WEBVTT

00:00:00.000 --> 00:00:01.464 Before we get started,

00:00:01.464 --> 00:00:05.500 I'd like to say a few introductory remarks.

00:00:05.500 --> 00:00:07.558 1st, just a reminder to keep your

00:00:07.558 --> 00:00:09.336 microphones on mute during the talk

00:00:09.336 --> 00:00:11.046 and during the discussion less you

00:00:11.046 --> 00:00:13.028 are speaking during that discussion.

00:00:13.028 --> 00:00:14.860 Also, if you'd like to ask questions,

00:00:14.860 --> 00:00:16.964 please hold them to the end of the

00:00:16.964 --> 00:00:18.997 talk or place them in the chat.

00:00:19.000 --> 00:00:21.212 In doing so, I'd like to encourage

00:00:21.212 --> 00:00:23.369 everyone to maintain a respectful stance,

00:00:23.370 --> 00:00:25.035 nuances, sometimes hard to discern

00:00:25.035 --> 00:00:27.400 in the format of a zoom call,

00:00:27.400 --> 00:00:29.745 and so it pays to be particularly

NOTE Confidence: 0.85625379

00:00:29.750 --> 00:00:31.850 thoughtful about this. Next,

NOTE Confidence: 0.86269116

00:00:31.850 --> 00:00:34.027 for those of you who are joining

NOTE Confidence: 0.86269116

00:00:34.027 --> 00:00:35.910 us from other institutions,

NOTE Confidence: 0.86269116

00:00:35.910 --> 00:00:38.486 a special welcome like attendees from Yale.

NOTE Confidence: 0.86269116

00:00:38.490 --> 00:00:41.076 If you'd like to receive CME credit,

NOTE Confidence: 0.86269116

00:00:41.076 --> 00:00:43.780 you may Trisha Doll will post information

NOTE Confidence: 0.86269116

00:00:43.780 --> 00:00:46.608 in the chat about how to sign up.

NOTE Confidence: 0.86269116

00:00:46.610 --> 00:00:48.082 She'll also post information

NOTE Confidence: 0.86269116

00:00:48.082 --> 00:00:50.300 about how to receive credit for

NOTE Confidence: 0.86269116

00:00:50.300 --> 00:00:53.040 participation in today's lecture.

NOTE Confidence: 0.86269116

00:00:53.040 --> 00:00:55.140 Finally, I'd like to announce that

NOTE Confidence: 0.86269116

00:00:55.140 --> 00:00:57.162 the Grand Round speaker next week

NOTE Confidence: 0.86269116

00:00:57.162 --> 00:00:58.942 will be Dean moves from Caltech,

NOTE Confidence: 0.86269116

00:00:58.942 --> 00:01:01.894 who will be speaking on space, time and fear.

NOTE Confidence: 0.86269116

00:01:01.894 --> 00:01:03.534 Survival decisions along defensive circuits,

NOTE Confidence: 0.86269116

00:01:03.540 --> 00:01:05.496 so I encourage you to attend

NOTE Confidence: 0.86269116

00:01:05.500 --> 00:01:06.817 next week as well.

NOTE Confidence: 0.86269116

00:01:06.817 --> 00:01:09.106 So with these introductory remarks behind us,

NOTE Confidence: 0.86269116

00:01:09.110 --> 00:01:10.750 I'm pleased to introduce our

NOTE Confidence: 0.86269116

00:01:10.750 --> 00:01:12.390 Grand round speaker Doctor Sarah.

NOTE Confidence: 0.86269116

00:01:12.390 --> 00:01:13.215 Yep.

NOTE Confidence: 0.86269116

00:01:13.215 --> 00:01:16.330 Doctor Yip received her PhD in

NOTE Confidence: 0.86269116

00:01:16.330 --> 00:01:19.107 psychiatry from the University of Oxford

NOTE Confidence: 0.86269116

00:01:19.107 --> 00:01:22.590 and in the United Kingdom in 2013.

NOTE Confidence: 0.86269116

00:01:22.590 --> 00:01:22.896 Subsequently,

NOTE Confidence: 0.86269116

00:01:22.896 --> 00:01:25.038 she came to Yale to complete a

NOTE Confidence: 0.86269116

00:01:25.038 --> 00:01:26.978 two year fellowship in Addiction

NOTE Confidence: 0.86269116

00:01:26.978 --> 00:01:29.088 Psychiatry within the Division of

NOTE Confidence: 0.86269116

00:01:29.088 --> 00:01:31.030 Substance Abuse in our Department.

NOTE Confidence: 0.86269116

00:01:31.030 --> 00:01:33.226 She was then promoted to Associate

NOTE Confidence: 0.86269116

00:01:33.230 --> 00:01:34.698 research Scientist and subsequently

NOTE Confidence: 0.86269116

00:01:34.698 --> 00:01:36.538 to assistant professor in 2016,

NOTE Confidence: 0.86269116

00:01:36.540 --> 00:01:38.634 and she holds a joint appointment

NOTE Confidence: 0.86269116

00:01:38.634 --> 00:01:40.570 in the Child Study Center.

NOTE Confidence: 0.86269116

00:01:40.570 --> 00:01:42.940 Ann in psychiatry.

NOTE Confidence: 0.86269116

00:01:42.940 --> 00:01:44.041 While at Yale,

NOTE Confidence: 0.86269116

00:01:44.041 --> 00:01:45.876 she is used Nuro psychiatric

NOTE Confidence: 0.86269116

00:01:45.876 --> 00:01:48.011 research methods to identify the

NOTE Confidence: 0.86269116

00:01:48.011 --> 00:01:49.795 biological mechanisms of addictions

NOTE Confidence: 0.86269116

00:01:49.795 --> 00:01:51.133 and their treatments.

NOTE Confidence: 0.86269116

00:01:51.140 --> 00:01:52.700 To support her efforts,

NOTE Confidence: 0.86269116

00:01:52.700 --> 00:01:54.260 she's been remarkably successful

NOTE Confidence: 0.86269116

00:01:54.260 --> 00:01:56.059 in obtaining external funding,

NOTE Confidence: 0.86269116

00:01:56.060 --> 00:01:58.520 including from the UK's Medical Research

NOTE Confidence: 0.86269116

00:01:58.520 --> 00:02:00.160 Council, Beijing Normal University,

NOTE Confidence: 0.86269116

00:02:00.160 --> 00:02:02.210 the National Center for Addiction,

NOTE Confidence: 0.86269116

00:02:02.210 --> 00:02:03.030 Substance Abuse,

NOTE Confidence: 0.86269116

00:02:03.030 --> 00:02:05.490 the Brain and Behavior Research Foundation,

NOTE Confidence: 0.86269116

00:02:05.490 --> 00:02:07.480 Naida, and, most recently,

NOTE Confidence: 0.86269116

00:02:07.480 --> 00:02:09.000 in IEEE.

NOTE Confidence: 0.86269116

00:02:09.000 --> 00:02:10.258 In this work,

NOTE Confidence: 0.86269116

00:02:10.258 --> 00:02:12.090 she's applied machine learning

NOTE Confidence: 0.86269116

00:02:12.090 --> 00:02:13.922 approaches to identify predictive

NOTE Confidence: 0.86269116

00:02:13.922 --> 00:02:15.815 neural mark rows of cocaine and

NOTE Confidence: 0.86269116

00:02:15.815 --> 00:02:18.160 opioid use as well as collection of

NOTE Confidence: 0.86269116

00:02:18.160 --> 00:02:19.992 neuroimaging data from individuals

NOTE Confidence: 0.86269116

00:02:19.992 --> 00:02:22.233 receiving different forms of medication

NOTE Confidence: 0.86269116

00:02:22.233 --> 00:02:23.840 assisted treatments for opioid

NOTE Confidence: 0.86269116

00:02:23.840 --> 00:02:25.440 use disorder or pharmacological

NOTE Confidence: 0.86269116

00:02:25.440 --> 00:02:26.606 challenges with medications,

NOTE Confidence: 0.86269116

00:02:26.606 --> 00:02:28.436 and most recently she's received

NOTE Confidence: 0.86269116

00:02:28.436 --> 00:02:31.108 funding from an I AAA to include

NOTE Confidence: 0.86269116

00:02:31.108 --> 00:02:32.640 predictive modeling of neuroimaging

NOTE Confidence: 0.86269116

00:02:32.640 --> 00:02:34.735 data from three large developmental

NOTE Confidence: 0.86269116

00:02:34.735 --> 00:02:36.499 cohorts to identify neural

NOTE Confidence: 0.86269116

00:02:36.499 --> 00:02:38.263 markers of alcohol initiation

NOTE Confidence: 0.873388706666667

00:02:38.270 --> 00:02:40.808 and misuse. Promises to be a

NOTE Confidence: 0.851209296

00:02:40.810 --> 00:02:42.370 very important work.

NOTE Confidence: 0.851209296

00:02:42.370 --> 00:02:45.450 Of note, in 2019 her work on

NOTE Confidence: 0.851209296

00:02:45.450 --> 00:02:47.490 connectome based modeling to predict

NOTE Confidence: 0.851209296

00:02:47.567 --> 00:02:50.117 treatment response in cocaine use

NOTE Confidence: 0.851209296

00:02:50.117 --> 00:02:53.785 disorder was cited as a top as the

NOTE Confidence: 0.851209296

00:02:53.785 --> 00:02:56.490 top basic science achievement of 2019

NOTE Confidence: 0.851209296

00:02:56.490 --> 00:02:59.110 by night as director Norvo Cough.

NOTE Confidence: 0.851209296

00:02:59.110 --> 00:03:00.910 Today we'll have the opportunity

NOTE Confidence: 0.851209296

00:03:00.910 --> 00:03:03.248 to learn more about this important

NOTE Confidence: 0.851209296

00:03:03.248 --> 00:03:05.738 work in her talk entitled Connectome

NOTE Confidence: 0.851209296

00:03:05.738 --> 00:03:07.734 based prediction of absence across

NOTE Confidence: 0.851209296

00:03:07.734 --> 00:03:11.570 drugs and brain states welcome Sarah.

NOTE Confidence: 0.8303813

00:03:11.570 --> 00:03:12.620 Thank you Stephanie,

NOTE Confidence: 0.8303813

00:03:12.620 --> 00:03:14.020 for that great introduction.

NOTE Confidence: 0.8303813

00:03:14.020 --> 00:03:16.470 It was one of the top basic

NOTE Confidence: 0.8303813

00:03:16.470 --> 00:03:19.750 science achievements, not the talk.

NOTE Confidence: 0.8303813

00:03:19.750 --> 00:03:21.650 I'm happy to provide support.

NOTE Confidence: 0.8303813

00:03:21.650 --> 00:03:22.790 That's our perspective.

NOTE Confidence: 0.8303813

00:03:22.790 --> 00:03:25.830 OK, let me just get my screen sharing.

NOTE Confidence: 0.77430546

00:03:33.180 --> 00:03:34.500 Can anyone see my slides?

NOTE Confidence: 0.7670263

00:03:36.710 --> 00:03:38.430 Yep yeah great OK great.

NOTE Confidence: 0.7670263

00:03:38.430 --> 00:03:40.726 So yes, Stephanie said I'm going to

NOTE Confidence: 0.7670263

00:03:40.726 --> 00:03:42.583 be presenting today on connectome

NOTE Confidence: 0.7670263

00:03:42.583 --> 00:03:44.203 based prediction of abstinence

NOTE Confidence: 0.7670263

00:03:44.203 --> 00:03:46.310 across drugs in Britain states.

NOTE Confidence: 0.7670263

00:03:46.310 --> 00:03:47.886 So this is work that my lab has

NOTE Confidence: 0.7670263

00:03:47.886 --> 00:03:49.402 been doing for a number of years

NOTE Confidence: 0.7670263

00:03:49.402 --> 00:03:50.896 to try to identify brain based

NOTE Confidence: 0.7670263

00:03:50.896 --> 00:03:52.356 predictors of treatment outcomes.

NOTE Confidence: 0.8262073

00:03:54.420 --> 00:03:56.604 I'm sure everyone here is aware of the

NOTE Confidence: 0.8262073

00:03:56.604 --> 00:03:58.397 current substances epidemic in this country,

NOTE Confidence: 0.8262073

00:03:58.400 --> 00:04:00.283 but I think it's nonetheless important to

NOTE Confidence: 0.8262073

00:04:00.283 --> 00:04:02.392 mention so this color map shows population

NOTE Confidence: 0.8262073

00:04:02.392 --> 00:04:04.557 level deaths per 100,000 individuals in the

NOTE Confidence: 0.8262073

00:04:04.557 --> 00:04:07.224 United States back in 2014, and as we know,

NOTE Confidence: 0.8262073

00:04:07.224 --> 00:04:09.390 these rates have continued to rise.

NOTE Confidence: 0.8262073

00:04:09.390 --> 00:04:10.662 And so, for example,

NOTE Confidence: 0.8262073

00:04:10.662 --> 00:04:11.934 annual opiate associated fatalities

NOTE Confidence: 0.8262073

00:04:11.934 --> 00:04:13.803 have exceeded those calls by firearms

NOTE Confidence: 0.8262073

00:04:13.803 --> 00:04:14.983 and motor vehicles combined,

NOTE Confidence: 0.8262073

00:04:14.990 --> 00:04:17.310 as well as those caused by HIV at

NOTE Confidence: 0.8262073

8

00:04:17.310 --> 00:04:19.340 the height of the AIDS epidemic.

NOTE Confidence: 0.8262073

00:04:19.340 --> 00:04:21.517 And although it's been much less publicized,

NOTE Confidence: 0.8262073

00:04:21.520 --> 00:04:23.410 there has been this concurrent rise and

NOTE Confidence: 0.8262073

00:04:23.410 --> 00:04:25.249 cocaine and stimulant associated fatalities.

NOTE Confidence: 0.8262073

00:04:25.250 --> 00:04:27.026 Therefore, we really do need improve

NOTE Confidence: 0.8262073

00:04:27.026 --> 00:04:28.584 strategies to combat the current

NOTE Confidence: 0.8262073

00:04:28.584 --> 00:04:30.534 substance use epidemic in this country,

NOTE Confidence: 0.8262073

00:04:30.540 --> 00:04:32.715 which is really the motivation

NOTE Confidence: 0.8262073

00:04:32.715 --> 00:04:35.390 for my labs or imaging work.

NOTE Confidence: 0.8262073

00:04:35.390 --> 00:04:37.350 So I often get asked why we would

NOTE Confidence: 0.8262073

00:04:37.350 --> 00:04:39.216 even using our imaging to predict

NOTE Confidence: 0.8262073

00:04:39.216 --> 00:04:41.190 treatment outcomes in the 1st place.

NOTE Confidence: 0.8262073

00:04:41.190 --> 00:04:41.736 After all,

NOTE Confidence: 0.8262073

00:04:41.736 --> 00:04:43.374 we're pretty fortunate in the addiction

NOTE Confidence: 0.8262073

00:04:43.374 --> 00:04:45.428 field with a large number of really

NOTE Confidence: 0.8262073

00:04:45.428 --> 00:04:46.883 excellent evidence based treatments that

NOTE Confidence: 0.8262073

00:04:46.935 --> 00:04:48.729 are very effective for some individuals.

NOTE Confidence: 0.8262073

00:04:48.730 --> 00:04:49.020 However,

NOTE Confidence: 0.8262073

00:04:49.020 --> 00:04:51.050 we also have a lot of between

NOTE Confidence: 0.8262073

00:04:51.050 --> 00:04:51.630 patient heterogeneity,

NOTE Confidence: 0.8262073

00:04:51.630 --> 00:04:53.268 which unfortunately means that the overall

NOTE Confidence: 0.8262073

00:04:53.268 --> 00:04:55.323 efficacy of any given treatment tends to

NOTE Confidence: 0.8262073

00:04:55.323 --> 00:04:56.843 be highly variable across individuals.

NOTE Confidence: 0.8262073

00:04:56.850 --> 00:04:57.792 Given this heterogeneity,

NOTE Confidence: 0.8262073

00:04:57.792 --> 00:04:59.362 it's perhaps not surprising that

NOTE Confidence: 0.8262073

00:04:59.362 --> 00:05:00.820 even gold standard treatments and

NOTE Confidence: 0.8262073

00:05:00.820 --> 00:05:02.967 have a high rates of relapse and that

NOTE Confidence: 0.8262073

00:05:02.967 --> 00:05:04.397 most individuals with a substance

NOTE Confidence: 0.8262073

00:05:04.397 --> 00:05:05.948 use disorder go through multiple

NOTE Confidence: 0.8262073

00:05:05.948 --> 00:05:07.142 failed treatment attempts.

NOTE Confidence: 0.8262073

00:05:07.142 --> 00:05:08.336 In other words,

NOTE Confidence: 0.8262073

00:05:08.340 --> 00:05:10.290 when it comes to addiction treatment,

NOTE Confidence: 0.8262073

00:05:10.290 --> 00:05:11.590 one treatment really doesn't

NOTE Confidence: 0.8262073

00:05:11.590 --> 00:05:12.890 fit all relapse rates.

NOTE Confidence: 0.8262073

00:05:12.890 --> 00:05:14.510 Following treatment also remain high,

NOTE Confidence: 0.8262073

00:05:14.510 --> 00:05:16.135 and for some substances this

NOTE Confidence: 0.8262073

00:05:16.135 --> 00:05:17.435 is a critical vulnerability.

NOTE Confidence: 0.8262073

00:05:17.440 --> 00:05:18.820 Vulnerability period for

NOTE Confidence: 0.8262073

00:05:18.820 --> 00:05:20.200 overdose associated death.

NOTE Confidence: 0.8262073

00:05:20.200 --> 00:05:21.862 And this problem is really further

NOTE Confidence: 0.8262073

00:05:21.862 --> 00:05:24.219 exacerbated by the fact that what I like

NOTE Confidence: 0.8262073

00:05:24.219 --> 00:05:25.709 to call traditional clinical variables.

NOTE Confidence: 0.8262073

00:05:25.710 --> 00:05:26.526 So for example,

NOTE Confidence: 0.8262073

00:05:26.526 --> 00:05:28.158 things like baseline severity don't tend

NOTE Confidence: 0.8262073

00:05:28.158 --> 00:05:30.272 to be all that helpful for predicting

NOTE Confidence: 0.8262073

00:05:30.272 --> 00:05:31.800 treatment response for relapse rates,

NOTE Confidence: 0.8262073

00:05:31.800 --> 00:05:33.405 meaning that we have unexplained

NOTE Confidence: 0.8262073

00:05:33.405 --> 00:05:34.689 sources of her originality

NOTE Confidence: 0.8262073

00:05:34.689 --> 00:05:35.920 influencing treatment outcomes.

NOTE Confidence: 0.8262073

00:05:35.920 --> 00:05:36.904 So within this context,

NOTE Confidence: 0.8262073

00:05:36.904 --> 00:05:38.380 a number of research groups have

NOTE Confidence: 0.8262073

00:05:38.425 --> 00:05:39.630 turned in our imaging measures

NOTE Confidence: 0.8262073

00:05:39.630 --> 00:05:41.228 to try to identify brain based

NOTE Confidence: 0.8262073

00:05:41.228 --> 00:05:42.596 predictors of treatment response.

NOTE Confidence: 0.81670505

00:05:45.120 --> 00:05:48.216 And so over the past 10 to 15 years,

NOTE Confidence: 0.81670505

00:05:48.220 --> 00:05:50.572 there's been a number of proof of

NOTE Confidence: 0.81670505

00:05:50.572 --> 00:05:52.000 concept studies looking brain,

NOTE Confidence: 0.81670505

00:05:52.000 --> 00:05:53.372 function and structure to

NOTE Confidence: 0.81670505

00:05:53.372 --> 00:05:54.744 treatment outcomes and addictions.

NOTE Confidence: 0.81670505

00:05:54.750 --> 00:05:55.617 So, for example,

NOTE Confidence: 0.81670505

00:05:55.617 --> 00:05:57.351 work by our group and others

NOTE Confidence: 0.81670505

00:05:57.351 --> 00:05:59.109 indicate that individual differences

NOTE Confidence: 0.81670505

12

00:05:59.109 --> 00:06:00.993 in pretreatment reward related

NOTE Confidence: 0.81670505

00:06:00.993 --> 00:06:02.871 activations are prospectively linked

NOTE Confidence: 0.81670505

00:06:02.871 --> 00:06:04.499 to within treatment abstinence.

NOTE Confidence: 0.81670505

00:06:04.500 --> 00:06:06.816 That changes in reward related activations,

NOTE Confidence: 0.81670505

00:06:06.820 --> 00:06:08.722 Ann May Co occur with reductions

NOTE Confidence: 0.81670505

00:06:08.722 --> 00:06:10.510 in substances and that individual

NOTE Confidence: 0.81670505

00:06:10.510 --> 00:06:12.354 differences in functional connectivity

NOTE Confidence: 0.81670505

00:06:12.354 --> 00:06:14.950 relate to both current cocaine use,

NOTE Confidence: 0.81670505

00:06:14.950 --> 00:06:17.630 an feature relapse to cocaine.

NOTE Confidence: 0.81670505

00:06:17.630 --> 00:06:18.184 So collectively,

NOTE Confidence: 0.81670505

00:06:18.184 --> 00:06:19.846 these and other studies are really

NOTE Confidence: 0.81670505

00:06:19.846 --> 00:06:21.399 supporting this overarching hypothesis,

NOTE Confidence: 0.81670505

00:06:21.400 --> 00:06:23.215 that individual differences in some

NOTE Confidence: 0.81670505

00:06:23.215 --> 00:06:25.975 aspects of the brain are indeed linked

NOTE Confidence: 0.81670505

00:06:25.975 --> 00:06:28.180 to differences in treatment outcomes.

NOTE Confidence: 0.81670505

00:06:28.180 --> 00:06:28.484 However,

NOTE Confidence: 0.81670505

00:06:28.484 --> 00:06:30.308 this work also has some limitations,

NOTE Confidence: 0.81670505

00:06:30.310 --> 00:06:32.128 so in particular most prior studies

NOTE Confidence: 0.81670505

00:06:32.128 --> 00:06:33.728 have relied on prospective associations

NOTE Confidence: 0.81670505

00:06:33.728 --> 00:06:35.750 and have used methods such as

NOTE Confidence: 0.81670505

00:06:35.750 --> 00:06:37.065 correlation and regression that

NOTE Confidence: 0.81670505

00:06:37.065 --> 00:06:38.815 have a tendency to overfit the data,

NOTE Confidence: 0.81670505

00:06:38.820 --> 00:06:41.280 leading to inflated effect size estimates.

NOTE Confidence: 0.81670505

00:06:41.280 --> 00:06:43.312 And so the problem with using the term

NOTE Confidence: 0.81670505

00:06:43.312 --> 00:06:45.119 prediction in this context in the

NOTE Confidence: 0.81670505

00:06:45.119 --> 00:06:46.991 context of symbol correlation or regression,

NOTE Confidence: 0.81670505

00:06:47.000 --> 00:06:49.070 is that true prediction requires

NOTE Confidence: 0.81670505

00:06:49.070 --> 00:06:52.000 application of a model to novel data.

NOTE Confidence: 0.81670505

00:06:52.000 --> 00:06:53.825 Machine learning approaches seek to

NOTE Confidence: 0.81670505

00:06:53.825 --> 00:06:55.650 produce overfitting via creation of

NOTE Confidence: 0.81670505

00:06:55.706 --> 00:06:57.687 a predictive model in a data driven

NOTE Confidence: 0.81670505

00:06:57.687 --> 00:06:59.720 manner manner using the training data set.

NOTE Confidence: 0.81670505

00:06:59.720 --> 00:07:01.550 And then application of that model

NOTE Confidence: 0.81670505

00:07:01.550 --> 00:07:03.659 to an independent test data set which

NOTE Confidence: 0.81670505

00:07:03.659 --> 00:07:05.327 is used for model validation and

NOTE Confidence: 0.81670505

00:07:05.327 --> 00:07:07.158 that distinction is really important

NOTE Confidence: 0.81670505

00:07:07.158 --> 00:07:09.402 because whereas the aim of traditional

NOTE Confidence: 0.81670505

00:07:09.410 --> 00:07:11.025 statistical approaches is to explain

NOTE Confidence: 0.81670505

00:07:11.025 --> 00:07:12.640 the relationship between two variables,

NOTE Confidence: 0.81670505

00:07:12.640 --> 00:07:15.027 the aim of machine learning approaches is

NOTE Confidence: 0.81670505

00:07:15.027 --> 00:07:16.840 to generate predictions in novel data,

NOTE Confidence: 0.81670505

00:07:16.840 --> 00:07:18.800 and I would argue that this type of

NOTE Confidence: 0.81670505

00:07:18.800 --> 00:07:20.843 approach is critical for the eventual

NOTE Confidence: 0.81670505

00:07:20.843 --> 00:07:22.343 translation of research findings

NOTE Confidence: 0.81670505

00:07:22.343 --> 00:07:23.620 into clinical settings,

NOTE Confidence: 0.81670505

00:07:23.620 --> 00:07:25.235 which is really a primary

NOTE Confidence: 0.81670505

00:07:25.235 --> 00:07:26.527 challenge of modern psychiatry.

