WEBVTT

NOTE duration: ”00:49:20.341”

NOTE Confidence: 0.9955371

00:00:00.399 --> 00:00:01.540 Good afternoon, everyone.

NOTE Confidence: 0.9661051

00:00:02.560 --> 00:00:04.500 It's my pleasure to introduce

NOTE Confidence: 0.9661051

00:00:04.799 --> 00:00:06.819 our, our grand rounds today.

NOTE Confidence: 0.9667559

00:00:07.200 --> 00:00:08.320 And, this is a very

NOTE Confidence: 0.9667559

00:00:08.320 --> 00:00:09.599 special grand rounds to me

NOTE Confidence: 0.9667559

00:00:09.599 --> 00:00:10.719 and to our center because

NOTE Confidence: 0.9667559

00:00:10.719 --> 00:00:12.559 we're presenting two t thirty

NOTE Confidence: 0.9667559

00:00:12.559 --> 00:00:13.219 two trainees.

NOTE Confidence: 0.98046595

00:00:13.825 --> 00:00:14.545 Before I do that, I

NOTE Confidence: 0.98046595

00:00:14.545 --> 00:00:15.425 just wanna give a shout

NOTE Confidence: 0.98046595

00:00:15.425 --> 00:00:17.665 out to, doctor Kareem Ibrahim.

NOTE Confidence: 0.98046595

00:00:17.665 --> 00:00:18.945 He'll be actually presenting next

NOTE Confidence: 0.98046595

00:00:18.945 --> 00:00:21.185 week on multimodal neuroimaging markers

NOTE Confidence: 0.98046595

00:00:21.185 --> 00:00:21.845 of transdiagnostic

NOTE Confidence: 0.96177673

00:00:22.305 --> 00:00:23.904 symptom domains in youth, the

NOTE Confidence: 0.96177673

00:00:23.904 --> 00:00:25.425 role of emotion regulation. And

NOTE Confidence: 0.96177673

00:00:25.425 --> 00:00:26.545 also, a shout out to

NOTE Confidence: 0.96177673

00:00:26.545 --> 00:00:27.505 him because he's also a

NOTE Confidence: 0.96177673

00:00:27.505 --> 00:00:28.564 t thirty two graduate.

NOTE Confidence: 0.99706966

00:00:29.679 --> 00:00:30.960 So, the first talk will

NOTE Confidence: 0.99706966

00:00:30.960 --> 00:00:32.019 be led by,

NOTE Confidence: 0.85785705

00:00:33.120 --> 00:00:33.860 Ellie Edgar,

NOTE Confidence: 0.9252803

00:00:34.559 --> 00:00:35.600 and her talk is the

NOTE Confidence: 0.9252803

00:00:35.600 --> 00:00:37.360 avoidant brain neurosignatures of risk

NOTE Confidence: 0.9252803

00:00:37.360 --> 00:00:38.720 avoidance in adolescence with a

NOTE Confidence: 0.9252803

00:00:38.720 --> 00:00:40.640 look toward early childhood measurement.

NOTE Confidence: 0.9252803

00:00:40.640 --> 00:00:41.600 So we she'll be talking

NOTE Confidence: 0.9252803

00:00:41.600 --> 00:00:42.100 about

NOTE Confidence: 0.99482137

00:00:42.784 --> 00:00:44.465 a preschool brat, but not

NOTE Confidence: 0.99482137

00:00:44.465 --> 00:00:45.684 the kind you think of.

NOTE Confidence: 0.9636778

00:00:46.305 --> 00:00:47.504 And, another shout out to

NOTE Confidence: 0.9636778

00:00:47.504 --> 00:00:48.644 her is that she's entertaining

NOTE Confidence: 0.9636778

00:00:48.704 --> 00:00:50.385 two job offers right now,

NOTE Confidence: 0.9636778

00:00:50.385 --> 00:00:51.745 academic job offers. So it's

NOTE Confidence: 0.9636778

00:00:51.745 --> 00:00:53.425 McDonald's or Burger King, we're

NOTE Confidence: 0.9636778

00:00:53.425 --> 00:00:54.644 thinking about. Yeah.

NOTE Confidence: 0.9685437

00:00:55.344 --> 00:00:56.704 And then secondly, I I

NOTE Confidence: 0.9685437

00:00:56.704 --> 00:00:57.524 wanna introduce

NOTE Confidence: 0.9767595

00:00:58.290 --> 00:00:59.809 doctor Dan Doyle, and he'll

NOTE Confidence: 0.9767595

00:00:59.809 --> 00:01:00.930 be speaking to us, another

NOTE Confidence: 0.9767595

00:01:00.930 --> 00:01:02.050 t thirty two graduate this

NOTE Confidence: 0.9767595

00:01:02.050 --> 00:01:02.550 year.

NOTE Confidence: 0.98291063

00:01:03.010 --> 00:01:04.130 He'll be sticking around to

NOTE Confidence: 0.98291063

00:01:04.130 --> 00:01:05.430 work on a k award

NOTE Confidence: 0.82987946

00:01:05.890 --> 00:01:08.690 with doctors Seston and Patty

NOTE Confidence: 0.82987946

00:01:08.690 --> 00:01:09.190 Bierman.

NOTE Confidence: 0.9925827

00:01:09.729 --> 00:01:10.229 And

NOTE Confidence: 0.9819424

00:01:10.625 --> 00:01:11.985 doctor Doyle, Dan's talk is

NOTE Confidence: 0.9819424

00:01:11.985 --> 00:01:14.225 deciphering genetic and circuit features

NOTE Confidence: 0.9819424

00:01:14.225 --> 00:01:14.965 of neurodevelopmental

NOTE Confidence: 0.99616957

00:01:15.424 --> 00:01:15.924 disorders.

NOTE Confidence: 0.9762277

00:01:16.305 --> 00:01:17.345 And lastly, I wanna give

NOTE Confidence: 0.9762277

00:01:17.345 --> 00:01:18.465 everyone a shout out online

NOTE Confidence: 0.9762277

00:01:18.465 --> 00:01:19.584 just to remind you that,

NOTE Confidence: 0.9762277

00:01:19.825 --> 00:01:21.104 our our own Trisha Doll

NOTE Confidence: 0.9762277

00:01:21.104 --> 00:01:22.305 has really ramped up our

NOTE Confidence: 0.9762277

00:01:22.305 --> 00:01:23.505 our treats here. So we

NOTE Confidence: 0.9762277

00:01:23.505 --> 00:01:25.205 have cheesecake and caramel brownies.

NOTE Confidence: 0.9762277

00:01:25.505 --> 00:01:27.000 I realize I'm creating a

NOTE Confidence: 0.9762277

00:01:27.000 --> 00:01:28.200 little bit of FOMO, and

NOTE Confidence: 0.9762277

00:01:28.200 --> 00:01:29.399 that's intentional. So we hope

NOTE Confidence: 0.9762277

00:01:29.399 --> 00:01:30.039 to see you at Grand

NOTE Confidence: 0.9762277

00:01:30.039 --> 00:01:30.920 Rounds in person in the

NOTE Confidence: 0.9762277

00:01:30.920 --> 00:01:32.219 future. Thank you.

NOTE Confidence: 0.9909291

00:01:40.105 --> 00:01:41.145 Awesome. Thank you for that

NOTE Confidence: 0.9909291

00:01:41.145 --> 00:01:43.225 introduction, doctor Crowley. So today,

NOTE Confidence: 0.9909291

00:01:43.225 --> 00:01:44.185 I'm gonna talk to you

NOTE Confidence: 0.9909291

00:01:44.185 --> 00:01:45.865 guys about my more recent

NOTE Confidence: 0.9909291

00:01:45.865 --> 00:01:46.365 research,

NOTE Confidence: 0.96206343

00:01:46.905 --> 00:01:47.945 here at the Courage Lab

NOTE Confidence: 0.96206343

00:01:47.945 --> 00:01:49.385 with doctor Crowley. So today,

NOTE Confidence: 0.96206343

00:01:49.385 --> 00:01:50.665 I'll be talking about neural

NOTE Confidence: 0.96206343

00:01:50.665 --> 00:01:52.045 signatures of risk avoidance

NOTE Confidence: 0.7699819

00:01:52.345 --> 00:01:53.005 in adolescents

NOTE Confidence: 0.98320854

00:01:53.620 --> 00:01:54.820 with a brief look towards

NOTE Confidence: 0.98320854

00:01:54.820 --> 00:01:56.200 early childhood measurement.

NOTE Confidence: 0.9426812

00:01:57.460 --> 00:01:59.140 But first, let's just picture

NOTE Confidence: 0.9426812

00:01:59.140 --> 00:02:00.740 this. So a teenager is

NOTE Confidence: 0.9426812

00:02:00.740 --> 00:02:01.700 standing at the edge of

NOTE Confidence: 0.9426812

00:02:01.700 --> 00:02:02.680 a diving board.

NOTE Confidence: 0.92686236

00:02:03.140 --> 00:02:04.760 Below them is deep water

NOTE Confidence: 0.92686236

00:02:04.820 --> 00:02:06.505 and around them are friends

NOTE Confidence: 0.92686236

00:02:06.505 --> 00:02:08.185 urging them to jump. Their

NOTE Confidence: 0.92686236

00:02:08.185 --> 00:02:09.625 hearts pounding, do they leap

NOTE Confidence: 0.92686236

00:02:09.625 --> 00:02:10.585 or do they take a

NOTE Confidence: 0.92686236

00:02:10.585 --> 00:02:11.325 step back?

NOTE Confidence: 0.9734448

00:02:11.865 --> 00:02:13.305 And so adolescence is often

NOTE Confidence: 0.9734448

00:02:13.305 --> 00:02:14.425 painted as a time of

NOTE Confidence: 0.9734448

00:02:14.425 --> 00:02:16.585 this reckless risk taking. Right?

NOTE Confidence: 0.9734448

00:02:16.585 --> 00:02:17.805 Driving too fast,

NOTE Confidence: 0.9785366

00:02:18.105 --> 00:02:19.625 breaking the rules, chasing a

NOTE Confidence: 0.9785366

00:02:19.625 --> 00:02:21.419 thrill. But there's also another

NOTE Confidence: 0.9785366

00:02:21.419 --> 00:02:22.620 side to this and that's

NOTE Confidence: 0.9785366

00:02:22.620 --> 00:02:23.120 avoidance.

NOTE Confidence: 0.9789178

00:02:23.900 --> 00:02:25.260 Just as some teens take

NOTE Confidence: 0.9789178

00:02:25.260 --> 00:02:27.120 that leap, others hesitate,

NOTE Confidence: 0.9624895

00:02:27.500 --> 00:02:29.040 hold back, and miss opportunities.

NOTE Confidence: 0.9829013

00:02:29.740 --> 00:02:31.100 And so what separates the

NOTE Confidence: 0.9829013

00:02:31.100 --> 00:02:31.919 risk takers

NOTE Confidence: 0.9506104

00:02:32.220 --> 00:02:33.120 from the avoiders?

NOTE Confidence: 0.99120516

00:02:33.505 --> 00:02:34.625 And how does each path

NOTE Confidence: 0.99120516

00:02:34.625 --> 00:02:35.905 shape their mental health and

NOTE Confidence: 0.99120516

00:02:35.905 --> 00:02:37.585 their future? And so today,

NOTE Confidence: 0.99120516

00:02:37.585 --> 00:02:39.745 I'll briefly discuss adolescent risk

NOTE Confidence: 0.99120516

00:02:39.745 --> 00:02:41.745 avoidance and why embracing risk

NOTE Confidence: 0.99120516

00:02:41.745 --> 00:02:43.044 can be just as consequential

NOTE Confidence: 0.99120516

00:02:43.105 --> 00:02:44.325 as embracing it.

NOTE Confidence: 0.9977684

00:02:45.950 --> 00:02:47.310 And so risk taking and

NOTE Confidence: 0.9977684

00:02:47.310 --> 00:02:49.630 risk avoidance enable individuals to

NOTE Confidence: 0.9977684

00:02:49.630 --> 00:02:51.550 adapt to a constantly evolving

NOTE Confidence: 0.9977684

00:02:51.550 --> 00:02:52.050 environment.

NOTE Confidence: 0.9942419

00:02:52.750 --> 00:02:54.770 These behaviors are complex reactions

NOTE Confidence: 0.9942419

00:02:54.910 --> 00:02:56.510 guided by both reflex and

NOTE Confidence: 0.9942419

00:02:56.510 --> 00:02:57.650 cognitive control.

NOTE Confidence: 0.953163

00:02:58.675 --> 00:03:00.035 And so contexts that elicit

NOTE Confidence: 0.953163

00:03:00.035 --> 00:03:02.135 both risk taking and avoidance

NOTE Confidence: 0.953163

00:03:02.275 --> 00:03:03.575 behaviors are ambiguous,

NOTE Confidence: 0.950055

00:03:04.194 --> 00:03:06.355 unpredictable, and or novel, and

NOTE Confidence: 0.950055

00:03:06.355 --> 00:03:07.175 these contexts

NOTE Confidence: 0.98324645

00:03:07.715 --> 00:03:09.235 often include the possibility of

NOTE Confidence: 0.98324645

00:03:09.235 --> 00:03:11.555 both reward and loss, such

NOTE Confidence: 0.98324645

00:03:11.555 --> 00:03:12.375 that the relative

NOTE Confidence: 0.9922345

00:03:12.820 --> 00:03:14.660 safety benefits of avoiding avoiding

NOTE Confidence: 0.9922345

00:03:14.660 --> 00:03:16.980 the situation or stimuli must

NOTE Confidence: 0.9922345

00:03:16.980 --> 00:03:18.840 be weighed against the possibility

NOTE Confidence: 0.9922345

00:03:18.900 --> 00:03:19.639 of sacrificing

NOTE Confidence: 0.9967849

00:03:19.940 --> 00:03:20.919 potential rewards.

NOTE Confidence: 0.9867847

00:03:22.980 --> 00:03:24.440 Now all of the decisions

NOTE Confidence: 0.9867847

00:03:24.500 --> 00:03:25.780 we make have some degree

NOTE Confidence: 0.9867847

00:03:25.780 --> 00:03:26.840 of risk involved,

NOTE Confidence: 0.993776

00:03:27.185 --> 00:03:28.305 and some degree of risk

NOTE Confidence: 0.993776

00:03:28.305 --> 00:03:29.905 taking is necessary, right, to

NOTE Confidence: 0.993776

00:03:29.905 --> 00:03:31.605 promote positive health outcomes,

NOTE Confidence: 0.9781583

00:03:31.905 --> 00:03:33.125 prepare for adulthood.

NOTE Confidence: 0.9976446

00:03:34.305 --> 00:03:35.444 But at the extremes,

NOTE Confidence: 0.9971933

00:03:35.745 --> 00:03:37.345 exaggerated risk taking can lead

NOTE Confidence: 0.9971933

00:03:37.345 --> 00:03:38.565 to negative consequences.

NOTE Confidence: 0.9450217

00:03:40.060 --> 00:03:40.860 At the other end of

NOTE Confidence: 0.9450217

00:03:40.860 --> 00:03:41.599 that spectrum,

NOTE Confidence: 0.9987772

00:03:42.060 --> 00:03:42.560 exaggerated

NOTE Confidence: 0.99296266

00:03:42.939 --> 00:03:44.720 risk avoidance is also associated

NOTE Confidence: 0.99296266

00:03:44.780 --> 00:03:46.319 with various types of dysfunction,

NOTE Confidence: 0.99717385

00:03:46.780 --> 00:03:48.220 and so both extremes lead

NOTE Confidence: 0.99717385

00:03:48.220 --> 00:03:49.280 to adverse outcomes.

NOTE Confidence: 0.997465

00:03:51.260 --> 00:03:53.420 But exaggerated risk avoidance plays

NOTE Confidence: 0.997465

00:03:53.420 --> 00:03:55.040 an important role in anxiety.

NOTE Confidence: 0.9925801

00:03:56.055 --> 00:03:57.255 So across all of the

NOTE Confidence: 0.9925801

00:03:57.255 --> 00:03:59.175 disorders under the anxiety umbrella

NOTE Confidence: 0.9925801

00:03:59.175 --> 00:04:01.195 in the DSM five, avoidance

NOTE Confidence: 0.9925801

00:04:01.255 --> 00:04:03.415 of stimuli or situations perceived

NOTE Confidence: 0.9925801

00:04:03.415 --> 00:04:05.415 as dangerous or threatening is

NOTE Confidence: 0.9925801

00:04:05.415 --> 00:04:06.615 a cardinal feature in the

NOTE Confidence: 0.9925801

00:04:06.615 --> 00:04:08.395 development and maintenance of anxiety.

NOTE Confidence: 0.99670446

00:04:09.400 --> 00:04:10.940 And so theories of cognitive

NOTE Confidence: 0.99670446

00:04:11.000 --> 00:04:13.000 behavior regard risk avoidance as

NOTE Confidence: 0.99670446

00:04:13.000 --> 00:04:14.940 a consequence of anxiety symptoms.

NOTE Confidence: 0.9921252

00:04:15.400 --> 00:04:17.000 For instance, the experience of

NOTE Confidence: 0.9921252

00:04:17.000 --> 00:04:18.360 anxiety can serve as a

NOTE Confidence: 0.9921252

00:04:18.360 --> 00:04:19.960 salient form of information to

NOTE Confidence: 0.9921252

00:04:19.960 --> 00:04:20.460 individuals,

NOTE Confidence: 0.9947245

00:04:21.240 --> 00:04:22.680 signaling the presence of threat

NOTE Confidence: 0.9947245

00:04:22.680 --> 00:04:23.420 in the environment.

