confidence: 0.872581660747528

00:58:19.480 --> 00:58:22.205 and in fact there is almost no  
NOTE Confidence: 0.872581660747528

00:58:22.205 --> 00:58:24.551 tolerance to smoking people that smoke  
NOTE Confidence: 0.872581660747528

00:58:24.551 --> 00:58:27.821 a pack a day smoker pack a day and  
NOTE Confidence: 0.872581660747528

00:58:27.821 --> 00:58:31.040 for 20 years they smoke a pack a day.  
NOTE Confidence: 0.872581660747528

00:58:31.040 --> 00:58:33.200 That's very different than the profile  
NOTE Confidence: 0.872581660747528

00:58:33.200 --> 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 --> 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 --> 00:58:44.530 a cute an acute deprivation state  
NOTE Confidence: 0.848867356777191

00:58:44.592 --> 00:58:46.380 that's that's simply reverse.

NOTE Confidence: 0.848867356777191  
00:58:46.380 --> 00:58:48.385 Ameliorated by the replacement of  
NOTE Confidence: 0.848867356777191  
00:58:48.385 --> 00:58:50.398 nicotine, and that's an that's  
NOTE Confidence: 0.848867356777191  
00:58:50.398 --> 00:58:52.408 shown cognitively as well as  
NOTE Confidence: 0.820339739322662  
00:58:52.410 --> 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 --> 00:58:59.239 We have a question in the chat box.  
NOTE Confidence: 0.820339739322662  
00:58:59.240 --> 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 --> 00:59:05.680 based ones like CBT effect these  
NOTE Confidence: 0.828417216028486  
00:59:05.680 --> 00:59:08.608 networks? I think all interventions are  
NOTE Confidence: 0.828417216028486  
00:59:08.608 --> 00:59:12.419 going to change if you change the brain.  
NOTE Confidence: 0.828417216028486  
00:59:12.420 --> 00:59:14.975 You're going to change the networks and  
NOTE Confidence: 0.828417216028486  
00:59:14.975 --> 00:59:17.619 whether we change them pharmacologically.  
NOTE Confidence: 0.828417216028486  
00:59:17.620 --> 00:59:19.096 Using noninvasive brain stimulation.  
NOTE Confidence: 0.828417216028486  
00:59:19.096 --> 00:59:21.310 Whether we use CBT or other  
NOTE Confidence: 0.828417216028486



00:59:21.368 --> 00:59:22.810 behavioral interventions.  
NOTE Confidence: 0.828417216028486

00:59:22.810 --> 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 --> 00:59:30.079 My long-term hope is that it's going  
NOTE Confidence: 0.828417216028486

00:59:30.079 --> 00:59:33.203 to be a combination therapy and you  
NOTE Confidence: 0.828417216028486

00:59:33.203 --> 00:59:36.337 and I would talk about this over  
NOTE Confidence: 0.828417216028486

00:59:36.337 --> 00:59:39.340 the years that it's going to be.  
NOTE Confidence: 0.828417216028486

00:59:39.340 --> 00:59:41.064 You know, supportive pharmacotherapy,  
NOTE Confidence: 0.828417216028486

00:59:41.064 --> 00:59:42.357 interventional behavioral interventions,  
NOTE Confidence: 0.828417216028486

00:59:42.360 --> 00:59:44.520 and with potentially neural modulation,  
NOTE Confidence: 0.828417216028486

00:59:44.520 --> 00:59:46.680 then that might enhance these  
NOTE Confidence: 0.828417216028486

00:59:46.680 --> 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 --> 01:00:00.500 really have a question just  
NOTE Confidence: 0.84974867105484

01:00:00.500 --> 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 --> 01:00:06.744 I'm actually a fourth year  
NOTE Confidence: 0.84974867105484  
01:00:06.744 --> 01:00:08.132 medical student at Howard.  
NOTE Confidence: 0.84974867105484  
01:00:08.132 --> 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 --> 01:00:12.636 Schottenfeld who passed it along and  
NOTE Confidence: 0.84974867105484  
01:00:12.640 --> 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 --> 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 --> 01:00:21.315 ago as a high school student.  
NOTE Confidence: 0.84974867105484  
01:00:21.315 --> 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 --> 01:00:28.594 to join a listening to everything  
NOTE Confidence: 0.84974867105484  
01:00:28.600 --> 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 --> 01:00:33.950 pursue science and medicine,  
NOTE Confidence: 0.84974867105484

01:00:33.950 --> 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 --> 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 --> 01:00:46.160 I will say one of the best parts of this job.  
NOTE Confidence: 0.846236169338226