NOTE Confidence: 0.81670505

00:07:26.530 --> 00:07:28.140 In addition, if used correctly,

NOTE Confidence: 0.81670505

00:07:28.140 --> 00:07:29.915 these approaches can be used

NOTE Confidence: 0.81670505

00:07:29.915 --> 00:07:31.335 for normal biological discovery.

NOTE Confidence: 0.81670505

00:07:31.340 --> 00:07:33.734 Which to me is also really important.

NOTE Confidence: 0.81670505

00:07:33.740 --> 00:07:35.104 So in my opinion,

NOTE Confidence: 0.81670505

00:07:35.104 --> 00:07:36.809 in addition to generating predictions

NOTE Confidence: 0.81670505

00:07:36.809 --> 00:07:37.859 in novel data,

NOTE Confidence: 0.81670505

00:07:37.860 --> 00:07:39.810 a primary goal of brain based

NOTE Confidence: 0.81670505

00:07:39.810 --> 00:07:41.540 clinical modeling should really be

NOTE Confidence: 0.81670505

00:07:41.540 --> 00:07:42.659 elucidation of mechanism.

NOTE Confidence: 0.81670505

00:07:42.660 --> 00:07:44.196 However, as we know,

NOTE Confidence: 0.81670505

00:07:44.196 --> 00:07:45.732 even highly predictive models

NOTE Confidence: 0.81670505

00:07:45.732 --> 00:07:48.810 often can be very little to enhance

NOTE Confidence: 0.81670505

00:07:48.810 --> 00:07:50.154 our mechanistic understanding.

NOTE Confidence: 0.81670505

00:07:50.160 --> 00:07:51.312 So throughout this talk,

NOTE Confidence: 0.81670505

00:07:51.312 --> 00:07:53.525 I'm really going to focus on maximizing

NOTE Confidence: 0.81670505

00:07:53.525 --> 00:07:55.645 nor biological discovery within the

NOTE Confidence: 0.81670505

00:07:55.645 --> 00:07:57.341 context of predictive modeling.

NOTE Confidence: 0.81670505

00:07:57.350 --> 00:07:59.718 In order to maximize this type of discovery,

NOTE Confidence: 0.81670505

00:07:59.720 --> 00:08:01.785 we use data driven whole brain methods.

NOTE Confidence: 0.81670505

00:08:01.790 --> 00:08:03.337 The reason for this is that given

NOTE Confidence: 0.81670505

00:08:03.337 --> 00:08:04.779 that recovery from addiction involves

NOTE Confidence: 0.81670505

00:08:04.779 --> 00:08:06.243 complex interactions across across

NOTE Confidence: 0.81670505

00:08:06.243 --> 00:08:07.707 clinical and biological domains,

NOTE Confidence: 0.81670505

00:08:07.710 --> 00:08:09.390 we think it's likely that it's even

NOTE Confidence: 0.81670505

00:08:09.390 --> 00:08:10.894 of abstinence also involves distributed

NOTE Confidence: 0.81670505

00:08:10.894 --> 00:08:12.734 processes for multiple brain regions.

NOTE Confidence: 0.81670505

00:08:12.740 --> 00:08:13.001 Therefore,

NOTE Confidence: 0.81670505

00:08:13.001 --> 00:08:15.089 all of the data and we showed you

NOTE Confidence: 0.81670505

00:08:15.089 --> 00:08:17.070 today is using a whole brain

NOTE Confidence: 0.81670505

00:08:17.070 --> 00:08:18.069 connectivity based approach,

NOTE Confidence: 0.81670505

00:08:18.070 --> 00:08:20.236 in which we're focusing on patterns

NOTE Confidence: 0.81670505

00:08:20.236 --> 00:08:22.050 of functional activity across the

NOTE Confidence: 0.81670505

00:08:22.050 --> 00:08:22.678 entire brain.

NOTE Confidence: 0.81670505

00:08:22.680 --> 00:08:24.402 The specific method I'm doing focusing

NOTE Confidence: 0.81670505

00:08:24.402 --> 00:08:26.222 on throughout this talk is referred

NOTE Confidence: 0.81670505

00:08:26.222 --> 00:08:28.094 to as connectome based predicted modeling,

NOTE Confidence: 0.81670505

00:08:28.100 --> 00:08:29.605 and unlike some other machine

NOTE Confidence: 0.81670505

00:08:29.605 --> 00:08:30.207 learning approaches,

NOTE Confidence: 0.81670505

00:08:30.210 --> 00:08:32.310 this is an entirely data driven technique.

NOTE Confidence: 0.81670505

00:08:32.310 --> 00:08:34.050 It doesn't require any a priori

NOTE Confidence: 0.81670505

00:08:34.050 --> 00:08:35.210 specification of networks or

NOTE Confidence: 0.81992507

00:08:35.262 --> 00:08:36.228 regions of interest.

NOTE Confidence: 0.81992507

00:08:36.230 --> 00:08:38.330 Therefore it's not only a predictive tool,

NOTE Confidence: 0.81992507

00:08:38.330 --> 00:08:40.510 but it's also a method

NOTE Confidence: 0.81992507

00:08:40.510 --> 00:08:41.818 of identifying networks.

NOTE Confidence: 0.81992507

18

00:08:41.820 --> 00:08:44.727 And so, prior to the data will be presenting.

NOTE Confidence: 0.81992507

00:08:44.730 --> 00:08:46.375 Today, connectome based modeling had

NOTE Confidence: 0.81992507

00:08:46.375 --> 00:08:48.383 been used to generate robust predictive

NOTE Confidence: 0.81992507

00:08:48.383 --> 00:08:50.855 models of measures such as IQ and attention,

NOTE Confidence: 0.81992507

00:08:50.860 --> 00:08:54.172 but it had never been applied to predict

NOTE Confidence: 0.81992507

00:08:54.172 --> 00:08:56.558 future behavior or clinical outcome.

NOTE Confidence: 0.81992507

00:08:56.560 --> 00:08:58.457 When we use a connectivity based approach,

NOTE Confidence: 0.81992507

00:08:58.460 --> 00:09:00.238 what we're doing is we're extracting time

NOTE Confidence: 0.81992507

00:09:00.238 --> 00:09:01.730 courses activity from multiple regions.

NOTE Confidence: 0.81992507

00:09:01.730 --> 00:09:03.165 It together encompass the entire

NOTE Confidence: 0.81992507

00:09:03.165 --> 00:09:04.895 brain to represented here by these

NOTE Confidence: 0.81992507

00:09:04.895 --> 00:09:06.347 cards in green and red voxels,

NOTE Confidence: 0.81992507

00:09:06.350 --> 00:09:07.952 and we simply correlate the patterns

NOTE Confidence: 0.81992507

00:09:07.952 --> 00:09:09.682 of activity across the time course of

NOTE Confidence: 0.81992507

00:09:09.682 --> 00:09:11.490 the whole scan to get a single summary

NOTE Confidence: 0.81992507

00:09:11.490 --> 00:09:13.165 statistic that summarizes the temporal

NOTE Confidence: 0.81992507

00:09:13.165 --> 00:09:15.020 coherence between those two brain regions.

NOTE Confidence: 0.81992507

00:09:15.020 --> 00:09:17.060 And we can do this for every single

NOTE Confidence: 0.81992507

00:09:17.118 --> 00:09:19.302 voxel in the brain to create a

NOTE Confidence: 0.81992507

00:09:19.302 --> 00:09:20.519 functional connectivity matrix or

NOTE Confidence: 0.81992507

00:09:20.519 --> 00:09:22.129 what we refer to as a connectome.

NOTE Confidence: 0.81992507

00:09:22.130 --> 00:09:24.122 So this single matrix Now summarizes

NOTE Confidence: 0.81992507

00:09:24.122 --> 00:09:25.450 whole brain connectivity patterns

NOTE Confidence: 0.81992507

00:09:25.506 --> 00:09:27.170 for all of the voxels in the brain.

NOTE Confidence: 0.81992507

00:09:27.170 --> 00:09:28.234 Or a single person,

NOTE Confidence: 0.81992507

00:09:28.234 --> 00:09:29.830 and there's data to indicate that

NOTE Confidence: 0.81992507

00:09:29.888 --> 00:09:31.648 these connectomes are both relatively

NOTE Confidence: 0.81992507

00:09:31.648 --> 00:09:33.056 unique to the individual,

NOTE Confidence: 0.81992507

00:09:33.060 --> 00:09:34.920 but also the patterns of connectivity

NOTE Confidence: 0.81992507

00:09:34.920 --> 00:09:35.850 within the connectome.

NOTE Confidence: 0.81992507

00:09:35.850 --> 00:09:38.562 Forgiven individual may vary as a

NOTE Confidence: 0.81992507

00:09:38.562 --> 00:09:41.090 function of task performance or what

NOTE Confidence: 0.81992507

00:09:41.090 --> 00:09:43.658 we like to refer to his brain state.

NOTE Confidence: 0.81992507

00:09:43.660 --> 00:09:45.232 The consistent with this notion of

NOTE Confidence: 0.81992507

00:09:45.232 --> 00:09:46.941 brain stay work by colleagues here

NOTE Confidence: 0.81992507

00:09:46.941 --> 00:09:48.753 at Yale has demonstrated that the

NOTE Confidence: 0.81992507

00:09:48.753 --> 00:09:50.466 accuracy of predictive models generated

NOTE Confidence: 0.81992507

00:09:50.466 --> 00:09:52.226 from connectivity data is improved

NOTE Confidence: 0.81992507

00:09:52.226 --> 00:09:54.230 when the input is connectivity data,

NOTE Confidence: 0.81992507

00:09:54.230 --> 00:09:55.530 computed joint task performance

NOTE Confidence: 0.81992507

00:09:55.530 --> 00:09:57.260 as opposed to join resting state.

NOTE Confidence: 0.81992507

00:09:57.260 --> 00:10:00.104 So here on your left you have the percent.

NOTE Confidence: 0.81992507

00:10:00.110 --> 00:10:01.769 Variance in IQ is explained by a

NOTE Confidence: 0.81992507

00:10:01.769 --> 00:10:03.134 predictive model built using different

NOTE Confidence: 0.81992507

00:10:03.134 --> 00:10:04.946 tasks from the Human Connectome Project.

NOTE Confidence: 0.81992507

00:10:04.950 --> 00:10:06.476 An on your right you have the

NOTE Confidence: 0.81992507

00:10:06.476 --> 00:10:07.871 same thing for the Philadelphia

NOTE Confidence: 0.81992507

00:10:07.871 --> 00:10:09.255 in or developmental Gore,

NOTE Confidence: 0.81992507

00:10:09.260 --> 00:10:10.828 and what I want to point out here

NOTE Confidence: 0.81992507

00:10:10.828 --> 00:10:12.802 is it in both cohorts the predictive

NOTE Confidence: 0.81992507

00:10:12.802 --> 00:10:14.332 accuracy of models built using

NOTE Confidence: 0.81992507

00:10:14.389 --> 00:10:16.249 resting state data is relatively low,

NOTE Confidence: 0.81992507

00:10:16.250 --> 00:10:18.760 so in both cases the model is only able to

NOTE Confidence: 0.81992507

00:10:18.823 --> 00:10:21.360 account for about 4% of the variance in IQ.

NOTE Confidence: 0.81992507

00:10:21.360 --> 00:10:22.893 The second thing I want to highlight

NOTE Confidence: 0.81992507

00:10:22.893 --> 00:10:24.536 is that the predictive accuracy of

NOTE Confidence: 0.81992507

00:10:24.536 --> 00:10:26.091 models generated from different types

NOTE Confidence: 0.81992507

00:10:26.091 --> 00:10:28.087 of task data is also highly variable,

NOTE Confidence: 0.81992507

00:10:28.090 --> 00:10:29.430 with some tasks accounting for

NOTE Confidence: 0.81992507

00:10:29.430 --> 00:10:31.660 up to 12% of the variance in IQ.

NOTE Confidence: 0.81992507

00:10:31.660 --> 00:10:32.700 Another accounting for less,

NOTE Confidence: 0.81992507

00:10:32.700 --> 00:10:34.260 so together this is suggesting that

NOTE Confidence: 0.81992507

00:10:34.309 --> 00:10:35.774 specific brain statement elations mean

NOTE Confidence: 0.81992507

00:10:35.774 --> 00:10:37.650 preferable for predicting a given behavior,

NOTE Confidence: 0.81992507

00:10:37.650 --> 00:10:39.666 which is an issue that I'm going to

NOTE Confidence: 0.81992507

00:10:39.666 --> 00:10:41.639 return to you throughout this talk,

NOTE Confidence: 0.81992507

00:10:41.640 --> 00:10:43.624 which brings me to the first bit of

NOTE Confidence: 0.81992507

00:10:43.624 --> 00:10:45.777 data will be presenting today in which

NOTE Confidence: 0.81992507

00:10:45.777 --> 00:10:47.707 we're using a connected based approach

NOTE Confidence: 0.81992507

00:10:47.707 --> 00:10:50.182 to try to put it to the clinical outcome.

NOTE Confidence: 0.81992507

00:10:50.190 --> 00:10:51.144 In this case,

NOTE Confidence: 0.81992507

00:10:51.144 --> 00:10:52.416 abstinence from cocaine during

NOTE Confidence: 0.81992507

00:10:52.416 --> 00:10:54.020 a 12 week treatment.

NOTE Confidence: 0.81992507

00:10:54.020 --> 00:10:55.180 The study design for this

NOTE Confidence: 0.81992507

00:10:55.180 --> 00:10:55.876 is relatively simple.

NOTE Confidence: 0.81992507

00:10:55.880 --> 00:10:57.135 We recruited patients and during

NOTE Confidence: 0.81992507

00:10:57.135 --> 00:10:58.878 a 12 treatment trial and scan them

NOTE Confidence: 0.81992507

00:10:58.878 --> 00:11:00.198 at the start of treatment and

NOTE Confidence: 0.81992507

00:11:00.198 --> 00:11:01.570 then again following treatment.

NOTE Confidence: 0.81992507

00:11:01.570 --> 00:11:03.210 All of our participants receiving

NOTE Confidence: 0.81992507

00:11:03.210 --> 00:11:04.850 methadone maintenance therapy for opiate

NOTE Confidence: 0.7997979

00:11:04.902 --> 00:11:06.784 use disorder, but we're now entering

NOTE Confidence: 0.7997979

00:11:06.784 --> 00:11:08.414 treatment for cocaine use disorder,

NOTE Confidence: 0.7997979

00:11:08.420 --> 00:11:10.958 so these are polysubstance using individuals.

NOTE Confidence: 0.7997979

00:11:10.960 --> 00:11:13.440 I'm not going to talk about the specific

NOTE Confidence: 0.7997979

00:11:13.440 --> 00:11:15.576 aspects of the 12 week trial today,

NOTE Confidence: 0.7997979

00:11:15.580 --> 00:11:16.744 but if you're interested,

NOTE Confidence: 0.7997979

00:11:16.744 --> 00:11:18.970 this was an RCT of behavioral therapy,

NOTE Confidence: 0.7997979

00:11:18.970 --> 00:11:20.818 with or without treatment with a

NOTE Confidence: 0.7997979

00:11:20.818 --> 00:11:22.050 cholinesterase inhibitor lanta mean,

NOTE Confidence: 0.7997979

00:11:22.050 --> 00:11:23.898 so the results of that are

NOTE Confidence: 0.7997979

00:11:23.898 --> 00:11:25.130 published in the Journal.

NOTE Confidence: 0.7997979

00:11:25.130 --> 00:11:26.715 Kinda looks like hydrate and

NOTE Confidence: 0.7997979

00:11:26.715 --> 00:11:28.520 consistent with the overall arc TR,

NOTE Confidence: 0.7997979

00:11:28.520 --> 00:11:30.356 nor imaging subsample was dominantly male,

NOTE Confidence: 0.7997979

00:11:30.360 --> 00:11:33.027 there mostly unemployed and the primary route

NOTE Confidence: 0.7997979

00:11:33.027 --> 00:11:35.088 of cocaine administration was via smoking.

NOTE Confidence: 0.7997979

00:11:35.090 --> 00:11:36.812 They also did a number of

NOTE Confidence: 0.7997979

00:11:36.812 --> 00:11:37.673 prior treatment attempts,

NOTE Confidence: 0.7997979

00:11:37.680 --> 00:11:39.493 including an average of three or more

NOTE Confidence: 0.7997979

00:11:39.493 --> 00:11:41.140 prior failed inpatient treatment attempts,

NOTE Confidence: 0.7997979

00:11:41.140 --> 00:11:43.183 and three or more for three or more prior

NOTE Confidence: 0.7997979

00:11:43.183 --> 00:11:44.879 failed outpatient treatment attempts,

NOTE Confidence: 0.7997979

00:11:44.880 --> 00:11:46.896 and they also had significant legal problems,

NOTE Confidence: 0.7997979

00:11:46.900 --> 00:11:48.622 so this is a very treatment

NOTE Confidence: 0.7997979

00:11:48.622 --> 00:11:50.064 refractory population, but it's also,

NOTE Confidence: 0.7997979

00:11:50.064 --> 00:11:52.578 you know, kind of a.

NOTE Confidence: 0.7997979

00:11:52.580 --> 00:11:56.200 It's not an unusual population.

NOTE Confidence: 0.7997979

00:11:56.200 --> 00:11:58.280 I'm not really going to drill down too

NOTE Confidence: 0.7997979

00:11:58.280 --> 00:12:00.210 much into the methods of CPM today,

NOTE Confidence: 0.7997979

00:12:00.210 --> 00:12:01.812 but I'm happy to answer questions

NOTE Confidence: 0.7997979

00:12:01.812 --> 00:12:02.880 if people are interested,

NOTE Confidence: 0.7997979

00:12:02.880 --> 00:12:04.851 but I do just want to give you sort

NOTE Confidence: 0.7997979

00:12:04.851 --> 00:12:07.146 of a general overview of the approach.

NOTE Confidence: 0.7997979

00:12:07.150 --> 00:12:08.480 So practically when we're doing

NOTE Confidence: 0.7997979

00:12:08.480 --> 00:12:09.544 a connecting based model,

NOTE Confidence: 0.7997979

00:12:09.550 --> 00:12:11.152 what we're doing is we're taking

NOTE Confidence: 0.7997979

00:12:11.152 --> 00:12:12.528 individual connectomes from a training

NOTE Confidence: 0.7997979

00:12:12.528 --> 00:12:14.341 data set and relating them to a

NOTE Confidence: 0.7997979

00:12:14.341 --> 00:12:15.420 behavioral variable of interest.

NOTE Confidence: 0.7997979

00:12:15.420 --> 00:12:17.289 So in this case that within treatment,

NOTE Confidence: 0.7997979

00:12:17.290 --> 00:12:18.879 abstinence and we do this using simple

NOTE Confidence: 0.7997979

00:12:18.879 --> 00:12:20.281 correlation in order to identify

NOTE Confidence: 0.7997979

00:12:20.281 --> 00:12:21.298 positive productive connections,

NOTE Confidence: 0.7997979

00:12:21.300 --> 00:12:23.169 or what we refer to as edges,

NOTE Confidence: 0.7997979

00:12:23.170 --> 00:12:24.496 as indicated by these red squares

NOTE Confidence: 0.7997979

00:12:24.496 --> 00:12:26.250 here and then we also identifying

NOTE Confidence: 0.7997979

00:12:26.250 --> 00:12:27.070 negative prediction.

NOTE Confidence: 0.7997979

00:12:27.070 --> 00:12:28.618 Productive connections as indicated

NOTE Confidence: 0.7997979

00:12:28.618 --> 00:12:30.166 by the green squares.

NOTE Confidence: 0.7997979

00:12:30.170 --> 00:12:31.694 So positive predictive connections

NOTE Confidence: 0.7997979

00:12:31.694 --> 00:12:33.599 are connections for which increased

NOTE Confidence: 0.7997979

00:12:33.599 --> 00:12:34.809 connectivity predicts absence,

NOTE Confidence: 0.7997979

00:12:34.810 --> 00:12:36.542 whereas negative predictive connections

NOTE Confidence: 0.7997979

00:12:36.542 --> 00:12:38.707 or connections for which decreased

NOTE Confidence: 0.7997979

00:12:38.707 --> 00:12:40.190 connectivity predicts abstinence.

NOTE Confidence: 0.7997979

00:12:40.190 --> 00:12:42.920 So this is our feature selection phase.

NOTE Confidence: 0.7997979

00:12:42.920 --> 00:12:44.420 We then create individual participant

NOTE Confidence: 0.7997979

00:12:44.420 --> 00:12:45.920 summary scores via just summing

NOTE Confidence: 0.7997979

00:12:45.972 --> 00:12:47.562 the edge weights identified in our

NOTE Confidence: 0.7997979

00:12:47.562 --> 00:12:49.175 feature selection phase so that each

NOTE Confidence: 0.7997979

00:12:49.175 --> 00:12:50.675 participant now just has two values.

NOTE Confidence: 0.7997979

00:12:50.680 --> 00:12:52.246 One is that positive summaries for

NOTE Confidence: 0.7997979

00:12:52.246 --> 00:12:53.720 another is a negative summers,

NOTE Confidence: 0.7997979

00:12:53.720 --> 00:12:55.414 or we then create our brain behavior

NOTE Confidence: 0.7997979

00:12:55.414 --> 00:12:56.843 model by entering these summary

NOTE Confidence: 0.7997979

00:12:56.843 --> 00:12:58.155 scores into predictive models.

NOTE Confidence: 0.7997979

00:12:58.160 --> 00:12:59.816 In this case, assuming linear relationships,

NOTE Confidence: 0.7997979

00:12:59.820 --> 00:13:01.683 so a simple Y equals MX plus B and

NOTE Confidence: 0.7997979

00:13:01.683 --> 00:13:03.802 then finally we apply this model to our

NOTE Confidence: 0.7997979

00:13:03.802 --> 00:13:05.721 testing data so we take connectivity

NOTE Confidence: 0.7997979

00:13:05.721 --> 00:13:07.845 matrices from the independent data set.

NOTE Confidence: 0.7997979

00:13:07.850 --> 00:13:09.500 We extract connectivity values from the

NOTE Confidence: 0.7997979

00:13:09.500 --> 00:13:11.448 edges we identified in our training data,

NOTE Confidence: 0.7997979

00:13:11.450 --> 00:13:12.940 set some them to create.

NOTE Confidence: 0.7997979

00:13:12.940 --> 00:13:14.500 Summary scores for new participants

NOTE Confidence: 0.7997979

00:13:14.500 --> 00:13:16.799 and enter those values into our brain

NOTE Confidence: 0.7997979

00:13:16.799 --> 00:13:18.509 behavior model to generate individual

NOTE Confidence: 0.7997979

00:13:18.509 --> 00:13:20.630 predictions of within treatment abstinence.

NOTE Confidence: 0.7997979

00:13:20.630 --> 00:13:21.250 And finally,

NOTE Confidence: 0.7997979

00:13:21.250 --> 00:13:22.800 although it's not shown here,

NOTE Confidence: 0.7997979

00:13:22.800 --> 00:13:24.570 we evaluate the performance of our

NOTE Confidence: 0.7997979

00:13:24.570 --> 00:13:26.195 model by comparing those predicted

NOTE Confidence: 0.7997979

00:13:26.195 --> 00:13:28.170 abstinence values with the actual

NOTE Confidence: 0.7997979

00:13:28.170 --> 00:13:29.750 within treatment abstinence values.

NOTE Confidence: 0.7997979

00:13:29.750 --> 00:13:31.232 And so we can compare actual

NOTE Confidence: 0.7997979

00:13:31.232 --> 00:13:31.726 predicted values.

NOTE Confidence: 0.7997979

00:13:31.730 --> 00:13:32.960 A number of different ways,

NOTE Confidence: 0.7997979

00:13:32.960 --> 00:13:33.932 which is an issue.

NOTE Confidence: 0.7997979

00:13:33.932 --> 00:13:36.419 I'm not really going to go into in this talk,

NOTE Confidence: 0.7997979

00:13:36.420 --> 00:13:37.650 but really the simplest way

NOTE Confidence: 0.7997979

00:13:37.650 --> 00:13:38.634 is just brain correlation.

NOTE Confidence: 0.8236762

00:13:38.640 --> 00:13:40.614 So that's what I'm going to be

NOTE Confidence: 0.8236762

00:13:40.614 --> 00:13:42.427 using to assess model performance

NOTE Confidence: 0.8236762

00:13:42.427 --> 00:13:44.227 throughout the talk today.