NOTE Confidence: 0.9799914

00:04:24.265 --> 00:04:26.105 And so this anxiety manifested

NOTE Confidence: 0.9799914

00:04:26.105 --> 00:04:27.885 in part by attentional biases

NOTE Confidence: 0.9799914

00:04:27.945 --> 00:04:29.865 towards threat and increased error

NOTE Confidence: 0.9799914

00:04:29.865 --> 00:04:30.365 monitoring

NOTE Confidence: 0.9836522

00:04:31.464 --> 00:04:33.385 may potentiate risk avoidant decision

NOTE Confidence: 0.9836522

00:04:33.385 --> 00:04:34.665 making as a means towards

NOTE Confidence: 0.9836522

00:04:34.665 --> 00:04:36.205 avoiding perceived threats.

NOTE Confidence: 0.979611

00:04:37.470 --> 00:04:38.830 Now it's also been proposed

NOTE Confidence: 0.979611

00:04:38.830 --> 00:04:40.029 that risk avoidance is a

NOTE Confidence: 0.979611

00:04:40.029 --> 00:04:42.050 cause and consequence of anxiety,

NOTE Confidence: 0.9986004

00:04:42.589 --> 00:04:43.710 and so this could suggest

NOTE Confidence: 0.9986004

00:04:43.710 --> 00:04:44.750 the presence of a self

NOTE Confidence: 0.9986004

00:04:44.750 --> 00:04:45.250 perpetuating

NOTE Confidence: 0.9996145

00:04:45.710 --> 00:04:46.210 cycle

NOTE Confidence: 0.88781184

00:04:47.070 --> 00:04:48.850 in which bias risk appraisals

NOTE Confidence: 0.90200245

00:04:49.390 --> 00:04:50.290 evoke anxiety,

NOTE Confidence: 0.9956553

00:04:51.255 --> 00:04:53.275 the experience of anxiety perpetuates

NOTE Confidence: 0.9956553

00:04:53.415 --> 00:04:55.255 the formation of negative risk

NOTE Confidence: 0.9956553

00:04:55.255 --> 00:04:55.755 appraisals,

NOTE Confidence: 0.996232

00:04:56.535 --> 00:04:58.555 negative risk appraisals and anxiety

NOTE Confidence: 0.996232

00:04:58.615 --> 00:04:59.975 both act as inputs into

NOTE Confidence: 0.996232

00:04:59.975 --> 00:05:02.055 the decision making process, and

NOTE Confidence: 0.996232

00:05:02.055 --> 00:05:04.075 risk avoidant decision making potentiates

NOTE Confidence: 0.996232

00:05:04.215 --> 00:05:06.295 pervasive patterns of risk avoidant

NOTE Confidence: 0.996232

00:05:06.295 --> 00:05:06.795 behavior.

NOTE Confidence: 0.9741424

00:05:08.430 --> 00:05:09.789 And so shifting gears slightly,

NOTE Confidence: 0.9741424

00:05:09.789 --> 00:05:11.069 we all know that EEG

NOTE Confidence: 0.9741424

00:05:11.069 --> 00:05:12.509 is a useful tool for

NOTE Confidence: 0.9741424

00:05:12.509 --> 00:05:14.430 delineating the neural underpinnings of

NOTE Confidence: 0.9741424

00:05:14.430 --> 00:05:15.650 a wide range of psychological

NOTE Confidence: 0.9741424

00:05:15.949 --> 00:05:16.449 processes.

NOTE Confidence: 0.9206146

00:05:16.990 --> 00:05:18.430 And so ERPs or event

NOTE Confidence: 0.9206146

00:05:18.430 --> 00:05:19.330 related potentials

NOTE Confidence: 0.85117954

00:05:19.654 --> 00:05:21.255 are phase and time locked

NOTE Confidence: 0.85117954

00:05:21.255 --> 00:05:21.755 neuroactivity

NOTE Confidence: 0.98381233

00:05:22.455 --> 00:05:24.535 created by averaging frequencies across

NOTE Confidence: 0.98381233

00:05:24.535 --> 00:05:25.595 multiple trials.

NOTE Confidence: 0.97999483

00:05:26.215 --> 00:05:27.495 And so within the context

NOTE Confidence: 0.97999483

00:05:27.495 --> 00:05:29.654 of risk, the FRN component

NOTE Confidence: 0.97999483

00:05:29.654 --> 00:05:31.335 of the N2 has received

NOTE Confidence: 0.97999483

00:05:31.335 --> 00:05:32.795 the most research focus.

NOTE Confidence: 0.9764868

00:05:33.120 --> 00:05:34.400 So the FRN is known

NOTE Confidence: 0.9764868

00:05:34.400 --> 00:05:35.760 to be sensitive to negative

NOTE Confidence: 0.9764868

00:05:35.760 --> 00:05:37.120 feedback, and we know that

NOTE Confidence: 0.9764868

00:05:37.120 --> 00:05:39.300 a greater amplitude is associated

NOTE Confidence: 0.9764868

00:05:39.360 --> 00:05:40.720 with risk taking in non

NOTE Confidence: 0.9764868

00:05:40.720 --> 00:05:42.420 anxious adults and adolescents.

NOTE Confidence: 0.9919502

00:05:43.040 --> 00:05:44.500 And further, it's been linked

NOTE Confidence: 0.9919502

00:05:44.640 --> 00:05:46.580 to anxiety in adult populations.

NOTE Confidence: 0.9481336

00:05:48.935 --> 00:05:50.775 Considerable research is also focused

NOTE Confidence: 0.9481336

00:05:50.775 --> 00:05:52.375 on the p three proposed

NOTE Confidence: 0.9481336

00:05:52.375 --> 00:05:54.294 to reflect attention orientation to

NOTE Confidence: 0.9481336

00:05:54.294 --> 00:05:55.435 unexpected events.

NOTE Confidence: 0.9869349

00:05:55.815 --> 00:05:56.694 And so we know a

NOTE Confidence: 0.9869349

00:05:56.694 --> 00:05:58.775 reduced amplitude is associated with

NOTE Confidence: 0.9869349

00:05:58.775 --> 00:06:01.095 risk taking in nonanxious adults

NOTE Confidence: 0.9869349

00:06:01.095 --> 00:06:01.835 and adolescents.

NOTE Confidence: 0.9961128

00:06:02.270 --> 00:06:03.310 It's also been linked to

NOTE Confidence: 0.9961128

00:06:03.310 --> 00:06:04.430 anxiety in both of these

NOTE Confidence: 0.9961128

00:06:04.430 --> 00:06:04.930 populations.

NOTE Confidence: 0.9123794

00:06:07.150 --> 00:06:08.510 But less work is focused

NOTE Confidence: 0.9123794

00:06:08.510 --> 00:06:09.710 on the p two, known

NOTE Confidence: 0.9123794

00:06:09.710 --> 00:06:11.550 to reflect sensory processes like

NOTE Confidence: 0.9123794

00:06:11.550 --> 00:06:13.730 attention following a feedback stimulus.

NOTE Confidence: 0.97738934

00:06:14.205 --> 00:06:15.164 And so what we do

NOTE Confidence: 0.97738934

00:06:15.164 --> 00:06:16.205 know is that a greater

NOTE Confidence: 0.97738934

00:06:16.205 --> 00:06:18.604 P2 amplitude is associated with

NOTE Confidence: 0.97738934

00:06:18.604 --> 00:06:20.044 higher levels of risk taking

NOTE Confidence: 0.97738934

00:06:20.044 --> 00:06:21.425 in non anxious adults.

NOTE Confidence: 0.95805436

00:06:23.485 --> 00:06:25.004 And finally, little work has

NOTE Confidence: 0.95805436

00:06:25.004 --> 00:06:26.764 assessed the LPP or slow

NOTE Confidence: 0.95805436

00:06:26.764 --> 00:06:27.264 wave

NOTE Confidence: 0.98651767

00:06:27.650 --> 00:06:29.650 proposed to reflect facilitated attention

NOTE Confidence: 0.98651767

00:06:29.650 --> 00:06:31.970 to emotionally or motivationally salient

NOTE Confidence: 0.98651767

00:06:31.970 --> 00:06:32.470 stimuli.

NOTE Confidence: 0.99547726

00:06:32.930 --> 00:06:34.389 And so a greater LPP

NOTE Confidence: 0.99547726

00:06:34.449 --> 00:06:34.949 amplitude

NOTE Confidence: 0.9847966

00:06:35.330 --> 00:06:37.009 is also associated with higher

NOTE Confidence: 0.9847966

00:06:37.009 --> 00:06:39.009 levels of risk taking, again,

NOTE Confidence: 0.9847966

00:06:39.009 --> 00:06:41.009 only demonstrated in non anxious

NOTE Confidence: 0.9847966

00:06:41.009 --> 00:06:41.509 adults.

NOTE Confidence: 0.98158306

00:06:43.475 --> 00:06:44.455 And so oscillatory

NOTE Confidence: 0.9746783

00:06:44.755 --> 00:06:46.755 dynamics complement ERPs in that

NOTE Confidence: 0.9746783

00:06:46.755 --> 00:06:47.475 they can be used to

NOTE Confidence: 0.9746783

00:06:47.475 --> 00:06:49.154 investigate phases of high or

NOTE Confidence: 0.9746783

00:06:49.154 --> 00:06:49.895 low excitability.

NOTE Confidence: 0.91287583

00:06:51.315 --> 00:06:53.315 One measure, event related spectral

NOTE Confidence: 0.91287583

00:06:53.315 --> 00:06:54.935 perturbation, or ERSPs,

NOTE Confidence: 0.99622446

00:06:55.570 --> 00:06:56.930 index the mean change in

NOTE Confidence: 0.99622446

00:06:56.930 --> 00:06:59.270 EEG power relative to baseline

NOTE Confidence: 0.99622446

00:06:59.410 --> 00:07:00.850 that is associated with the

NOTE Confidence: 0.99622446

00:07:00.850 --> 00:07:02.950 presentation of stimuli or execution

NOTE Confidence: 0.99622446

00:07:03.090 --> 00:07:03.750 of responses.

NOTE Confidence: 0.9768444

00:07:04.850 --> 00:07:06.290 And a common target for

NOTE Confidence: 0.9768444

00:07:06.290 --> 00:07:07.890 assessing the neural dynamics of

NOTE Confidence: 0.9768444

00:07:07.890 --> 00:07:10.195 uncertain or risky situations is

NOTE Confidence: 0.9768444

00:07:10.195 --> 00:07:12.055 theta band oscillatory power.

NOTE Confidence: 0.96108544

00:07:13.395 --> 00:07:15.335 So mid frontal theta reflects

NOTE Confidence: 0.96108544

00:07:15.395 --> 00:07:17.655 medial prefrontal cortex processes,

NOTE Confidence: 0.9884006

00:07:17.955 --> 00:07:19.475 which are highly sensitive to

NOTE Confidence: 0.9884006

00:07:19.475 --> 00:07:21.655 tasks involving novelty, conflict,

NOTE Confidence: 0.9814805

00:07:22.035 --> 00:07:23.795 punishment, and error, as well

NOTE Confidence: 0.9814805

00:07:23.795 --> 00:07:24.935 as feedback processing.

NOTE Confidence: 0.9772774

00:07:26.169 --> 00:07:27.690 Mid frontal theta has also

NOTE Confidence: 0.9772774

00:07:27.690 --> 00:07:29.470 been identified in the generation

NOTE Confidence: 0.9772774

00:07:29.530 --> 00:07:31.129 of event related mid frontal

NOTE Confidence: 0.9772774

00:07:31.129 --> 00:07:32.110 voltage negativities,

NOTE Confidence: 0.99164385

00:07:32.569 --> 00:07:33.530 like the n two, and

NOTE Confidence: 0.99164385

00:07:33.530 --> 00:07:34.409 we'll come back to that

NOTE Confidence: 0.99164385

00:07:34.409 --> 00:07:34.909 later.

NOTE Confidence: 0.98280436

00:07:35.770 --> 00:07:36.889 But theta power has been

NOTE Confidence: 0.98280436

00:07:36.889 --> 00:07:38.810 found to reflect individual differences

NOTE Confidence: 0.98280436

00:07:38.810 --> 00:07:40.190 in risk taking in adults.

NOTE Confidence: 0.97193635

00:07:40.705 --> 00:07:41.985 But only one study has

NOTE Confidence: 0.97193635

00:07:41.985 --> 00:07:43.105 linked it to anxiety in

NOTE Confidence: 0.97193635

00:07:43.105 --> 00:07:45.045 the context of risk, demonstrating

NOTE Confidence: 0.97193635

00:07:45.105 --> 00:07:46.245 that highly anxious

NOTE Confidence: 0.99043936

00:07:46.705 --> 00:07:48.945 adults showed amplified mid frontal

NOTE Confidence: 0.99043936

00:07:48.945 --> 00:07:50.785 theta power before making a

NOTE Confidence: 0.99043936

00:07:50.785 --> 00:07:52.225 less risky choice during a

NOTE Confidence: 0.99043936

00:07:52.225 --> 00:07:53.045 risk game.

NOTE Confidence: 0.9755965

00:07:54.940 --> 00:07:56.380 Now aside from gaps in

NOTE Confidence: 0.9755965

00:07:56.380 --> 00:07:57.820 the amount and types of

NOTE Confidence: 0.9755965

00:07:57.820 --> 00:07:59.920 ERP research and theta oscillatory

NOTE Confidence: 0.9755965

00:08:00.060 --> 00:08:01.900 dynamic research, if you didn't

NOTE Confidence: 0.9755965

00:08:01.900 --> 00:08:03.500 notice, all of these studies

NOTE Confidence: 0.9755965

00:08:03.500 --> 00:08:04.620 were in the context of

NOTE Confidence: 0.9755965

00:08:04.620 --> 00:08:05.440 risk taking,

NOTE Confidence: 0.93166846

00:08:05.820 --> 00:08:07.280 and that's a direct result

NOTE Confidence: 0.6950022

00:08:19.025 --> 00:08:19.525 performance,

NOTE Confidence: 0.9859163

00:08:20.130 --> 00:08:21.830 as well as avoidance motivation,

NOTE Confidence: 0.9859163

00:08:21.890 --> 00:08:23.350 so the potential for loss.

NOTE Confidence: 0.98758847

00:08:23.890 --> 00:08:24.770 And so this makes it

NOTE Confidence: 0.98758847

00:08:24.770 --> 00:08:26.130 difficult to determine if an

NOTE Confidence: 0.98758847

00:08:26.130 --> 00:08:28.450 individual shows risk avoidance or

NOTE Confidence: 0.98758847

00:08:28.450 --> 00:08:29.670 low approach motivation.

NOTE Confidence: 0.88658595

00:08:31.810 --> 00:08:33.010 And so Crowley et al

NOTE Confidence: 0.88658595

00:08:33.010 --> 00:08:34.304 addressed this gap by inverting

NOTE Confidence: 0.88658595

00:08:34.365 --> 00:08:36.285 the existing balloon analog risk

NOTE Confidence: 0.88658595

00:08:36.285 --> 00:08:37.425 task or BART.

NOTE Confidence: 0.9528517

00:08:38.125 --> 00:08:39.405 This new task, going to

NOTE Confidence: 0.9528517

00:08:39.405 --> 00:08:41.345 the balloon risk avoidance task,

NOTE Confidence: 0.9528517

00:08:41.485 --> 00:08:43.645 biases participants towards the perception

NOTE Confidence: 0.9528517

00:08:43.645 --> 00:08:44.304 of risk.

NOTE Confidence: 0.97575074

00:08:44.845 --> 00:08:46.125 And so each of thirty

NOTE Confidence: 0.97575074

00:08:46.125 --> 00:08:47.565 trials starts with the balloon

NOTE Confidence: 0.97575074

00:08:47.565 --> 00:08:48.845 being inflated next to the

NOTE Confidence: 0.97575074

00:08:48.845 --> 00:08:49.820 meter. And if you look

NOTE Confidence: 0.97575074

00:08:49.820 --> 00:08:50.980 at the meter, it ranges

NOTE Confidence: 0.97575074

00:08:50.980 --> 00:08:52.340 from that blue to red,

NOTE Confidence: 0.97575074

00:08:52.340 --> 00:08:53.860 so it's safe to more

NOTE Confidence: 0.97575074

00:08:53.860 --> 00:08:55.400 dangerous as you go up.

NOTE Confidence: 0.9944148

00:08:55.940 --> 00:08:57.460 And during each trial, an

NOTE Confidence: 0.9944148

00:08:57.460 --> 00:08:59.220 eight second timer imposes a

NOTE Confidence: 0.9944148

00:08:59.220 --> 00:09:00.980 mild time pressure, and this

NOTE Confidence: 0.9944148

00:09:00.980 --> 00:09:02.179 is for the participant to

NOTE Confidence: 0.9944148

00:09:02.179 --> 00:09:03.700 decide how much to deflate

NOTE Confidence: 0.9944148

00:09:03.700 --> 00:09:04.440 each balloon.

NOTE Confidence: 0.9985076

00:09:04.934 --> 00:09:06.135 If no action is taken,

NOTE Confidence: 0.9985076

00:09:06.135 --> 00:09:07.355 the balloon will pop.