01:00:46.160 --> 01:00:48.344 The absolute best parts of this job.  
NOTE Confidence: 0.846236169338226

01:00:48.350 --> 01:00:50.228 Other students working in the lab,  
NOTE Confidence: 0.846236169338226

01:00:50.230 --> 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 --> 01:00:55.670 we have a number of programs at  
NOTE Confidence: 0.846236169338226

01:00:55.670 --> 01:00:57.292 the intramural program and we  
NOTE Confidence: 0.846236169338226

01:00:57.292 --> 01:00:58.990 get students in at all levels,  
NOTE Confidence: 0.846236169338226

01:00:58.990 --> 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 --> 01:01:03.500 think wonderful.  
NOTE Confidence: 0.777802288532257  
01:01:03.500 --> 01:01:05.040 Well, thank you Justin.  
NOTE Confidence: 0.777802288532257  
01:01:05.040 --> 01:01:08.028 I hope we can interact you over to Yale  
NOTE Confidence: 0.777802288532257  
01:01:08.028 --> 01:01:10.827 for your post medical school years.  
NOTE Confidence: 0.777802288532257  
01:01:10.830 --> 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 --> 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 --> 01:01:37.039 study when you had the error made  
NOTE Confidence: 0.864145636558533

01:01:37.040 --> 01:01:39.854 and you gave the feedback of the  
NOTE Confidence: 0.864145636558533

01:01:39.854 --> 01:01:42.076 negative frowny phase versus the  
NOTE Confidence: 0.864145636558533

01:01:42.076 --> 01:01:44.416 error made an ambiguous feedback.  
NOTE Confidence: 0.864145636558533

01:01:44.420 --> 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 --> 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 --> 01:01:57.080 the speed that I that I.  
NOTE Confidence: 0.878468342125416

01:01:57.080 --> 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 --> 01:02:03.550 so I wanted to tease you with it.  
NOTE Confidence: 0.878468342125416

01:02:03.550 --> 01:02:05.020 Yeah there were two bars.  
NOTE Confidence: 0.878468342125416

01:02:05.020 --> 01:02:07.036 If you can think of the slide there  
NOTE Confidence: 0.878468342125416

01:02:07.036 --> 01:02:09.077 are two bars to the right that  
NOTE Confidence: 0.878468342125416

01:02:09.077 --> 01:02:10.929 we're both yellow and those were

NOTE Confidence: 0.878468342125416  
01:02:10.929 --> 01:02:12.867 the those were the non informative  
NOTE Confidence: 0.878468342125416  
01:02:12.867 --> 01:02:15.016 feedback and it was sort of a  
NOTE Confidence: 0.878468342125416  
01:02:15.016 --> 01:02:15.898 neutral activity activation.  
NOTE Confidence: 0.76599109172821  
01:02:18.140 --> 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 --> 01:02:35.710 Sorry I'm trying to unmute myself  
NOTE Confidence: 0.859870076179504  
01:02:35.710 --> 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 --> 01:02:44.199 series of studies that you know  
NOTE Confidence: 0.859870076179504  
01:02:44.199 --> 01:02:46.410 are all connect and makes sense.  
NOTE Confidence: 0.859870076179504  
01:02:46.410 --> 01:02:49.470 I wish we were also lucky to have results  
NOTE Confidence: 0.859870076179504

01:02:49.470 --> 01:02:52.270 which kind of all fit together so well.  
NOTE Confidence: 0.859870076179504

01:02:52.270 --> 01:02:54.000 So thank you for that.  
NOTE Confidence: 0.859870076179504

01:02:54.000 --> 01:02:57.450 I guess my question is more of a general one,  
NOTE Confidence: 0.859870076179504

01:02:57.450 --> 01:03:00.501 which is a lot of the studies that you  
NOTE Confidence: 0.859870076179504

01:03:00.501 --> 01:03:02.620 presented were in the adult brain.  
NOTE Confidence: 0.859870076179504

01:03:02.620 --> 01:03:04.004 If I understand correctly.  
NOTE Confidence: 0.859870076179504

01:03:04.004 --> 01:03:06.451 You know now we are in the  
NOTE Confidence: 0.859870076179504

01:03:06.451 --> 01:03:08.209 in the US and World Wide.  
NOTE Confidence: 0.859870076179504

01:03:08.210 --> 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 --> 01:03:14.602 in youth and have you know I would.  
NOTE Confidence: 0.859870076179504

01:03:14.610 --> 01:03:16.584 I would think knowing little bit that  
NOTE Confidence: 0.859870076179504

01:03:16.584 --> 01:03:19.026 I do about the youth brain that you  
NOTE Confidence: 0.859870076179504