NOTE Confidence: 0.8236762

00:13:44.230 --> 00:13:46.198 For this study, with a couple of different

NOTE Confidence: 0.8236762

00:13:46.198 --> 00:13:48.237 types of functional data to choose from.

NOTE Confidence: 0.8236762

00:13:48.240 --> 00:13:49.304 So during pretreatment scanning,

NOTE Confidence: 0.8236762

00:13:49.304 --> 00:13:50.368 everyone perform two tasks.

NOTE Confidence: 0.8236762

00:13:50.370 --> 00:13:52.344 One was a basic cognitive control task

NOTE Confidence: 0.8236762

00:13:52.344 --> 00:13:54.789 and the other one was a classic reward

NOTE Confidence: 0.8236762

00:13:54.789 --> 00:13:56.660 task and monetary incentive void task.

NOTE Confidence: 0.8236762

00:13:56.660 --> 00:13:58.778 And so, given that we were

NOTE Confidence: 0.8236762

00:13:58.778 --> 00:14:00.190 interested in cocaine use.

NOTE Confidence: 0.8236762

00:14:00.190 --> 00:14:01.675 We chose to either word

NOTE Confidence: 0.8236762

00:14:01.675 --> 00:14:03.160 task because at that time,

NOTE Confidence: 0.8236762

00:14:03.160 --> 00:14:04.650 at least to my mind,

NOTE Confidence: 0.8236762

00:14:04.650 --> 00:14:06.378 the data linking cocaine use to

NOTE Confidence: 0.8236762

00:14:06.378 --> 00:14:08.183 reward was stronger than the data

NOTE Confidence: 0.8236762

00:14:08.183 --> 00:14:09.688 linking it to cognitive control,

NOTE Confidence: 0.8236762

00:14:09.690 --> 00:14:11.472 and so using the data acquired

NOTE Confidence: 0.8236762

00:14:11.472 --> 00:14:12.363 Dreamer Award task,

NOTE Confidence: 0.8236762

00:14:12.370 --> 00:14:13.598 we compute individual participant

NOTE Confidence: 0.8236762

00:14:13.598 --> 00:14:15.440 connectivity matrices and we feed this

NOTE Confidence: 0.8236762

00:14:15.486 --> 00:14:16.944 into our connectome based model along

NOTE Confidence: 0.8236762

00:14:16.944 --> 00:14:18.899 with our measure of instrument abstinence,

NOTE Confidence: 0.8236762

00:14:18.900 --> 00:14:20.682 which was defined as the percentage

NOTE Confidence: 0.8236762

00:14:20.682 --> 00:14:22.251 of BI weekly urine specimens

NOTE Confidence: 0.8236762

00:14:22.251 --> 00:14:23.871 that were negative for cocaine

NOTE Confidence: 0.8236762

00:14:23.871 --> 00:14:25.780 during the 12 week treatment.

NOTE Confidence: 0.8236762

00:14:25.780 --> 00:14:28.855 So is the biologically verified

NOTE Confidence: 0.8236762

00:14:28.855 --> 00:14:31.315 dimensional measure of absence?

NOTE Confidence: 0.8236762

00:14:31.320 --> 00:14:33.049 So here we have our initial model

NOTE Confidence: 0.8236762

00:14:33.049 --> 00:14:35.401 results here on the Y axis we have

NOTE Confidence: 0.8236762

00:14:35.401 --> 00:14:36.649 individual participant abstinence values

NOTE Confidence: 0.8236762

00:14:36.649 --> 00:14:38.279 as predicted by our brain behavior

NOTE Confidence: 0.8236762

00:14:38.279 --> 00:14:40.916 model and on the X axis we have actual

NOTE Confidence: 0.8236762

00:14:40.916 --> 00:14:42.636 absolute values for each participant.

NOTE Confidence: 0.8236762

00:14:42.640 --> 00:14:44.740 And so typically when we use correlation,

NOTE Confidence: 0.8236762

00:14:44.740 --> 00:14:46.240 we're trying to explain the

NOTE Confidence: 0.8236762

00:14:46.240 --> 00:14:47.440 variance between two variables.

NOTE Confidence: 0.8236762

00:14:47.440 --> 00:14:49.827 But here we're just using it to

NOTE Confidence: 0.8236762

00:14:49.827 --> 00:14:50.850 characterize predictive accuracy

NOTE Confidence: 0.8236762

00:14:50.907 --> 00:14:52.451 or the correspondence between

NOTE Confidence: 0.8236762

00:14:52.451 --> 00:14:53.995 actual and predicted values.

NOTE Confidence: 0.8236762

00:14:54.000 --> 00:14:56.000 And so you can see that our model

NOTE Confidence: 0.8236762

00:14:56.000 --> 00:14:57.250 has relatively good predictive

NOTE Confidence: 0.8236762

00:14:57.250 --> 00:14:58.995 accuracy with this German 0.42,

NOTE Confidence: 0.8236762

00:14:59.000 --> 00:15:01.002 which means that about 20% of the

NOTE Confidence: 0.8236762

00:15:01.002 --> 00:15:02.332 variance in within treatment abstinence

NOTE Confidence: 0.8236762

00:15:02.332 --> 00:15:03.842 is accounted for by connectivity

NOTE Confidence: 0.8236762

00:15:03.842 --> 00:15:05.166 within our abstinence networks,

NOTE Confidence: 0.8236762

00:15:05.170 --> 00:15:06.457 and interesting Lee,

NOTE Confidence: 0.8236762

00:15:06.457 --> 00:15:08.173 this correspondence is greater

NOTE Confidence: 0.8236762

00:15:08.173 --> 00:15:09.460 than that absorbed.

NOTE Confidence: 0.8236762

00:15:09.460 --> 00:15:10.895 If we just relate absence

NOTE Confidence: 0.8236762

00:15:10.895 --> 00:15:12.043 to another level variable,

NOTE Confidence: 0.8236762

00:15:12.050 --> 00:15:14.066 for example related to baseline cocaine use,

NOTE Confidence: 0.8236762

00:15:14.070 --> 00:15:15.785 indicating that are connected based

NOTE Confidence: 0.8236762

00:15:15.785 --> 00:15:17.500 model has greater predictive accuracy

NOTE Confidence: 0.8236762

00:15:17.555 --> 00:15:19.247 than traditional clinical variables.

NOTE Confidence: 0.8236762

00:15:19.250 --> 00:15:21.326 So in addition to generating predictions,

NOTE Confidence: 0.8236762

00:15:21.330 --> 00:15:22.374 this approach also,

NOTE Confidence: 0.8236762

00:15:22.374 --> 00:15:23.070 of course,

NOTE Confidence: 0.8236762

00:15:23.070 --> 00:15:25.499 identifies networks just as a heads up.

NOTE Confidence: 0.8236762

00:15:25.500 --> 00:15:27.112 Networks identified using whole

NOTE Confidence: 0.8236762

00:15:27.112 --> 00:15:28.724 connectome based approaches are

NOTE Confidence: 0.8236762

00:15:28.724 --> 00:15:30.426 typically complex and can be

NOTE Confidence: 0.8236762

00:15:30.426 --> 00:15:31.542 composed of multiple adjacent

NOTE Confidence: 0.8236762

00:15:31.542 --> 00:15:33.130 and non Jason's brain regions.

NOTE Confidence: 0.8236762

00:15:33.130 --> 00:15:35.206 As was certainly the case here.

NOTE Confidence: 0.8236762

00:15:35.210 --> 00:15:38.153 So here on your left you can see the

NOTE Confidence: 0.8236762

00:15:38.153 --> 00:15:41.109 positive network shown in red as a reminder.

NOTE Confidence: 0.8236762

00:15:41.110 --> 00:15:43.245 The positive network includes connections

NOTE Confidence: 0.8236762

00:15:43.245 --> 00:15:44.953 which increased connectivity predicts

NOTE Confidence: 0.8236762

00:15:44.953 --> 00:15:47.114 absence and on the right you can see

NOTE Confidence: 0.8236762

00:15:47.114 --> 00:15:48.785 the negative network which corresponds

NOTE Confidence: 0.8236762

00:15:48.785 --> 00:15:50.573 to connections which decreased

NOTE Confidence: 0.8236762

00:15:50.573 --> 00:15:51.914 connectivity predicts abstinence.

NOTE Confidence: 0.8236762

00:15:51.920 --> 00:15:53.666 And so while these networks are

NOTE Confidence: 0.8236762

00:15:53.666 --> 00:15:54.830 certainly complex and arguably

NOTE Confidence: 0.8236762

00:15:54.879 --> 00:15:56.339 pretty hard to interpret when

NOTE Confidence: 0.8236762

00:15:56.339 --> 00:15:57.507 presented in this fashion,

NOTE Confidence: 0.8236762

00:15:57.510 --> 00:15:59.512 it's important to point out that actually

NOTE Confidence: 0.8236762

00:15:59.512 --> 00:16:01.062 the combined number of connections

NOTE Confidence: 0.8236762

00:16:01.062 --> 00:16:02.976 within the positive and the negative

NOTE Confidence: 0.8236762

00:16:02.976 --> 00:16:04.559 network together is only around 500,

NOTE Confidence: 0.8236762

00:16:04.560 --> 00:16:06.324 which is actually less than than

NOTE Confidence: 0.8236762

00:16:06.324 --> 00:16:09.368 2% of all possible connections.

NOTE Confidence: 0.8236762

00:16:09.370 --> 00:16:10.294 In other words,

NOTE Confidence: 0.8236762

00:16:10.294 --> 00:16:11.526 despite this visual complexity,

NOTE Confidence: 0.8236762

00:16:11.530 --> 00:16:12.770 these are actually quite

NOTE Confidence: 0.8236762

00:16:12.770 --> 00:16:13.390 specific connections.

NOTE Confidence: 0.78052706

00:16:17.070 --> 00:16:18.743 So there are a number of standard

NOTE Confidence: 0.78052706

00:16:18.743 --> 00:16:20.752 ways in which we can now start

NOTE Confidence: 0.78052706

00:16:20.752 --> 00:16:21.992 to summarize these connections

NOTE Confidence: 0.78052706

00:16:21.992 --> 00:16:23.430 to facilitate interpretation.

NOTE Confidence: 0.78052706

00:16:23.430 --> 00:16:25.080 So one simple way of characterizing

NOTE Confidence: 0.78052706

00:16:25.080 --> 00:16:26.578 our networks is to summarize

NOTE Confidence: 0.78052706

00:16:26.578 --> 00:16:28.278 them by a connection distance.

NOTE Confidence: 0.78052706

00:16:28.280 --> 00:16:30.317 So for each nodal connection we can

NOTE Confidence: 0.78052706

00:16:30.317 --> 00:16:31.560 compute Euclidean distance using

NOTE Confidence: 0.78052706

00:16:31.560 --> 00:16:33.125 central coordinates for each node.

NOTE Confidence: 0.78052706

00:16:33.130 --> 00:16:34.948 And if we apply this to

NOTE Confidence: 0.78052706

00:16:34.948 --> 00:16:35.857 our abstinence networks,

NOTE Confidence: 0.78052706

00:16:35.860 --> 00:16:38.076 what we find is that both networks include

NOTE Confidence: 0.78052706

00:16:38.076 --> 00:16:40.099 both short and long range connections.

NOTE Confidence: 0.78052706

00:16:40.100 --> 00:16:41.296 However, positive absence network,

NOTE Confidence: 0.78052706

00:16:41.296 --> 00:16:43.090 the network for which increased connectivity

NOTE Confidence: 0.78052706

00:16:43.129 --> 00:16:44.337 predicts more within treatments,

NOTE Confidence: 0.78052706

00:16:44.340 --> 00:16:46.004 is characterized by predominantly

NOTE Confidence: 0.78052706

00:16:46.004 --> 00:16:46.836 longer interactions.

NOTE Confidence: 0.78052706

00:16:46.840 --> 00:16:48.450 Where is our negative network,

NOTE Confidence: 0.78052706

00:16:48.450 --> 00:16:50.376 the network for which decreased connectivity

NOTE Confidence: 0.78052706

00:16:50.376 --> 00:16:51.660 predicts more within treatment.

NOTE Confidence: 0.78052706

00:16:51.660 --> 00:16:52.940 Abstinence is characterized by

NOTE Confidence: 0.78052706

00:16:52.940 --> 00:16:54.220 predominantly shorter range connections,

NOTE Confidence: 0.78052706

00:16:54.220 --> 00:16:55.556 which makes intuitive sense

NOTE Confidence: 0.78052706

00:16:55.556 --> 00:16:56.892 because longer range connections

NOTE Confidence: 0.78052706

00:16:56.892 --> 00:16:59.114 tend to be involved in the higher

NOTE Confidence: 0.78052706

00:16:59.114 --> 00:17:00.314 order more complex processes.

NOTE Confidence: 0.75752413

00:17:02.540 --> 00:17:04.451 Another way in which we can summarize

NOTE Confidence: 0.75752413

00:17:04.451 --> 00:17:05.819 these networks is of course,

NOTE Confidence: 0.75752413

00:17:05.820 --> 00:17:07.195 anatomically so these circle plots

NOTE Confidence: 0.75752413

00:17:07.195 --> 00:17:08.570 summarize network connectivity based on

NOTE Confidence: 0.75752413

00:17:08.615 --> 00:17:10.175 the number of connections between mappers.

NOTE Confidence: 0.75752413

00:17:10.180 --> 00:17:11.272 They'll brain regions which

NOTE Confidence: 0.75752413

00:17:11.272 --> 00:17:12.637 are listed on your left,

NOTE Confidence: 0.75752413

00:17:12.640 --> 00:17:14.890 so from the top of each circle brain brain

NOTE Confidence: 0.75752413

00:17:14.890 --> 00:17:16.740 regions are represented in grafana top,

NOTE Confidence: 0.75752413

00:17:16.740 --> 00:17:17.820 and as amical order,

NOTE Confidence: 0.75752413

00:17:17.820 --> 00:17:19.170 with lines coming from the

NOTE Confidence: 0.75752413

00:17:19.170 --> 00:17:20.559 red portions of the top,

NOTE Confidence: 0.75752413

00:17:20.560 --> 00:17:22.135 or responding to prefrontal cortical

NOTE Confidence: 0.75752413

00:17:22.135 --> 00:17:23.710 connections in lines coming from

NOTE Confidence: 0.75752413

00:17:23.758 --> 00:17:25.648 the purple bits at the bottom

NOTE Confidence: 0.75752413

00:17:25.648 --> 00:17:26.908 corresponding to brainstem connections.

NOTE Confidence: 0.75752413

00:17:26.910 --> 00:17:28.240 And from left to right,

NOTE Confidence: 0.75752413

00:17:28.240 --> 00:17:29.328 network connectivity is threshold

NOTE Confidence: 0.75752413

00:17:29.328 --> 00:17:31.253 with a different levels based on the

NOTE Confidence: 0.75752413

00:17:31.253 --> 00:17:32.735 total number of connections for brain,

NOTE Confidence: 0.75752413

00:17:32.740 --> 00:17:34.774 region and so you can see that if we

NOTE Confidence: 0.75752413

00:17:34.774 --> 00:17:36.690 use a liberal threshold, for example,

NOTE Confidence: 0.75752413

00:17:36.690 --> 00:17:38.690 we look at all brain regions with five

NOTE Confidence: 0.75752413

00:17:38.747 --> 00:17:40.955 or more connections showing here on the left.

NOTE Confidence: 0.75752413

00:17:40.960 --> 00:17:42.016 Our networks remains somewhat

NOTE Confidence: 0.75752413

00:17:42.016 --> 00:17:42.808 difficult to interpret.

NOTE Confidence: 0.75752413

00:17:42.810 --> 00:17:43.075 However,

NOTE Confidence: 0.75752413

00:17:43.075 --> 00:17:44.930 if we take a more conservative threshold,

NOTE Confidence: 0.75752413

00:17:44.930 --> 00:17:46.932 for example only focusing on regions with

NOTE Confidence: 0.75752413

00:17:46.932 --> 00:17:49.228 12 or more connections on the right.

NOTE Confidence: 0.75752413

00:17:49.230 --> 00:17:51.225 Our networks begin to be a bit

NOTE Confidence: 0.75752413

00:17:51.225 --> 00:17:51.795 more interpretable,

NOTE Confidence: 0.75752413

00:17:51.800 --> 00:17:52.610 so for example,

NOTE Confidence: 0.75752413

00:17:52.610 --> 00:17:54.500 we can see that the positive abstinence

NOTE Confidence: 0.75752413

00:17:54.552 --> 00:17:56.552 network shown in red at the top is

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NOTE Confidence: 0.75752413

00:17:56.552 --> 00:17:58.079 characterized by right prefrontal node

NOTE Confidence: 0.75752413

00:17:58.079 --> 00:17:59.699 with connections to temporal limbic

NOTE Confidence: 0.75752413

00:17:59.699 --> 00:18:01.256 and left frontal cortical regions,

NOTE Confidence: 0.75752413

00:18:01.256 --> 00:18:03.751 and we can also see that the negative

NOTE Confidence: 0.75752413

00:18:03.751 --> 00:18:05.665 network here at the bottom is

NOTE Confidence: 0.75752413

00:18:05.665 --> 00:18:07.819 characterized by a temporal node with

NOTE Confidence: 0.75752413

00:18:07.819 --> 00:18:10.093 connections to limit and cerebellar nodes.

NOTE Confidence: 0.75752413

00:18:10.100 --> 00:18:11.836 Another way we can begin to understand

NOTE Confidence: 0.75752413

00:18:11.836 --> 00:18:13.536 the anatomy of our absence networks

NOTE Confidence: 0.75752413

00:18:13.536 --> 00:18:15.036 is via their spatial overlap

NOTE Confidence: 0.75752413

00:18:15.036 --> 00:18:16.439 with Canonical neural networks.

NOTE Confidence: 0.75752413

00:18:16.440 --> 00:18:17.244 So for example,

NOTE Confidence: 0.75752413

00:18:17.244 --> 00:18:18.852 via their overlap with the frontal

NOTE Confidence: 0.75752413

00:18:18.852 --> 00:18:20.758 parietal salients and default mode networks,

NOTE Confidence: 0.75752413

00:18:20.760 --> 00:18:23.160 all of which had previously

NOTE Confidence: 0.75752413

00:18:23.160 --> 00:18:25.080 been implicated in addictions.

NOTE Confidence: 0.75752413

00:18:25.080 --> 00:18:26.128 When we do this,

NOTE Confidence: 0.75752413

00:18:26.128 --> 00:18:27.176 we can characterize connectivity

NOTE Confidence: 0.75752413

00:18:27.176 --> 00:18:29.135 based on the number of connections

NOTE Confidence: 0.75752413

00:18:29.135 --> 00:18:30.515 between these established networks.

NOTE Confidence: 0.75752413

00:18:30.520 --> 00:18:32.278 So here we have matrices summarizing

NOTE Confidence: 0.75752413

00:18:32.278 --> 00:18:34.114 overlap between these networks for the

NOTE Confidence: 0.75752413

00:18:34.114 --> 00:18:35.644 positive and negative network separately,

NOTE Confidence: 0.75752413

00:18:35.650 --> 00:18:37.582 and for each matrix the cells represent

NOTE Confidence: 0.75752413

00:18:37.582 --> 00:18:39.124 the total number of connections

NOTE Confidence: 0.75752413

00:18:39.124 --> 00:18:40.779 within and between each network,

NOTE Confidence: 0.75752413

00:18:40.780 --> 00:18:42.290 with darker colors indicating a

NOTE Confidence: 0.75752413

00:18:42.290 --> 00:18:43.498 greater number of connections,

NOTE Confidence: 0.75752413

00:18:43.500 --> 00:18:45.537 and so we can see the positive

NOTE Confidence: 0.75752413

00:18:45.537 --> 00:18:47.218 network is characterized by a large

NOTE Confidence: 0.75752413

00:18:47.218 --> 00:18:48.712 number of frontal parietal to me

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NOTE Confidence: 0.75752413

00:18:48.712 --> 00:18:50.449 and medial frontal connections,

NOTE Confidence: 0.75752413

00:18:50.450 --> 00:18:52.650 as well as by a lot of salience

NOTE Confidence: 0.75752413

00:18:52.650 --> 00:18:54.546 and motor sensory connections as

NOTE Confidence: 0.75752413

00:18:54.546 --> 00:18:57.096 indicated by these dark red boxes.

NOTE Confidence: 0.75752413

00:18:57.100 --> 00:18:59.260 We can also see that the negative network

NOTE Confidence: 0.75752413

00:18:59.260 --> 00:19:01.159 includes a large number of salience,

NOTE Confidence: 0.75752413

00:19:01.160 --> 00:19:02.900 default mode, and medial frontal connections,

NOTE Confidence: 0.75752413

00:19:02.900 --> 00:19:04.930 as indicated by the dark blue boxes,

NOTE Confidence: 0.75752413

00:19:04.930 --> 00:19:06.370 and these differences become even

NOTE Confidence: 0.75752413

00:19:06.370 --> 00:19:08.135 more apparent if we directly compare

NOTE Confidence: 0.75752413

00:19:08.135 --> 00:19:09.505 the number of connections within

NOTE Confidence: 0.75752413

00:19:09.505 --> 00:19:11.840 each network so we can see that the

NOTE Confidence: 0.75752413

00:19:11.840 --> 00:19:13.325 positive network includes more frontal

NOTE Confidence: 0.75752413

00:19:13.325 --> 00:19:14.698 parietal to medial frontal connections,

NOTE Confidence: 0.75752413

00:19:14.698 --> 00:19:16.300 as well as more salient subcortical

NOTE Confidence: 0.75752413

00:19:16.346 --> 00:19:17.399 motor sensory connections.

NOTE Confidence: 0.75752413

00:19:17.400 --> 00:19:18.172 In contrast,

NOTE Confidence: 0.75752413

00:19:18.172 --> 00:19:20.102 the negative network includes more

NOTE Confidence: 0.75752413

00:19:20.102 --> 00:19:21.689 connections between the medial

NOTE Confidence: 0.75752413

00:19:21.689 --> 00:19:23.539 frontal network and the salience

NOTE Confidence: 0.75752413

00:19:23.539 --> 00:19:25.019 in default mode connections.

NOTE Confidence: 0.75752413

00:19:25.020 --> 00:19:26.700 So based on these differences,

NOTE Confidence: 0.75752413

00:19:26.700 --> 00:19:28.380 we generated a theoretical network

NOTE Confidence: 0.75752413

00:19:28.380 --> 00:19:30.060 based model of cocaine abstinence.

NOTE Confidence: 0.75752413

00:19:30.060 --> 00:19:31.645 We propose the cocaine abstinence

NOTE Confidence: 0.75752413

00:19:31.645 --> 00:19:33.230 is positively predicted by increased

NOTE Confidence: 0.7954006

00:19:33.284 --> 00:19:35.029 connectivity within and between frontal

NOTE Confidence: 0.7954006

00:19:35.029 --> 00:19:36.774 parietal and medial frontal networks.

NOTE Confidence: 0.7954006

00:19:36.780 --> 00:19:38.550 As a reminder, these are networks

NOTE Confidence: 0.7954006

00:19:38.550 --> 00:19:40.192 involved in coordination of attention

NOTE Confidence: 0.7954006

00:19:40.192 --> 00:19:41.820 and executive control processes,

43

NOTE Confidence: 0.7954006

00:19:41.820 --> 00:19:43.787 and so we think they might contribute

NOTE Confidence: 0.7954006

00:19:43.787 --> 00:19:45.377 within two and abstinence via

NOTE Confidence: 0.7954006

00:19:45.377 --> 00:19:47.453 coordination of the top down process

NOTE Confidence: 0.7954006

00:19:47.453 --> 00:19:49.549 is necessary for treatment engagement.

NOTE Confidence: 0.7954006

00:19:49.550 --> 00:19:50.402 So for example,

NOTE Confidence: 0.7954006

00:19:50.402 --> 00:19:51.822 things like acquisition of new

NOTE Confidence: 0.7954006

00:19:51.822 --> 00:19:53.522 skills or enhanced control over

NOTE Confidence: 0.7954006

00:19:53.522 --> 00:19:55.322 impulsive behaviors or data further

NOTE Confidence: 0.7954006

00:19:55.322 --> 00:19:57.060 suggests that cocaine abstinence.

NOTE Confidence: 0.7954006

00:19:57.060 --> 00:19:59.224 Is positively predicted by

NOTE Confidence: 0.7954006

00:19:59.224 --> 00:20:00.306 increased connectivity.

NOTE Confidence: 0.7954006

00:20:00.310 --> 00:20:01.925 Within salient subcortical motor sensory

NOTE Confidence: 0.7954006

00:20:01.925 --> 00:20:03.980 regions and so these are networks

NOTE Confidence: 0.7954006

00:20:03.980 --> 00:20:05.890 involved in coordination of salience,

NOTE Confidence: 0.7954006

00:20:05.890 --> 00:20:06.781 encoding and reward.