NOTE Confidence: 0.9937202

00:09:09.255 --> 00:09:10.455 Now when the balloon is

NOTE Confidence: 0.9937202

00:09:10.455 --> 00:09:12.135 initially inflated, it's worth the

NOTE Confidence: 0.9937202

00:09:12.135 --> 00:09:13.495 full value of one hundred

NOTE Confidence: 0.9937202

00:09:13.495 --> 00:09:14.395 and ten points.

NOTE Confidence: 0.9697317

00:09:14.855 --> 00:09:16.455 Participants give up points to

NOTE Confidence: 0.9697317

00:09:16.455 --> 00:09:17.515 deflate the balloon,

NOTE Confidence: 0.9715825

00:09:17.880 --> 00:09:19.340 reducing the risk or likelihood

NOTE Confidence: 0.9715825

00:09:19.400 --> 00:09:20.520 that it will pop, but

NOTE Confidence: 0.9715825

00:09:20.520 --> 00:09:22.440 also decreasing the balloon's value

NOTE Confidence: 0.9715825

00:09:22.440 --> 00:09:23.400 and in turn the amount

NOTE Confidence: 0.9715825

00:09:23.400 --> 00:09:24.280 of points that they can

NOTE Confidence: 0.9715825

00:09:24.280 --> 00:09:25.420 earn for that trial.

NOTE Confidence: 0.9917474

00:09:26.920 --> 00:09:28.200 And so the more air

NOTE Confidence: 0.9917474

00:09:28.200 --> 00:09:29.400 that they release from the

NOTE Confidence: 0.9917474

00:09:29.400 --> 00:09:31.160 balloon, the safer the balloon

NOTE Confidence: 0.9917474

00:09:31.160 --> 00:09:32.684 is, but the point value

NOTE Confidence: 0.9917474

00:09:32.684 --> 00:09:33.804 of the trial is lower

NOTE Confidence: 0.9917474

00:09:33.804 --> 00:09:35.264 as indicated up top.

NOTE Confidence: 0.9974964

00:09:35.725 --> 00:09:36.845 The less air that is

NOTE Confidence: 0.9974964

00:09:36.845 --> 00:09:38.625 released, the higher the likelihood

NOTE Confidence: 0.9974964

00:09:38.684 --> 00:09:39.964 it will pop, but the

NOTE Confidence: 0.9974964

00:09:39.964 --> 00:09:41.245 point value of the trial

NOTE Confidence: 0.9974964

00:09:41.245 --> 00:09:42.764 is higher as indicated on

NOTE Confidence: 0.9974964

00:09:42.764 --> 00:09:43.985 the bottom of the screen.

NOTE Confidence: 0.9858843

00:09:45.509 --> 00:09:46.630 And so if the balloon

NOTE Confidence: 0.9858843

00:09:46.630 --> 00:09:47.589 does not pop, we call

NOTE Confidence: 0.9858843

00:09:47.589 --> 00:09:48.889 this successful avoidance.

NOTE Confidence: 0.9997053

00:09:49.589 --> 00:09:50.790 And if the balloon pops,

NOTE Confidence: 0.9997053

00:09:50.790 --> 00:09:52.570 we call this unsuccessful avoidance.

NOTE Confidence: 0.9963434

00:09:54.309 --> 00:09:55.429 And so in their initial

NOTE Confidence: 0.9963434

00:09:55.429 --> 00:09:57.209 study, Crowley and colleagues demonstrated

NOTE Confidence: 0.9963434

00:09:57.350 --> 00:09:59.029 that risk avoidant behavior on

NOTE Confidence: 0.9963434

00:09:59.029 --> 00:10:01.415 the BRAT was positively related

NOTE Confidence: 0.9963434

00:10:01.415 --> 00:10:03.735 to overall adolescent anxiety and

NOTE Confidence: 0.9963434

00:10:03.735 --> 00:10:04.635 fearful temperament.

NOTE Confidence: 0.9790595

00:10:05.335 --> 00:10:07.015 Moreover, the BART, which measures

NOTE Confidence: 0.9790595

00:10:07.015 --> 00:10:08.615 both risk avoidance and approach

NOTE Confidence: 0.9790595

00:10:08.615 --> 00:10:10.395 motivation, like I mentioned earlier,

NOTE Confidence: 0.9790595

00:10:10.615 --> 00:10:12.455 was unrelated to anxiety in

NOTE Confidence: 0.9790595

00:10:12.455 --> 00:10:14.429 their study, highlighting the utility

NOTE Confidence: 0.9790595

00:10:14.429 --> 00:10:15.790 of the BRAT for studying

NOTE Confidence: 0.9790595

00:10:15.790 --> 00:10:17.089 risk avoidance specifically.

NOTE Confidence: 0.9746518

00:10:18.670 --> 00:10:20.110 And so given these promising

NOTE Confidence: 0.9746518

00:10:20.110 --> 00:10:21.709 behavioral results, the first study

NOTE Confidence: 0.9746518

00:10:21.709 --> 00:10:23.389 I will discuss today builds

NOTE Confidence: 0.9746518

00:10:23.389 --> 00:10:24.910 directly on these findings by

NOTE Confidence: 0.9746518

00:10:24.910 --> 00:10:26.589 examining the neural dynamics of

NOTE Confidence: 0.9746518

00:10:26.589 --> 00:10:27.949 youth risk avoidance during the

NOTE Confidence: 0.9746518

00:10:27.949 --> 00:10:28.449 BRAT.

NOTE Confidence: 0.9762571

00:10:29.765 --> 00:10:31.205 And so our sample consisted

NOTE Confidence: 0.9762571

00:10:31.205 --> 00:10:33.205 of fifty nine adolescents eleven

NOTE Confidence: 0.9762571

00:10:33.205 --> 00:10:34.585 to nineteen years of age.

NOTE Confidence: 0.9762571

00:10:34.804 --> 00:10:35.925 The BRAT was used with

NOTE Confidence: 0.9762571

00:10:35.925 --> 00:10:38.005 concurrent EEG to measure ERPs

NOTE Confidence: 0.9762571

00:10:38.005 --> 00:10:39.705 and theta oscillatory dynamics

NOTE Confidence: 0.99629194

00:10:40.085 --> 00:10:41.465 in response to unsuccessful

NOTE Confidence: 0.9923005

00:10:41.925 --> 00:10:43.945 and successful risk avoidance conditions.

NOTE Confidence: 0.9647744

00:10:44.709 --> 00:10:46.149 And the social phobia and

NOTE Confidence: 0.9647744

00:10:46.149 --> 00:10:48.390 anxiety inventory for children was

NOTE Confidence: 0.9647744

00:10:48.390 --> 00:10:49.510 used to drive groups of

NOTE Confidence: 0.9647744

00:10:49.510 --> 00:10:50.970 high and low social anxiety.

NOTE Confidence: 0.978264

00:10:53.269 --> 00:10:55.450 Alright. Now first, youth reporting

NOTE Confidence: 0.978264

00:10:55.510 --> 00:10:57.290 high levels of social anxiety

NOTE Confidence: 0.85890806

00:10:57.670 --> 00:10:59.529 exhibited larger p two,

NOTE Confidence: 0.91106004

00:10:59.945 --> 00:11:00.445 LPP,

NOTE Confidence: 0.99841005

00:11:00.905 --> 00:11:03.245 and FRN amplitudes to unsuccessful

NOTE Confidence: 0.995934

00:11:03.785 --> 00:11:05.885 compared to successful risk avoidance.

NOTE Confidence: 0.97577065

00:11:06.825 --> 00:11:08.445 However, there is no significant

NOTE Confidence: 0.97577065

00:11:08.585 --> 00:11:10.285 difference in P3 amplitude

NOTE Confidence: 0.998317

00:11:10.745 --> 00:11:11.725 between successful

NOTE Confidence: 0.9926208

00:11:12.300 --> 00:11:13.820 and unsuccessful avoidance as a

NOTE Confidence: 0.9926208

00:11:13.820 --> 00:11:15.840 function of social anxiety level.

NOTE Confidence: 0.99898046

00:11:16.220 --> 00:11:17.500 But across the whole sample

NOTE Confidence: 0.99898046

00:11:17.500 --> 00:11:18.160 of youth,

NOTE Confidence: 0.8995081

00:11:18.700 --> 00:11:20.220 youth show smaller p three

NOTE Confidence: 0.8995081

00:11:20.220 --> 00:11:21.520 responses to unsuccessful

NOTE Confidence: 0.9959613

00:11:21.900 --> 00:11:23.760 relative to successful avoidance.

NOTE Confidence: 0.9842683

00:11:25.585 --> 00:11:27.265 And so second, youth with

NOTE Confidence: 0.9842683

00:11:27.265 --> 00:11:29.045 higher levels of social anxiety

NOTE Confidence: 0.97679317

00:11:29.345 --> 00:11:31.045 showed smaller theta responses

NOTE Confidence: 0.99877834

00:11:31.345 --> 00:11:32.804 following successful avoidance

NOTE Confidence: 0.99224705

00:11:33.265 --> 00:11:34.385 compared to those with low

NOTE Confidence: 0.99224705

00:11:34.385 --> 00:11:35.845 levels of social anxiety.

NOTE Confidence: 0.99515915

00:11:37.950 --> 00:11:39.470 And that same exact effect

NOTE Confidence: 0.99515915

00:11:39.470 --> 00:11:41.650 was found for unsuccessful avoidance.

NOTE Confidence: 0.99515915

00:11:41.870 --> 00:11:43.230 Those with higher levels of

NOTE Confidence: 0.99515915

00:11:43.230 --> 00:11:45.550 social anxiety showed smaller theta

NOTE Confidence: 0.99515915

00:11:45.550 --> 00:11:47.070 power responses than those with

NOTE Confidence: 0.99515915

00:11:47.070 --> 00:11:48.850 lower levels of social anxiety.

NOTE Confidence: 0.96155393

00:11:52.035 --> 00:11:53.475 And so first, the p

NOTE Confidence: 0.96155393

00:11:53.475 --> 00:11:55.715 two, FRN, and LPP, but

NOTE Confidence: 0.96155393

00:11:55.715 --> 00:11:57.495 not p three, for unsuccessful

NOTE Confidence: 0.96155393

00:11:57.635 --> 00:11:58.775 avoidance significantly

NOTE Confidence: 0.99849

00:11:59.155 --> 00:12:01.075 differentiated high and low social

NOTE Confidence: 0.99849

00:12:01.075 --> 00:12:02.054 anxiety groups.

NOTE Confidence: 0.9766997

00:12:02.355 --> 00:12:03.929 So regarding the p two,

NOTE Confidence: 0.9766997

00:12:04.250 --> 00:12:05.929 overall, youth with greater levels

NOTE Confidence: 0.9766997

00:12:05.929 --> 00:12:07.450 of social anxiety may have

NOTE Confidence: 0.9766997

00:12:07.450 --> 00:12:08.910 expected to avoid losing,

NOTE Confidence: 0.98259073

00:12:09.210 --> 00:12:10.490 and this was indeed reflected

NOTE Confidence: 0.98259073

00:12:10.490 --> 00:12:11.929 in our behavioral data. So

NOTE Confidence: 0.98259073

00:12:11.929 --> 00:12:13.309 they gave up more points

NOTE Confidence: 0.98259073

00:12:13.610 --> 00:12:14.890 and took less risk than

NOTE Confidence: 0.98259073

00:12:14.890 --> 00:12:16.089 those with lower levels of

NOTE Confidence: 0.98259073

00:12:16.089 --> 00:12:16.910 social anxiety.

NOTE Confidence: 0.93037105

00:12:17.255 --> 00:12:18.135 And so, in turn, this

NOTE Confidence: 0.93037105

00:12:18.135 --> 00:12:19.255 risk avoidance may have been

NOTE Confidence: 0.93037105

00:12:19.255 --> 00:12:20.375 reflected in that P two

NOTE Confidence: 0.93037105

00:12:20.375 --> 00:12:20.875 amplitude.

NOTE Confidence: 0.984154

00:12:22.054 --> 00:12:23.255 And we know the FRN

NOTE Confidence: 0.984154

00:12:23.255 --> 00:12:24.774 is sensitive to negative feedback.

NOTE Confidence: 0.984154

00:12:24.774 --> 00:12:25.975 So given that youth with

NOTE Confidence: 0.984154

00:12:25.975 --> 00:12:27.675 high levels of social anxiety

NOTE Confidence: 0.984154

00:12:27.975 --> 00:12:29.770 tended to avoid risk, they

NOTE Confidence: 0.984154

00:12:29.770 --> 00:12:30.890 might have been surprised when

NOTE Confidence: 0.984154

00:12:30.890 --> 00:12:32.089 they let more air out

NOTE Confidence: 0.984154

00:12:32.089 --> 00:12:33.370 of the balloon, a safer

NOTE Confidence: 0.984154

00:12:33.370 --> 00:12:35.150 balloon, but it still popped,

NOTE Confidence: 0.984154

00:12:35.370 --> 00:12:36.990 reflected by a larger FRN

NOTE Confidence: 0.984154

00:12:37.050 --> 00:12:37.550 response.

NOTE Confidence: 0.9648784

00:12:39.690 --> 00:12:41.770 The larger LPP amplitude in

NOTE Confidence: 0.9648784

00:12:41.770 --> 00:12:43.464 youth with social anxiety might

NOTE Confidence: 0.9648784

00:12:43.464 --> 00:12:45.785 indicate greater sustained attention to

NOTE Confidence: 0.9648784

00:12:45.785 --> 00:12:47.324 unsuccessful risk avoidance,

NOTE Confidence: 0.99963295

00:12:47.785 --> 00:12:49.324 supporting the view that individuals

NOTE Confidence: 0.99963295

00:12:49.464 --> 00:12:50.605 with social anxiety

NOTE Confidence: 0.99838203

00:12:50.985 --> 00:12:53.384 might exhibit attentional negativity biases

NOTE Confidence: 0.99838203

00:12:53.384 --> 00:12:54.605 to aversive stimuli.

NOTE Confidence: 0.98422134

00:12:55.670 --> 00:12:57.429 And regarding the P3, we

NOTE Confidence: 0.98422134

00:12:57.429 --> 00:12:58.550 didn't find the effect as

NOTE Confidence: 0.98422134

00:12:58.550 --> 00:13:00.009 a function of social anxiety,

NOTE Confidence: 0.98422134

00:13:00.149 --> 00:13:01.190 and so we might have

NOTE Confidence: 0.98422134

00:13:01.190 --> 00:13:02.870 found a smaller amplitude for

NOTE Confidence: 0.98422134

00:13:02.870 --> 00:13:03.370 unsuccessful

NOTE Confidence: 0.9934615

00:13:03.910 --> 00:13:05.990 relative to successful avoidance across

NOTE Confidence: 0.9934615

00:13:05.990 --> 00:13:06.970 the whole sample

NOTE Confidence: 0.99570435

00:13:07.350 --> 00:13:08.550 because of the loss of

NOTE Confidence: 0.99570435

00:13:08.550 --> 00:13:09.670 points for those with low

NOTE Confidence: 0.99570435

00:13:09.670 --> 00:13:11.050 levels of social anxiety

NOTE Confidence: 0.9703077

00:13:11.745 --> 00:13:12.945 and the loss of avoiding

NOTE Confidence: 0.9703077

00:13:12.945 --> 00:13:14.225 risk for those with high

NOTE Confidence: 0.9703077

00:13:14.225 --> 00:13:16.145 levels of social anxiety. And

NOTE Confidence: 0.9703077

00:13:16.145 --> 00:13:17.505 so for both groups, some

NOTE Confidence: 0.9703077

00:13:17.505 --> 00:13:18.945 type of loss was reflected

NOTE Confidence: 0.9703077

00:13:18.945 --> 00:13:20.405 in the reduced P three.

NOTE Confidence: 0.97310185

00:13:22.145 --> 00:13:23.585 Now second, higher levels of

NOTE Confidence: 0.97310185

00:13:23.585 --> 00:13:25.425 social anxiety were associated with

NOTE Confidence: 0.97310185

00:13:25.425 --> 00:13:27.490 mid frontal theta for successful

NOTE Confidence: 0.97310185

00:13:27.490 --> 00:13:28.950 and unsuccessful avoidance.

NOTE Confidence: 0.99394184

00:13:29.730 --> 00:13:30.929 And in youth with higher

NOTE Confidence: 0.99394184

00:13:30.929 --> 00:13:32.769 levels of social anxiety, we

NOTE Confidence: 0.99394184

00:13:32.769 --> 00:13:34.529 found this reduced mid frontal

NOTE Confidence: 0.99394184

00:13:34.529 --> 00:13:36.690 theta response in conjunction with

NOTE Confidence: 0.99394184

00:13:36.690 --> 00:13:38.709 an increased FRN response.

NOTE Confidence: 0.97274244

00:13:39.934 --> 00:13:42.335 Both responses, though, differentiated risk

NOTE Confidence: 0.97274244

00:13:42.335 --> 00:13:44.015 avoidance in youth with social

NOTE Confidence: 0.97274244

00:13:44.015 --> 00:13:44.515 anxiety,

NOTE Confidence: 0.99279547

00:13:44.895 --> 00:13:46.515 albeit in the opposite direction,

NOTE Confidence: 0.9984845

00:13:46.895 --> 00:13:48.915 highlighting the importance of contrasting

NOTE Confidence: 0.9984845

00:13:49.054 --> 00:13:50.195 oscillatory dynamics

NOTE Confidence: 0.99663186

00:13:50.655 --> 00:13:52.095 and ERPs in order to

NOTE Confidence: 0.99663186

00:13:52.095 --> 00:13:53.475 develop a more comprehensive

NOTE Confidence: 0.9984685

00:13:54.209 --> 00:13:56.370 explanation and potential biomarker for

NOTE Confidence: 0.9984685

00:13:56.370 --> 00:13:57.110 risk avoidance

NOTE Confidence: 0.9948051

00:13:57.490 --> 00:13:59.110 in socially anxious youth.