01:03:19.026 --> 01:03:21.335 would anticipate that a lot of the  
NOTE Confidence: 0.859870076179504

01:03:21.335 --> 01:03:22.771 flexibility or inflexibility that  
NOTE Confidence: 0.859870076179504

01:03:22.771 --> 01:03:25.185 you're seeing in the adult brain would

NOTE Confidence: 0.859870076179504  
01:03:25.185 --> 01:03:27.135 reflect very differently in the youth  
NOTE Confidence: 0.859870076179504  
01:03:27.135 --> 01:03:29.007 brain is what my understanding is.  
NOTE Confidence: 0.859870076179504  
01:03:29.010 --> 01:03:30.774 Could you maybe speak a little  
NOTE Confidence: 0.859870076179504  
01:03:30.774 --> 01:03:32.850 bit to what you would expect?  
NOTE Confidence: 0.859870076179504  
01:03:32.850 --> 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 --> 01:03:40.035 that's a great question.  
NOTE Confidence: 0.90646356344223  
01:03:40.040 --> 01:03:42.328 So we have studied only adults as you,  
NOTE Confidence: 0.90646356344223  
01:03:42.330 --> 01:03:44.895 as you alluded to. 18 to 60 year olds.  
NOTE Confidence: 0.90646356344223  
01:03:44.900 --> 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 --> 01:03:53.851 of smoking that nobody thought  
NOTE Confidence: 0.90646356344223  
01:03:53.851 --> 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 --> 01:03:59.807 high school and not be a smoker,  
NOTE Confidence: 0.90646356344223



01:03:59.810 --> 01:04:02.085 the likelihood of them smoking is very,  
NOTE Confidence: 0.90646356344223

01:04:02.090 --> 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 --> 01:04:09.238 and we know that you as you just alluded to,  
NOTE Confidence: 0.90646356344223

01:04:09.240 --> 01:04:11.190 that that's the time of greatest  
NOTE Confidence: 0.90646356344223

01:04:11.190 --> 01:04:12.490 flexibility in the brain,  
NOTE Confidence: 0.90646356344223

01:04:12.490 --> 01:04:13.624 greatest developmental plasticity.  
NOTE Confidence: 0.90646356344223

01:04:13.624 --> 01:04:16.270 And so we have two things going  
NOTE Confidence: 0.90646356344223

01:04:16.331 --> 01:04:18.119 on right with beating the brain  
NOTE Confidence: 0.90646356344223

01:04:18.119 --> 01:04:19.942 up with this foreign substance at  
NOTE Confidence: 0.90646356344223

01:04:19.942 --> 01:04:21.944 the same time that the brain is.  
NOTE Confidence: 0.90646356344223

01:04:21.950 --> 01:04:22.800 Is maturing.  
NOTE Confidence: 0.90646356344223

01:04:22.800 --> 01:04:25.350 And so you would expect that  
NOTE Confidence: 0.90646356344223

01:04:25.350 --> 01:04:28.417 one of the reasons perhaps why,  
NOTE Confidence: 0.90646356344223

01:04:28.420 --> 01:04:29.617 as an adult,

NOTE Confidence: 0.90646356344223  
01:04:29.617 --> 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 --> 01:04:36.620 is that that plasticity is  
NOTE Confidence: 0.90646356344223  
01:04:36.620 --> 01:04:38.670 well locked in right now.  
NOTE Confidence: 0.90646356344223  
01:04:38.670 --> 01:04:41.556 Which of those circuits potentially were  
NOTE Confidence: 0.90646356344223  
01:04:41.556 --> 01:04:44.988 affected the most at that at that time?  
NOTE Confidence: 0.90646356344223  
01:04:44.990 --> 01:04:48.280 I do have data in my pocket  
NOTE Confidence: 0.90646356344223  
01:04:48.280 --> 01:04:52.229 that is not ready for primetime.  
NOTE Confidence: 0.90646356344223  
01:04:52.230 --> 01:04:55.954 The the animal studies that I showed  
NOTE Confidence: 0.90646356344223  
01:04:55.954 --> 01:04:59.469 you that that Robin Keeley did.  
NOTE Confidence: 0.90646356344223  
01:04:59.470 --> 01:05:02.806 We repeated in in neonatal rats.  
NOTE Confidence: 0.90646356344223  
01:05:02.810 --> 01:05:08.130 So we we started this at P.  
NOTE Confidence: 0.90646356344223  
01:05:08.130 --> 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 --> 01:05:17.122 different starting points along  
NOTE Confidence: 0.90646356344223