NOTE Confidence: 0.7954006

00:20:06.781 --> 00:20:08.563 So we think that these networks

NOTE Confidence: 0.7954006

00:20:08.563 --> 00:20:09.745 could support motivational

NOTE Confidence: 0.7954006

00:20:09.745 --> 00:20:11.830 processes and relevant in treatment.

NOTE Confidence: 0.7954006

00:20:11.830 --> 00:20:12.464 For example,

NOTE Confidence: 0.7954006

00:20:12.464 --> 00:20:14.366 willingness to change in shoring up

NOTE Confidence: 0.7954006

00:20:14.366 --> 00:20:16.567 of non drug reward processing or

NOTE Confidence: 0.7954006

00:20:16.567 --> 00:20:18.452 attending double turn it rewards.

NOTE Confidence: 0.7954006

00:20:18.460 --> 00:20:18.782 Finally,

NOTE Confidence: 0.7954006

00:20:18.782 --> 00:20:20.392 our data indicate that absence

NOTE Confidence: 0.7954006

00:20:20.392 --> 00:20:22.067 is further predicted by decreased

NOTE Confidence: 0.7954006

00:20:22.067 --> 00:20:23.702 connectivity between these two systems

NOTE Confidence: 0.7954006

00:20:23.702 --> 00:20:25.890 and so based on prior connectivity

NOTE Confidence: 0.7954006

00:20:25.890 --> 00:20:27.530 working cocaine use disorder,

NOTE Confidence: 0.7954006

00:20:27.530 --> 00:20:29.315 we actually think that appropriate

NOTE Confidence: 0.7954006

00:20:29.315 --> 00:20:31.100 separation between these two systems.

NOTE Confidence: 0.7954006

00:20:31.100 --> 00:20:32.685 Could relate to greater behavioral

NOTE Confidence: 0.7954006

00:20:32.685 --> 00:20:33.953 flexibility or decreased compulsivity

NOTE Confidence: 0.7954006

00:20:33.953 --> 00:20:35.764 as might be required for behavior

NOTE Confidence: 0.7954006

00:20:35.764 --> 00:20:36.634 change during treatment,

NOTE Confidence: 0.7954006

00:20:36.640 --> 00:20:38.110 so this model is really building

NOTE Confidence: 0.7954006

00:20:38.110 --> 00:20:39.566 on prior models of addiction

NOTE Confidence: 0.7954006

00:20:39.566 --> 00:20:41.258 emphasizing separation of frontal,

NOTE Confidence: 0.7954006

00:20:41.260 --> 00:20:42.308 parietal and salience networks

NOTE Confidence: 0.7954006

00:20:42.308 --> 00:20:44.275 such as model put forth by Elliot

NOTE Confidence: 0.7954006

00:20:44.275 --> 00:20:46.020 Stein colleagues where we're also

NOTE Confidence: 0.7954006

00:20:46.020 --> 00:20:47.416 incorporating medial frontal motor,

NOTE Confidence: 0.7954006

00:20:47.420 --> 00:20:48.616 sensory and subcortical networks.

NOTE Confidence: 0.7954006

00:20:48.616 --> 00:20:49.812 Provide a theoretical framework

NOTE Confidence: 0.7954006

00:20:49.812 --> 00:20:50.810 for future research,

NOTE Confidence: 0.7954006

00:20:50.810 --> 00:20:52.966 and so our hope is that by

NOTE Confidence: 0.7954006

00:20:52.966 --> 00:20:53.890 proposing this framework,

NOTE Confidence: 0.7954006

00:20:53.890 --> 00:20:56.362 we can encourage others to test

NOTE Confidence: 0.7954006

00:20:56.362 --> 00:20:58.739 these hypothesis in their own data.

NOTE Confidence: 0.7954006

00:20:58.740 --> 00:21:00.882 So the last thing I want to point out

NOTE Confidence: 0.7954006

00:21:00.882 --> 00:21:03.387 on this slide is that so when we're

NOTE Confidence: 0.7954006

00:21:03.387 --> 00:21:05.410 when we're computing our connectivity,

NOTE Confidence: 0.7954006

00:21:05.410 --> 00:21:06.614 matrices were basically we're

NOTE Confidence: 0.7954006

00:21:06.614 --> 00:21:08.420 taking the time course across the

NOTE Confidence: 0.7954006

00:21:08.469 --> 00:21:09.949 entire rewards get broad tasks,

NOTE Confidence: 0.7954006

00:21:09.950 --> 00:21:11.465 so we're not modeling events

NOTE Confidence: 0.7954006

00:21:11.465 --> 00:21:12.677 of interest at all.

NOTE Confidence: 0.7954006

00:21:12.680 --> 00:21:14.486 We're just basing it on the

NOTE Confidence: 0.7954006

00:21:14.486 --> 00:21:15.690 overall pattern of connectivity

NOTE Confidence: 0.7954006

00:21:15.745 --> 00:21:16.917 across the entire task.

NOTE Confidence: 0.7954006

00:21:16.920 --> 00:21:17.718 But Despite that,

NOTE Confidence: 0.7954006

00:21:17.718 --> 00:21:19.314 I think that our findings are

NOTE Confidence: 0.7954006

00:21:19.314 --> 00:21:20.920 actually somewhat intuitive when we

NOTE Confidence: 0.7954006

00:21:20.920 --> 00:21:22.535 consider them within the specific

NOTE Confidence: 0.7954006

00:21:22.535 --> 00:21:24.187 context of reward task performance,

NOTE Confidence: 0.7954006

00:21:24.190 --> 00:21:25.715 which of course would require

NOTE Confidence: 0.7954006

00:21:25.715 --> 00:21:26.935 coordination of both attentional

NOTE Confidence: 0.7954006

00:21:26.935 --> 00:21:28.241 and cognitive control processes

NOTE Confidence: 0.7954006

00:21:28.241 --> 00:21:29.831 as well as assailants encoding

NOTE Confidence: 0.7954006

00:21:29.831 --> 00:21:31.400 and reward response behaviors.

NOTE Confidence: 0.7954006

00:21:31.400 --> 00:21:32.135 So, so again,

NOTE Confidence: 0.7954006

00:21:32.135 --> 00:21:33.850 this is just starting to hint at

NOTE Confidence: 0.7954006

00:21:33.905 --> 00:21:35.795 this possibility that Brain State

NOTE Confidence: 0.7954006

00:21:35.795 --> 00:21:37.685 might matter for predictive modeling.

NOTE Confidence: 0.7954006

00:21:37.690 --> 00:21:39.322 Also tested the ability of the

NOTE Confidence: 0.7954006

00:21:39.322 --> 00:21:40.410 identified networks for abstinence

NOTE Confidence: 0.7954006

00:21:40.460 --> 00:21:41.300 following treatment.

NOTE Confidence: 0.7954006

00:21:41.300 --> 00:21:43.211 So for this analysis we simply create

NOTE Confidence: 0.7954006

00:21:43.211 --> 00:21:44.693 summary scores by summing edge

NOTE Confidence: 0.7954006

00:21:44.693 --> 00:21:46.208 weights for the nodes identified

NOTE Confidence: 0.7954006

00:21:46.208 --> 00:21:47.620 in our original analysis.

NOTE Confidence: 0.7954006

00:21:47.620 --> 00:21:49.474 So we're taking our absence networks

NOTE Confidence: 0.7954006

00:21:49.474 --> 00:21:51.914 and we're using them as a mask to

NOTE Confidence: 0.7954006

00:21:51.914 --> 00:21:53.636 extract values from post treatment data,

NOTE Confidence: 0.7954006

00:21:53.640 --> 00:21:55.464 and we enter those into correlational

NOTE Confidence: 0.7954006

00:21:55.464 --> 00:21:57.260 analysis with percent days of absence.

NOTE Confidence: 0.7954006

00:21:57.260 --> 00:21:58.932 During six month follow up and we find

NOTE Confidence: 0.7954006

00:21:58.932 --> 00:22:00.494 that post treatment network strengths

NOTE Confidence: 0.7954006

00:22:00.494 --> 00:22:02.324 were in fact significantly correlated

NOTE Confidence: 0.7954006

00:22:02.324 --> 00:22:03.580 with posttreatment abstinence,

NOTE Confidence: 0.7954006

00:22:03.580 --> 00:22:04.507 suggesting relative consistency

NOTE Confidence: 0.7954006

00:22:04.507 --> 00:22:05.743 of this relationship overtime

NOTE Confidence: 0.7954006

00:22:05.743 --> 00:22:06.890 further consistent with that.

NOTE Confidence: 0.7954006

00:22:06.890 --> 00:22:08.565 When we just compare pre

NOTE Confidence: 0.7954006

00:22:08.565 --> 00:22:09.570 versus post treatment.

NOTE Confidence: 0.7954006

00:22:09.570 --> 00:22:11.646 Connectivity strength we see no changes,

NOTE Confidence: 0.7954006

00:22:11.650 --> 00:22:13.370 overtime raising the possibility

NOTE Confidence: 0.7954006

00:22:13.370 --> 00:22:15.520 that these effects are somewhat

NOTE Confidence: 0.7954006

00:22:15.520 --> 00:22:17.169 stable within individuals.

NOTE Confidence: 0.7954006

00:22:17.170 --> 00:22:18.490 But the big question is,

NOTE Confidence: 0.82973784

00:22:18.490 --> 00:22:20.250 is not really whether or not these effects

NOTE Confidence: 0.82973784

00:22:20.250 --> 00:22:21.900 are stable within individuals overtime,

NOTE Confidence: 0.82973784

00:22:21.900 --> 00:22:23.478 but whether or not this fact

NOTE Confidence: 0.82973784

00:22:23.478 --> 00:22:24.530 replicates an independent sample,

NOTE Confidence: 0.82973784

00:22:24.530 --> 00:22:26.285 because that's really the whole

NOTE Confidence: 0.82973784

00:22:26.285 --> 00:22:28.040 point of using something like

NOTE Confidence: 0.82973784

00:22:28.105 --> 00:22:29.717 a machine learning approach.

NOTE Confidence: 0.82973784

00:22:29.720 --> 00:22:31.268 So the analysis of and show

NOTE Confidence: 0.82973784

00:22:31.268 --> 00:22:33.318 you up to now were run using.

NOTE Confidence: 0.82973784

00:22:33.320 --> 00:22:35.000 They gotta leave one out cross

NOTE Confidence: 0.82973784

00:22:35.000 --> 00:22:36.742 validation scheme in which for each

NOTE Confidence: 0.82973784

00:22:36.742 --> 00:22:38.167 for a single participants predicted

NOTE Confidence: 0.82973784

00:22:38.167 --> 00:22:40.348 value or what we refer to as the

NOTE Confidence: 0.82973784

00:22:40.348 --> 00:22:41.883 left out participant is generated by

NOTE Confidence: 0.82973784

00:22:41.883 --> 00:22:43.654 taking the data from all of their

NOTE Confidence: 0.82973784

00:22:43.654 --> 00:22:44.976 participants in the training data

NOTE Confidence: 0.82973784

00:22:44.976 --> 00:22:46.747 set an iterative manner and so all

NOTE Confidence: 0.82973784

00:22:46.803 --> 00:22:48.558 participants have a predicted value.

NOTE Confidence: 0.82973784

00:22:48.560 --> 00:22:50.216 But that approach can also be

NOTE Confidence: 0.82973784

00:22:50.216 --> 00:22:51.044 prone to overfitting,

NOTE Confidence: 0.82973784

00:22:51.050 --> 00:22:53.658 so we wanted to also have an external

NOTE Confidence: 0.82973784

00:22:53.658 --> 00:22:55.778 validation sample which was no small

NOTE Confidence: 0.82973784

00:22:55.778 --> 00:22:57.178 feat because pretreatment Norman

NOTE Confidence: 0.82973784

00:22:57.178 --> 00:22:59.308 data is pretty hard to come by.

NOTE Confidence: 0.82973784

00:22:59.310 --> 00:23:00.670 However, things to Kathy, Carolyn,

NOTE Confidence: 0.82973784

00:23:00.670 --> 00:23:01.456 Mark, but Enza,

NOTE Confidence: 0.82973784

00:23:01.456 --> 00:23:02.766 we managed to cobble together

NOTE Confidence: 0.82973784

00:23:02.766 --> 00:23:03.650 a replication sample.

NOTE Confidence: 0.82973784

00:23:03.650 --> 00:23:05.498 I'm not going to go too much

NOTE Confidence: 0.82973784

00:23:05.498 --> 00:23:07.168 into the details of that today,

NOTE Confidence: 0.82973784

00:23:07.170 --> 00:23:08.544 but it was 45 individuals about

NOTE Confidence: 0.82973784

00:23:08.544 --> 00:23:10.111 a third of whom were taking

NOTE Confidence: 0.82973784

00:23:10.111 --> 00:23:11.899 methadone for opiate use or now

NOTE Confidence: 0.82973784

00:23:11.899 --> 00:23:13.130 seeking treatment for cocaine.

NOTE Confidence: 0.82973784

00:23:13.130 --> 00:23:14.490 As in our original sample,

NOTE Confidence: 0.82973784

00:23:14.490 --> 00:23:16.205 but 2/3 of the replication sample were

NOTE Confidence: 0.82973784

00:23:16.205 --> 00:23:18.008 not on methadone and work independently,

NOTE Confidence: 0.82973784

00:23:18.010 --> 00:23:19.636 and they're also scan prior to

NOTE Confidence: 0.82973784

00:23:19.636 --> 00:23:20.720 us totally separate treatment.

NOTE Confidence: 0.82973784

00:23:20.720 --> 00:23:22.070 Trial involving a different medication.

NOTE Confidence: 0.82973784

00:23:22.070 --> 00:23:23.696 So this is a very heterogeneous

NOTE Confidence: 0.82973784

00:23:23.696 --> 00:23:25.185 replication sample, was at least.

NOTE Confidence: 0.82973784

00:23:25.185 --> 00:23:27.075 For replication sample were again just

NOTE Confidence: 0.82973784

00:23:27.075 --> 00:23:28.747 creating summary scores by summing

NOTE Confidence: 0.82973784

00:23:28.747 --> 00:23:30.697 edge weights with nodes identified in

NOTE Confidence: 0.82973784

00:23:30.757 --> 00:23:32.652 our original analysis and entering

NOTE Confidence: 0.82973784

00:23:32.652 --> 00:23:34.168 them into correlation analysis.

NOTE Confidence: 0.82973784

00:23:34.170 --> 00:23:35.390 Their biological measure absence

NOTE Confidence: 0.82973784

00:23:35.390 --> 00:23:37.589 percent cocaine for yarns and in fact

NOTE Confidence: 0.82973784

00:23:37.589 --> 00:23:39.503 we find the same relationship between

NOTE Confidence: 0.82973784

00:23:39.503 --> 00:23:40.980 network strengthen within treatment.

NOTE Confidence: 0.82973784

00:23:40.980 --> 00:23:43.080 Abstinence in this heterogeneous

NOTE Confidence: 0.82973784

00:23:43.080 --> 00:23:44.130 independent sample.

NOTE Confidence: 0.82973784

00:23:44.130 --> 00:23:46.027 Just to summarize that first data set.

NOTE Confidence: 0.82973784

00:23:46.030 --> 00:23:47.584 These data demonstrate the ability of

NOTE Confidence: 0.82973784

00:23:47.584 --> 00:23:48.949 a recently developed machine learning

NOTE Confidence: 0.82973784

00:23:48.949 --> 00:23:50.359 approach for Dick Truman Outcomes.

NOTE Confidence: 0.82973784

00:23:50.360 --> 00:23:51.173 In this case,

NOTE Confidence: 0.82973784

00:23:51.173 --> 00:23:52.257 abstinence from cocaine germ

NOTE Confidence: 0.82973784

00:23:52.257 --> 00:23:52.799 phobia treatment.

NOTE Confidence: 0.82973784

00:23:52.800 --> 00:23:54.697 I didn't show you the data today,

NOTE Confidence: 0.82973784

00:23:54.700 --> 00:23:56.355 but we recently replicated this

NOTE Confidence: 0.82973784

00:23:56.355 --> 00:23:58.010 in a second external sample.

NOTE Confidence: 0.82973784

00:23:58.010 --> 00:23:59.809 Networks that we are identified with her

NOTE Confidence: 0.82973784

00:23:59.809 --> 00:24:01.899 bus and they were relatively unchanged,

NOTE Confidence: 0.82973784

00:24:01.900 --> 00:24:02.496 involved analysis,

NOTE Confidence: 0.82973784

00:24:02.496 --> 00:24:03.390 controlling for other

NOTE Confidence: 0.82973784

00:24:03.390 --> 00:24:04.284 baseline clinical variables.

NOTE Confidence: 0.82973784

00:24:04.290 --> 00:24:05.292 So for example,

NOTE Confidence: 0.82973784

00:24:05.292 --> 00:24:06.962 methadone dose or days of

NOTE Confidence: 0.82973784

00:24:06.962 --> 00:24:08.340 past month calcaneus.

NOTE Confidence: 0.82973784

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00:24:08.340 --> 00:24:09.504 Post treatment connectivity within

00:24:09.504 --> 00:24:10.668 these networks also predicted

00:24:10.668 --> 00:24:12.045 absent certain follow up and our

00:24:12.045 --> 00:24:12.985 networks are not changed from

00:24:12.985 --> 00:24:14.272 pre to posttreatment raising the

00:24:14.272 --> 00:24:15.332 possibility that this relationship

00:24:15.332 --> 00:24:16.929 might be somewhat consistent overtime,

00:24:16.929 --> 00:24:19.400 which is a point that will come

00:24:19.462 --> 00:24:21.198 back to at the end of my talk.

00:24:21.200 --> 00:24:22.862 But first I want to return

00:24:22.862 --> 00:24:24.400 this issue of Brain State.

00:24:24.400 --> 00:24:25.930 And which brings me to the

00:24:25.930 --> 00:24:27.300 second part of my talk,

00:24:27.300 --> 00:24:28.806 in which we've begun looking into

00:24:28.806 --> 00:24:30.470 whether brain states are drug specific.

00:24:30.470 --> 00:24:32.227 So this is work that was recently

NOTE Confidence: 0.82973784

00:24:32.227 --> 00:24:34.108 published and look at their psychiatry and

NOTE Confidence: 0.82973784

00:24:34.108 --> 00:24:36.020 was led by Doctor Sarah Legiance Teen,

NOTE Confidence: 0.82973784

00:24:36.020 --> 00:24:37.514 a very talented former postdoc in

NOTE Confidence: 0.82973784

00:24:37.514 --> 00:24:39.724 my lab who was recently who recently

NOTE Confidence: 0.82973784

00:24:39.724 --> 00:24:41.649 received her appointment to assistant

NOTE Confidence: 0.82973784

00:24:41.649 --> 00:24:43.200 professor here in Psychiatry.

NOTE Confidence: 0.82973784

00:24:43.200 --> 00:24:44.740 So the clinical rationale for

NOTE Confidence: 0.82973784

00:24:44.740 --> 00:24:46.280 this work really came from

NOTE Confidence: 0.8145461

00:24:46.342 --> 00:24:47.962 some MA work done by Epstein

NOTE Confidence: 0.8145461

00:24:47.962 --> 00:24:49.649 and colleagues a few years ago,

NOTE Confidence: 0.8145461

00:24:49.650 --> 00:24:50.935 so this was an electronic

NOTE Confidence: 0.8145461

00:24:50.935 --> 00:24:52.220 diary study of 114 methadone

NOTE Confidence: 0.8145461

00:24:52.272 --> 00:24:53.748 treat individuals with cocaine,

NOTE Confidence: 0.8145461

00:24:53.750 --> 00:24:55.215 an opiate dependence so very

NOTE Confidence: 0.8145461

00:24:55.215 --> 00:24:56.680 similar to our Poly substance.

NOTE Confidence: 0.8145461

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00:24:56.680 --> 00:24:57.792 Using our image example,

NOTE Confidence: 0.8145461

00:24:57.792 --> 00:24:59.797 and in this study what they did

NOTE Confidence: 0.8145461

00:24:59.797 --> 00:25:01.212 was ask participants to track

NOTE Confidence: 0.8145461

00:25:01.212 --> 00:25:02.830 changes in mood and craving,

NOTE Confidence: 0.8145461

00:25:02.830 --> 00:25:04.516 and to document their substance use

NOTE Confidence: 0.8145461

00:25:04.516 --> 00:25:05.981 within an animated framework and

NOTE Confidence: 0.8145461

00:25:05.981 --> 00:25:07.745 what they found was a differential

NOTE Confidence: 0.8145461

00:25:07.745 --> 00:25:08.969 Association between positive versus

NOTE Confidence: 0.8145461

00:25:08.969 --> 00:25:10.439 negative mood States and future

NOTE Confidence: 0.8145461

00:25:10.439 --> 00:25:12.027 substances such that cocaine use

NOTE Confidence: 0.8145461

00:25:12.027 --> 00:25:13.655 was most robustly associated

NOTE Confidence: 0.8145461

00:25:13.655 --> 00:25:16.072 with having been exposed to the

NOTE Confidence: 0.8145461

00:25:16.072 --> 00:25:18.263 drug or being in a positive mood.

NOTE Confidence: 0.8145461

00:25:18.270 --> 00:25:19.503 Suggesting possible links

NOTE Confidence: 0.8145461

00:25:19.503 --> 00:25:21.147 with impulsivity and reward,

NOTE Confidence: 0.8145461

00:25:21.150 --> 00:25:23.205 but heroin craving was associated

NOTE Confidence: 0.8145461

00:25:23.205 --> 00:25:25.260 with increases in negative affect,

NOTE Confidence: 0.8145461

00:25:25.260 --> 00:25:27.865 suggesting possible links with emotion

NOTE Confidence: 0.8145461

00:25:27.865 --> 00:25:29.949 regulation or inhibitory control.

NOTE Confidence: 0.8145461

00:25:29.950 --> 00:25:31.738 And so, based on this finding,

NOTE Confidence: 0.8145461

00:25:31.740 --> 00:25:33.462 the different mood states predict opiate

NOTE Confidence: 0.8145461

00:25:33.462 --> 00:25:35.629 versus cocaine use in the same individuals.

NOTE Confidence: 0.8145461

00:25:35.630 --> 00:25:37.406 We wanted to test the hypothesis

NOTE Confidence: 0.8145461

00:25:37.406 --> 00:25:38.945 that maybe different brain states

NOTE Confidence: 0.8145461

00:25:38.945 --> 00:25:40.450 might be more closely linked

NOTE Confidence: 0.8145461

00:25:40.450 --> 00:25:41.910 to opiate versus cocaine use.

NOTE Confidence: 0.8145461

00:25:41.910 --> 00:25:44.438 In our image example.

NOTE Confidence: 0.8145461

00:25:44.440 --> 00:25:45.580 So for this analysis,

NOTE Confidence: 0.8145461

00:25:45.580 --> 00:25:47.290 instead of focusing on cocaine use,

NOTE Confidence: 0.8145461

00:25:47.290 --> 00:25:48.720 we're focusing on opiate use.

NOTE Confidence: 0.8145461

00:25:48.720 --> 00:25:49.004 However,

NOTE Confidence: 0.8145461

00:25:49.004 --> 00:25:50.708 the primary simple is the same,

NOTE Confidence: 0.8145461

00:25:50.710 --> 00:25:52.705 so as I mentioned in the beginning

NOTE Confidence: 0.8145461

00:25:52.705 --> 00:25:53.560 of this talk,

NOTE Confidence: 0.8145461

00:25:53.560 --> 00:25:55.306 when I introduced our sample despite

NOTE Confidence: 0.8145461

00:25:55.306 --> 00:25:56.700 seeking treatment for cocaine use,

NOTE Confidence: 0.8145461

00:25:56.700 --> 00:25:58.812 all of our participants at Coco

NOTE Confidence: 0.8145461

00:25:58.812 --> 00:25:59.868 get use disorder.

NOTE Confidence: 0.8145461

00:25:59.870 --> 00:26:00.986 And we're currently methadone

NOTE Confidence: 0.8145461

00:26:00.986 --> 00:26:02.948 maintained and in fact it did turn

NOTE Confidence: 0.8145461

00:26:02.948 --> 00:26:04.804 out that there was a fair amount of

NOTE Confidence: 0.8145461

00:26:04.804 --> 00:26:06.317 residual to be used in this sample.

NOTE Confidence: 0.8145461

00:26:06.320 --> 00:26:08.296 If you're interested in the details on that,

NOTE Confidence: 0.8145461

00:26:08.300 --> 00:26:09.680 I'll refer you to the clinical

NOTE Confidence: 0.8145461

00:26:09.680 --> 00:26:11.030 paper led by Kathy Carroll,

NOTE Confidence: 0.8145461

00:26:11.030 --> 00:26:12.738 but just briefly so you can sort

NOTE Confidence: 0.8145461

00:26:12.738 --> 00:26:13.760 of understand that data.