NOTE Confidence: 0.97527987

00:14:00.929 --> 00:14:02.209 And so now thinking back

NOTE Confidence: 0.97527987

00:14:02.209 --> 00:14:03.089 to the beginning of this

NOTE Confidence: 0.97527987

00:14:03.089 --> 00:14:03.589 presentation,

NOTE Confidence: 0.99506986

00:14:04.050 --> 00:14:05.250 we know that adolescence is

NOTE Confidence: 0.99506986

00:14:05.250 --> 00:14:06.629 that time of risk taking

NOTE Confidence: 0.9864247

00:14:06.965 --> 00:14:08.105 and reckless impulsivity,

NOTE Confidence: 0.9819081

00:14:08.485 --> 00:14:10.005 and these characteristics are very

NOTE Confidence: 0.9819081

00:14:10.005 --> 00:14:11.765 often associated with teen alcohol

NOTE Confidence: 0.9819081

00:14:11.765 --> 00:14:13.525 use. But what about risk

NOTE Confidence: 0.9819081

00:14:13.525 --> 00:14:15.605 avoidance and alcohol use? And

NOTE Confidence: 0.9819081

00:14:15.605 --> 00:14:16.725 so in the second study

NOTE Confidence: 0.9819081

00:14:16.725 --> 00:14:18.245 I will discuss today, we

NOTE Confidence: 0.9819081

00:14:18.245 --> 00:14:20.770 assessed risk avoidance, theta, and

NOTE Confidence: 0.9819081

00:14:20.770 --> 00:14:22.930 anxiety sensitivity as predictors of

NOTE Confidence: 0.9819081

00:14:22.930 --> 00:14:24.710 age of adolescent alcohol initiation.

NOTE Confidence: 0.9779867

00:14:26.450 --> 00:14:27.570 So a new sample of

NOTE Confidence: 0.9779867

00:14:27.570 --> 00:14:29.410 one hundred seventeen youth, thirteen

NOTE Confidence: 0.9779867

00:14:29.410 --> 00:14:30.690 to seventeen years of age,

NOTE Confidence: 0.9779867

00:14:30.690 --> 00:14:31.190 participated.

NOTE Confidence: 0.9689795

00:14:31.650 --> 00:14:32.930 They received the BRAT with

NOTE Confidence: 0.9689795

00:14:32.930 --> 00:14:34.690 concurrent EEG to assess mid

NOTE Confidence: 0.9689795

00:14:34.690 --> 00:14:36.705 frontal theta and the revised

NOTE Confidence: 0.9689795

00:14:36.765 --> 00:14:39.565 childhood anxiety sensitivity index to

NOTE Confidence: 0.9689795

00:14:39.565 --> 00:14:40.945 assess anxiety sensitivity.

NOTE Confidence: 0.98530686

00:14:42.925 --> 00:14:44.605 And so first, youth showed

NOTE Confidence: 0.98530686

00:14:44.605 --> 00:14:46.685 significantly higher mid frontal theta

NOTE Confidence: 0.98530686

00:14:46.685 --> 00:14:47.825 power for unsuccessful

NOTE Confidence: 0.9256095

00:14:48.285 --> 00:14:49.985 compared to successful avoidants.

NOTE Confidence: 0.9990266

00:14:50.780 --> 00:14:51.680 And that's demonstrated

NOTE Confidence: 0.99991864

00:14:52.060 --> 00:14:52.960 in this picture

NOTE Confidence: 0.98061275

00:14:55.100 --> 00:14:56.060 as well as in this

NOTE Confidence: 0.98061275

00:14:56.060 --> 00:14:56.560 one.

NOTE Confidence: 0.9763367

00:15:01.260 --> 00:15:02.860 And so second, lower mid

NOTE Confidence: 0.9763367

00:15:02.860 --> 00:15:05.120 frontal theta power following unsuccessful

NOTE Confidence: 0.9763367

00:15:05.340 --> 00:15:05.840 avoidance

NOTE Confidence: 0.9963955

00:15:06.175 --> 00:15:08.175 was associated with greater anxiety

NOTE Confidence: 0.9963955

00:15:08.175 --> 00:15:08.675 sensitivity,

NOTE Confidence: 0.998006

00:15:09.135 --> 00:15:10.335 but this relation was not

NOTE Confidence: 0.998006

00:15:10.335 --> 00:15:11.955 evident for successful avoidance.

NOTE Confidence: 0.98554707

00:15:14.735 --> 00:15:16.015 And finally, we found that

NOTE Confidence: 0.98554707

00:15:16.015 --> 00:15:17.935 mid frontal theta power following

NOTE Confidence: 0.98554707

00:15:17.935 --> 00:15:19.155 unsuccessful avoidance

NOTE Confidence: 0.9989571

00:15:19.720 --> 00:15:21.820 moderated the relation between anxiety

NOTE Confidence: 0.9989571

00:15:21.880 --> 00:15:22.380 sensitivity

NOTE Confidence: 0.9954933

00:15:22.920 --> 00:15:24.780 and alcohol initiation age.

NOTE Confidence: 0.99617285

00:15:25.240 --> 00:15:26.600 So those with high levels

NOTE Confidence: 0.99617285

00:15:26.600 --> 00:15:28.280 of mid frontal theta following

NOTE Confidence: 0.99617285

00:15:28.280 --> 00:15:29.420 unsuccessful avoidance

NOTE Confidence: 0.98663205

00:15:29.800 --> 00:15:31.320 showed a decrease in alcohol

NOTE Confidence: 0.98663205

00:15:31.320 --> 00:15:33.000 initiation age as their CASI

NOTE Confidence: 0.98663205

00:15:33.000 --> 00:15:33.980 scores increased.

NOTE Confidence: 0.9992458

00:15:34.305 --> 00:15:36.005 So the more anxiety sensitive,

NOTE Confidence: 0.9992458

00:15:36.145 --> 00:15:37.745 the younger the age of

NOTE Confidence: 0.9992458

00:15:37.745 --> 00:15:38.725 alcohol initiation.

NOTE Confidence: 0.986104

00:15:40.065 --> 00:15:41.745 Conversely, youth with low levels

NOTE Confidence: 0.986104

00:15:41.745 --> 00:15:43.345 of mid frontal theta following

NOTE Confidence: 0.986104

00:15:43.345 --> 00:15:44.485 unsuccessful avoidance

NOTE Confidence: 0.9977238

00:15:44.865 --> 00:15:46.464 showed an increase in alcohol

NOTE Confidence: 0.9977238

00:15:46.464 --> 00:15:48.225 initiation age as CASI scores

NOTE Confidence: 0.9977238

00:15:48.225 --> 00:15:50.000 increased. So the more anxiety

NOTE Confidence: 0.9977238

00:15:50.060 --> 00:15:51.740 sensitive here, the older the

NOTE Confidence: 0.9977238

00:15:51.740 --> 00:15:53.040 age of alcohol initiation.

NOTE Confidence: 0.9790096

00:15:57.020 --> 00:15:58.460 And so consistent with the

NOTE Confidence: 0.9790096

00:15:58.460 --> 00:16:00.300 non anxious subsample in study

NOTE Confidence: 0.9790096

00:16:00.300 --> 00:16:02.714 one, adolescents exhibited higher mid

NOTE Confidence: 0.9790096

00:16:02.714 --> 00:16:04.894 frontal theta power following unsuccessful

NOTE Confidence: 0.97725695

00:16:05.355 --> 00:16:07.035 compared to successful avoidance on

NOTE Confidence: 0.97725695

00:16:07.035 --> 00:16:07.695 the BRAT.

NOTE Confidence: 0.9972197

00:16:09.274 --> 00:16:10.875 Also consistent with the socially

NOTE Confidence: 0.9972197

00:16:10.875 --> 00:16:12.810 anxious subsample in study one,

NOTE Confidence: 0.9897698

00:16:13.290 --> 00:16:15.130 lower mid frontal theta following

NOTE Confidence: 0.9897698

00:16:15.130 --> 00:16:17.210 unsuccessful avoidance was associated with

NOTE Confidence: 0.9897698

00:16:17.210 --> 00:16:18.590 greater anxiety sensitivity.

NOTE Confidence: 0.9743685

00:16:20.250 --> 00:16:22.410 Now adolescents categorized as as

NOTE Confidence: 0.9743685

00:16:22.410 --> 00:16:24.490 exhibiting high theta power tended

NOTE Confidence: 0.9743685

00:16:24.490 --> 00:16:26.564 to initiate alcohol at earlier

NOTE Confidence: 0.9743685

00:16:26.564 --> 00:16:28.504 ages as their anxiety sensitivity

NOTE Confidence: 0.9743685

00:16:28.564 --> 00:16:29.545 scores increased.

NOTE Confidence: 0.99301606

00:16:30.245 --> 00:16:32.004 Considering this finding in conjunction

NOTE Confidence: 0.99301606

00:16:32.004 --> 00:16:33.865 with the motivational drinking model,

NOTE Confidence: 0.99301606

00:16:34.004 --> 00:16:35.865 it's possible that high anxiety

NOTE Confidence: 0.99301606

00:16:36.004 --> 00:16:36.985 sensitive individuals

NOTE Confidence: 0.99934584

00:16:37.605 --> 00:16:39.045 might initiate drinking at a

NOTE Confidence: 0.99934584

00:16:39.045 --> 00:16:40.720 younger age to cope with

NOTE Confidence: 0.99934584

00:16:40.720 --> 00:16:42.420 their elevated anxiety symptoms

NOTE Confidence: 0.95970356

00:16:43.040 --> 00:16:44.640 because it's challenging to shift

NOTE Confidence: 0.95970356

00:16:44.640 --> 00:16:46.000 to a different, perhaps more

NOTE Confidence: 0.95970356

00:16:46.000 --> 00:16:48.000 positive activity once presented with

NOTE Confidence: 0.95970356

00:16:48.000 --> 00:16:48.500 alcohol

NOTE Confidence: 0.9718034

00:16:49.040 --> 00:16:50.500 or a combination of both.

NOTE Confidence: 0.9718034

00:16:50.560 --> 00:16:51.760 So if they're drinking to

NOTE Confidence: 0.9718034

00:16:51.760 --> 00:16:53.300 cope with their anxiety sensitivity

NOTE Confidence: 0.9718034

00:16:53.440 --> 00:16:54.340 and are successful,

NOTE Confidence: 0.99952

00:16:54.915 --> 00:16:57.235 negative reinforcement supports continuation of

NOTE Confidence: 0.99952

00:16:57.235 --> 00:16:58.135 alcohol use.

NOTE Confidence: 0.96687967

00:16:59.714 --> 00:17:01.894 Now, conversely, low theta category

NOTE Confidence: 0.96687967

00:17:01.955 --> 00:17:02.455 adolescents

NOTE Confidence: 0.9756158

00:17:02.915 --> 00:17:04.355 tended to initiate at later

NOTE Confidence: 0.9756158

00:17:04.355 --> 00:17:06.295 ages as their anxiety sensitivity

NOTE Confidence: 0.9756158

00:17:06.434 --> 00:17:07.335 scores increased.

NOTE Confidence: 0.98520434

00:17:07.820 --> 00:17:09.580 And so decreased theta power

NOTE Confidence: 0.98520434

00:17:09.580 --> 00:17:11.420 might reflect an adolescent's ability

NOTE Confidence: 0.98520434

00:17:11.420 --> 00:17:12.320 to shift attention

NOTE Confidence: 0.99551

00:17:12.619 --> 00:17:14.320 from alcohol and its consequences

NOTE Confidence: 0.99207705

00:17:14.700 --> 00:17:16.160 to other goals and activities.

NOTE Confidence: 0.947952

00:17:16.540 --> 00:17:18.320 And so adolescents with greater

NOTE Confidence: 0.947952

00:17:18.380 --> 00:17:19.359 anxiety sensitivity

NOTE Confidence: 0.9913471

00:17:19.820 --> 00:17:21.340 would initiate alcohol use at

NOTE Confidence: 0.9913471

00:17:21.340 --> 00:17:22.755 a later age because they're

NOTE Confidence: 0.9913471

00:17:22.755 --> 00:17:24.275 typically more risk avoidant than

NOTE Confidence: 0.9913471

00:17:24.275 --> 00:17:25.175 their less anxiously

NOTE Confidence: 0.99652916

00:17:25.555 --> 00:17:26.615 sensitive counterparts.

NOTE Confidence: 0.9762377

00:17:28.675 --> 00:17:30.035 And so shifting gears just

NOTE Confidence: 0.9762377

00:17:30.035 --> 00:17:31.075 one more time, we'll talk

NOTE Confidence: 0.9762377

00:17:31.075 --> 00:17:32.115 a little bit about current

NOTE Confidence: 0.9762377

00:17:32.115 --> 00:17:33.234 directions. So what I'm doing

NOTE Confidence: 0.9762377

00:17:33.234 --> 00:17:34.675 right now is measuring risk

NOTE Confidence: 0.9762377

00:17:34.675 --> 00:17:36.215 avoidance in early childhood.

NOTE Confidence: 0.97753274

00:17:37.869 --> 00:17:39.630 And so critically many children

NOTE Confidence: 0.97753274

00:17:39.630 --> 00:17:41.309 show elevated anxiety and a

NOTE Confidence: 0.97753274

00:17:41.309 --> 00:17:43.309 proclivity to avoid novelty and

NOTE Confidence: 0.97753274

00:17:43.309 --> 00:17:44.770 risk very early in life.

NOTE Confidence: 0.97753274

00:17:44.990 --> 00:17:45.869 And a good number of

NOTE Confidence: 0.97753274

00:17:45.869 --> 00:17:47.070 these children might fail to

NOTE Confidence: 0.97753274

00:17:47.070 --> 00:17:48.990 actualize their potential by not

NOTE Confidence: 0.97753274

00:17:48.990 --> 00:17:50.050 taking risks interpersonally,

NOTE Confidence: 0.9858523

00:17:50.744 --> 00:17:51.945 in the classroom, or on

NOTE Confidence: 0.9858523

00:17:51.945 --> 00:17:53.545 the sports field. And so

NOTE Confidence: 0.9858523

00:17:53.545 --> 00:17:55.244 imagine if we could identify

NOTE Confidence: 0.99885035

00:17:55.625 --> 00:17:57.005 a risk avoidance proclivity

NOTE Confidence: 0.99401253

00:17:57.305 --> 00:17:58.445 earlier in life.

NOTE Confidence: 0.9370763

00:17:59.785 --> 00:18:00.984 But to date, no studies

NOTE Confidence: 0.9370763

00:18:00.984 --> 00:18:02.345 have assessed risk avoidance in

NOTE Confidence: 0.9370763

00:18:02.345 --> 00:18:03.565 preschool age children,

NOTE Confidence: 0.9986927

00:18:04.530 --> 00:18:05.810 and only two studies have

NOTE Confidence: 0.9986927

00:18:05.810 --> 00:18:06.950 assessed risk taking.

NOTE Confidence: 0.9816596

00:18:07.490 --> 00:18:08.690 And so the first study,

NOTE Confidence: 0.9816596

00:18:08.690 --> 00:18:10.070 consistent with work in adolescents

NOTE Confidence: 0.9816596

00:18:10.210 --> 00:18:12.050 and adults, shows that highly

NOTE Confidence: 0.9816596

00:18:12.050 --> 00:18:14.790 exuberant preschoolers, so characterized by

NOTE Confidence: 0.9816596

00:18:14.850 --> 00:18:16.150 more positive reactivity

NOTE Confidence: 0.9776705

00:18:16.705 --> 00:18:18.725 to novelty, greater approach behavior,

NOTE Confidence: 0.9776705

00:18:18.785 --> 00:18:19.285 sociability,

NOTE Confidence: 0.9993195

00:18:19.665 --> 00:18:21.045 they had a greater propensity

NOTE Confidence: 0.9993195

00:18:21.105 --> 00:18:22.225 for risk taking at five

NOTE Confidence: 0.9993195

00:18:22.225 --> 00:18:23.125 years of age.

NOTE Confidence: 0.93334305

00:18:24.705 --> 00:18:25.905 And not a surprise, the

NOTE Confidence: 0.93334305

00:18:25.905 --> 00:18:27.425 second study found that the

NOTE Confidence: 0.93334305

00:18:27.425 --> 00:18:30.085 anxiety related constructs behavioral inhibition,

NOTE Confidence: 0.9145725

00:18:30.470 --> 00:18:32.310 so characterized by vigilance towards

NOTE Confidence: 0.9145725

00:18:32.310 --> 00:18:34.950 novelty, heightened negative act affect,

NOTE Confidence: 0.9145725

00:18:34.950 --> 00:18:36.410 withdrawal from unfamiliar

NOTE Confidence: 0.9973934

00:18:36.790 --> 00:18:37.770 social situations

NOTE Confidence: 0.9574366

00:18:38.390 --> 00:18:39.830 was not associated with risk

NOTE Confidence: 0.9574366

00:18:39.830 --> 00:18:41.109 taking in children at four

NOTE Confidence: 0.9574366

00:18:41.109 --> 00:18:42.090 years of age.