01:05:17.122 --> 01:05:20.079 development and we allowed them  
NOTE Confidence: 0.90646356344223

01:05:20.079 --> 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 --> 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 --> 01:05:33.967 one of the nice things we have in  
NOTE Confidence: 0.90646356344223

01:05:33.967 --> 01:05:36.464 animal magnet. We can do scanning.  
NOTE Confidence: 0.90646356344223

01:05:36.464 --> 01:05:39.362 I think we scan these these rats  
NOTE Confidence: 0.90646356344223

01:05:39.362 --> 01:05:41.997 four times across the development.  
NOTE Confidence: 0.90646356344223

01:05:42.000 --> 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 --> 01:05:49.806 heads around itself,  
NOTE Confidence: 0.90646356344223

01:05:49.810 --> 01:05:52.033 give me a call in a couple of months  
NOTE Confidence: 0.90646356344223

01:05:52.033 --> 01:05:54.115 an I'll have some data for you,  
NOTE Confidence: 0.90646356344223

01:05:54.120 --> 01:05:55.992 but it's a critical question that

NOTE Confidence: 0.90646356344223

01:05:55.992 --> 01:05:57.910 we think that this really is.

NOTE Confidence: 0.90646356344223

01:05:57.910 --> 01:06:00.410 Something that that's very relevant

NOTE Confidence: 0.90646356344223

01:06:00.410 --> 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 --> 01:06:08.591 curious to know whether this process

NOTE Confidence: 0.890278100967407

01:06:08.591 --> 01:06:10.921 that is changing that you're

NOTE Confidence: 0.890278100967407

01:06:10.921 --> 01:06:13.309 describing you know with nicotine.

NOTE Confidence: 0.890278100967407

01:06:13.310 --> 01:06:15.977 The timeliness of that and how it

NOTE Confidence: 0.890278100967407

01:06:15.977 --> 01:06:18.598 changes in younger populations will be

NOTE Confidence: 0.890278100967407

01:06:18.598 --> 01:06:20.938 very interesting to examine because

NOTE Confidence: 0.890278100967407

01:06:20.938 --> 01:06:24.007 you know you don't get the same

NOTE Confidence: 0.890278100967407

01:06:24.007 --> 01:06:26.057 profile of nicotine withdrawal in

NOTE Confidence: 0.861741483211518

01:06:26.060 --> 01:06:27.716 younger populations too, so.

NOTE Confidence: 0.861741483211518

01:06:27.716 --> 01:06:30.200 Really, I'm really glad you mentioned that.

NOTE Confidence: 0.861741483211518

01:06:30.200 --> 01:06:32.258 So kids when they stop smoking do

NOTE Confidence: 0.861741483211518

01:06:32.258 --> 01:06:34.937 not have a very serious effective  
NOTE Confidence: 0.861741483211518

01:06:34.937 --> 01:06:40.221 withdrawal syndrome. I. That that's.  
NOTE Confidence: 0.861741483211518

01:06:40.221 --> 01:06:43.750 Fascinating. Any other there  
NOTE Confidence: 0.868219435214996

01:06:43.750 --> 01:06:46.490 is another question in chat.  
NOTE Confidence: 0.868219435214996

01:06:46.490 --> 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 --> 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 --> 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 --> 01:07:18.591 the end that I didn't punish you with  
NOTE Confidence: 0.820001661777496

01:07:18.591 --> 01:07:21.476 to look at at fractionating as we're  
NOTE Confidence: 0.820001661777496

01:07:21.476 --> 01:07:23.486 beginning to fractionate the phenotype,  
NOTE Confidence: 0.820001661777496

01:07:23.490 --> 01:07:25.940 so we're not doing a particularly good  
NOTE Confidence: 0.820001661777496