NOTE Confidence: 0.8145461

00:26:13.760 --> 00:26:15.248 Here we have survival curves indicating

NOTE Confidence: 0.8145461

00:26:15.248 --> 00:26:17.014 the time to 1st submission of a

NOTE Confidence: 0.8145461

00:26:17.014 --> 00:26:18.472 non methadone will be a positive

NOTE Confidence: 0.8145461

00:26:18.472 --> 00:26:19.980 urine screen during this whole week

NOTE Confidence: 0.8145461

00:26:19.980 --> 00:26:21.696 treatment and we can see that on

NOTE Confidence: 0.8145461

00:26:21.696 --> 00:26:22.940 average about 50% of participants

NOTE Confidence: 0.8145461

00:26:22.940 --> 00:26:24.440 in this study submitted at least

NOTE Confidence: 0.8145461

00:26:24.440 --> 00:26:26.084 one non methadone opiate positive

NOTE Confidence: 0.8145461

00:26:26.084 --> 00:26:27.179 urine during treatment.

NOTE Confidence: 0.8145461

00:26:27.180 --> 00:26:29.462 This is also true of the newer

NOTE Confidence: 0.8145461

00:26:29.462 --> 00:26:30.114 imaging subsample,

NOTE Confidence: 0.8145461

00:26:30.120 --> 00:26:31.720 for which the mean percentage

NOTE Confidence: 0.8145461

00:26:31.720 --> 00:26:33.320 of opiate negative yarns meted

NOTE Confidence: 0.8145461

00:26:33.376 --> 00:26:35.026 during treatment was about 65%,

NOTE Confidence: 0.8145461

00:26:35.030 --> 00:26:36.660 indicating of course at about

NOTE Confidence: 0.8145461

00:26:36.660 --> 00:26:38.298 35% of specimens tested positive

NOTE Confidence: 0.8145461

00:26:38.298 --> 00:26:39.606 for non methadone opiates.

NOTE Confidence: 0.7534767

00:26:42.510 --> 00:26:44.596 For this analysis we again just calculate

NOTE Confidence: 0.7534767

00:26:44.596 --> 00:26:45.490 functional connectivity matrices,

NOTE Confidence: 0.7534767

00:26:45.490 --> 00:26:47.331 but this time we're doing using the

NOTE Confidence: 0.7534767

00:26:47.331 --> 00:26:48.487 data acquired during performance

NOTE Confidence: 0.7534767

00:26:48.487 --> 00:26:50.377 or cognitive control task and we

NOTE Confidence: 0.7534767

00:26:50.377 --> 00:26:51.982 entered those matrices into our

NOTE Confidence: 0.7534767

00:26:51.982 --> 00:26:53.812 print behavior model along with their

NOTE Confidence: 0.7534767

00:26:53.812 --> 00:26:56.260 biological measure of abstinence.

NOTE Confidence: 0.7534767

00:26:56.260 --> 00:26:58.294 And so this is the result of that model

NOTE Confidence: 0.7534767

00:26:58.294 --> 00:27:00.728 here on the Y access we again have

NOTE Confidence: 0.7534767

00:27:00.728 --> 00:27:01.983 individual participant absence values

NOTE Confidence: 0.7534767

00:27:01.983 --> 00:27:03.922 as predicted by the brain behavior model

NOTE Confidence: 0.7534767

00:27:03.922 --> 00:27:06.181 and on the X axis we have the actual

NOTE Confidence: 0.7534767

00:27:06.181 --> 00:27:07.769 abstinence values for each participant,

NOTE Confidence: 0.7534767

00:27:07.770 --> 00:27:08.862 again as a reminder.

NOTE Confidence: 0.7534767

00:27:08.862 --> 00:27:10.227 Typically when we use correlation,

NOTE Confidence: 0.7534767

00:27:10.230 --> 00:27:12.022 we're using it to try to explain

NOTE Confidence: 0.7534767

00:27:12.022 --> 00:27:13.519 the variance between two variables,

NOTE Confidence: 0.7534767

00:27:13.520 --> 00:27:15.408 But here we're just using the up to

NOTE Confidence: 0.7534767

00:27:15.408 --> 00:27:16.240 characterize predictive accuracy

NOTE Confidence: 0.7534767

00:27:16.240 --> 00:27:17.500 or the correspondence between

NOTE Confidence: 0.7534767

00:27:17.500 --> 00:27:18.445 actual encrypted values.

NOTE Confidence: 0.7534767

00:27:18.450 --> 00:27:19.820 And as you can see,

NOTE Confidence: 0.7534767

00:27:19.820 --> 00:27:21.190 our model has relatively good

NOTE Confidence: 0.7534767

00:27:21.190 --> 00:27:22.560 predictive accuracy with aspirin 0.34,

NOTE Confidence: 0.7534767

00:27:22.560 --> 00:27:24.502 which means at about 12% of the

NOTE Confidence: 0.7534767

00:27:24.502 --> 00:27:25.646 variance and within treatment

NOTE Confidence: 0.7534767

00:27:25.646 --> 00:27:27.477 opiate use is accounted for by

NOTE Confidence: 0.7534767

00:27:27.477 --> 00:27:28.749 connectivity within this network.

NOTE Confidence: 0.7534767

00:27:28.750 --> 00:27:30.335 So for Contacts that's comparable

NOTE Confidence: 0.7534767

00:27:30.335 --> 00:27:32.308 to the amount of variance explained

NOTE Confidence: 0.7534767

00:27:32.308 --> 00:27:34.306 by similar approaches that seek to

NOTE Confidence: 0.7534767

00:27:34.306 --> 00:27:36.489 predict rate like behaviors such as IQ.

NOTE Confidence: 0.7534767

00:27:36.490 --> 00:27:37.880 As their cocaine network that

NOTE Confidence: 0.7534767

00:27:37.880 --> 00:27:38.992 will be at network,

NOTE Confidence: 0.7534767

00:27:39.000 --> 00:27:40.944 we identified his complex that includes

NOTE Confidence: 0.7534767

00:27:40.944 --> 00:27:42.240 connections between multiple adjacent

NOTE Confidence: 0.7534767

00:27:42.287 --> 00:27:43.820 and non adjacent brain regions and in

NOTE Confidence: 0.7534767

00:27:43.820 --> 00:27:45.375 fact or opiate network is actually

NOTE Confidence: 0.7534767

00:27:45.375 --> 00:27:47.085 somewhat larger than the cocaine network.

NOTE Confidence: 0.7534767

00:27:47.090 --> 00:27:48.480 So with the positive and

NOTE Confidence: 0.7534767

00:27:48.480 --> 00:27:49.314 negative networks together,

NOTE Confidence: 0.7534767

00:27:49.320 --> 00:27:51.630 including just under 1000 edges.

NOTE Confidence: 0.7534767

00:27:51.630 --> 00:27:53.634 So that's almost twice the size

NOTE Confidence: 0.7534767

00:27:53.634 --> 00:27:54.970 of the cocaine network.

NOTE Confidence: 0.7534767

00:27:54.970 --> 00:27:56.635 However, it's still less than

NOTE Confidence: 0.7534767

00:27:56.635 --> 00:27:57.972 3% of possible connections,

NOTE Confidence: 0.7534767

00:27:57.972 --> 00:28:01.328 so again, and despite the visual.

NOTE Confidence: 0.7534767

00:28:01.330 --> 00:28:02.414 Complexity to actually quite

NOTE Confidence: 0.7534767

00:28:02.414 --> 00:28:02.956 specific connections,

NOTE Confidence: 0.7534767

00:28:02.960 --> 00:28:04.320 you can understand the anatomy

NOTE Confidence: 0.7534767

00:28:04.320 --> 00:28:05.408 of her opiate network.

NOTE Confidence: 0.7534767

00:28:05.410 --> 00:28:07.042 We can again summarize it by

NOTE Confidence: 0.7534767

00:28:07.042 --> 00:28:08.130 overlap with Canonical networks.

NOTE Confidence: 0.7534767

00:28:08.130 --> 00:28:10.027 So for example by overlap of medial,

NOTE Confidence: 0.7534767

00:28:10.030 --> 00:28:11.390 frontal and default mode networks

NOTE Confidence: 0.7534767

00:28:11.390 --> 00:28:12.478 when we do this,

NOTE Confidence: 0.7534767

00:28:12.480 --> 00:28:14.237 we can see that at least relative

NOTE Confidence: 0.7534767

00:28:14.237 --> 00:28:15.470 to the cocaine network,

NOTE Confidence: 0.7534767

00:28:15.470 --> 00:28:17.374 the opiate network is somewhat more sparse,

NOTE Confidence: 0.7534767

00:28:17.380 --> 00:28:19.548 and it does not include any within network,

NOTE Confidence: 0.7534767

00:28:19.550 --> 00:28:20.330 medial, frontal,

NOTE Confidence: 0.7534767

00:28:20.330 --> 00:28:21.890 or default mode connections.

NOTE Confidence: 0.7534767

00:28:21.890 --> 00:28:23.840 So despite including more edges overall,

NOTE Confidence: 0.7534767

00:28:23.840 --> 00:28:25.488 that will be it.

NOTE Confidence: 0.7534767

00:28:25.488 --> 00:28:27.548 Network is distributed across fewer

NOTE Confidence: 0.7534767

00:28:27.548 --> 00:28:28.630 Canonical networks.

NOTE Confidence: 0.7534767

00:28:28.630 --> 00:28:29.882 Directly compare positive versus

NOTE Confidence: 0.7534767

00:28:29.882 --> 00:28:30.508 negative networks.

NOTE Confidence: 0.7534767

00:28:30.510 --> 00:28:32.178 We find that positive network we

NOTE Confidence: 0.7534767

00:28:32.178 --> 00:28:33.679 follow the positive network included

NOTE Confidence: 0.7534767

00:28:33.679 --> 00:28:35.015 relatively more within network

NOTE Confidence: 0.7534767

00:28:35.015 --> 00:28:37.110 connections in the motor sensory network,

NOTE Confidence: 0.7534767

00:28:37.110 --> 00:28:39.030 whereas the negative network was

NOTE Confidence: 0.7534767

00:28:39.030 --> 00:28:40.566 characterized by more connections

NOTE Confidence: 0.7534767

00:28:40.566 --> 00:28:42.174 between the Motors and sorry

NOTE Confidence: 0.7534767

00:28:42.174 --> 00:28:43.920 network and rental prior to default

NOTE Confidence: 0.7534767

00:28:43.974 --> 00:28:45.689 mode and medial frontal networks.

NOTE Confidence: 0.7534767

00:28:45.690 --> 00:28:47.314 I have to say we were somewhat

NOTE Confidence: 0.7534767

00:28:47.314 --> 00:28:49.050 surprised that a large number of

NOTE Confidence: 0.7534767

00:28:49.050 --> 00:28:50.690 Motors motor sensor connections here.

NOTE Confidence: 0.7534767

00:28:50.690 --> 00:28:52.349 So what we've done is it also

NOTE Confidence: 0.7534767

00:28:52.349 --> 00:28:53.688 taken a virtual lesion approach

NOTE Confidence: 0.7534767

00:28:53.688 --> 00:28:55.683 with these data in which we just

NOTE Confidence: 0.7534767

00:28:55.683 --> 00:28:57.521 knock out all the nodes overlap

NOTE Confidence: 0.7534767

00:28:57.521 --> 00:28:59.021 with the given conical network,

NOTE Confidence: 0.7534767

00:28:59.030 --> 00:29:01.254 and we find that when we do this,

NOTE Confidence: 0.7534767

00:29:01.260 --> 00:29:02.645 despite the ceilings in child's

NOTE Confidence: 0.7534767

00:29:02.645 --> 00:29:03.476 motor sensory component,

NOTE Confidence: 0.7534767

00:29:03.480 --> 00:29:04.870 if we completely remove it,

NOTE Confidence: 0.7534767

00:29:04.870 --> 00:29:05.982 remaining connections still are

NOTE Confidence: 0.7534767

00:29:05.982 --> 00:29:07.094 sufficient in product abstinence.

NOTE Confidence: 0.7534767

00:29:07.100 --> 00:29:08.372 And actually we find the same

NOTE Confidence: 0.7534767

00:29:08.372 --> 00:29:10.406 thing if we if we knockout other

NOTE Confidence: 0.7534767

00:29:10.406 --> 00:29:11.540 individual clinical networks.

NOTE Confidence: 0.7534767

00:29:11.540 --> 00:29:12.024 For example,

NOTE Confidence: 0.7534767

00:29:12.024 --> 00:29:13.960 if we just knock out the default mode

NOTE Confidence: 0.79277724

00:29:14.017 --> 00:29:16.264 connections, really indicating that those.

NOTE Confidence: 0.79277724

00:29:16.264 --> 00:29:18.344 Single Canonical network alone is

NOTE Confidence: 0.79277724

00:29:18.344 --> 00:29:20.098 required to support abstinence.

NOTE Confidence: 0.79277724

00:29:20.100 --> 00:29:21.940 Salty understanding we again proposed

NOTE Confidence: 0.79277724

00:29:21.940 --> 00:29:23.780 a theoretical model that summarizes

NOTE Confidence: 0.79277724

00:29:23.836 --> 00:29:25.246 key aspects of this network,

NOTE Confidence: 0.79277724

00:29:25.250 --> 00:29:26.765 so this figure just emphasizes

NOTE Confidence: 0.79277724

00:29:26.765 --> 00:29:28.280 the absence was associated with

NOTE Confidence: 0.79277724

00:29:28.337 --> 00:29:30.297 increased within network motor sensor

NOTE Confidence: 0.79277724

00:29:30.297 --> 00:29:31.865 connectivity and increased between

NOTE Confidence: 0.79277724

00:29:31.865 --> 00:29:33.598 network connectivity of motor sensory

NOTE Confidence: 0.79277724

00:29:33.598 --> 00:29:35.536 and salience networks and of default

NOTE Confidence: 0.79277724

00:29:35.540 --> 00:29:37.550 mode and frontal parietal networks

NOTE Confidence: 0.79277724

00:29:37.550 --> 00:29:40.400 as indicated by the red lines here.

NOTE Confidence: 0.79277724

00:29:40.400 --> 00:29:42.206 And models also highlighting the absence,

NOTE Confidence: 0.79277724

00:29:42.210 --> 00:29:43.770 was further associated with decreased

NOTE Confidence: 0.79277724

00:29:43.770 --> 00:29:45.330 connectivity between the motor sensory

NOTE Confidence: 0.79277724

00:29:45.374 --> 00:29:46.809 network and medial frontal default

NOTE Confidence: 0.79277724

00:29:46.809 --> 00:29:48.244 mode and frontal parietal networks,

NOTE Confidence: 0.79277724

00:29:48.250 --> 00:29:50.056 as indicated by the blue lines,

NOTE Confidence: 0.79277724

00:29:50.060 --> 00:29:50.590 and again,

NOTE Confidence: 0.79277724

00:29:50.590 --> 00:29:52.710 our hope is that by summarizing the data

NOTE Confidence: 0.79277724

00:29:52.768 --> 00:29:54.588 in this somewhat simplistic manner,

NOTE Confidence: 0.79277724

00:29:54.590 --> 00:29:56.753 we can encourage others to test these

NOTE Confidence: 0.79277724

00:29:56.753 --> 00:29:58.792 theories in their own datasets to

NOTE Confidence: 0.79277724

00:29:58.792 --> 00:30:00.547 further guide nor biological risk.

NOTE Confidence: 0.79277724

00:30:00.550 --> 00:30:02.622 We've also made all of the masks of

NOTE Confidence: 0.79277724

00:30:02.622 --> 00:30:04.548 our actual absence networks public,

NOTE Confidence: 0.79277724

00:30:04.550 --> 00:30:07.820 and along with the associated code.

NOTE Confidence: 0.79277724

00:30:07.820 --> 00:30:09.310 Because we're interested in mechanism,

NOTE Confidence: 0.79277724

00:30:09.310 --> 00:30:10.020 of course,

NOTE Confidence: 0.79277724

00:30:10.020 --> 00:30:11.795 very interested in anatomical overlap

NOTE Confidence: 0.79277724

00:30:11.795 --> 00:30:13.910 between the cocaine and obeah networks.

NOTE Confidence: 0.79277724

00:30:13.910 --> 00:30:14.207 However,

NOTE Confidence: 0.79277724

00:30:14.207 --> 00:30:14.504 Interestingly,

NOTE Confidence: 0.79277724

00:30:14.504 --> 00:30:15.989 only compare edges across networks,

NOTE Confidence: 0.79277724

00:30:15.990 --> 00:30:17.766 we actually saw very little overlap,

NOTE Confidence: 0.79277724

00:30:17.770 --> 00:30:19.849 so less than 1% of edges shared.

NOTE Confidence: 0.79277724

00:30:19.850 --> 00:30:22.235 So here on your left we have edges their

NOTE Confidence: 0.79277724

00:30:22.235 --> 00:30:24.598 common to both cocaine and opiate networks,

NOTE Confidence: 0.79277724

00:30:24.600 --> 00:30:26.214 with the red lines indicating shared

NOTE Confidence: 0.79277724

00:30:26.214 --> 00:30:28.010 positive edges and the blue lines

NOTE Confidence: 0.79277724

00:30:28.010 --> 00:30:29.350 indicating shared negative edges.

NOTE Confidence: 0.79277724

00:30:29.350 --> 00:30:30.840 And as you can see,

NOTE Confidence: 0.79277724

00:30:30.840 --> 00:30:33.216 there's only a total of 8 shared edges.

NOTE Confidence: 0.79277724

00:30:33.220 --> 00:30:33.517 Overall,

NOTE Confidence: 0.79277724

00:30:33.517 --> 00:30:36.190 I realized I left off the figure legend here.

NOTE Confidence: 0.79277724

00:30:36.190 --> 00:30:37.270 So just for reference,

NOTE Confidence: 0.79277724

00:30:37.270 --> 00:30:38.620 the positive shared edges include

NOTE Confidence: 0.79277724

00:30:38.620 --> 00:30:39.711 a prefrontal, prefrontal,

NOTE Confidence: 0.79277724

00:30:39.711 --> 00:30:40.494 and limbic connections,

NOTE Confidence: 0.79277724

00:30:40.494 --> 00:30:42.441 as well as a subcortical to parietal

NOTE Confidence: 0.79277724

00:30:42.441 --> 00:30:43.789 connection and negative straight

NOTE Confidence: 0.79277724

00:30:43.789 --> 00:30:45.904 edges include parietal, still in bed,

NOTE Confidence: 0.79277724

00:30:45.904 --> 00:30:47.008 and supportable connections.

NOTE Confidence: 0.79277724

00:30:47.010 --> 00:30:47.618 In addition,

NOTE Confidence: 0.79277724

00:30:47.618 --> 00:30:49.442 we also identified several edges that

NOTE Confidence: 0.79277724

00:30:49.442 --> 00:30:50.820 have opposite opposite associations

NOTE Confidence: 0.79277724

00:30:50.820 --> 00:30:52.620 with opiate versus cocaine use,

NOTE Confidence: 0.79277724

00:30:52.620 --> 00:30:54.600 so these are edges for which,

NOTE Confidence: 0.79277724

00:30:54.600 --> 00:30:55.218 for example,

NOTE Confidence: 0.79277724

00:30:55.218 --> 00:30:56.763 increased connectivity is a positive

NOTE Confidence: 0.79277724

00:30:56.763 --> 00:30:58.230 predictor of cocaine abstinence,

NOTE Confidence: 0.79277724

00:30:58.230 --> 00:30:59.880 but for which decreased connectivity

NOTE Confidence: 0.79277724

00:30:59.880 --> 00:31:01.200 is a positive character.

NOTE Confidence: 0.79277724

00:31:01.200 --> 00:31:02.380 Opiate abstinence,

NOTE Confidence: 0.79277724

00:31:02.380 --> 00:31:04.150 or vice versa.

NOTE Confidence: 0.79277724

00:31:04.150 --> 00:31:05.865 Cities opposing edges are including

NOTE Confidence: 0.79277724

00:31:05.865 --> 00:31:06.894 connection between prefrontal

NOTE Confidence: 0.79277724

00:31:06.894 --> 00:31:08.595 and cerebellar regions as well as

NOTE Confidence: 0.79277724

00:31:08.595 --> 00:31:09.810 the temporal and vital cortices.

NOTE Confidence: 0.79277724

00:31:09.810 --> 00:31:11.300 And as you can see,

NOTE Confidence: 0.79277724

00:31:11.300 --> 00:31:12.790 there are more opposing edges

NOTE Confidence: 0.79277724

00:31:12.790 --> 00:31:13.684 than consistent edges.

NOTE Confidence: 0.79277724

00:31:13.690 --> 00:31:15.205 So these data together really

NOTE Confidence: 0.79277724

00:31:15.205 --> 00:31:16.417 indicating that the neural

NOTE Confidence: 0.79277724

00:31:16.417 --> 00:31:17.913 substrates of cocaine opiate use

NOTE Confidence: 0.79277724

00:31:17.913 --> 00:31:19.343 disorder may be largely disposable.

NOTE Confidence: 0.7633291

00:31:24.500 --> 00:31:26.276 We've also been looking into the

NOTE Confidence: 0.7633291

00:31:26.276 --> 00:31:27.460 specificity of these networks.

NOTE Confidence: 0.7633291

00:31:27.460 --> 00:31:28.644 Are predicting specific drugs

NOTE Confidence: 0.7633291

00:31:28.644 --> 00:31:29.828 across different brain states,

NOTE Confidence: 0.7633291

00:31:29.830 --> 00:31:31.552 so the data I just showed you

NOTE Confidence: 0.7633291

00:31:31.552 --> 00:31:33.063 indicated the cocaine obit network

NOTE Confidence: 0.7633291

00:31:33.063 --> 00:31:34.858 have pretty limited anatomical overlap.

NOTE Confidence: 0.7633291

00:31:34.860 --> 00:31:36.040 However one network was

NOTE Confidence: 0.7633291

00:31:36.040 --> 00:31:37.515 driver from reward task data,

NOTE Confidence: 0.7633291

00:31:37.520 --> 00:31:39.170 another was drive from cognitive data

NOTE Confidence: 0.7633291

00:31:39.170 --> 00:31:41.224 and I haven't yet shown you whether

NOTE Confidence: 0.7633291

00:31:41.224 --> 00:31:43.024 the opiate network also related to

NOTE Confidence: 0.7633291

00:31:43.024 --> 00:31:44.630 cocaine abstinence or vice versa,

NOTE Confidence: 0.7633291

00:31:44.630 --> 00:31:46.639 and I also haven't yet presented data

NOTE Confidence: 0.7633291

00:31:46.639 --> 00:31:48.254 to determine whether the relationship

NOTE Confidence: 0.7633291

00:31:48.254 --> 00:31:49.658 between network connectivity and

NOTE Confidence: 0.7633291

00:31:49.658 --> 00:31:51.859 substances is in fact task dependent.

NOTE Confidence: 0.7633291

00:31:51.860 --> 00:31:53.000 Or in other words,

NOTE Confidence: 0.7633291

00:31:53.000 --> 00:31:54.710 whether or not connect me findings

NOTE Confidence: 0.7633291

00:31:54.772 --> 00:31:56.120 hold across brain states.

NOTE Confidence: 0.7633291

00:31:56.120 --> 00:31:57.640 So to answer this question,

NOTE Confidence: 0.7633291

00:31:57.640 --> 00:31:59.327 first we looked at the impact of

NOTE Confidence: 0.7633291

00:31:59.327 --> 00:32:01.279 brain state on network identification.

NOTE Confidence: 0.7633291

00:32:01.280 --> 00:32:03.050 So we repeat our connectome based

NOTE Confidence: 0.7633291

00:32:03.050 --> 00:32:04.593 model of opiate abstinence using

NOTE Confidence: 0.7633291

00:32:04.593 --> 00:32:06.447 reward instead of cognitive task data,

NOTE Confidence: 0.7633291

00:32:06.450 --> 00:32:09.186 and we find that as I just showed you,

NOTE Confidence: 0.7633291

00:32:09.190 --> 00:32:11.339 we are able to predict opiate abstinence

NOTE Confidence: 0.7633291

00:32:11.339 --> 00:32:12.840 using cognitive control house data.

NOTE Confidence: 0.7633291

00:32:12.840 --> 00:32:13.151 However,

NOTE Confidence: 0.7633291

00:32:13.151 --> 00:32:15.017 we're not able to predict opiate

NOTE Confidence: 0.7633291

00:32:15.017 --> 00:32:16.479 abstinence using reward task data.