NOTE Confidence: 0.97932714

00:18:42.390 --> 00:18:43.750 And so although these studies

NOTE Confidence: 0.97932714

00:18:43.750 --> 00:18:44.730 provide an important

NOTE Confidence: 0.9949023

00:18:45.425 --> 00:18:47.025 foundation for risk taking in

NOTE Confidence: 0.9949023

00:18:47.025 --> 00:18:49.345 children, crucial knowledge gaps remain

NOTE Confidence: 0.9949023

00:18:49.345 --> 00:18:50.645 regarding risk avoidance.

NOTE Confidence: 0.96229523

00:18:51.265 --> 00:18:52.625 And so setting the foundation

NOTE Confidence: 0.96229523

00:18:52.625 --> 00:18:54.085 for future work on developmental

NOTE Confidence: 0.96229523

00:18:54.145 --> 00:18:55.125 risk for anxiety,

NOTE Confidence: 0.9376447

00:18:55.425 --> 00:18:56.785 I received the Yale Child

NOTE Confidence: 0.9376447

00:18:56.785 --> 00:18:58.545 Study Center Trainee Pilot Research

NOTE Confidence: 0.9376447

00:18:58.545 --> 00:19:00.480 Grant to examine two aims

NOTE Confidence: 0.9376447

00:19:00.720 --> 00:19:02.960 involving the behavioral and neural

NOTE Confidence: 0.9376447

00:19:02.960 --> 00:19:04.480 indices of risk avoidance in

NOTE Confidence: 0.9376447

00:19:04.480 --> 00:19:06.020 relation to symptoms of anxiety

NOTE Confidence: 0.9376447

00:19:06.240 --> 00:19:07.840 and temperament in preschool aged

NOTE Confidence: 0.9376447

00:19:07.840 --> 00:19:08.340 children.

NOTE Confidence: 0.98793334

00:19:09.679 --> 00:19:10.640 And so this is what

NOTE Confidence: 0.98793334

00:19:10.640 --> 00:19:11.520 it looks like. So I

NOTE Confidence: 0.98793334

00:19:11.520 --> 00:19:13.040 slightly modified the BRAT by

NOTE Confidence: 0.98793334

00:19:13.040 --> 00:19:14.320 first changing the value of

NOTE Confidence: 0.98793334

00:19:14.320 --> 00:19:14.980 the balloons

NOTE Confidence: 0.99869776

00:19:15.304 --> 00:19:16.125 from numerical points

NOTE Confidence: 0.9746616

00:19:16.825 --> 00:19:18.505 to candies. And second, by

NOTE Confidence: 0.9746616

00:19:18.505 --> 00:19:19.965 exchanging the total point

NOTE Confidence: 0.9827786

00:19:20.345 --> 00:19:21.465 count with a jar that's

NOTE Confidence: 0.9827786

00:19:21.465 --> 00:19:22.984 filled with candies. And so

NOTE Confidence: 0.9827786

00:19:22.984 --> 00:19:24.664 the preschool BRAT also features

NOTE Confidence: 0.9827786

00:19:24.664 --> 00:19:26.424 more training, like, before the

NOTE Confidence: 0.9827786

00:19:26.424 --> 00:19:27.705 task in order for children

NOTE Confidence: 0.9827786

00:19:27.705 --> 00:19:29.225 to fully grasp the task

NOTE Confidence: 0.9827786

00:19:29.225 --> 00:19:30.809 at hand. And so data

NOTE Confidence: 0.9827786

00:19:30.809 --> 00:19:32.090 collection for this is currently

NOTE Confidence: 0.9827786

00:19:32.090 --> 00:19:32.590 ongoing,

NOTE Confidence: 0.9952112

00:19:32.970 --> 00:19:34.010 but I look forward to

NOTE Confidence: 0.9952112

00:19:34.010 --> 00:19:35.210 analyzing and writing it up

NOTE Confidence: 0.9952112

00:19:35.210 --> 00:19:36.650 in a manuscript as well

NOTE Confidence: 0.9952112

00:19:36.650 --> 00:19:37.850 as building on them in

NOTE Confidence: 0.9952112

00:19:37.850 --> 00:19:39.230 a future grant application.

NOTE Confidence: 0.9793006

00:19:40.970 --> 00:19:41.850 And so that's all we

NOTE Confidence: 0.9793006

00:19:41.850 --> 00:19:42.730 have time for today, and

NOTE Confidence: 0.9793006

00:19:42.730 --> 00:19:43.450 so I'd like to thank

NOTE Confidence: 0.9793006

00:19:43.450 --> 00:19:44.945 you all for listening and

NOTE Confidence: 0.9793006

00:19:44.945 --> 00:19:45.845 for your attention.

NOTE Confidence: 0.92826414

00:19:59.260 --> 00:20:00.140 Just turning it on. Here

NOTE Confidence: 0.92826414

00:20:00.140 --> 00:20:00.960 we go.

NOTE Confidence: 0.9754202

00:20:03.179 --> 00:20:04.400 Can you hear me? Okay.

NOTE Confidence: 0.8174077

00:20:05.340 --> 00:20:05.840 Questions.

NOTE Confidence: 0.8919998

00:20:06.140 --> 00:20:07.119 You have five minutes.

NOTE Confidence: 0.9790531

00:20:11.524 --> 00:20:12.644 Thank you. I just wanted

NOTE Confidence: 0.9790531

00:20:12.644 --> 00:20:14.265 to ask you about how

NOTE Confidence: 0.9790531

00:20:14.404 --> 00:20:16.585 how you determined alcohol initiation

NOTE Confidence: 0.9790531

00:20:16.804 --> 00:20:18.085 in adolescence. So was it

NOTE Confidence: 0.9790531

00:20:18.085 --> 00:20:19.044 just the first time they

NOTE Confidence: 0.9790531

00:20:19.044 --> 00:20:20.804 ever tried alcohol, or was

NOTE Confidence: 0.9790531

00:20:20.804 --> 00:20:21.684 it that they were using

NOTE Confidence: 0.9790531

00:20:21.684 --> 00:20:22.184 it

NOTE Confidence: 0.9753955

00:20:22.484 --> 00:20:23.684 more consistently? How how was

NOTE Confidence: 0.9753955

00:20:23.684 --> 00:20:25.030 that categorized? Oh, yeah. In

NOTE Confidence: 0.9753955

00:20:25.030 --> 00:20:26.310 this study, it was categorized

NOTE Confidence: 0.9753955

00:20:26.310 --> 00:20:27.450 as their first use.

NOTE Confidence: 0.98936814

00:20:32.630 --> 00:20:33.510 Thank you for a great

NOTE Confidence: 0.98936814

00:20:33.510 --> 00:20:34.010 presentation.

NOTE Confidence: 0.96804875

00:20:35.590 --> 00:20:36.630 Can you comment a little

NOTE Confidence: 0.96804875

00:20:36.630 --> 00:20:38.605 bit about the, sample of

NOTE Confidence: 0.96804875

00:20:38.605 --> 00:20:40.705 participants? Is it community volunteers

NOTE Confidence: 0.96804875

00:20:40.765 --> 00:20:42.365 or clinical sample? And if

NOTE Confidence: 0.96804875

00:20:42.365 --> 00:20:43.185 there was any,

NOTE Confidence: 0.891477

00:20:44.445 --> 00:20:45.805 medication that they would take

NOTE Confidence: 0.891477

00:20:45.805 --> 00:20:47.185 in a co occurring disorders

NOTE Confidence: 0.891477

00:20:47.244 --> 00:20:48.305 that were recorded?

NOTE Confidence: 0.9964978

00:20:49.340 --> 00:20:50.540 Yeah. So both of these

NOTE Confidence: 0.9964978

00:20:50.540 --> 00:20:51.359 were community

NOTE Confidence: 0.99707496

00:20:51.900 --> 00:20:52.400 based

NOTE Confidence: 0.97280705

00:20:52.700 --> 00:20:54.800 samples. So we recruited by,

NOTE Confidence: 0.97280705

00:20:54.940 --> 00:20:56.400 like, a mass mail out.

NOTE Confidence: 0.94966614

00:21:02.665 --> 00:21:03.465 Thank you, Ellie. That was

NOTE Confidence: 0.94966614

00:21:03.465 --> 00:21:05.385 an incredibly clear presentation. And

NOTE Confidence: 0.94966614

00:21:05.385 --> 00:21:06.744 either of the institutions that

NOTE Confidence: 0.94966614

00:21:06.744 --> 00:21:07.465 have given you a job

NOTE Confidence: 0.94966614

00:21:07.465 --> 00:21:08.345 offer will be lucky to

NOTE Confidence: 0.94966614

00:21:08.345 --> 00:21:09.005 have you.

NOTE Confidence: 0.9225752

00:21:09.625 --> 00:21:11.225 I so, in terms of

NOTE Confidence: 0.9225752

00:21:11.305 --> 00:21:12.265 I think you're you're getting

NOTE Confidence: 0.9225752

00:21:12.265 --> 00:21:13.225 to this in the last

NOTE Confidence: 0.9225752

00:21:13.225 --> 00:21:15.065 pilot study. Is there what's

NOTE Confidence: 0.9225752

00:21:15.065 --> 00:21:16.840 known about developmental change in

NOTE Confidence: 0.9225752

00:21:16.840 --> 00:21:18.859 theta power and the oscillatory

NOTE Confidence: 0.9225752

00:21:19.080 --> 00:21:20.359 dynamics that you mentioned that

NOTE Confidence: 0.9225752

00:21:20.440 --> 00:21:21.720 in your introduction? Does that

NOTE Confidence: 0.9225752

00:21:21.720 --> 00:21:23.720 show developmental change from childhood

NOTE Confidence: 0.9225752

00:21:23.720 --> 00:21:24.299 to adolescence?

NOTE Confidence: 0.9946789

00:21:25.480 --> 00:21:26.760 That's a very good question,

NOTE Confidence: 0.9946789

00:21:26.760 --> 00:21:27.799 and I have not yet

NOTE Confidence: 0.9946789

00:21:27.799 --> 00:21:29.065 looked into that. But that's

NOTE Confidence: 0.9946789

00:21:29.065 --> 00:21:29.945 something I would like to

NOTE Confidence: 0.9946789

00:21:29.945 --> 00:21:31.225 look into in the future

NOTE Confidence: 0.9946789

00:21:31.225 --> 00:21:32.765 as I connect these

NOTE Confidence: 0.9997482

00:21:33.385 --> 00:21:33.885 different

NOTE Confidence: 0.9743412

00:21:34.425 --> 00:21:36.265 areas of development. And it

NOTE Confidence: 0.9743412

00:21:36.265 --> 00:21:37.225 sounds like that data that

NOTE Confidence: 0.9743412

00:21:37.225 --> 00:21:38.185 you'll generate in your last

NOTE Confidence: 0.9743412

00:21:38.185 --> 00:21:39.065 study will help you do

NOTE Confidence: 0.9743412

00:21:39.065 --> 00:21:39.965 that. Yeah.

NOTE Confidence: 0.36596593

00:21:42.100 --> 00:21:42.600 Anyone

NOTE Confidence: 0.98876595

00:21:42.980 --> 00:21:44.580 else? Well, thank you, Ellie.

NOTE Confidence: 0.98876595

00:21:44.580 --> 00:21:45.960 Nice job. Thank you.

NOTE Confidence: 0.8363107

00:21:51.059 --> 00:21:52.759 Without further ado, doctor DeAndoio.

NOTE Confidence: 0.9986323

00:22:10.350 --> 00:22:12.350 Okay. So I'm gonna change

NOTE Confidence: 0.9986323

00:22:12.350 --> 00:22:13.890 gears pretty drastically.

NOTE Confidence: 0.7907672

00:22:15.390 --> 00:22:16.990 I'm a postdoc in Kathak

NOTE Confidence: 0.7907672

00:22:16.990 --> 00:22:18.530 Patapi Raman in the labs,

NOTE Confidence: 0.98616326

00:22:18.910 --> 00:22:19.970 and so we don't

NOTE Confidence: 0.9741937

00:22:20.270 --> 00:22:21.630 really see patients. We don't

NOTE Confidence: 0.9741937

00:22:21.630 --> 00:22:22.510 do a lot with human

NOTE Confidence: 0.9741937

00:22:22.510 --> 00:22:24.095 work. But I wanna point

NOTE Confidence: 0.9741937

00:22:24.095 --> 00:22:25.135 out at the beginning that

NOTE Confidence: 0.9741937

00:22:25.135 --> 00:22:26.755 Ellie brought up these different

NOTE Confidence: 0.9741937

00:22:26.815 --> 00:22:27.875 circuits or

NOTE Confidence: 0.9927691

00:22:28.175 --> 00:22:30.255 kind of connectivity responses that

NOTE Confidence: 0.9927691

00:22:30.255 --> 00:22:30.915 are important

NOTE Confidence: 0.9948071

00:22:31.695 --> 00:22:33.315 for risk avoidance or,

NOTE Confidence: 0.9769575

00:22:34.015 --> 00:22:36.115 alcohol initiation, these different factors.

NOTE Confidence: 0.9846912

00:22:36.655 --> 00:22:38.280 And we wanna understand how

NOTE Confidence: 0.9846912

00:22:38.359 --> 00:22:39.800 the development of those circuits

NOTE Confidence: 0.9846912

00:22:39.800 --> 00:22:41.420 occurs kind of throughout

NOTE Confidence: 0.9525734

00:22:42.520 --> 00:22:44.040 throughout life as well as

NOTE Confidence: 0.9525734

00:22:44.040 --> 00:22:45.720 especially during early development. And

NOTE Confidence: 0.9525734

00:22:45.720 --> 00:22:46.220 so

NOTE Confidence: 0.9810133

00:22:46.760 --> 00:22:47.640 not only how do they

NOTE Confidence: 0.9810133

00:22:47.640 --> 00:22:48.600 function, but how do they

NOTE Confidence: 0.9810133

00:22:48.600 --> 00:22:49.820 form in the first place?

NOTE Confidence: 0.99665177

00:22:50.600 --> 00:22:51.340 And so

NOTE Confidence: 0.9631804

00:22:53.045 --> 00:22:54.725 in Katak and Anad's labs,

NOTE Confidence: 0.9631804

00:22:54.725 --> 00:22:56.165 we're interested in the development

NOTE Confidence: 0.9631804

00:22:56.165 --> 00:22:57.525 of the cerebral cortex. Right?

NOTE Confidence: 0.9631804

00:22:57.525 --> 00:22:58.725 This is the outermost part

NOTE Confidence: 0.9631804

00:22:58.725 --> 00:22:59.684 of the brain, kind of

NOTE Confidence: 0.9631804

00:22:59.684 --> 00:23:01.465 the bark, and it's essential

NOTE Confidence: 0.9631804

00:23:01.605 --> 00:23:03.285 for our conscious thoughts, actions,

NOTE Confidence: 0.9631804

00:23:03.285 --> 00:23:04.025 and perceptions.

NOTE Confidence: 0.97669

00:23:04.609 --> 00:23:05.810 And this cortex is a

NOTE Confidence: 0.97669

00:23:05.810 --> 00:23:08.050 laminated structure. It's conveniently split

NOTE Confidence: 0.97669

00:23:08.050 --> 00:23:09.750 into six individual layers

NOTE Confidence: 0.9935473

00:23:10.050 --> 00:23:12.130 with unique molecular identities and

NOTE Confidence: 0.9935473

00:23:12.130 --> 00:23:12.950 unique connectivities.

NOTE Confidence: 0.9601823

00:23:13.970 --> 00:23:15.650 So the upper layers, just

NOTE Confidence: 0.9601823

00:23:15.650 --> 00:23:16.950 layers two through four,

NOTE Confidence: 0.9745941

00:23:17.365 --> 00:23:19.044 send projections largely within the

NOTE Confidence: 0.9745941

00:23:19.044 --> 00:23:19.544 cortex.

NOTE Confidence: 0.98376375

00:23:19.845 --> 00:23:20.804 They could be within the

NOTE Confidence: 0.98376375

00:23:20.804 --> 00:23:22.085 same hemisphere or across the

NOTE Confidence: 0.98376375

00:23:22.085 --> 00:23:23.445 midline through structures like the

NOTE Confidence: 0.98376375

00:23:23.445 --> 00:23:24.345 corpus callosum

NOTE Confidence: 0.99176484

00:23:24.725 --> 00:23:26.164 to help integrate and process

NOTE Confidence: 0.99176484

00:23:26.164 --> 00:23:26.664 information.

NOTE Confidence: 0.95250314

00:23:27.445 --> 00:23:28.804 And by contrast, the deep

NOTE Confidence: 0.95250314

00:23:28.804 --> 00:23:30.244 layers here in red and

NOTE Confidence: 0.95250314

00:23:30.244 --> 00:23:32.024 green, layers five and six,

NOTE Confidence: 0.9926264

00:23:32.390 --> 00:23:33.750 send their projections largely out

NOTE Confidence: 0.9926264

00:23:33.750 --> 00:23:35.130 of the cortex to subcortical

NOTE Confidence: 0.9926264

00:23:35.270 --> 00:23:36.550 structures in the thalamus or

NOTE Confidence: 0.9926264

00:23:36.550 --> 00:23:37.590 in the spinal cord to

NOTE Confidence: 0.9926264

00:23:37.590 --> 00:23:38.970 help control movement.