01:07:25.940 --> 01:07:28.418 job at looking at individual differences

NOTE Confidence: 0.820001661777496  
01:07:28.418 --> 01:07:31.142 with with interventions of any sort,  
NOTE Confidence: 0.820001661777496  
01:07:31.150 --> 01:07:32.990 there is the nicotine metabolism  
NOTE Confidence: 0.820001661777496  
01:07:32.990 --> 01:07:35.333 ratio work that Karen Lerman has  
NOTE Confidence: 0.820001661777496  
01:07:35.333 --> 01:07:37.073 shown for individual differences  
NOTE Confidence: 0.820001661777496  
01:07:37.073 --> 01:07:39.248 with slow versus fast metabolizers.  
NOTE Confidence: 0.820001661777496  
01:07:39.250 --> 01:07:42.118 And we know that slow metabolizers  
NOTE Confidence: 0.820001661777496  
01:07:42.118 --> 01:07:45.075 seem to do better with, well,  
NOTE Confidence: 0.820001661777496  
01:07:45.075 --> 01:07:47.015 buitron fast metabolizers seem  
NOTE Confidence: 0.820001661777496  
01:07:47.015 --> 01:07:49.440 to do better with NRT.  
NOTE Confidence: 0.820001661777496  
01:07:49.440 --> 01:07:52.737 That's one of the best examples I  
NOTE Confidence: 0.820001661777496  
01:07:52.737 --> 01:07:55.440 know of fractionating the phenotype.  
NOTE Confidence: 0.820001661777496  
01:07:55.440 --> 01:07:56.800 I would hope that.  
NOTE Confidence: 0.820001661777496  
01:07:56.800 --> 01:07:59.772 If we all get to do this wonderful  
NOTE Confidence: 0.820001661777496  
01:07:59.772 --> 01:08:03.587 job for a few more years that we we  
NOTE Confidence: 0.820001661777496  
01:08:03.587 --> 01:08:06.809 can get down the road to begin to do.  
NOTE Confidence: 0.820001661777496

01:08:06.810 --> 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 --> 01:08:12.654 fact the well buitron 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 --> 01:08:18.230 I mean if you think about it.  
NOTE Confidence: 0.820001661777496

01:08:18.230 --> 01:08:21.275 NRT works in 1015% of the people.  
NOTE Confidence: 0.820001661777496

01:08:21.280 --> 01:08:23.450 Well buitron, 20 ish percent.  
NOTE Confidence: 0.820001661777496

01:08:23.450 --> 01:08:25.270 Varena clean thirtyish percent  
NOTE Confidence: 0.820001661777496

01:08:25.270 --> 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 --> 01:08:35.137 people 100% of the time.  
NOTE Confidence: 0.820001661777496

01:08:35.140 --> 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 --> 01:08:39.319 but we just don't know who they are right?  
NOTE Confidence: 0.820001661777496

01:08:39.320 --> 01:08:41.091 And we also don't know if they're  
NOTE Confidence: 0.820001661777496

01:08:41.091 --> 01:08:42.959 the same people or if these are

NOTE Confidence: 0.820001661777496  
01:08:42.959 --> 01:08:44.279 in fact independent Co boards.  
NOTE Confidence: 0.820001661777496  
01:08:44.280 --> 01:08:45.580 So it's a great question.  
NOTE Confidence: 0.820001661777496  
01:08:45.580 --> 01:08:46.624 We're not there yet.  
NOTE Confidence: 0.820001661777496  
01:08:46.624 --> 01:08:48.190 It's sort of the Holy Grail,  
NOTE Confidence: 0.820001661777496  
01:08:48.190 --> 01:08:49.202 at least in my.  
NOTE Confidence: 0.820001661777496  
01:08:49.202 --> 01:08:50.720 In my thinking that we can  
NOTE Confidence: 0.820001661777496  
01:08:50.783 --> 01:08:52.108 do that at some point.  
NOTE Confidence: 0.826059877872467  
01:08:56.650 --> 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 --> 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 --> 01:09:14.728 That wasn't my hand raised.  
NOTE Confidence: 0.826059877872467



01:09:14.728 --> 01:09:15.826 That was me  
NOTE Confidence: 0.628543972969055

01:09:15.830 --> 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 --> 01:09:23.789 see any good options? Trisha. I  
NOTE Confidence: 0.867055237293243

01:09:23.790 --> 01:09:25.810 think we are all set.  
NOTE Confidence: 0.867055237293243

01:09:25.810 --> 01:09:28.244 I don't see any other hands  
NOTE Confidence: 0.867055237293243

01:09:28.244 --> 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 --> 01:09:36.752 stimulating talk.  
NOTE Confidence: 0.867055237293243

01:09:36.752 --> 01:09:39.594 It's got everybody's juices going and we.  
NOTE Confidence: 0.867055237293243

01:09:39.600 --> 01:09:41.822 Now we will be following up on  
NOTE Confidence: 0.867055237293243

01:09:41.822 --> 01:09:43.730 your papers and things like that.  
NOTE Confidence: 0.867055237293243

01:09:43.730 --> 01:09:44.588 Thanks so much.  
NOTE Confidence: 0.867055237293243

01:09:44.588 --> 01:09:46.590 I know it's really early where you  
NOTE Confidence: 0.867055237293243

01:09:46.654 --> 01:09:48.537 are and you've taken the you woken

NOTE Confidence: 0.867055237293243

01:09:48.537 --> 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 --> 01:09:56.480 Thank you everyone, thanks.