NOTE Confidence: 0.7633291

00:32:16.480 --> 00:32:16.789 Similarly,

NOTE Confidence: 0.7633291

00:32:16.789 --> 00:32:18.952 when we repeat our model of cocaine

NOTE Confidence: 0.7633291

00:32:18.952 --> 00:32:20.230 abstinence using cognitive data

NOTE Confidence: 0.7633291

00:32:20.230 --> 00:32:21.740 instead of reward task data.

NOTE Confidence: 0.7633291

00:32:21.740 --> 00:32:23.679 We find that we're only able to

NOTE Confidence: 0.7633291

00:32:23.679 --> 00:32:25.223 identify a cocaine network using

NOTE Confidence: 0.7633291

00:32:25.223 --> 00:32:26.519 the reward task data,

NOTE Confidence: 0.7633291

00:32:26.520 --> 00:32:27.654 demonstrating the identification

NOTE Confidence: 0.7633291

00:32:27.654 --> 00:32:29.544 of both obit cocaine abstinence

NOTE Confidence: 0.7633291

00:32:29.544 --> 00:32:31.389 networks was brain state specific.

NOTE Confidence: 0.7633291

00:32:31.390 --> 00:32:33.442 So having established that next we

NOTE Confidence: 0.7633291

00:32:33.442 --> 00:32:35.849 wanted to test whether once identified

NOTE Confidence: 0.7633291

00:32:35.849 --> 00:32:37.793 relationships between networks and

NOTE Confidence: 0.7633291

00:32:37.793 --> 00:32:40.214 specific substances might hold or

NOTE Confidence: 0.7633291

00:32:40.214 --> 00:32:41.846 generalize across brain states.

NOTE Confidence: 0.7633291

00:32:41.850 --> 00:32:43.310 To her on the left,

NOTE Confidence: 0.7633291

00:32:43.310 --> 00:32:44.470 with the Association between

NOTE Confidence: 0.7633291

00:32:44.470 --> 00:32:45.340 the in treatment,

NOTE Confidence: 0.7633291

00:32:45.340 --> 00:32:46.504 opiate abstinence and connectivity

NOTE Confidence: 0.7633291

00:32:46.504 --> 00:32:47.668 within the cocaine network,

NOTE Confidence: 0.7633291

00:32:47.670 --> 00:32:49.130 and as you can see,

NOTE Confidence: 0.7633291

00:32:49.130 --> 00:32:50.803 there's no relationship and on the right

NOTE Confidence: 0.7633291

00:32:50.803 --> 00:32:52.908 we have the relationship between cocaine,

NOTE Confidence: 0.7633291

00:32:52.910 --> 00:32:54.074 network connectivity and abstinence

NOTE Confidence: 0.7633291

00:32:54.074 --> 00:32:55.238 across different brain states.

NOTE Confidence: 0.7633291

00:32:55.240 --> 00:32:56.848 So for these analysis we're taking

NOTE Confidence: 0.7633291

00:32:56.848 --> 00:32:58.600 the cocaine cocaine network that were

NOTE Confidence: 0.7633291

00:32:58.600 --> 00:33:00.175 identified using reward task performance,

NOTE Confidence: 0.7633291

00:33:00.180 --> 00:33:02.259 using it as a mask to extract

NOTE Confidence: 0.7633291

00:33:02.259 --> 00:33:03.500 connectivity during cognitive task

NOTE Confidence: 0.7633291

00:33:03.500 --> 00:33:04.960 performance and also during resting

NOTE Confidence: 0.7633291

00:33:04.960 --> 00:33:07.273 state and what we find is that we

NOTE Confidence: 0.7633291

00:33:07.273 --> 00:33:08.905 again see a modest linear relationship

NOTE Confidence: 0.7633291

00:33:08.910 --> 00:33:10.298 between network connectivity and

NOTE Confidence: 0.7633291

00:33:10.298 --> 00:33:11.686 within treatment cocaine abstinence.

NOTE Confidence: 0.7633291

00:33:11.690 --> 00:33:14.189 So together these data indicate that all

NOTE Confidence: 0.7633291

00:33:14.189 --> 00:33:16.199 cocaine network does not generalize.

NOTE Confidence: 0.7633291

00:33:16.200 --> 00:33:17.325 Predict opiate abstinence,

NOTE Confidence: 0.7633291

00:33:17.325 --> 00:33:18.825 the relationship between cocaine,

NOTE Confidence: 0.7633291

00:33:18.830 --> 00:33:21.005 network connectivity and cocaine abstinence

NOTE Confidence: 0.7633291

00:33:21.005 --> 00:33:24.009 does in fact generalize across brain states.

NOTE Confidence: 0.7633291

00:33:24.010 --> 00:33:25.450 We see a very similar

NOTE Confidence: 0.7633291

00:33:25.450 --> 00:33:26.602 pattern with opiate network,

NOTE Confidence: 0.7633291

00:33:26.610 --> 00:33:28.451 so on the left we have the

NOTE Confidence: 0.7633291

00:33:28.451 --> 00:33:29.790 Association between within treatment,

NOTE Confidence: 0.7633291

00:33:29.790 --> 00:33:30.078 cocaine,

NOTE Confidence: 0.7633291

00:33:30.078 --> 00:33:30.942 abstinence and connectivity,

NOTE Confidence: 0.7633291

00:33:30.942 --> 00:33:32.382 even though be it network.

NOTE Confidence: 0.7633291

00:33:32.390 --> 00:33:33.775 This time during cognitive task

NOTE Confidence: 0.7633291

00:33:33.775 --> 00:33:35.484 performance and you can see that

NOTE Confidence: 0.7633291

00:33:35.484 --> 00:33:36.844 there is no significant Association

NOTE Confidence: 0.7633291

00:33:36.844 --> 00:33:38.920 where we take the network that we

NOTE Confidence: 0.7633291

00:33:38.920 --> 00:33:40.475 identified using cognitive task data.

NOTE Confidence: 0.7633291

00:33:40.480 --> 00:33:42.300 Use it as a mask to extract

NOTE Confidence: 0.7633291

00:33:42.300 --> 00:33:43.462 connectivity during reward task

NOTE Confidence: 0.7633291

00:33:43.462 --> 00:33:45.107 performance or during resting state.

NOTE Confidence: 0.7633291

00:33:45.110 --> 00:33:47.028 We again see a positive Association between

NOTE Confidence: 0.7633291

00:33:47.028 --> 00:33:48.580 network connectivity and within treatment.

NOTE Confidence: 0.7633291

00:33:48.580 --> 00:33:50.800 Abstinence would be absence.

NOTE Confidence: 0.7633291

00:33:50.800 --> 00:33:51.138 Again,

NOTE Confidence: 0.7633291

00:33:51.138 --> 00:33:53.166 indicating that while the opiate network

NOTE Confidence: 0.7633291

00:33:53.166 --> 00:33:55.040 does not generalize predict cocaine,

NOTE Confidence: 0.7633291

00:33:55.040 --> 00:33:56.920 use the relationship between

NOTE Confidence: 0.7633291

00:33:56.920 --> 00:33:58.800 opioid network connectivity and

NOTE Confidence: 0.7633291

00:33:58.800 --> 00:34:00.667 opiate abstinence does generalize

NOTE Confidence: 0.7633291

00:34:00.667 --> 00:34:01.966 across brain states.

NOTE Confidence: 0.7633291

00:34:01.970 --> 00:34:03.548 So I don't want to overly

NOTE Confidence: 0.7633291

00:34:03.548 --> 00:34:04.337 believer this point,

NOTE Confidence: 0.7633291

00:34:04.340 --> 00:34:05.642 but this is just to show

NOTE Confidence: 0.7633291

00:34:05.642 --> 00:34:06.510 you that we've run

NOTE Confidence: 0.7977975

00:34:06.563 --> 00:34:08.278 all possible combinations of this.

NOTE Confidence: 0.7977975

00:34:08.280 --> 00:34:10.051 So, for example, we've looked at whether

NOTE Confidence: 0.7977975

00:34:10.051 --> 00:34:11.392 opiate network connectivity during resting

NOTE Confidence: 0.7977975

00:34:11.392 --> 00:34:12.747 state relates to cocaine abstinence,

NOTE Confidence: 0.7977975

00:34:12.750 --> 00:34:14.328 and in all cases the specificity

NOTE Confidence: 0.7977975

00:34:14.328 --> 00:34:15.380 of these effects remains.

NOTE Confidence: 0.7977975

00:34:15.380 --> 00:34:16.344 So. In other words,

NOTE Confidence: 0.7977975

00:34:16.344 --> 00:34:17.549 we're seeing a double dissociation

NOTE Confidence: 0.7977975

00:34:17.549 --> 00:34:19.249 such that the cocaine network is

NOTE Confidence: 0.7977975

00:34:19.249 --> 00:34:20.377 consistently unrelated opiate use,

NOTE Confidence: 0.7977975

00:34:20.380 --> 00:34:22.780 and vice versa.

NOTE Confidence: 0.7977975

00:34:22.780 --> 00:34:24.310 As of the cocaine data,

NOTE Confidence: 0.7977975

00:34:24.310 --> 00:34:26.100 we've looked into the relationship

NOTE Confidence: 0.7977975

00:34:26.100 --> 00:34:27.890 between connectivity within the opiate

NOTE Confidence: 0.7977975

00:34:27.943 --> 00:34:29.587 network at post treatment and subsequent

NOTE Confidence: 0.7977975

00:34:29.587 --> 00:34:31.837 opiate use at 6 month follow up and

79

NOTE Confidence: 0.7977975

00:34:31.837 --> 00:34:33.481 we again find a similar relationship

NOTE Confidence: 0.7977975

00:34:33.490 --> 00:34:34.714 between post treatment activity

NOTE Confidence: 0.7977975

00:34:34.714 --> 00:34:35.938 and abstinence following treatment,

NOTE Confidence: 0.7977975

00:34:35.940 --> 00:34:37.572 potentially indicating some consistently

NOTE Confidence: 0.7977975

00:34:37.572 --> 00:34:38.796 this relationship overtime.

NOTE Confidence: 0.7977975

00:34:38.800 --> 00:34:40.145 And when we compare connectivity

NOTE Confidence: 0.7977975

00:34:40.145 --> 00:34:41.490 within the opiate network from

NOTE Confidence: 0.7977975

00:34:41.537 --> 00:34:42.517 free to post treatment,

NOTE Confidence: 0.7977975

00:34:42.520 --> 00:34:44.389 we also don't see any significant changes,

NOTE Confidence: 0.7977975

00:34:44.390 --> 00:34:45.884 further suggesting stability

NOTE Confidence: 0.7977975

00:34:45.884 --> 00:34:47.378 of these effects.

NOTE Confidence: 0.7977975

00:34:47.380 --> 00:34:49.060 Which is interesting to me,

NOTE Confidence: 0.7977975

00:34:49.060 --> 00:34:50.730 touches on an important point,

NOTE Confidence: 0.7977975

00:34:50.730 --> 00:34:52.400 which is that networks contributing

NOTE Confidence: 0.7977975

00:34:52.400 --> 00:34:54.428 to treatment response may in fact

NOTE Confidence: 0.7977975

00:34:54.428 --> 00:34:56.216 be distinct from those that change

NOTE Confidence: 0.7977975

00:34:56.216 --> 00:34:58.283 with treatment or that are directly

NOTE Confidence: 0.7977975

00:34:58.283 --> 00:34:59.775 implicated in disease pathology.

NOTE Confidence: 0.7977975

00:34:59.780 --> 00:35:00.815 So for example,

NOTE Confidence: 0.7977975

00:35:00.815 --> 00:35:02.540 brain regions for Tim's treatment

NOTE Confidence: 0.7977975

00:35:02.540 --> 00:35:04.742 responses and other disorders such as

NOTE Confidence: 0.7977975

00:35:04.742 --> 00:35:06.552 depression often have limited overlap

NOTE Confidence: 0.7977975

00:35:06.552 --> 00:35:08.808 with regions consistently found to

NOTE Confidence: 0.7977975

00:35:08.808 --> 00:35:10.644 differentiate patients from controls.

NOTE Confidence: 0.7977975

00:35:10.650 --> 00:35:12.025 Another possibility is the brain

NOTE Confidence: 0.7977975

00:35:12.025 --> 00:35:13.125 regions that predict treatment

NOTE Confidence: 0.7977975

00:35:13.125 --> 00:35:14.583 outcomes may just be different from

NOTE Confidence: 0.7977975

00:35:14.583 --> 00:35:15.728 those that change with treatment,

NOTE Confidence: 0.7977975

00:35:15.730 --> 00:35:17.508 and so at first I know that

NOTE Confidence: 0.7977975

00:35:17.508 --> 00:35:18.270 sounds counter intuitive,

NOTE Confidence: 0.7977975

00:35:18.270 --> 00:35:19.794 but when you think about it

NOTE Confidence: 0.7977975

00:35:19.794 --> 00:35:20.810 in a clinical context,

NOTE Confidence: 0.7977975

00:35:20.810 --> 00:35:22.075 we know that factors that

NOTE Confidence: 0.7977975

00:35:22.075 --> 00:35:22.834 predict treatment response.

NOTE Confidence: 0.7977975

00:35:22.840 --> 00:35:23.659 So for example,

NOTE Confidence: 0.7977975

00:35:23.659 --> 00:35:25.297 motivation to change can be distinct

NOTE Confidence: 0.7977975

00:35:25.297 --> 00:35:27.029 from those that change with treatment

NOTE Confidence: 0.7977975

00:35:27.029 --> 00:35:29.019 such as the acquisition of new skills.

NOTE Confidence: 0.7977975

00:35:29.020 --> 00:35:30.802 Thus the same may be true

NOTE Confidence: 0.7977975

00:35:30.802 --> 00:35:31.693 for neural networks.

NOTE Confidence: 0.7977975

00:35:31.700 --> 00:35:32.011 Further,

NOTE Confidence: 0.7977975

00:35:32.011 --> 00:35:33.566 it's possible that changes with

NOTE Confidence: 0.7977975

00:35:33.566 --> 00:35:35.116 an absence networks may take

NOTE Confidence: 0.7977975

00:35:35.116 --> 00:35:36.915 time to emerge and may only be

NOTE Confidence: 0.7977975

00:35:36.915 --> 00:35:38.259 detectable months after treatment,

NOTE Confidence: 0.7977975

00:35:38.260 --> 00:35:39.958 and that theory is consistent with

NOTE Confidence: 0.7977975

00:35:39.958 --> 00:35:41.090 data demonstrating the abstinence

NOTE Confidence: 0.7977975

00:35:41.139 --> 00:35:42.679 rates continue to improve following

NOTE Confidence: 0.7977975

00:35:42.679 --> 00:35:43.603 some behavioral treatments

NOTE Confidence: 0.7977975

00:35:43.603 --> 00:35:44.810 for cocaine use disorder.

NOTE Confidence: 0.7977975

00:35:44.810 --> 00:35:45.101 Thus,

NOTE Confidence: 0.7977975

00:35:45.101 --> 00:35:46.847 it stands to reason that the

NOTE Confidence: 0.7977975

00:35:46.847 --> 00:35:48.987 same may be true for the brain.

NOTE Confidence: 0.7977975

00:35:48.990 --> 00:35:52.838 Neural change may just take time to emerge.

NOTE Confidence: 0.7977975

00:35:52.840 --> 00:35:54.526 And so we began trying to

NOTE Confidence: 0.7977975

00:35:54.526 --> 00:35:55.650 explore that first possibility.

NOTE Confidence: 0.7977975

00:35:55.650 --> 00:35:57.519 The possibility that our networks are not

NOTE Confidence: 0.7977975

00:35:57.519 --> 00:35:59.298 only predictive of future substance use,

NOTE Confidence: 0.7977975

00:35:59.300 --> 00:36:01.148 but that they also just may be altered

NOTE Confidence: 0.7977975

00:36:01.148 --> 00:36:02.959 relative to healthy control individuals,

NOTE Confidence: 0.7977975

00:36:02.960 --> 00:36:05.125 and therefore perhaps linked to

NOTE Confidence: 0.7977975

00:36:05.125 --> 00:36:06.857 addiction pathophysiology more generally.

NOTE Confidence: 0.7977975

00:36:06.860 --> 00:36:08.695 Theoretical basis for looking into

NOTE Confidence: 0.7977975

00:36:08.695 --> 00:36:10.163 comparisons with healthy controls

NOTE Confidence: 0.7977975

00:36:10.163 --> 00:36:11.966 comes from really nicely by Hugh

NOTE Confidence: 0.7977975

00:36:11.966 --> 00:36:13.641 Garavan and colleagues from a few

NOTE Confidence: 0.7977975

00:36:13.641 --> 00:36:15.039 years ago in which they propose

NOTE Confidence: 0.7977975

00:36:15.039 --> 00:36:16.350 a couple of different scenarios

NOTE Confidence: 0.7977975

00:36:16.350 --> 00:36:17.875 for what prolonged absence might

NOTE Confidence: 0.7977975

00:36:17.875 --> 00:36:19.589 look like at the brain level.

NOTE Confidence: 0.7977975

00:36:19.590 --> 00:36:21.070 So here at the top,

NOTE Confidence: 0.7977975

00:36:21.070 --> 00:36:22.714 they propose that one scenario would

NOTE Confidence: 0.7977975

00:36:22.714 --> 00:36:24.497 be that recovery from addiction could

NOTE Confidence: 0.7977975

00:36:24.497 --> 00:36:26.399 involve some sort of restoration of

NOTE Confidence: 0.7977975

00:36:26.399 --> 00:36:28.169 premorbid brain function in the middle,

NOTE Confidence: 0.7977975

00:36:28.170 --> 00:36:29.695 they propose that an alternative

NOTE Confidence: 0.7977975

00:36:29.695 --> 00:36:31.220 hypothesis could be that prolonged

NOTE Confidence: 0.7977975

00:36:31.267 --> 00:36:32.959 recovery may in fact require some

NOTE Confidence: 0.7977975

00:36:32.959 --> 00:36:34.087 sort of hyper functionality.

NOTE Confidence: 0.7977975

00:36:34.090 --> 00:36:35.845 Brain regions involved in absence

NOTE Confidence: 0.7977975

00:36:35.845 --> 00:36:37.600 maintenance to above the level

NOTE Confidence: 0.7977975

00:36:37.658 --> 00:36:39.250 observed in healthy controls.

NOTE Confidence: 0.7977975

00:36:39.250 --> 00:36:39.708 Or finally,

NOTE Confidence: 0.7977975

00:36:39.708 --> 00:36:41.540 a third option at the bottom is the

NOTE Confidence: 0.79146427

00:36:41.591 --> 00:36:43.697 individuals in recovery from addiction may

NOTE Confidence: 0.79146427

00:36:43.697 --> 00:36:45.590 continue to exhibit decreased function,

NOTE Confidence: 0.79146427

00:36:45.590 --> 00:36:47.100 thereby confirming vulnerability for relapse.

NOTE Confidence: 0.79146427

00:36:47.100 --> 00:36:48.816 So just unpack that a bit

NOTE Confidence: 0.79146427

00:36:48.816 --> 00:36:50.420 more based on this model.

NOTE Confidence: 0.79146427

00:36:50.420 --> 00:36:52.052 If we were to compare absence

NOTE Confidence: 0.79146427

00:36:52.052 --> 00:36:53.459 networks to healthy controls and

NOTE Confidence: 0.79146427

00:36:53.459 --> 00:36:54.819 we found that absent individuals

NOTE Confidence: 0.79146427

00:36:54.819 --> 00:36:56.357 had similar levels of network

NOTE Confidence: 0.79146427

00:36:56.357 --> 00:36:57.969 strength relative healthy controls,

NOTE Confidence: 0.79146427

00:36:57.970 --> 00:37:00.119 we might conclude that what we're seeing

NOTE Confidence: 0.79146427

00:37:00.119 --> 00:37:02.578 is a return to premorbid functioning.

NOTE Confidence: 0.79146427

00:37:02.580 --> 00:37:02.850 Alternatively,

NOTE Confidence: 0.79146427

00:37:02.850 --> 00:37:04.740 if we were to find the individuals

NOTE Confidence: 0.79146427

00:37:04.740 --> 00:37:06.388 who achieve abstinence have increased

NOTE Confidence: 0.79146427

00:37:06.388 --> 00:37:08.158 network strength relative to controls,

NOTE Confidence: 0.79146427

00:37:08.160 --> 00:37:09.645 we might conclude that we're

NOTE Confidence: 0.79146427

00:37:09.645 --> 00:37:11.512 seeing is an elevation of brain

NOTE Confidence: 0.79146427

00:37:11.512 --> 00:37:13.117 function or a hyper recovery.

NOTE Confidence: 0.79146427

00:37:13.120 --> 00:37:13.670 And finally,

NOTE Confidence: 0.79146427

00:37:13.670 --> 00:37:15.595 if we were to find the abstinent

NOTE Confidence: 0.79146427

00:37:15.595 --> 00:37:16.980 individuals at decreased network

NOTE Confidence: 0.79146427

00:37:16.980 --> 00:37:18.388 strength relative to controls,

NOTE Confidence: 0.79146427

00:37:18.390 --> 00:37:20.748 we might interpret that as indicating

NOTE Confidence: 0.79146427

00:37:20.748 --> 00:37:22.320 continued vulnerability for relapse.

NOTE Confidence: 0.79146427

00:37:22.320 --> 00:37:23.790 So to test these theories,

NOTE Confidence: 0.79146427

00:37:23.790 --> 00:37:24.882 we've computed connectomes from

NOTE Confidence: 0.79146427

00:37:24.882 --> 00:37:26.520 identical task data for 38 age

NOTE Confidence: 0.79146427

00:37:26.567 --> 00:37:28.137 and sex matched non substance

NOTE Confidence: 0.79146427

00:37:28.137 --> 00:37:29.079 using control participants.

NOTE Confidence: 0.79146427

00:37:29.080 --> 00:37:30.844 And we've compared this to our

NOTE Confidence: 0.79146427

00:37:30.844 --> 00:37:32.020 Poly substance using sample.

NOTE Confidence: 0.79146427

00:37:32.020 --> 00:37:33.994 So here I'm just showing your binarization

NOTE Confidence: 0.79146427

00:37:33.994 --> 00:37:35.840 of the data I present earlier.

NOTE Confidence: 0.79146427

00:37:35.840 --> 00:37:37.466 So we have cocaine network sent

NOTE Confidence: 0.79146427

00:37:37.466 --> 00:37:38.550 for individuals to achieve

NOTE Confidence: 0.79146427

00:37:38.602 --> 00:37:39.958 some abstinence from cocaine.

NOTE Confidence: 0.79146427

00:37:39.960 --> 00:37:41.857 Drug treatment on the left and network

NOTE Confidence: 0.79146427

00:37:41.857 --> 00:37:43.667 show and for individuals who did

NOTE Confidence: 0.79146427

00:37:43.667 --> 00:37:45.545 not achieve absence on the right.

NOTE Confidence: 0.79146427

00:37:45.550 --> 00:37:47.222 And when we add in our controls what

NOTE Confidence: 0.79146427

00:37:47.222 --> 00:37:49.348 we find is it non substance using

NOTE Confidence: 0.79146427

00:37:49.348 --> 00:37:50.676 individuals or actually intermediary

NOTE Confidence: 0.79146427

00:37:50.676 --> 00:37:52.439 between responders and nonresponders.

NOTE Confidence: 0.79146427

00:37:52.440 --> 00:37:54.155 Such that our treatment responders

NOTE Confidence: 0.79146427

00:37:54.155 --> 00:37:55.527 actually have increased network

NOTE Confidence: 0.79146427

00:37:55.527 --> 00:37:57.132 strength relative to controls and

NOTE Confidence: 0.79146427

00:37:57.132 --> 00:37:58.642 our non responders have decreased

NOTE Confidence: 0.79146427

00:37:58.642 --> 00:38:00.367 network strength relative to controls.

NOTE Confidence: 0.79146427

00:38:00.370 --> 00:38:01.930 We again seem very similar pattern

NOTE Confidence: 0.79146427

00:38:01.930 --> 00:38:04.019 when we look at our opiate network,

NOTE Confidence: 0.79146427

00:38:04.020 --> 00:38:05.418 we find that our control group

NOTE Confidence: 0.79146427

00:38:05.418 --> 00:38:06.350 is again intermediary between

NOTE Confidence: 0.79146427

00:38:06.395 --> 00:38:07.715 responders and nonresponders with

NOTE Confidence: 0.79146427

00:38:07.715 --> 00:38:09.035 responders have increased network

NOTE Confidence: 0.79146427

00:38:09.035 --> 00:38:10.209 strength relative to controls.

NOTE Confidence: 0.79146427

00:38:10.210 --> 00:38:11.610 Although the difference between

NOTE Confidence: 0.79146427

00:38:11.610 --> 00:38:13.360 the controls and the non

NOTE Confidence: 0.79146427

00:38:13.360 --> 00:38:14.970 responders here isn't significant.