NOTE Confidence: 0.9996549

00:23:39.510 --> 00:23:40.970 And these layers are situated

NOTE Confidence: 0.99704087

00:23:41.510 --> 00:23:42.470 right in the middle of

NOTE Confidence: 0.99704087

00:23:42.470 --> 00:23:43.610 the cortex between

NOTE Confidence: 0.9295601

00:23:44.150 --> 00:23:45.350 the deep most part, the

NOTE Confidence: 0.9295601

00:23:45.350 --> 00:23:47.234 subplate, and the top most

NOTE Confidence: 0.9295601

00:23:47.234 --> 00:23:48.835 part, the marginal zone or

NOTE Confidence: 0.9295601

00:23:48.835 --> 00:23:49.655 layer one.

NOTE Confidence: 0.9973936

00:23:50.435 --> 00:23:52.515 And despite these diverse neuronal

NOTE Confidence: 0.9973936

00:23:52.515 --> 00:23:54.215 identities and projection types,

NOTE Confidence: 0.9883834

00:23:54.835 --> 00:23:56.035 these neurons are all actually

NOTE Confidence: 0.9883834

00:23:56.035 --> 00:23:57.234 generated from the same pool

NOTE Confidence: 0.9883834

00:23:57.234 --> 00:23:58.855 of neural progenitor cells.

NOTE Confidence: 0.9490047

00:23:59.419 --> 00:24:00.960 This happens in a sequential

NOTE Confidence: 0.9490047

00:24:01.100 --> 00:24:02.859 inside out manner generally and

NOTE Confidence: 0.9490047

00:24:02.859 --> 00:24:04.240 begins with the deep layers,

NOTE Confidence: 0.9490047

00:24:04.460 --> 00:24:06.380 subplate six five, and then

NOTE Confidence: 0.9490047

00:24:06.380 --> 00:24:07.820 continues to the upper layers

NOTE Confidence: 0.9490047

00:24:07.820 --> 00:24:08.799 four two three

NOTE Confidence: 0.99859065

00:24:09.260 --> 00:24:10.400 four three two.

NOTE Confidence: 0.8818165

00:24:10.859 --> 00:24:11.600 And so,

NOTE Confidence: 0.98065877

00:24:12.335 --> 00:24:14.175 generally, our labs are interested

NOTE Confidence: 0.98065877

00:24:14.175 --> 00:24:16.275 in three main questions. First,

NOTE Confidence: 0.98065877

00:24:16.335 --> 00:24:17.295 and one that I'll not

NOTE Confidence: 0.98065877

00:24:17.295 --> 00:24:18.734 really focus on today, is

NOTE Confidence: 0.98065877

00:24:18.734 --> 00:24:19.935 how are all of these

NOTE Confidence: 0.98065877

00:24:19.935 --> 00:24:21.715 distinct neuronal types are generated

NOTE Confidence: 0.98065877

00:24:21.775 --> 00:24:22.655 from the same pool of

NOTE Confidence: 0.98065877

00:24:22.655 --> 00:24:23.155 progenitors?

NOTE Confidence: 0.9896747

00:24:24.109 --> 00:24:25.710 Second, how they ultimately wire

NOTE Confidence: 0.9896747

00:24:25.710 --> 00:24:27.230 together to form brain circuits

NOTE Confidence: 0.9896747

00:24:27.230 --> 00:24:27.950 and how they end up

NOTE Confidence: 0.9896747

00:24:27.950 --> 00:24:29.150 being functional in the long

NOTE Confidence: 0.9896747

00:24:29.150 --> 00:24:29.650 run.

NOTE Confidence: 0.9815436

00:24:30.190 --> 00:24:32.030 And then third, what aspects

NOTE Confidence: 0.9815436

00:24:32.030 --> 00:24:33.630 of these processes are altered

NOTE Confidence: 0.9815436

00:24:33.630 --> 00:24:34.830 in humans, and how can

NOTE Confidence: 0.9815436

00:24:34.830 --> 00:24:36.130 they contribute to neurodevelopmental

NOTE Confidence: 0.78030473

00:24:36.590 --> 00:24:37.090 disorders.

NOTE Confidence: 0.99420226

00:24:39.055 --> 00:24:39.695 And so

NOTE Confidence: 0.7888956

00:24:40.895 --> 00:24:41.395 oh,

NOTE Confidence: 0.9366714

00:24:43.695 --> 00:24:44.575 so here we can see

NOTE Confidence: 0.9366714

00:24:44.575 --> 00:24:45.455 kind of an example of

NOTE Confidence: 0.9366714

00:24:45.455 --> 00:24:47.075 their different molecular identities.

NOTE Confidence: 0.9907589

00:24:47.455 --> 00:24:48.655 Just like the schematic, you

NOTE Confidence: 0.9907589

00:24:48.655 --> 00:24:50.015 can see the subplate here

NOTE Confidence: 0.9907589

00:24:50.015 --> 00:24:51.855 in purple, layer six in

NOTE Confidence: 0.9907589

00:24:51.855 --> 00:24:52.355 green,

NOTE Confidence: 0.9906377

00:24:52.669 --> 00:24:54.029 layer five in red, two

NOTE Confidence: 0.9906377

00:24:54.029 --> 00:24:54.990 through four in blue, and

NOTE Confidence: 0.9906377

00:24:54.990 --> 00:24:56.429 then one in kind of

NOTE Confidence: 0.9906377

00:24:56.429 --> 00:24:56.929 brown.

NOTE Confidence: 0.9500159

00:24:58.669 --> 00:24:59.789 But I first wanna highlight

NOTE Confidence: 0.9500159

00:24:59.789 --> 00:25:01.150 a couple examples of why

NOTE Confidence: 0.9500159

00:25:01.150 --> 00:25:02.690 this is relevant for understanding

NOTE Confidence: 0.9500159

00:25:02.750 --> 00:25:04.270 the human condition. So we

NOTE Confidence: 0.9500159

00:25:04.270 --> 00:25:05.470 focus on a layer six

NOTE Confidence: 0.9500159

00:25:05.470 --> 00:25:06.990 marker, TBR one, here in

NOTE Confidence: 0.9500159

00:25:06.990 --> 00:25:07.490 green.

NOTE Confidence: 0.9811724

00:25:08.115 --> 00:25:09.475 Its role in brain development

NOTE Confidence: 0.9811724

00:25:09.475 --> 00:25:10.755 is pretty well studied over

NOTE Confidence: 0.9811724

00:25:10.755 --> 00:25:12.435 the past twenty or so

NOTE Confidence: 0.9811724

00:25:12.435 --> 00:25:12.935 years,

NOTE Confidence: 0.99643373

00:25:13.955 --> 00:25:15.234 both here at Yale and

NOTE Confidence: 0.99643373

00:25:15.234 --> 00:25:15.734 outside.

NOTE Confidence: 0.99636704

00:25:16.275 --> 00:25:17.795 And so mutations in TBR

NOTE Confidence: 0.99636704

00:25:17.795 --> 00:25:19.575 one are associated with intellectual

NOTE Confidence: 0.99636704

00:25:19.795 --> 00:25:21.715 developmental disorder and autism with

NOTE Confidence: 0.99636704

00:25:21.715 --> 00:25:22.535 speech delay.

NOTE Confidence: 0.9674429

00:25:22.915 --> 00:25:24.260 And here you can see

NOTE Confidence: 0.9674429

00:25:24.260 --> 00:25:25.940 two different t one weighted

NOTE Confidence: 0.9674429

00:25:25.940 --> 00:25:26.440 MRIs

NOTE Confidence: 0.9889467

00:25:26.899 --> 00:25:28.419 from different patients, both of

NOTE Confidence: 0.9889467

00:25:28.419 --> 00:25:30.440 whom have frontal pachygyria.

NOTE Confidence: 0.9921807

00:25:31.700 --> 00:25:33.140 And while we can see

NOTE Confidence: 0.9921807

00:25:33.140 --> 00:25:34.820 these alterations in human data,

NOTE Confidence: 0.9921807

00:25:34.820 --> 00:25:36.020 it can be really difficult

NOTE Confidence: 0.9921807

00:25:36.020 --> 00:25:37.035 to kind of get a

NOTE Confidence: 0.9921807

00:25:37.035 --> 00:25:38.555 deeper understanding of what's going

NOTE Confidence: 0.9921807

00:25:38.555 --> 00:25:40.255 on, what causes these different

NOTE Confidence: 0.9921807

00:25:40.315 --> 00:25:40.815 phenotypes.

NOTE Confidence: 0.9985824

00:25:41.515 --> 00:25:42.335 And so

NOTE Confidence: 0.97363573

00:25:42.875 --> 00:25:43.835 to get at that, we

NOTE Confidence: 0.97363573

00:25:43.835 --> 00:25:44.815 turn to mice.

NOTE Confidence: 0.9854601

00:25:45.994 --> 00:25:47.615 So luckily, we have exceptional

NOTE Confidence: 0.9854601

00:25:47.675 --> 00:25:48.955 mouse genetic tools that can

NOTE Confidence: 0.9854601

00:25:48.955 --> 00:25:50.235 help us understand the different

NOTE Confidence: 0.9854601

00:25:50.235 --> 00:25:52.420 molecular bases of typical and

NOTE Confidence: 0.9854601

00:25:52.420 --> 00:25:53.640 divergent brain development.

NOTE Confidence: 0.98695624

00:25:54.020 --> 00:25:55.060 And so here in the

NOTE Confidence: 0.98695624

00:25:55.060 --> 00:25:56.260 bottom, this is now a

NOTE Confidence: 0.98695624

00:25:56.260 --> 00:25:57.400 mouse brain. So

NOTE Confidence: 0.9431392

00:25:58.260 --> 00:25:59.780 mice have smooth brains. They

NOTE Confidence: 0.9431392

00:25:59.780 --> 00:26:01.160 don't have psoas or gyri.

NOTE Confidence: 0.981969

00:26:02.260 --> 00:26:03.300 And here in green, you

NOTE Confidence: 0.981969

00:26:03.300 --> 00:26:04.500 can see a coronal section

NOTE Confidence: 0.981969

00:26:04.500 --> 00:26:05.619 in which we have projections

NOTE Confidence: 0.981969

00:26:05.619 --> 00:26:06.900 from the thumb from the

NOTE Confidence: 0.981969

00:26:06.900 --> 00:26:07.400 cortex

NOTE Confidence: 0.9775038

00:26:08.155 --> 00:26:09.535 up around into the thalamus,

NOTE Confidence: 0.9917824

00:26:09.994 --> 00:26:11.355 and a sagittal section where

NOTE Confidence: 0.9917824

00:26:11.355 --> 00:26:12.475 we don't yet have much

NOTE Confidence: 0.9917824

00:26:12.475 --> 00:26:12.975 innervation

NOTE Confidence: 0.9973939

00:26:13.595 --> 00:26:14.795 down into the midbrain and

NOTE Confidence: 0.9973939

00:26:14.795 --> 00:26:16.095 through the cerebral peduncles.

NOTE Confidence: 0.9722019

00:26:17.115 --> 00:26:18.234 And, normally, this is what

NOTE Confidence: 0.9722019

00:26:18.234 --> 00:26:19.115 we would see at this

NOTE Confidence: 0.9722019

00:26:19.115 --> 00:26:19.615 stage.

NOTE Confidence: 0.9859103

00:26:19.915 --> 00:26:20.715 But if we were to

NOTE Confidence: 0.9859103

00:26:20.715 --> 00:26:21.994 take away TBR one from

NOTE Confidence: 0.9859103

00:26:21.994 --> 00:26:23.115 these mice, you can see

NOTE Confidence: 0.9859103

00:26:23.115 --> 00:26:23.855 on the bottom,

NOTE Confidence: 0.9973829

00:26:25.490 --> 00:26:27.109 the connections are altered drastically.

NOTE Confidence: 0.9973829

00:26:27.169 --> 00:26:28.770 So instead of projections going

NOTE Confidence: 0.9973829

00:26:28.770 --> 00:26:29.809 from the cortex to the

NOTE Confidence: 0.9973829

00:26:29.809 --> 00:26:30.309 thalamus,

NOTE Confidence: 0.97997534

00:26:30.609 --> 00:26:32.470 they dive more ventrally towards

NOTE Confidence: 0.97997534

00:26:32.530 --> 00:26:33.270 the hypothalamus.

NOTE Confidence: 0.9977174

00:26:34.369 --> 00:26:36.210 And there's also exuberant outgrowth

NOTE Confidence: 0.9977174

00:26:36.210 --> 00:26:37.490 of these projections into the

NOTE Confidence: 0.9977174

00:26:37.490 --> 00:26:39.030 midbrain and cerebral peduncles.

NOTE Confidence: 0.9956183

00:26:40.315 --> 00:26:41.515 And so using these tools,

NOTE Confidence: 0.9956183

00:26:41.515 --> 00:26:42.235 we're able to get a

NOTE Confidence: 0.9956183

00:26:42.235 --> 00:26:43.994 better understanding of how developing

NOTE Confidence: 0.9956183

00:26:43.994 --> 00:26:45.994 circuits are altered following gene

NOTE Confidence: 0.9956183

00:26:45.994 --> 00:26:47.375 mutations seen in patients.

NOTE Confidence: 0.9725885

00:26:47.675 --> 00:26:48.875 We're kind of able to

NOTE Confidence: 0.9725885

00:26:48.875 --> 00:26:50.255 fine tune this and say,

NOTE Confidence: 0.9725885

00:26:50.315 --> 00:26:51.675 okay, in this scenario, we

NOTE Confidence: 0.9725885

00:26:51.675 --> 00:26:52.955 took out the entirety of

NOTE Confidence: 0.9725885

00:26:52.955 --> 00:26:54.480 the TBR one gene. This

NOTE Confidence: 0.9725885

00:26:54.480 --> 00:26:55.559 is not always the case

NOTE Confidence: 0.9725885

00:26:55.559 --> 00:26:56.760 in human patients. They may

NOTE Confidence: 0.9725885

00:26:56.760 --> 00:26:58.359 have a frame shift or

NOTE Confidence: 0.9725885

00:26:58.359 --> 00:26:59.900 a partially functional protein.

NOTE Confidence: 0.99895906

00:27:00.440 --> 00:27:01.880 And so we're able to

NOTE Confidence: 0.99895906

00:27:01.880 --> 00:27:03.320 adjust our mice to get

NOTE Confidence: 0.99895906

00:27:03.320 --> 00:27:04.359 a sense of those different

NOTE Confidence: 0.99895906

00:27:04.359 --> 00:27:05.640 changes as well. And for

NOTE Confidence: 0.99895906

00:27:05.640 --> 00:27:07.000 TBR one, for example, this

NOTE Confidence: 0.99895906

00:27:07.000 --> 00:27:08.220 has been done by

NOTE Confidence: 0.97664887

00:27:08.595 --> 00:27:10.355 Brian O'Rourke and Kevin Wright's

NOTE Confidence: 0.97664887

00:27:10.355 --> 00:27:11.575 groups in Oregon,

NOTE Confidence: 0.9806611

00:27:12.434 --> 00:27:14.135 to study different patient mutations

NOTE Confidence: 0.9806611

00:27:14.275 --> 00:27:15.715 of TBR one to look

NOTE Confidence: 0.9806611

00:27:15.715 --> 00:27:16.695 at circuit connectivity.

NOTE Confidence: 0.9714099

00:27:18.674 --> 00:27:19.554 And then one of the

NOTE Confidence: 0.9714099

00:27:19.554 --> 00:27:21.119 most obvious and drastic cases

NOTE Confidence: 0.9714099

00:27:21.119 --> 00:27:22.560 in which studying these genes

NOTE Confidence: 0.9714099

00:27:22.560 --> 00:27:24.240 has been informative is mutations

NOTE Confidence: 0.9714099

00:27:24.240 --> 00:27:25.760 in the Rheeland gene. So

NOTE Confidence: 0.9714099

00:27:25.760 --> 00:27:27.760 Rheeland is expressed largely in

NOTE Confidence: 0.9714099

00:27:27.760 --> 00:27:29.460 layer one marginal zone neurons,

NOTE Confidence: 0.9354916

00:27:29.920 --> 00:27:31.280 but mutations in this gene

NOTE Confidence: 0.9354916

00:27:31.280 --> 00:27:33.040 are associated with Norman Roberts

NOTE Confidence: 0.9354916

00:27:33.040 --> 00:27:34.980 syndrome, which also has lysencephaly.

NOTE Confidence: 0.8889012

00:27:35.280 --> 00:27:36.420 You can see pretty much

NOTE Confidence: 0.8889012

00:27:36.635 --> 00:27:37.455 smooth brain,

NOTE Confidence: 0.97943294

00:27:39.035 --> 00:27:40.635 and altered lamination of the

NOTE Confidence: 0.97943294

00:27:40.635 --> 00:27:41.835 cortex. So the layers are

NOTE Confidence: 0.97943294

00:27:41.835 --> 00:27:43.435 actually in the opposite order

NOTE Confidence: 0.97943294

00:27:43.435 --> 00:27:44.494 that we would expect.

NOTE Confidence: 0.92974627

00:27:45.195 --> 00:27:46.895 But at first, our understanding

NOTE Confidence: 0.92974627

00:27:47.115 --> 00:27:48.635 of the real end function

NOTE Confidence: 0.92974627

00:27:48.635 --> 00:27:49.755 might be hampered by using

NOTE Confidence: 0.92974627

00:27:49.755 --> 00:27:51.455 mice because they're normally lysencephalic.