NOTE Confidence: 0.79146427

00:38:14.970 --> 00:38:17.290 So for both the cocaine and opiate networks,

NOTE Confidence: 0.79146427

00:38:17.290 --> 00:38:19.250 we're seeing this powder in the treatment

NOTE Confidence: 0.79146427

00:38:19.250 --> 00:38:20.480 responders have greater network,

NOTE Confidence: 0.79146427

00:38:20.480 --> 00:38:21.626 strengthen control participants.

NOTE Confidence: 0.79146427

00:38:21.626 --> 00:38:22.008 Again,

NOTE Confidence: 0.79146427

00:38:22.008 --> 00:38:24.300 consistent with this notion of an

NOTE Confidence: 0.79146427

00:38:24.360 --> 00:38:26.280 elevation of function relative to

NOTE Confidence: 0.79146427

00:38:26.280 --> 00:38:27.816 controls or hyper functionality.

NOTE Confidence: 0.79146427

00:38:27.820 --> 00:38:29.230 Most recently we've been applying

NOTE Confidence: 0.79146427

00:38:29.230 --> 00:38:31.348 this same approach to try to identify

NOTE Confidence: 0.79146427

00:38:31.348 --> 00:38:32.988 predictors of cannabis use outcomes,

NOTE Confidence: 0.79146427

00:38:32.990 --> 00:38:35.414 which I think is a really important issue,

89

00:38:35.420 --> 00:38:37.862 particularly within the context of the

00:38:37.862 --> 00:38:40.040 changing legislation in this country.

00:38:40.040 --> 00:38:40.904 Started my talk.

00:38:40.904 --> 00:38:42.632 I really focused on cocaine and

00:38:42.632 --> 00:38:44.471 opiates and I referenced increased

00:38:44.471 --> 00:38:46.346 overdose kristallen treatment as a

00:38:46.346 --> 00:38:48.055 significant motivator for identifying

00:38:48.055 --> 00:38:49.759 brain based predictors outcomes.

00:38:49.760 --> 00:38:51.566 And so while cannabis of course

00:38:51.566 --> 00:38:53.858 poses much less of an overdose risk,

00:38:53.860 --> 00:38:55.792 assuming it hasn't been mixed with

00:38:55.792 --> 00:38:57.320 another illicit substance cannabis use,

00:38:57.320 --> 00:38:58.580 none of nonetheless remains

00:38:58.580 --> 00:38:59.210 extremely prevalent,

00:38:59.210 --> 00:39:01.541 so approximately 15% of you as adults

00:39:01.541 --> 00:39:03.619 reported past year use back in 2017,

NOTE Confidence: 0.79146427

00:39:03.620 --> 00:39:05.258 and that number is likely higher

NOTE Confidence: 0.79146427

00:39:05.258 --> 00:39:07.143 now given all the ongoing changes

NOTE Confidence: 0.79146427

00:39:07.143 --> 00:39:08.978 to legislation in this country.

NOTE Confidence: 0.79146427

00:39:08.980 --> 00:39:10.870 So not only is cannabis use

NOTE Confidence: 0.79146427

00:39:10.870 --> 00:39:12.130 potentially becoming more prevalent,

NOTE Confidence: 0.79146427

00:39:12.130 --> 00:39:13.570 it's also becoming stronger,

NOTE Confidence: 0.79146427

00:39:13.570 --> 00:39:16.098 so the blue line here corresponds to

NOTE Confidence: 0.79146427

00:39:16.098 --> 00:39:17.946 the proportion of THC in cannabis

NOTE Confidence: 0.79146427

00:39:17.946 --> 00:39:20.088 samples over the past 20 years or so.

NOTE Confidence: 0.79146427

00:39:20.090 --> 00:39:21.505 And the green line corresponds

NOTE Confidence: 0.79146427

00:39:21.505 --> 00:39:22.920 to the portion of CVD,

NOTE Confidence: 0.77770895

00:39:22.920 --> 00:39:24.340 and as you can see,

NOTE Confidence: 0.77770895

00:39:24.340 --> 00:39:25.904 cannabis is becoming significantly

NOTE Confidence: 0.77770895

00:39:25.904 --> 00:39:28.250 stronger or composed of a significantly

NOTE Confidence: 0.77770895

00:39:28.308 --> 00:39:30.156 higher ratio of THC relative to CD.

NOTE Confidence: 0.77770895

00:39:30.160 --> 00:39:31.320 For these analysis we're

NOTE Confidence: 0.77770895

00:39:31.320 --> 00:39:32.190 combining aggregate pretreatment

NOTE Confidence: 0.77770895

00:39:32.190 --> 00:39:33.779 data from 2 separate arctis,

NOTE Confidence: 0.77770895

00:39:33.780 --> 00:39:35.290 one led by Kathy Carroll,

NOTE Confidence: 0.77770895

00:39:35.290 --> 00:39:36.800 another led by Brian Killick,

NOTE Confidence: 0.77770895

00:39:36.800 --> 00:39:39.216 and by combining data from these two samples,

NOTE Confidence: 0.77770895

00:39:39.220 --> 00:39:40.886 we end up with Nora merging data

NOTE Confidence: 0.77770895

00:39:40.886 --> 00:39:42.333 that needs our quality control

NOTE Confidence: 0.77770895

00:39:42.333 --> 00:39:44.028 criteria for 58 individuals of

NOTE Confidence: 0.77770895

00:39:44.028 --> 00:39:45.560 primary cannabis use disorder.

NOTE Confidence: 0.77718

00:39:48.290 --> 00:39:50.036 For these analysis we again have

NOTE Confidence: 0.77718

00:39:50.036 --> 00:39:51.552 connectivity matrices that we generate

NOTE Confidence: 0.77718

00:39:51.552 --> 00:39:53.328 from both cognitive control and reward

NOTE Confidence: 0.77718

00:39:53.328 --> 00:39:55.328 task data which we enter interpretive

NOTE Confidence: 0.77718

00:39:55.328 --> 00:39:57.093 model along with their dimensional

NOTE Confidence: 0.77718

00:39:57.093 --> 00:40:00.183 biological measure of abstinence. Surprise.

NOTE Confidence: 0.77718

00:40:00.183 --> 00:40:02.287 What we find is that we're able to

NOTE Confidence: 0.77718

00:40:02.287 --> 00:40:04.039 generate accurate predictive models of

NOTE Confidence: 0.77718

00:40:04.039 --> 00:40:06.187 cannabis abstinence using both data types,

NOTE Confidence: 0.77718

00:40:06.190 --> 00:40:07.465 suggesting that both cognitive and

NOTE Confidence: 0.77718

00:40:07.465 --> 00:40:09.145 reward related brain states are relevant

NOTE Confidence: 0.77718

00:40:09.145 --> 00:40:10.597 for understanding cannabis abstinence.

NOTE Confidence: 0.77718

00:40:10.600 --> 00:40:12.736 So here, on the left we have the

NOTE Confidence: 0.77718

00:40:12.736 --> 00:40:13.650 correspondence between predicted

NOTE Confidence: 0.77718

00:40:13.650 --> 00:40:15.300 and actual abstinence values for

NOTE Confidence: 0.77718

00:40:15.300 --> 00:40:17.059 the cognitive tasks shown in Gray,

NOTE Confidence: 0.77718

00:40:17.060 --> 00:40:20.060 and for the reward tasks shown in white.

NOTE Confidence: 0.77718

00:40:20.060 --> 00:40:22.316 And what we can see is that for

NOTE Confidence: 0.77718

00:40:22.316 --> 00:40:23.490 both types of data,

NOTE Confidence: 0.77718

00:40:23.490 --> 00:40:25.485 the spearings was hovering just under .4,

NOTE Confidence: 0.77718

00:40:25.490 --> 00:40:27.212 indicating that about 16% of the

93

NOTE Confidence: 0.77718

00:40:27.212 --> 00:40:28.734 variance and within treatment cannabis

NOTE Confidence: 0.77718

00:40:28.734 --> 00:40:30.654 abstinence can be accounted for by

NOTE Confidence: 0.77718

00:40:30.654 --> 00:40:32.080 connectivity within these networks.

NOTE Confidence: 0.77718

00:40:32.080 --> 00:40:34.054 As with the cocaine and opiate networks,

NOTE Confidence: 0.77718

00:40:34.060 --> 00:40:35.300 we've also tested the generalizability

NOTE Confidence: 0.77718

00:40:35.300 --> 00:40:36.946 of this effect to an independent

NOTE Confidence: 0.77718

00:40:36.946 --> 00:40:38.020 sample of individuals.

NOTE Confidence: 0.77718

00:40:38.020 --> 00:40:39.440 The primary cocaine use disorder,

NOTE Confidence: 0.77718

00:40:39.440 --> 00:40:41.987 the results of which are shown on your right,

NOTE Confidence: 0.77718

00:40:41.990 --> 00:40:43.400 and as you can see,

NOTE Confidence: 0.77718

00:40:43.400 --> 00:40:45.098 we found that the cannabis network

NOTE Confidence: 0.77718

00:40:45.098 --> 00:40:46.230 does not generalize further,

NOTE Confidence: 0.77718

00:40:46.230 --> 00:40:48.054 indicating substance specificity of

NOTE Confidence: 0.77718

00:40:48.054 --> 00:40:49.878 our different abstinence networks.

NOTE Confidence: 0.77718

00:40:49.880 --> 00:40:51.952 We're only just starting to dig down

NOTE Confidence: 0.77718

00:40:51.952 --> 00:40:53.850 into the anatomy of these network,

NOTE Confidence: 0.77718

00:40:53.850 --> 00:40:56.082 but so far the anatomy of the networks

NOTE Confidence: 0.77718

00:40:56.082 --> 00:40:57.685 identified during reward and cognitive

NOTE Confidence: 0.77718

00:40:57.685 --> 00:40:59.335 tasks do have some similarities,

NOTE Confidence: 0.77718

00:40:59.340 --> 00:41:01.338 so these cord plots are summarizing

NOTE Confidence: 0.77718

00:41:01.338 --> 00:41:03.059 positive network connections for the

NOTE Confidence: 0.77718

00:41:03.059 --> 00:41:04.411 network identified during cognitive

NOTE Confidence: 0.77718

00:41:04.411 --> 00:41:06.446 task performance on your left and

NOTE Confidence: 0.77718

00:41:06.446 --> 00:41:08.210 reward task performance on your right.

NOTE Confidence: 0.77718

00:41:08.210 --> 00:41:09.992 So these plants are really similar

NOTE Confidence: 0.77718

00:41:09.992 --> 00:41:12.087 to the other circle plots are

NOTE Confidence: 0.77718

00:41:12.087 --> 00:41:12.939 presented previously,

NOTE Confidence: 0.77718

00:41:12.940 --> 00:41:13.614 but here,

NOTE Confidence: 0.77718

00:41:13.614 --> 00:41:14.962 instead of summarizing macroscale

NOTE Confidence: 0.77718

00:41:14.962 --> 00:41:15.973 regional connectivity there,

NOTE Confidence: 0.77718

00:41:15.980 --> 00:41:17.021 summarizing connectivity between

NOTE Confidence: 0.77718

00:41:17.021 --> 00:41:19.450 Canonical networks and we can see that

NOTE Confidence: 0.77718

00:41:19.507 --> 00:41:21.265 for both tasks the cannabis network

NOTE Confidence: 0.77718

00:41:21.265 --> 00:41:23.219 is characterized by high degrees of

NOTE Confidence: 0.77718

00:41:23.219 --> 00:41:25.029 connections between frontal parietal and

NOTE Confidence: 0.77718

00:41:25.029 --> 00:41:27.107 motor sensory networks as indicated by

NOTE Confidence: 0.77718

00:41:27.107 --> 00:41:29.840 these sort of blue to pink arcs here.

NOTE Confidence: 0.77718

00:41:29.840 --> 00:41:31.868 But we also see some differences.

NOTE Confidence: 0.77718

00:41:31.870 --> 00:41:32.548 For example,

NOTE Confidence: 0.77718

00:41:32.548 --> 00:41:34.582 we see differences in patterns of

NOTE Confidence: 0.77718

00:41:34.582 --> 00:41:35.966 connectivity related to salience

NOTE Confidence: 0.77718

00:41:35.966 --> 00:41:36.938 and visual networks.

NOTE Confidence: 0.77718

00:41:36.940 --> 00:41:38.750 These differences are more striking.

NOTE Confidence: 0.77718

00:41:38.750 --> 00:41:40.170 When we compare the negative

NOTE Confidence: 0.77718

00:41:40.170 --> 00:41:41.590 connections so connections to which

NOTE Confidence: 0.77718

00:41:41.636 --> 00:41:43.188 decreased connectivity is positive,

NOTE Confidence: 0.77718

96

00:41:43.190 --> 00:41:44.111 productive cannabis abstinence.

NOTE Confidence: 0.77718

00:41:44.111 --> 00:41:45.953 So here we're seeing clear differences

NOTE Confidence: 0.77718

00:41:45.953 --> 00:41:47.593 in patterns of connectivity between

NOTE Confidence: 0.77718

00:41:47.593 --> 00:41:49.203 salience and motor sensory networks,

NOTE Confidence: 0.77718

00:41:49.210 --> 00:41:51.390 characterized by these sort of

NOTE Confidence: 0.77718

00:41:51.390 --> 00:41:53.134 phase to pink arcs.

NOTE Confidence: 0.77718

00:41:53.140 --> 00:41:55.135 And we can also see that joint

NOTE Confidence: 0.77718

00:41:55.135 --> 00:41:55.990 cognitive task performance.

NOTE Confidence: 0.77718

00:41:55.990 --> 00:41:57.736 The model is identifying a number

NOTE Confidence: 0.77718

00:41:57.736 --> 00:41:59.227 of connections between the default

NOTE Confidence: 0.77718

00:41:59.227 --> 00:42:00.859 mode and frontal network as shown

NOTE Confidence: 0.77718

00:42:00.859 --> 00:42:02.259 by the screens beige dark,

NOTE Confidence: 0.77718

00:42:02.260 --> 00:42:04.312 which we're not seeing in the

NOTE Confidence: 0.77718

00:42:04.312 --> 00:42:06.030 reward task model at all.

NOTE Confidence: 0.77718

00:42:06.030 --> 00:42:08.010 So as I said, these are brand new data.

NOTE Confidence: 0.77718

00:42:08.010 --> 00:42:09.240 We're still working on drilling down

NOTE Confidence: 0.77718

00:42:09.240 --> 00:42:10.650 into the anatomy of these networks.

NOTE Confidence: 0.77718

00:42:10.650 --> 00:42:13.116 A lot of the work with this stuff comes

NOTE Confidence: 0.77718

00:42:13.116 --> 00:42:15.337 after you've already done your model.

NOTE Confidence: 0.77718

00:42:15.340 --> 00:42:15.894 But really,

NOTE Confidence: 0.77718

00:42:15.894 --> 00:42:17.279 these findings are just again

NOTE Confidence: 0.77718

00:42:17.279 --> 00:42:18.675 highlighting this idea that brain

NOTE Confidence: 0.77718

00:42:18.675 --> 00:42:20.211 State may be a significant factor

NOTE Confidence: 0.77718

00:42:20.211 --> 00:42:21.548 for generation of optimal models.

NOTE Confidence: 0.77718

00:42:21.550 --> 00:42:23.590 So even if we're trying to predict the

NOTE Confidence: 0.77718

00:42:23.590 --> 00:42:25.328 same behavior in the same individuals,

NOTE Confidence: 0.82947934

00:42:25.330 --> 00:42:27.822 the connections that we can identify should

NOTE Confidence: 0.82947934

00:42:27.822 --> 00:42:30.281 be partially dependent on the brain state

NOTE Confidence: 0.82947934

00:42:30.281 --> 00:42:32.285 that participant was in during acquisition.

NOTE Confidence: 0.82947934

00:42:32.290 --> 00:42:35.494 That's all the day I wanted to show you

NOTE Confidence: 0.82947934

00:42:35.494 --> 00:42:37.310 today, which I think demonstrates with

NOTE Confidence: 0.82947934

00:42:37.310 --> 00:42:39.295 ability of our approach to generate

NOTE Confidence: 0.82947934

00:42:39.295 --> 00:42:41.187 specific externally valid predictions,

NOTE Confidence: 0.82947934

00:42:41.190 --> 00:42:43.675 but also to provide more biological insight.

NOTE Confidence: 0.82947934

00:42:43.680 --> 00:42:45.400 So hopefully we've demonstrated today

NOTE Confidence: 0.82947934

00:42:45.400 --> 00:42:47.544 is that networks identified using this

NOTE Confidence: 0.82947934

00:42:47.544 --> 00:42:49.732 approach are clinically relevant. That is,

NOTE Confidence: 0.82947934

00:42:49.732 --> 00:42:51.868 there able to predict treatment response.

NOTE Confidence: 0.82947934

00:42:51.870 --> 00:42:54.096 Is there also externally valid or able

NOTE Confidence: 0.82947934

00:42:54.096 --> 00:42:55.909 to generalize product specific behaviors

NOTE Confidence: 0.82947934

00:42:55.909 --> 00:42:57.914 and novel symbols and individuals?

NOTE Confidence: 0.82947934

00:42:57.920 --> 00:42:59.700 In addition, despite their complexity,

NOTE Confidence: 0.82947934

00:42:59.700 --> 00:43:01.475 these networks are in fact

NOTE Confidence: 0.82947934

00:43:01.475 --> 00:43:02.185 biologically meaningful,

NOTE Confidence: 0.82947934

00:43:02.190 --> 00:43:05.016 and that they're composed the specific

NOTE Confidence: 0.82947934

00:43:05.016 --> 00:43:06.900 connections observing specific behaviors.

NOTE Confidence: 0.82947934

00:43:06.900 --> 00:43:08.944 And finally, these networks are a bust.

NOTE Confidence: 0.82947934

00:43:08.950 --> 00:43:10.420 A common sources of variance,

NOTE Confidence: 0.82947934

00:43:10.420 --> 00:43:11.880 so they predict even after

NOTE Confidence: 0.82947934

00:43:11.880 --> 00:43:13.048 controlling for severity treatments.

NOTE Confidence: 0.82947934

00:43:13.050 --> 00:43:15.838 I mentor medication status.

NOTE Confidence: 0.82947934

00:43:15.840 --> 00:43:17.532 If you're interested in applying predictive

NOTE Confidence: 0.82947934

00:43:17.532 --> 00:43:18.900 modeling approaches your own data,

NOTE Confidence: 0.82947934

00:43:18.900 --> 00:43:20.568 I recommend checking out the August

NOTE Confidence: 0.82947934

00:43:20.568 --> 00:43:21.680 issue of biological psychiatry,

NOTE Confidence: 0.82947934

00:43:21.680 --> 00:43:22.234 CNN I,

NOTE Confidence: 0.82947934

00:43:22.234 --> 00:43:24.173 which is dedicated to data driven approaches.

NOTE Confidence: 0.82947934

00:43:24.180 --> 00:43:26.000 This includes our our review paper that

NOTE Confidence: 0.82947934

00:43:26.000 --> 00:43:27.391 covers recommendations for best practices

NOTE Confidence: 0.82947934

00:43:27.391 --> 00:43:28.811 in cross validated biomarker research

NOTE Confidence: 0.82947934

00:43:28.811 --> 00:43:30.569 within the specific context of addictions.

NOTE Confidence: 0.82947934

00:43:30.570 --> 00:43:30.787 However,

NOTE Confidence: 0.82947934

00:43:30.787 --> 00:43:32.523 I think that many of the issues that

NOTE Confidence: 0.82947934

00:43:32.523 --> 00:43:34.490 we cover really applied to clinical

NOTE Confidence: 0.82947934

00:43:34.490 --> 00:43:35.854 predictive modeling more generally,

NOTE Confidence: 0.82947934

00:43:35.860 --> 00:43:37.743 which is probably why I figure summarizing

NOTE Confidence: 0.82947934

00:43:37.743 --> 00:43:40.027 the work for this approach made the cover.

NOTE Confidence: 0.82947934

00:43:40.030 --> 00:43:40.584 So again,

NOTE Confidence: 0.82947934

00:43:40.584 --> 00:43:42.246 if you're interested in these approaches,

NOTE Confidence: 0.82947934

00:43:42.250 --> 00:43:45.596 I suggest that you check that out.

NOTE Confidence: 0.82947934

00:43:45.600 --> 00:43:46.052 Just briefly,

NOTE Confidence: 0.82947934

00:43:46.052 --> 00:43:47.634 I'm not going to go into all

NOTE Confidence: 0.82947934

00:43:47.634 --> 00:43:48.949 the recommendations here,

NOTE Confidence: 0.82947934

00:43:48.950 --> 00:43:50.742 but I do want to just highlight

NOTE Confidence: 0.82947934

00:43:50.742 --> 00:43:52.020 a few key points,

NOTE Confidence: 0.82947934

00:43:52.020 --> 00:43:53.808 one of which is careful consideration

NOTE Confidence: 0.82947934

00:43:53.808 --> 00:43:55.670 of the window of assessment.

NOTE Confidence: 0.82947934

00:43:55.670 --> 00:43:57.441 So while scanning prior to a clinical

NOTE Confidence: 0.82947934

00:43:57.441 --> 00:43:59.150 intervention is often considered desirable,

NOTE Confidence: 0.82947934

00:43:59.150 --> 00:44:00.928 it's important term it's getting during this

NOTE Confidence: 0.82947934

00:44:00.928 --> 00:44:02.630 time can introduce unnecessary confounds,

NOTE Confidence: 0.82947934

00:44:02.630 --> 00:44:04.080 such as effects of acute

NOTE Confidence: 0.82947934

00:44:04.080 --> 00:44:04.950 intoxication or withdrawal.

NOTE Confidence: 0.82947934

00:44:04.950 --> 00:44:06.980 In the case of addiction or mood,

NOTE Confidence: 0.82947934

00:44:06.980 --> 00:44:08.123 state or psychosis.

NOTE Confidence: 0.82947934

00:44:08.123 --> 00:44:10.409 In the case of other disorders.

NOTE Confidence: 0.82947934

00:44:10.410 --> 00:44:11.010 In addition,

NOTE Confidence: 0.82947934

00:44:11.010 --> 00:44:12.510 scanning prior to clinical intervention

NOTE Confidence: 0.82947934

00:44:12.510 --> 00:44:14.750 may not be feasible in this treatment.

NOTE Confidence: 0.82947934

00:44:14.750 --> 00:44:15.797 Initiation is delayed,

NOTE Confidence: 0.82947934

00:44:15.797 --> 00:44:17.542 which may place unnecessary burden

NOTE Confidence: 0.82947934

00:44:17.542 --> 00:44:18.740 on the patient.

NOTE Confidence: 0.82947934

00:44:18.740 --> 00:44:20.693 I also want to emphasize the importance

NOTE Confidence: 0.82947934

00:44:20.693 --> 00:44:21.971 of employing multiple performance

NOTE Confidence: 0.82947934

00:44:21.971 --> 00:44:23.916 metrics for quantifying model accuracy,

NOTE Confidence: 0.82947934

00:44:23.920 --> 00:44:26.520 which I didn't go into too much today.

NOTE Confidence: 0.82947934

00:44:26.520 --> 00:44:27.188 But again,

NOTE Confidence: 0.82947934

00:44:27.188 --> 00:44:28.858 it's interview paper and also

NOTE Confidence: 0.82947934

00:44:28.858 --> 00:44:30.326 important of setting realistic

NOTE Confidence: 0.82947934

00:44:30.326 --> 00:44:31.946 expectations for effect size

NOTE Confidence: 0.82947934

00:44:31.946 --> 00:44:33.971 estimates when you're talking about

NOTE Confidence: 0.82947934

00:44:34.035 --> 00:44:36.010 results from cross validated models.

NOTE Confidence: 0.82947934

00:44:36.010 --> 00:44:36.315 Finally,

NOTE Confidence: 0.82947934

00:44:36.315 --> 00:44:38.145 I want to emphasize the importance

NOTE Confidence: 0.82947934

00:44:38.145 --> 00:44:40.126 of conducting post hoc testing to

NOTE Confidence: 0.82947934

00:44:40.126 --> 00:44:41.474 provide elucidation of mechanism,

NOTE Confidence: 0.82947934

00:44:41.480 --> 00:44:43.418 as without this findings or models,

NOTE Confidence: 0.82947934

00:44:43.420 --> 00:44:44.488 even with high accuracy,

NOTE Confidence: 0.82947934

00:44:44.488 --> 00:44:46.548 can do very little to advance our

NOTE Confidence: 0.82947934

00:44:46.548 --> 00:44:48.568 understanding of the underlying neurobiology,

NOTE Confidence: 0.82947934

00:44:48.570 --> 00:44:50.995 which is essential for informing

NOTE Confidence: 0.82947934

00:44:50.995 --> 00:44:52.450 novel treatment development.