NOTE Confidence: 0.9986534

00:27:52.270 --> 00:27:53.630 So lysencephaly is not a

NOTE Confidence: 0.9986534

00:27:53.630 --> 00:27:54.830 phenotype that we can observe

NOTE Confidence: 0.9986534

00:27:54.830 --> 00:27:55.490 in them.

NOTE Confidence: 0.99413997

00:27:56.590 --> 00:27:57.950 However, if we look at

NOTE Confidence: 0.99413997

00:27:57.950 --> 00:27:59.550 DTI data from a control

NOTE Confidence: 0.99413997

00:27:59.550 --> 00:28:00.850 mouse here on the left,

NOTE Confidence: 0.9920669

00:28:01.869 --> 00:28:03.010 you can see thalamocortical

NOTE Confidence: 0.98100054

00:28:03.390 --> 00:28:05.070 projections here in green. They

NOTE Confidence: 0.98100054

00:28:05.070 --> 00:28:06.965 enter the cortex, then they

NOTE Confidence: 0.98100054

00:28:06.965 --> 00:28:08.505 kind of organize into these

NOTE Confidence: 0.84965956

00:28:08.885 --> 00:28:09.705 discrete structures.

NOTE Confidence: 0.98978806

00:28:10.325 --> 00:28:11.225 By contrast,

NOTE Confidence: 0.99872714

00:28:11.605 --> 00:28:12.265 if we

NOTE Confidence: 0.80945957

00:28:12.805 --> 00:28:14.025 delete the real engine,

NOTE Confidence: 0.9963123

00:28:14.565 --> 00:28:15.945 alter the cortical lamination,

NOTE Confidence: 0.93424237

00:28:16.405 --> 00:28:17.145 these thalamocortical

NOTE Confidence: 0.96417916

00:28:17.445 --> 00:28:19.285 projections no longer organize into

NOTE Confidence: 0.96417916

00:28:19.285 --> 00:28:20.310 their discrete structures.

NOTE Confidence: 0.98586255

00:28:23.030 --> 00:28:24.310 And these examples kind of

NOTE Confidence: 0.98586255

00:28:24.310 --> 00:28:25.750 illustrate that we can effectively

NOTE Confidence: 0.98586255

00:28:25.750 --> 00:28:26.550 use mice to get a

NOTE Confidence: 0.98586255

00:28:26.550 --> 00:28:28.150 much deeper understanding of circuit

NOTE Confidence: 0.98586255

00:28:28.150 --> 00:28:29.670 development and the alterations that

NOTE Confidence: 0.98586255

00:28:29.670 --> 00:28:31.450 may occur in brain disorders.

NOTE Confidence: 0.9918851

00:28:32.150 --> 00:28:34.070 But thalamocortical connectivity is a

NOTE Confidence: 0.9918851

00:28:34.070 --> 00:28:35.515 great example for that because

NOTE Confidence: 0.9918851

00:28:35.515 --> 00:28:36.635 as these signals are sent

NOTE Confidence: 0.9918851

00:28:36.635 --> 00:28:37.595 from the thalamus to the

NOTE Confidence: 0.9918851

00:28:37.595 --> 00:28:39.355 cortex, they're often important for

NOTE Confidence: 0.9918851

00:28:39.355 --> 00:28:41.275 sensory processing and often altered

NOTE Confidence: 0.9918851

00:28:41.275 --> 00:28:42.815 in neurodevelopmental disorders.

NOTE Confidence: 0.985264

00:28:43.355 --> 00:28:44.554 So seeing how they're really

NOTE Confidence: 0.985264

00:28:44.554 --> 00:28:45.595 changing can help us get

NOTE Confidence: 0.985264

00:28:45.595 --> 00:28:47.115 a better sense of of

NOTE Confidence: 0.985264

00:28:47.115 --> 00:28:48.315 the connections that we may

NOTE Confidence: 0.985264

00:28:48.315 --> 00:28:50.119 be seeing, and maybe it's

NOTE Confidence: 0.985264

00:28:50.119 --> 00:28:51.580 EEG or something else.

NOTE Confidence: 0.9560026

00:28:53.480 --> 00:28:55.399 And so thalamic cortical projections

NOTE Confidence: 0.9560026

00:28:55.399 --> 00:28:57.179 follow a very stereotype developmental

NOTE Confidence: 0.9560026

00:28:57.320 --> 00:28:59.000 trajectory. These ages at the

NOTE Confidence: 0.9560026

00:28:59.000 --> 00:29:00.940 top, you can ignore unless

NOTE Confidence: 0.97834593

00:29:01.240 --> 00:29:02.440 you wanna know about mouse

NOTE Confidence: 0.97834593

00:29:02.440 --> 00:29:03.340 ages. But,

NOTE Confidence: 0.9685489

00:29:04.945 --> 00:29:05.985 initially, they grow out of

NOTE Confidence: 0.9685489

00:29:05.985 --> 00:29:07.345 the thalamus here in magenta

NOTE Confidence: 0.9685489

00:29:07.345 --> 00:29:08.965 and into the developing striatum.

NOTE Confidence: 0.9809548

00:29:09.665 --> 00:29:10.785 They then reach into the

NOTE Confidence: 0.9809548

00:29:10.785 --> 00:29:12.065 cortex, and they wait there,

NOTE Confidence: 0.9809548

00:29:12.065 --> 00:29:13.265 and they kind of they

NOTE Confidence: 0.9809548

00:29:13.265 --> 00:29:14.225 go through what's called a

NOTE Confidence: 0.9809548

00:29:14.225 --> 00:29:15.425 waiting period. It's been really

NOTE Confidence: 0.9809548

00:29:15.425 --> 00:29:16.245 well described,

NOTE Confidence: 0.99965364

00:29:16.945 --> 00:29:17.845 for the last

NOTE Confidence: 0.9428574

00:29:18.500 --> 00:29:19.880 thirty to forty years,

NOTE Confidence: 0.98279995

00:29:20.980 --> 00:29:21.940 while they wait for their

NOTE Confidence: 0.98279995

00:29:21.940 --> 00:29:23.060 layer four targets to be

NOTE Confidence: 0.98279995

00:29:23.060 --> 00:29:24.420 born and migrate. So they

NOTE Confidence: 0.98279995

00:29:24.420 --> 00:29:25.860 have nothing to connect with

NOTE Confidence: 0.98279995

00:29:25.860 --> 00:29:26.600 at this point.

NOTE Confidence: 0.96104753

00:29:27.140 --> 00:29:28.340 They later grow into the

NOTE Confidence: 0.96104753

00:29:28.340 --> 00:29:30.100 cortex and then finally they

NOTE Confidence: 0.96104753

00:29:30.100 --> 00:29:32.020 organize into discrete structures. So

NOTE Confidence: 0.96104753

00:29:32.020 --> 00:29:33.355 in the mouse, an example

NOTE Confidence: 0.96104753

00:29:33.355 --> 00:29:34.395 of this are the whisker

NOTE Confidence: 0.96104753

00:29:34.395 --> 00:29:34.895 barrels.

NOTE Confidence: 0.9959581

00:29:35.275 --> 00:29:36.955 This organization corresponds to the

NOTE Confidence: 0.9959581

00:29:36.955 --> 00:29:38.395 sensory information from each of

NOTE Confidence: 0.9959581

00:29:38.395 --> 00:29:39.835 the mouse's whiskers. So we

NOTE Confidence: 0.9959581

00:29:39.835 --> 00:29:41.674 know exactly what location corresponds

NOTE Confidence: 0.9959581

00:29:41.674 --> 00:29:42.715 to which whisker on their

NOTE Confidence: 0.9959581

00:29:42.715 --> 00:29:43.215 face.

NOTE Confidence: 0.9974353

00:29:43.835 --> 00:29:44.335 But

NOTE Confidence: 0.9815228

00:29:44.955 --> 00:29:45.835 why do we care so

NOTE Confidence: 0.9815228

00:29:45.835 --> 00:29:47.054 much about thalamocortical

NOTE Confidence: 0.98678565

00:29:47.434 --> 00:29:47.934 connections?

NOTE Confidence: 0.96486074

00:29:48.840 --> 00:29:50.280 And so the thalamus sends

NOTE Confidence: 0.96486074

00:29:50.280 --> 00:29:51.559 projections to a variety of

NOTE Confidence: 0.96486074

00:29:51.559 --> 00:29:53.480 cortical regions, including the prefrontal

NOTE Confidence: 0.96486074

00:29:53.480 --> 00:29:55.179 cortex that Ali brought up,

NOTE Confidence: 0.8885231

00:29:55.640 --> 00:29:57.419 somatomotor regions, and more.

NOTE Confidence: 0.9706633

00:29:57.720 --> 00:29:59.400 And these connections are altered,

NOTE Confidence: 0.9706633

00:29:59.400 --> 00:30:00.840 both increase and decrease in

NOTE Confidence: 0.9706633

00:30:00.840 --> 00:30:02.840 various brain disorders. For example,

NOTE Confidence: 0.9706633

00:30:02.840 --> 00:30:04.140 schizophrenia and bipolar

NOTE Confidence: 0.9997731

00:30:04.975 --> 00:30:05.475 have

NOTE Confidence: 0.96455467

00:30:05.934 --> 00:30:08.575 reduced or increased connectivity depending

NOTE Confidence: 0.96455467

00:30:08.575 --> 00:30:09.695 on which areas you look

NOTE Confidence: 0.96455467

00:30:09.695 --> 00:30:10.975 at. The same for major

NOTE Confidence: 0.96455467

00:30:10.975 --> 00:30:13.054 depressive disorder. And autism also

NOTE Confidence: 0.96455467

00:30:13.054 --> 00:30:14.735 has reports of increased thalamus

NOTE Confidence: 0.96455467

00:30:14.735 --> 00:30:15.934 to temporal and thalamus to

NOTE Confidence: 0.96455467

00:30:15.934 --> 00:30:17.794 somatic motor and parietal connectivity

NOTE Confidence: 0.96455467

00:30:17.934 --> 00:30:18.434 patterns.

NOTE Confidence: 0.99809337

00:30:19.215 --> 00:30:19.955 And so

NOTE Confidence: 0.96847785

00:30:21.450 --> 00:30:22.890 we see all these reports

NOTE Confidence: 0.96847785

00:30:22.890 --> 00:30:24.650 of changes, but the hard

NOTE Confidence: 0.96847785

00:30:24.650 --> 00:30:25.610 part is how do these

NOTE Confidence: 0.96847785

00:30:25.610 --> 00:30:27.450 projections and connections develop in

NOTE Confidence: 0.96847785

00:30:27.450 --> 00:30:28.809 the first place? So are

NOTE Confidence: 0.96847785

00:30:28.809 --> 00:30:29.770 they getting set up the

NOTE Confidence: 0.96847785

00:30:29.770 --> 00:30:30.970 wrong way to begin with?

NOTE Confidence: 0.96847785

00:30:30.970 --> 00:30:33.150 But and at that level,

NOTE Confidence: 0.96847785

00:30:33.290 --> 00:30:34.910 what are the molecular components

NOTE Confidence: 0.96847785

00:30:34.970 --> 00:30:36.135 kind of regulating that?

NOTE Confidence: 0.99600154

00:30:36.935 --> 00:30:37.675 And so

NOTE Confidence: 0.95846915

00:30:38.295 --> 00:30:39.175 so what I'll talk a

NOTE Confidence: 0.95846915

00:30:39.175 --> 00:30:40.315 little bit about today,

NOTE Confidence: 0.988016

00:30:41.735 --> 00:30:42.935 and this is an ongoing

NOTE Confidence: 0.988016

00:30:42.935 --> 00:30:44.395 project in the lab and

NOTE Confidence: 0.93245226

00:30:45.415 --> 00:30:46.855 along with another lab in

NOTE Confidence: 0.93245226

00:30:46.855 --> 00:30:48.075 Germany. And so

NOTE Confidence: 0.9914063

00:30:48.929 --> 00:30:49.889 we really wanna get a

NOTE Confidence: 0.9914063

00:30:49.889 --> 00:30:51.250 complete understanding of how these

NOTE Confidence: 0.9914063

00:30:51.250 --> 00:30:52.450 circuits come to form during

NOTE Confidence: 0.9914063

00:30:52.450 --> 00:30:54.370 development and then to map

NOTE Confidence: 0.9914063

00:30:54.370 --> 00:30:55.649 this assembly and how they

NOTE Confidence: 0.9914063

00:30:55.649 --> 00:30:56.149 refine

NOTE Confidence: 0.9961365

00:30:56.690 --> 00:30:58.129 over time. So this is

NOTE Confidence: 0.9961365

00:30:58.129 --> 00:30:58.629 collaboratively

NOTE Confidence: 0.9096291

00:30:58.929 --> 00:31:00.690 done with Rachel Bandler, another

NOTE Confidence: 0.9096291

00:31:00.690 --> 00:31:02.129 great postdoc in the Pattabhi

NOTE Confidence: 0.9096291

00:31:02.129 --> 00:31:04.095 Raman and Sustin Labs, who's

NOTE Confidence: 0.960187

00:31:04.635 --> 00:31:05.615 also in the NRTP.

NOTE Confidence: 0.9585031

00:31:07.115 --> 00:31:08.475 And then Connor Lynch, who's

NOTE Confidence: 0.9585031

00:31:08.475 --> 00:31:09.375 a very talented

NOTE Confidence: 0.9109838

00:31:09.835 --> 00:31:10.575 oh, no.

NOTE Confidence: 0.9631398

00:31:11.435 --> 00:31:12.875 A very talented grad student

NOTE Confidence: 0.9631398

00:31:12.875 --> 00:31:14.075 in Christian Meyer's lab in

NOTE Confidence: 0.9631398

00:31:14.075 --> 00:31:14.575 Germany.

NOTE Confidence: 0.9980573

00:31:15.355 --> 00:31:16.015 And so

NOTE Confidence: 0.9803648

00:31:16.670 --> 00:31:18.370 traditionally, we would use immuno

NOTE Confidence: 0.9803648

00:31:18.429 --> 00:31:20.110 staining on sections to assess

NOTE Confidence: 0.9803648

00:31:20.110 --> 00:31:21.390 projections. And so here is

NOTE Confidence: 0.9803648

00:31:21.390 --> 00:31:22.910 another mouse brain. In green,

NOTE Confidence: 0.9803648

00:31:22.910 --> 00:31:23.710 you can see all the

NOTE Confidence: 0.9803648

00:31:23.710 --> 00:31:24.990 projections from the thalamus to

NOTE Confidence: 0.9803648

00:31:24.990 --> 00:31:25.650 the cortex.

NOTE Confidence: 0.99191713

00:31:26.030 --> 00:31:27.470 Here's an example of those

NOTE Confidence: 0.99191713

00:31:27.470 --> 00:31:29.730 whisker barrel structures in practice.

NOTE Confidence: 0.9910891

00:31:31.615 --> 00:31:32.815 But this restricts what we

NOTE Confidence: 0.9910891

00:31:32.815 --> 00:31:34.175 can truly assess. And so

NOTE Confidence: 0.9910891

00:31:34.175 --> 00:31:35.775 to bypass this limitation in

NOTE Confidence: 0.9910891

00:31:35.775 --> 00:31:37.695 the lab, we've implemented whole

NOTE Confidence: 0.9910891

00:31:37.695 --> 00:31:39.155 brain clearing and imaging

NOTE Confidence: 0.9390212

00:31:39.535 --> 00:31:40.895 so we can investigate entire

NOTE Confidence: 0.9390212

00:31:40.895 --> 00:31:42.275 brains without sectioning

NOTE Confidence: 0.9701919

00:31:43.070 --> 00:31:44.750 or artifacts or different staining

NOTE Confidence: 0.9701919

00:31:44.750 --> 00:31:45.890 issues. And so,

NOTE Confidence: 0.96556866

00:31:47.550 --> 00:31:48.670 as an example here, you

NOTE Confidence: 0.96556866

00:31:48.670 --> 00:31:49.630 can see this is an

NOTE Confidence: 0.96556866

00:31:49.630 --> 00:31:50.770 entire mouse brain,

NOTE Confidence: 0.9965494

00:31:51.710 --> 00:31:52.830 with all the layer five

NOTE Confidence: 0.9965494

00:31:52.830 --> 00:31:53.970 neurons in red.

NOTE Confidence: 0.9979752

00:31:54.830 --> 00:31:55.570 And so

NOTE Confidence: 0.99507874

00:31:55.870 --> 00:31:56.565 as we

NOTE Confidence: 0.99888784

00:31:57.125 --> 00:31:58.085 spin it, we can see

NOTE Confidence: 0.99888784

00:31:58.085 --> 00:31:59.605 all the projections coming from

NOTE Confidence: 0.99888784

00:31:59.605 --> 00:32:00.105 those

NOTE Confidence: 0.98449534

00:32:00.644 --> 00:32:02.725 those neurons as well, such

NOTE Confidence: 0.98449534

00:32:02.725 --> 00:32:03.225 as

NOTE Confidence: 0.93004924

00:32:04.965 --> 00:32:06.725 through the internal capsule, down

NOTE Confidence: 0.93004924

00:32:06.725 --> 00:32:08.105 past the ponds, and then

NOTE Confidence: 0.93004924

00:32:08.325 --> 00:32:09.625 the pyramidal decussation.