NOTE Confidence: 0.82947934

00:44:52.450 --> 00:44:53.434 So in this context,

NOTE Confidence: 0.82947934

00:44:53.434 --> 00:44:54.910 it's important to consider model findings

NOTE Confidence: 0.82947934

00:44:54.954 --> 00:44:56.609 across multiple levels of interpretation,

NOTE Confidence: 0.82947934

00:44:56.610 --> 00:44:58.654 with the most basic level being the

NOTE Confidence: 0.82947934

00:44:58.654 --> 00:45:00.197 connections themselves and the most

NOTE Confidence: 0.82947934

00:45:00.197 --> 00:45:01.727 abstract level being the overarching

NOTE Confidence: 0.82947934

00:45:01.727 --> 00:45:03.364 or biological model which can be

NOTE Confidence: 0.82947934

00:45:03.364 --> 00:45:04.690 used to guide treatment and act

NOTE Confidence: 0.82947934

00:45:04.690 --> 00:45:07.630 as a basis for further testing.

NOTE Confidence: 0.82947934

00:45:07.630 --> 00:45:09.274 Within the context of a region

NOTE Confidence: 0.82947934

00:45:09.274 --> 00:45:10.370 of interest of region

NOTE Confidence: 0.83260494

00:45:10.432 --> 00:45:11.860 of interest based approach,

NOTE Confidence: 0.83260494

00:45:11.860 --> 00:45:13.370 one simple method of determining

NOTE Confidence: 0.83260494

00:45:13.370 --> 00:45:14.578 significance of different features.

NOTE Confidence: 0.83260494

00:45:14.580 --> 00:45:16.065 So significance of individual regions

NOTE Confidence: 0.83260494

00:45:16.065 --> 00:45:18.500 of interest or networks is to just rerun

NOTE Confidence: 0.83260494

00:45:18.500 --> 00:45:20.005 the model excluding specific features.

NOTE Confidence: 0.83260494

00:45:20.010 --> 00:45:21.804 This is that sort of virtual

NOTE Confidence: 0.83260494

00:45:21.804 --> 00:45:23.464 lesion approach that I talked

NOTE Confidence: 0.83260494

00:45:23.464 --> 00:45:25.469 about earlier with Soviet network.

NOTE Confidence: 0.83260494

00:45:25.470 --> 00:45:27.838 And we do this in order to determine

NOTE Confidence: 0.83260494

00:45:27.838 --> 00:45:29.358 which features were necessary

NOTE Confidence: 0.83260494

00:45:29.358 --> 00:45:31.098 for optimal model performance.

NOTE Confidence: 0.83260494

00:45:31.100 --> 00:45:33.564 So for example, to ask the question,

NOTE Confidence: 0.83260494

00:45:33.570 --> 00:45:35.770 does a middle volume contribute

NOTE Confidence: 0.83260494

00:45:35.770 --> 00:45:37.530 to overall model performance?

NOTE Confidence: 0.83260494

00:45:37.530 --> 00:45:39.336 Similarly, we can rerun the model

NOTE Confidence: 0.83260494

00:45:39.336 --> 00:45:40.540 only including selected features,

105

NOTE Confidence: 0.83260494

00:45:40.540 --> 00:45:42.458 and that will enable determination of the

NOTE Confidence: 0.83260494

00:45:42.458 --> 00:45:44.149 relative weight of specific features.

NOTE Confidence: 0.83260494

00:45:44.150 --> 00:45:45.956 So that would answer the question

NOTE Confidence: 0.83260494

00:45:45.956 --> 00:45:47.505 what is the predictability of

NOTE Confidence: 0.83260494

00:45:47.505 --> 00:45:48.669 amygdala volume by itself,

NOTE Confidence: 0.83260494

00:45:48.670 --> 00:45:50.770 and so these are really simple steps,

NOTE Confidence: 0.83260494

00:45:50.770 --> 00:45:52.576 but people often skip over them,

NOTE Confidence: 0.83260494

00:45:52.580 --> 00:45:55.812 so this is just a reminder that elucidation

NOTE Confidence: 0.83260494

00:45:55.812 --> 00:45:58.456 should also be a goal of prediction.

NOTE Confidence: 0.83260494

00:45:58.460 --> 00:45:59.620 We have several ongoing

NOTE Confidence: 0.83260494

00:45:59.620 --> 00:46:01.070 projects to extend this work,

NOTE Confidence: 0.83260494

00:46:01.070 --> 00:46:02.405 including our one focusing on

NOTE Confidence: 0.83260494

00:46:02.405 --> 00:46:03.740 neural markers of opiate use

NOTE Confidence: 0.83260494

00:46:03.792 --> 00:46:05.128 during the postpartum period,

NOTE Confidence: 0.83260494

00:46:05.130 --> 00:46:06.330 among women receiving methadone,

NOTE Confidence: 0.83260494

00:46:06.330 --> 00:46:08.432 we also have a pilot project which

NOTE Confidence: 0.83260494

00:46:08.432 --> 00:46:10.189 we're using real time fMRI to try

NOTE Confidence: 0.83260494

00:46:10.189 --> 00:46:11.366 to directly target connectivity

NOTE Confidence: 0.83260494

00:46:11.366 --> 00:46:13.244 within that will be at network,

NOTE Confidence: 0.83260494

00:46:13.250 --> 00:46:14.840 so we're interested in whether these

NOTE Confidence: 0.83260494

00:46:14.840 --> 00:46:16.440 connections are in fact modifiable,

NOTE Confidence: 0.83260494

00:46:16.440 --> 00:46:18.180 and we also have some medication.

NOTE Confidence: 0.83260494

00:46:18.180 --> 00:46:21.450 Studies were looking into that too.

NOTE Confidence: 0.83260494

00:46:21.450 --> 00:46:23.109 A sort of separate side of my

NOTE Confidence: 0.83260494

00:46:23.109 --> 00:46:24.989 lab work is also developmental,

NOTE Confidence: 0.83260494

00:46:24.990 --> 00:46:26.334 so we've also been using a

NOTE Confidence: 0.83260494

00:46:26.334 --> 00:46:27.740 connectome based approach to identify

NOTE Confidence: 0.83260494

00:46:27.740 --> 00:46:29.120 developmental mechanisms initiation,

NOTE Confidence: 0.83260494

00:46:29.120 --> 00:46:30.595 which is an ongoing collaboration

NOTE Confidence: 0.83260494

00:46:30.595 --> 00:46:31.775 with Dustin and Godfrey.

NOTE Confidence: 0.83260494

00:46:31.780 --> 00:46:33.250 Pearls in here at Yale,

NOTE Confidence: 0.83260494

00:46:33.250 --> 00:46:37.106 but also with Mary Heitzig in Hugh Garavan.

NOTE Confidence: 0.83260494

00:46:37.110 --> 00:46:38.630 There's also other studies that

NOTE Confidence: 0.83260494

00:46:38.630 --> 00:46:40.640 we wanted were not funded for yet,

NOTE Confidence: 0.83260494

00:46:40.640 --> 00:46:42.397 so we just received a very promising

NOTE Confidence: 0.83260494

00:46:42.397 --> 00:46:44.206 initial score from another or one

NOTE Confidence: 0.83260494

00:46:44.206 --> 00:46:45.546 focusing on developmental mechanisms

NOTE Confidence: 0.83260494

00:46:45.546 --> 00:46:46.952 of initiation, but this time,

NOTE Confidence: 0.83260494

00:46:46.952 --> 00:46:48.660 using the ABCD data set and including

NOTE Confidence: 0.83260494

00:46:48.706 --> 00:46:50.626 considerations ivkova 19 related factors,

NOTE Confidence: 0.83260494

00:46:50.630 --> 00:46:52.105 and that's a collaboration with

NOTE Confidence: 0.83260494

00:46:52.105 --> 00:46:52.990 Danilo Stockem ago.

NOTE Confidence: 0.83260494

00:46:52.990 --> 00:46:53.307 Finally,

NOTE Confidence: 0.83260494

00:46:53.307 --> 00:46:54.892 we're very interested in extending

NOTE Confidence: 0.83260494

00:46:54.892 --> 00:46:56.802 our work across different scanners in

NOTE Confidence: 0.83260494

00:46:56.802 --> 00:46:58.292 clinical settings and also interested

NOTE Confidence: 0.83260494

00:46:58.292 --> 00:46:59.752 in looking into potential sex

NOTE Confidence: 0.83260494

00:46:59.752 --> 00:47:01.808 differences in it will be at Nora markers,

NOTE Confidence: 0.83260494

00:47:01.810 --> 00:47:03.532 and so we've recently applied for

NOTE Confidence: 0.83260494

00:47:03.532 --> 00:47:05.040 funding to pursue that works,

NOTE Confidence: 0.83260494

00:47:05.040 --> 00:47:08.136 so fingers crossed on that one.

NOTE Confidence: 0.83260494

00:47:08.140 --> 00:47:09.796 I'll end there, but I want to just

NOTE Confidence: 0.83260494

00:47:09.796 --> 00:47:11.210 thank all of my collaborators,

NOTE Confidence: 0.83260494

00:47:11.210 --> 00:47:12.862 and because of the coauthors on the

NOTE Confidence: 0.83260494

00:47:12.862 --> 00:47:14.510 data presented today, and also my Cal,

NOTE Confidence: 0.83260494

00:47:14.510 --> 00:47:15.685 my mentor is Kathy Carolyn,

NOTE Confidence: 0.83260494

00:47:15.690 --> 00:47:16.634 Mark, but Enzo, also,

NOTE Confidence: 0.83260494

00:47:16.634 --> 00:47:17.106 of course,

NOTE Confidence: 0.83260494

00:47:17.110 --> 00:47:18.454 when I think everyone in my lab

NOTE Confidence: 0.83260494

00:47:18.454 --> 00:47:20.192 and all of the funders who make

NOTE Confidence: 0.83260494

00:47:20.192 --> 00:47:21.587 this research possible and thanks,

NOTE Confidence: 0.83260494

00:47:21.590 --> 00:47:22.770 all of you for listening.

NOTE Confidence: 0.87370175

00:47:26.150 --> 00:47:27.923 Thank you so much Sarah.

NOTE Confidence: 0.87370175

00:47:27.923 --> 00:47:30.310 We can we have a little time

NOTE Confidence: 0.87370175

00:47:30.389 --> 00:47:32.529 if there are any questions.

NOTE Confidence: 0.87370175

00:47:32.530 --> 00:47:35.154 It was a really great talk and

NOTE Confidence: 0.87370175

00:47:35.154 --> 00:47:36.276 very sophisticated systematic

NOTE Confidence: 0.87370175

00:47:36.276 --> 00:47:38.150 work that you've been doing.

NOTE Confidence: 0.9165679

00:47:40.190 --> 00:47:40.800 Thank you.

NOTE Confidence: 0.86263376

00:47:49.950 --> 00:47:51.690 Chris, go ahead.

NOTE Confidence: 0.86263376

00:47:51.690 --> 00:47:53.420 Yes Sarah great great talk.

NOTE Confidence: 0.86263376

00:47:53.420 --> 00:47:55.486 Thank you in your quick summary

NOTE Confidence: 0.86263376

00:47:55.486 --> 00:47:56.868 of the predictive modeling.

NOTE Confidence: 0.86263376

00:47:56.868 --> 00:47:58.246 You emphasize that you're

NOTE Confidence: 0.86263376

00:47:58.246 --> 00:48:01.130 looking at linear relationships.

NOTE Confidence: 0.86263376

00:48:01.130 --> 00:48:02.081 And the computational

NOTE Confidence: 0.86263376

00:48:02.081 --> 00:48:03.666 accessory for that is clear,

NOTE Confidence: 0.86263376

00:48:03.670 --> 00:48:05.580 but it also may be limiting

NOTE Confidence: 0.86263376

00:48:05.580 --> 00:48:07.174 because you may have threshold

NOTE Confidence: 0.86263376

00:48:07.174 --> 00:48:08.758 or other non linear relationships

NOTE Confidence: 0.86370313

00:48:08.760 --> 00:48:10.032 that are equally important.

NOTE Confidence: 0.86370313

00:48:10.032 --> 00:48:12.574 Or more important is there is it possible

NOTE Confidence: 0.86370313

00:48:12.574 --> 00:48:13.846 to incorporate nonlinear relationships?

NOTE Confidence: 0.86370313

00:48:13.846 --> 00:48:16.076 Or does the parameter space just blow

NOTE Confidence: 0.86370313

00:48:16.076 --> 00:48:18.298 up so quickly that that can't be

NOTE Confidence: 0.86370313

00:48:18.300 --> 00:48:19.890 done? That's a great question.

NOTE Confidence: 0.86370313

00:48:19.890 --> 00:48:21.510 I believe that Dustin Shine

NOTE Confidence: 0.86370313

00:48:21.510 --> 00:48:23.709 Host is working on some of that.

NOTE Confidence: 0.86370313

00:48:23.710 --> 00:48:26.198 I mean, you could use a kernel or

NOTE Confidence: 0.86370313

00:48:26.198 --> 00:48:27.563 something like that. Absolutely.

NOTE Confidence: 0.86370313

00:48:27.563 --> 00:48:30.387 I mean there's no reason why you couldn't.

NOTE Confidence: 0.86370313

00:48:30.390 --> 00:48:32.441 I mean, again, I find the interpretation

NOTE Confidence: 0.86370313

00:48:32.441 --> 00:48:34.832 even just with the linear so hard

NOTE Confidence: 0.86370313

00:48:34.832 --> 00:48:36.647 if we're talking about mechanistic

NOTE Confidence: 0.86370313

00:48:36.647 --> 00:48:37.672 understanding, but absolutely,

NOTE Confidence: 0.86370313

00:48:37.672 --> 00:48:39.989 especially if you have data that aren't.

NOTE Confidence: 0.86370313

00:48:39.990 --> 00:48:41.976 Yeah, yes, that would be great.

NOTE Confidence: 0.86370313

00:48:41.980 --> 00:48:43.630 We should do that next.

NOTE Confidence: 0.8620014

00:48:44.920 --> 00:48:46.560 Well, it enter related question

NOTE Confidence: 0.8620014

00:48:46.560 --> 00:48:47.872 that motivated that question.

NOTE Confidence: 0.8620014

00:48:47.872 --> 00:48:49.840 Is your predictions the amount of

NOTE Confidence: 0.8620014

00:48:49.840 --> 00:48:51.478 variance that you're explaining? You're

NOTE Confidence: 0.8620014

00:48:51.480 --> 00:48:53.776 getting up to 16% or something that's

NOTE Confidence: 0.8620014

00:48:53.776 --> 00:48:55.414 clearly impressive and validates that

NOTE Confidence: 0.8620014

00:48:55.414 --> 00:48:57.060 you're looking at something real.

NOTE Confidence: 0.8620014

00:48:57.060 --> 00:48:59.026 But it's a long way from

NOTE Confidence: 0.8620014

00:48:59.026 --> 00:49:00.010 clinical utility, absolutely.

NOTE Confidence: 0.8620014

00:49:00.010 --> 00:49:02.298 And so I was wondering whether incorporating

NOTE Confidence: 0.8620014

00:49:02.300 --> 00:49:03.947 nonlinear relationships would be a

NOTE Confidence: 0.8620014

00:49:03.947 --> 00:49:06.242 way to bump that up more quickly,

NOTE Confidence: 0.8620014

00:49:06.242 --> 00:49:08.206 but I wonder what other thoughts

NOTE Confidence: 0.8620014

00:49:08.206 --> 00:49:10.507 you have about what the future steps

NOTE Confidence: 0.8620014

00:49:10.507 --> 00:49:12.796 in this line of research might be.

NOTE Confidence: 0.8620014

00:49:12.800 --> 00:49:16.370 That will get us to. 85%.

NOTE Confidence: 0.85067517

00:49:17.440 --> 00:49:18.740 Whatever the threshold may

NOTE Confidence: 0.85067517

00:49:18.740 --> 00:49:21.647 may need to be for this to become clinical,

NOTE Confidence: 0.85067517

00:49:21.650 --> 00:49:22.303 clinically actionable?

NOTE Confidence: 0.85067517

00:49:22.303 --> 00:49:24.242 Yeah, absolutely, that's a great question.

NOTE Confidence: 0.85067517

00:49:24.242 --> 00:49:26.046 I mean, I think. You know,

NOTE Confidence: 0.85067517

00:49:26.046 --> 00:49:27.780 so we've done some stuff where

NOTE Confidence: 0.85067517

00:49:27.843 --> 00:49:30.279 we've been for the cocaine data in

NOTE Confidence: 0.85067517

00:49:30.279 --> 00:49:31.860 the external replication example,

NOTE Confidence: 0.85067517

00:49:31.860 --> 00:49:33.869 where we combine in other clinical features.

NOTE Confidence: 0.85067517

00:49:33.870 --> 00:49:36.152 So if we just add in, you know.

NOTE Confidence: 0.85067517

00:49:36.152 --> 00:49:37.868 So we take the network strength,

NOTE Confidence: 0.85067517

00:49:37.870 --> 00:49:39.502 but then we add in baseline

NOTE Confidence: 0.85067517

00:49:39.502 --> 00:49:41.299 severity or past month cocaine use,

NOTE Confidence: 0.85067517

00:49:41.300 --> 00:49:42.956 which are things that by themselves

NOTE Confidence: 0.85067517

00:49:42.956 --> 00:49:44.450 aren't sufficient to predict outcome.

NOTE Confidence: 0.85067517

00:49:44.450 --> 00:49:46.738 We do find that the model accuracy improves,

NOTE Confidence: 0.85067517

00:49:46.740 --> 00:49:49.025 so when we do that, if we're doing,

NOTE Confidence: 0.85067517

00:49:49.025 --> 00:49:51.310 just say yes, no any absence from treatment,

NOTE Confidence: 0.85067517

00:49:51.310 --> 00:49:53.283 we can get up to 71% accuracy.

NOTE Confidence: 0.85067517

00:49:53.283 --> 00:49:55.307 But again, this all needs to be validated

NOTE Confidence: 0.85067517

00:49:55.307 --> 00:49:56.919 in different clinical settings.

NOTE Confidence: 0.85067517

00:49:56.920 --> 00:49:59.160 And and all that stuff like this is,

NOTE Confidence: 0.85067517

00:49:59.160 --> 00:50:00.400 you know, and if.

NOTE Confidence: 0.85067517

00:50:00.400 --> 00:50:01.934 Magnets, so the multisite application

NOTE Confidence: 0.85067517

00:50:01.934 --> 00:50:03.770 that I mentioned at the end,

NOTE Confidence: 0.85067517

00:50:03.770 --> 00:50:05.863 I'm really excited about and I think

NOTE Confidence: 0.85067517

00:50:05.863 --> 00:50:08.659 it's sort of the next step to try to

NOTE Confidence: 0.85067517

00:50:08.659 --> 00:50:10.499 understand if these things are real,

NOTE Confidence: 0.85067517

00:50:10.500 --> 00:50:14.546 so we'll see what their viewers think.

NOTE Confidence: 0.85067517

00:50:14.550 --> 00:50:16.135 Thanks.

NOTE Confidence: 0.85067517

00:50:16.135 --> 00:50:17.720 Thinking.

NOTE Confidence: 0.85067517

00:50:17.720 --> 00:50:19.323 He said that was beautiful

NOTE Confidence: 0.85067517

00:50:19.323 --> 00:50:20.610 and really convincing data,

NOTE Confidence: 0.85067517

00:50:20.610 --> 00:50:22.210 especially the way you generalized

NOTE Confidence: 0.85067517

00:50:22.210 --> 00:50:23.820 across those discrete patient samples.

NOTE Confidence: 0.85067517

00:50:23.820 --> 00:50:26.710 And So what I was curious about is if

NOTE Confidence: 0.85067517

00:50:26.710 --> 00:50:29.053 you could have any task you wanted in

NOTE Confidence: 0.85067517

00:50:29.053 --> 00:50:31.075 the scanner because you're using these

NOTE Confidence: 0.85067517

00:50:31.075 --> 00:50:32.810 cognitive control and reward tasks

NOTE Confidence: 0.85067517

00:50:32.810 --> 00:50:34.922 that are sort of proxies for constructs,

NOTE Confidence: 0.85067517

00:50:34.922 --> 00:50:37.066 do you think are relevant and you've

NOTE Confidence: 0.85067517

00:50:37.066 --> 00:50:39.226 shown variants with different task states?

NOTE Confidence: 0.85067517

00:50:39.230 --> 00:50:41.150 What do you think the ideal

NOTE Confidence: 0.85067517

00:50:41.150 --> 00:50:43.838 task would be for prediction?

NOTE Confidence: 0.85067517

00:50:43.840 --> 00:50:45.004 So it's possible the

NOTE Confidence: 0.85067517

00:50:45.004 --> 00:50:46.459 answer might be drug use,

NOTE Confidence: 0.85067517

00:50:46.460 --> 00:50:48.206 and I'm not a huge huge

NOTE Confidence: 0.85067517

00:50:48.206 --> 00:50:49.079 cue reactivity person,

NOTE Confidence: 0.85067517

00:50:49.080 --> 00:50:51.699 but I think that that could be the answer.

NOTE Confidence: 0.85067517

00:50:51.700 --> 00:50:53.440 At least an opiate use disorder,

NOTE Confidence: 0.85067517

00:50:53.440 --> 00:50:55.484 but the clinics that I work with

NOTE Confidence: 0.85067517

00:50:55.484 --> 00:50:58.098 tend not to want us to show drug use,

NOTE Confidence: 0.85067517

00:50:58.100 --> 00:51:00.137 and so I don't know that that's

NOTE Confidence: 0.85067517

00:51:00.137 --> 00:51:01.010 necessarily the best.

NOTE Confidence: 0.85067517

00:51:01.010 --> 00:51:01.576 I mean,

NOTE Confidence: 0.85067517

00:51:01.576 --> 00:51:04.210 one thing that I think would be really cool,

NOTE Confidence: 0.85067517

00:51:04.210 --> 00:51:06.247 and it Brian Killick and Kathy Carolyn.

NOTE Confidence: 0.85067517

00:51:06.250 --> 00:51:08.140 I've been talking about is so the

NOTE Confidence: 0.85067517

00:51:08.140 --> 00:51:09.907 type of behavioral therapy that we

NOTE Confidence: 0.85067517

00:51:09.907 --> 00:51:11.713 were receiving in the Poly substance

NOTE Confidence: 0.85067517

00:51:11.713 --> 00:51:13.478 using sample is this computerized

NOTE Confidence: 0.85067517

00:51:13.478 --> 00:51:15.238 CBT that Kathy Carroll developed.

NOTE Confidence: 0.85067517

00:51:15.240 --> 00:51:17.072 And we think it would be really cool

NOTE Confidence: 0.85067517

00:51:17.072 --> 00:51:18.907 to scan patients while they're viewing

NOTE Confidence: 0.85067517

00:51:18.907 --> 00:51:21.207 the computerized CBT and so then see

NOTE Confidence: 0.85067517

00:51:21.207 --> 00:51:23.383 if that is a better predictor of treatment.

NOTE Confidence: 0.85067517

00:51:23.390 --> 00:51:24.790 Response to CDT itself, right?

NOTE Confidence: 0.85067517

00:51:24.790 --> 00:51:27.513 So if you get them in the

NOTE Confidence: 0.85067517

00:51:27.513 --> 00:51:29.560 brain state of therapy?

NOTE Confidence: 0.85067517

00:51:29.560 --> 00:51:30.312 So yeah,

NOTE Confidence: 0.85067517

00:51:30.312 --> 00:51:32.568 lots of different directions to go,

NOTE Confidence: 0.85067517

00:51:32.570 --> 00:51:32.940 thanks.

NOTE Confidence: 0.8507915

00:51:43.990 --> 00:51:46.789 Any other questions? Comments.

NOTE Confidence: 0.765057

00:51:50.450 --> 00:51:53.213 Seen a few things in the chat saying what

NOTE Confidence: 0.765057

00:51:53.213 --> 00:51:55.668 a wonderful talk it's been, Sarah. Oh yeah.

NOTE Confidence: 0.8998035

00:52:01.630 --> 00:52:03.898 OK, well if there are no other

NOTE Confidence: 0.8998035

00:52:03.898 --> 00:52:05.862 comments will close for today and

NOTE Confidence: 0.8998035

00:52:05.862 --> 00:52:08.046 thank you so much for a really

NOTE Confidence: 0.8998035

00:52:08.046 --> 00:52:10.268 terrific presentation and stimulating.

NOTE Confidence: 0.8998035

00:52:10.270 --> 00:52:13.150 And I'm sure this will lead to some

NOTE Confidence: 0.8998035

00:52:13.150 --> 00:52:14.590 additional collaborations with your

NOTE Confidence: 0.8998035

00:52:14.590 --> 00:52:16.750 colleagues here at Yale and elsewhere.

NOTE Confidence: 0.8998035

00:52:16.750 --> 00:52:17.887 So thank you.