NOTE Confidence: 0.99085027

00:32:10.990 --> 00:32:12.350 So we're able to assess

NOTE Confidence: 0.99085027

00:32:12.350 --> 00:32:13.250 entire circuits,

NOTE Confidence: 0.9992982

00:32:13.950 --> 00:32:14.450 but

NOTE Confidence: 0.969409

00:32:14.750 --> 00:32:16.510 these circuits have multiple components.

NOTE Confidence: 0.969409

00:32:16.510 --> 00:32:17.890 What connects with what?

NOTE Confidence: 0.9992895

00:32:18.510 --> 00:32:19.950 So how do we label

NOTE Confidence: 0.9992895

00:32:19.950 --> 00:32:21.570 true connections between cells?

NOTE Confidence: 0.9555994

00:32:22.745 --> 00:32:23.705 So to get at this

NOTE Confidence: 0.9555994

00:32:23.705 --> 00:32:25.385 question, we take an advantage

NOTE Confidence: 0.9555994

00:32:25.385 --> 00:32:26.685 of the rabies virus.

NOTE Confidence: 0.9957026

00:32:28.985 --> 00:32:30.345 And so the rabies virus

NOTE Confidence: 0.9957026

00:32:30.345 --> 00:32:31.545 was first used for tracing

NOTE Confidence: 0.9957026

00:32:31.545 --> 00:32:32.905 studies in the late nineteen

NOTE Confidence: 0.9957026

00:32:32.905 --> 00:32:33.405 eighties,

NOTE Confidence: 0.998936

00:32:34.585 --> 00:32:35.545 but it has become more

NOTE Confidence: 0.998936

00:32:35.545 --> 00:32:36.985 prominent and optimized over the

NOTE Confidence: 0.998936

00:32:36.985 --> 00:32:38.445 last twenty years or so.

NOTE Confidence: 0.9880883

00:32:38.800 --> 00:32:40.240 And so what makes the

NOTE Confidence: 0.9880883

00:32:40.240 --> 00:32:41.440 rabies virus special is that

NOTE Confidence: 0.9880883

00:32:41.440 --> 00:32:42.800 by modifying it, we're able

NOTE Confidence: 0.9880883

00:32:42.800 --> 00:32:44.320 to control what cells are

NOTE Confidence: 0.9880883

00:32:44.320 --> 00:32:45.120 able to take up the

NOTE Confidence: 0.9880883

00:32:45.120 --> 00:32:46.800 virus initially. We would call

NOTE Confidence: 0.9880883

00:32:46.800 --> 00:32:48.640 those starter cells. And second,

NOTE Confidence: 0.9880883

00:32:48.640 --> 00:32:50.820 it travels retrogradely, so back

NOTE Confidence: 0.99894017

00:32:51.285 --> 00:32:52.585 from a projection

NOTE Confidence: 0.97955215

00:32:53.365 --> 00:32:54.725 via a synapse. So we're

NOTE Confidence: 0.97955215

00:32:54.725 --> 00:32:56.425 able to identify what monosynaptically

NOTE Confidence: 0.9759783

00:32:56.885 --> 00:32:58.085 connects to our starter cells.

NOTE Confidence: 0.9759783

00:32:58.085 --> 00:32:59.445 So what forms a functional

NOTE Confidence: 0.9759783

00:32:59.445 --> 00:33:00.805 circuit with the cell we

NOTE Confidence: 0.9759783

00:33:00.805 --> 00:33:01.785 initially infected?

NOTE Confidence: 0.9843593

00:33:03.205 --> 00:33:04.825 So in this scenario,

NOTE Confidence: 0.9874403

00:33:05.510 --> 00:33:06.710 here, our red cell is

NOTE Confidence: 0.9874403

00:33:06.710 --> 00:33:07.750 any cell that is able

NOTE Confidence: 0.9874403

00:33:07.750 --> 00:33:08.790 to be a starter cell.

NOTE Confidence: 0.9874403

00:33:08.790 --> 00:33:09.750 It's able to take up

NOTE Confidence: 0.9874403

00:33:09.750 --> 00:33:10.730 the rabies virus.

NOTE Confidence: 0.9932691

00:33:11.830 --> 00:33:13.530 A yellow cell is

NOTE Confidence: 0.98871154

00:33:14.310 --> 00:33:15.670 a starter cell that has

NOTE Confidence: 0.98871154

00:33:15.670 --> 00:33:16.870 taken up the rabies virus,

NOTE Confidence: 0.98871154

00:33:16.870 --> 00:33:18.070 so it's both red and

NOTE Confidence: 0.98871154

00:33:18.070 --> 00:33:18.570 green.

NOTE Confidence: 0.98479235

00:33:18.925 --> 00:33:20.205 And then anything that connects

NOTE Confidence: 0.98479235

00:33:20.205 --> 00:33:21.965 to that starter cell is

NOTE Confidence: 0.98479235

00:33:21.965 --> 00:33:23.005 only green. It has the

NOTE Confidence: 0.98479235

00:33:23.005 --> 00:33:24.365 rabies virus, but not the

NOTE Confidence: 0.98479235

00:33:24.365 --> 00:33:26.125 ability to be a starter

NOTE Confidence: 0.98479235

00:33:26.125 --> 00:33:26.625 cell.

NOTE Confidence: 0.95626765

00:33:28.285 --> 00:33:30.205 So basically, we know which

NOTE Confidence: 0.95626765

00:33:30.205 --> 00:33:32.045 neurons form synaptic connections with

NOTE Confidence: 0.95626765

00:33:32.045 --> 00:33:32.785 each other.

NOTE Confidence: 0.9920206

00:33:33.230 --> 00:33:34.110 And so once we got

NOTE Confidence: 0.9920206

00:33:34.110 --> 00:33:35.150 this tool kind of working

NOTE Confidence: 0.9920206

00:33:35.150 --> 00:33:36.830 within the lab, we utilized

NOTE Confidence: 0.9920206

00:33:36.830 --> 00:33:37.710 it in the context of

NOTE Confidence: 0.9920206

00:33:37.710 --> 00:33:38.990 the frontal cortex. We think

NOTE Confidence: 0.9920206

00:33:38.990 --> 00:33:40.430 this is a really important

NOTE Confidence: 0.9920206

00:33:40.430 --> 00:33:41.870 region. The prefrontal cortex is

NOTE Confidence: 0.9920206

00:33:41.870 --> 00:33:43.790 greatly expanded in humans compared

NOTE Confidence: 0.9920206

00:33:43.790 --> 00:33:44.610 to other primates.

NOTE Confidence: 0.9744964

00:33:44.910 --> 00:33:45.790 And so let's get a

NOTE Confidence: 0.9744964

00:33:45.790 --> 00:33:47.070 sense of how the initial

NOTE Confidence: 0.9744964

00:33:47.070 --> 00:33:48.370 circuits are made even

NOTE Confidence: 0.9997747

00:33:48.815 --> 00:33:50.195 prior to human evolution.

NOTE Confidence: 0.9839562

00:33:51.615 --> 00:33:53.235 And so, again, this is

NOTE Confidence: 0.9983405

00:33:53.535 --> 00:33:55.235 mouse genetics on your left.

NOTE Confidence: 0.9889584

00:33:55.934 --> 00:33:57.135 I'm not gonna go into

NOTE Confidence: 0.9889584

00:33:57.135 --> 00:33:58.355 detail about it.

NOTE Confidence: 0.9983505

00:33:58.655 --> 00:33:59.155 But

NOTE Confidence: 0.9827251

00:34:00.495 --> 00:34:01.554 based on the

NOTE Confidence: 0.9993753

00:34:02.080 --> 00:34:03.380 the approach we took,

NOTE Confidence: 0.9977573

00:34:03.760 --> 00:34:05.440 all excitatory neurons within the

NOTE Confidence: 0.9977573

00:34:05.440 --> 00:34:07.460 cortex are potential starter cells.

NOTE Confidence: 0.9884123

00:34:09.120 --> 00:34:10.560 But we inject the rabies

NOTE Confidence: 0.9884123

00:34:10.560 --> 00:34:12.239 virus directly into the frontal

NOTE Confidence: 0.9884123

00:34:12.239 --> 00:34:13.600 cortex, and so here is

NOTE Confidence: 0.9884123

00:34:13.600 --> 00:34:14.880 a cleared brain on your

NOTE Confidence: 0.9884123

00:34:14.880 --> 00:34:15.380 right.

NOTE Confidence: 0.9951375

00:34:16.055 --> 00:34:17.015 And you can see the

NOTE Confidence: 0.9951375

00:34:17.015 --> 00:34:18.295 injection site here in kind

NOTE Confidence: 0.9951375

00:34:18.295 --> 00:34:19.195 of this magenta

NOTE Confidence: 0.80505955

00:34:19.815 --> 00:34:20.315 screen.

NOTE Confidence: 0.969077

00:34:20.855 --> 00:34:22.055 And so we perform these

NOTE Confidence: 0.969077

00:34:22.055 --> 00:34:24.055 experiments in mice right after

NOTE Confidence: 0.969077

00:34:24.055 --> 00:34:25.095 birth, so the day they

NOTE Confidence: 0.969077

00:34:25.095 --> 00:34:25.975 were born, and then we

NOTE Confidence: 0.969077

00:34:25.975 --> 00:34:27.015 wait a week. This is

NOTE Confidence: 0.969077

00:34:27.015 --> 00:34:29.335 relatively similar to late mid

NOTE Confidence: 0.969077

00:34:29.335 --> 00:34:30.935 fetal stage for humans. So

NOTE Confidence: 0.969077

00:34:30.935 --> 00:34:31.435 really

NOTE Confidence: 0.94410384

00:34:31.950 --> 00:34:33.570 what's happening during development.

NOTE Confidence: 0.99478257

00:34:35.150 --> 00:34:36.050 And so

NOTE Confidence: 0.9653731

00:34:36.430 --> 00:34:37.550 as a reminder, again, the

NOTE Confidence: 0.9653731

00:34:37.550 --> 00:34:39.630 magenta cells are potential starter

NOTE Confidence: 0.9653731

00:34:39.630 --> 00:34:40.930 cells and their projections.

NOTE Confidence: 0.98179394

00:34:41.390 --> 00:34:42.270 You can see we hit

NOTE Confidence: 0.98179394

00:34:42.270 --> 00:34:43.469 part of motor cortex as

NOTE Confidence: 0.98179394

00:34:43.469 --> 00:34:45.150 the corticospinal tract is labeled

NOTE Confidence: 0.98179394

00:34:45.150 --> 00:34:45.825 here as well,

NOTE Confidence: 0.9822951

00:34:46.385 --> 00:34:48.065 whereas the green cells are

NOTE Confidence: 0.9822951

00:34:48.065 --> 00:34:49.665 the inputs to those starters.

NOTE Confidence: 0.9822951

00:34:49.665 --> 00:34:51.025 So what made a functional

NOTE Confidence: 0.9822951

00:34:51.025 --> 00:34:52.625 connection with them within the

NOTE Confidence: 0.9822951

00:34:52.625 --> 00:34:53.825 first postnatal week of a

NOTE Confidence: 0.9822951

00:34:53.825 --> 00:34:54.724 mouse's life.

NOTE Confidence: 0.99267846

00:34:56.065 --> 00:34:57.505 And so taking a closer

NOTE Confidence: 0.99267846

00:34:57.505 --> 00:34:58.625 look at the three d

NOTE Confidence: 0.99267846

00:34:58.625 --> 00:34:59.125 image,

NOTE Confidence: 0.91713226

00:34:59.890 --> 00:35:00.390 maybe,

NOTE Confidence: 0.97503054

00:35:01.090 --> 00:35:02.290 you can see we get

NOTE Confidence: 0.97503054

00:35:02.290 --> 00:35:04.210 robust green labeling, especially in

NOTE Confidence: 0.97503054

00:35:04.210 --> 00:35:04.710 these

NOTE Confidence: 0.9982803

00:35:05.010 --> 00:35:05.510 subcortical

NOTE Confidence: 0.84995973

00:35:05.890 --> 00:35:06.390 structures.

NOTE Confidence: 0.92985046

00:35:06.930 --> 00:35:08.369 Here, where the laser pointer

NOTE Confidence: 0.92985046

00:35:08.369 --> 00:35:09.910 is is the thalamus.

NOTE Confidence: 0.99057525

00:35:10.369 --> 00:35:11.330 And so we can kind

NOTE Confidence: 0.99057525

00:35:11.330 --> 00:35:12.609 of go through our entire

NOTE Confidence: 0.99057525

00:35:12.609 --> 00:35:14.130 brain and follow every single

NOTE Confidence: 0.99057525

00:35:14.130 --> 00:35:15.270 neuron that's traced.

NOTE Confidence: 0.93963325

00:35:16.955 --> 00:35:18.155 And you saw the bright

NOTE Confidence: 0.93963325

00:35:18.155 --> 00:35:18.975 green there.

NOTE Confidence: 0.9927147

00:35:19.515 --> 00:35:20.235 And so if we take

NOTE Confidence: 0.9927147

00:35:20.235 --> 00:35:21.935 just a snippet of that,

NOTE Confidence: 0.9652511

00:35:23.114 --> 00:35:24.575 this is the mouse's thymus,

NOTE Confidence: 0.9672675

00:35:25.755 --> 00:35:27.435 and here's cortex. This is

NOTE Confidence: 0.9672675

00:35:27.435 --> 00:35:28.540 the injection side, and we

NOTE Confidence: 0.9672675

00:35:28.540 --> 00:35:29.500 can see that we get

NOTE Confidence: 0.9672675

00:35:29.500 --> 00:35:31.579 really robust labeling of medial

NOTE Confidence: 0.9672675

00:35:31.579 --> 00:35:32.079 dorsal,

NOTE Confidence: 0.9638978

00:35:32.859 --> 00:35:33.920 VPM, VPL,

NOTE Confidence: 0.99924785

00:35:34.219 --> 00:35:34.719 and

NOTE Confidence: 0.9937434

00:35:35.020 --> 00:35:36.799 VM nuclei of the thalamus.

NOTE Confidence: 0.99939317

00:35:37.339 --> 00:35:39.020 So during the early development

NOTE Confidence: 0.99939317

00:35:39.020 --> 00:35:39.760 of the mouse,

NOTE Confidence: 0.9989985

00:35:40.355 --> 00:35:41.795 the thalamus is making robust

NOTE Confidence: 0.9989985

00:35:41.795 --> 00:35:43.654 connections from these distinct nuclei

NOTE Confidence: 0.99925846

00:35:44.114 --> 00:35:45.335 to the frontal cortex.

NOTE Confidence: 0.9977955

00:35:45.875 --> 00:35:46.614 And so

NOTE Confidence: 0.991994

00:35:47.315 --> 00:35:48.355 how do we make sense

NOTE Confidence: 0.991994

00:35:48.355 --> 00:35:50.295 of these different cells? Right?

NOTE Confidence: 0.94936985

00:35:50.594 --> 00:35:51.635 Do we care what cell

NOTE Confidence: 0.94936985

00:35:51.635 --> 00:35:52.594 synapse down to what or

NOTE Confidence: 0.94936985

00:35:52.594 --> 00:35:53.895 just region to region?

NOTE Confidence: 0.9841856

00:35:54.489 --> 00:35:55.530 And so in addition to

NOTE Confidence: 0.9841856

00:35:55.530 --> 00:35:56.570 imaging, we're able to get

NOTE Confidence: 0.9841856

00:35:56.570 --> 00:35:58.170 the gene expression profiles for

NOTE Confidence: 0.9841856

00:35:58.170 --> 00:35:59.450 each of these green cells

NOTE Confidence: 0.9841856

00:35:59.450 --> 00:36:01.150 with single cell RNA seq.

NOTE Confidence: 0.98541427

00:36:01.530 --> 00:36:02.969 And so by taking those

NOTE Confidence: 0.98541427

00:36:02.969 --> 00:36:04.910 green cells and sequencing them,

NOTE Confidence: 0.98541427

00:36:04.969 --> 00:36:06.090 we're able to get this

NOTE Confidence: 0.98541427

00:36:06.090 --> 00:36:07.315 UMAP. So this is a

NOTE Confidence: 0.98541427

00:36:07.315 --> 00:36:08.375 two d representation

NOTE Confidence: 0.9860834

00:36:08.675 --> 00:36:09.715 of all the green cells

NOTE Confidence: 0.9860834

00:36:09.715 --> 00:36:11.075 that we've sequenced from one

NOTE Confidence: 0.9860834

00:36:11.075 --> 00:36:12.755 mouse brain, so any cell

NOTE Confidence: 0.9860834

00:36:12.755 --> 00:36:14.215 that had the rabies virus.

NOTE Confidence: 0.9912883

00:36:14.995 --> 00:36:16.535 Each dot is a cell.

NOTE Confidence: 0.9912883

00:36:16.835 --> 00:36:17.875 And based off the gene

NOTE Confidence: 0.9912883

00:36:17.875 --> 00:36:20.215 expression profiles, we identify what

NOTE Confidence: 0.9938189

00:36:20.619 --> 00:36:21.980 putative cell type they are,

NOTE Confidence: 0.9938189

00:36:21.980 --> 00:36:23.280 what we think they are.

NOTE Confidence: 0.99924964

00:36:24.140 --> 00:36:25.339 And what's really exciting is

NOTE Confidence: 0.99924964

00:36:25.339 --> 00:36:26.460 that we see green cells

NOTE Confidence: 0.99924964

00:36:26.460 --> 00:36:26.960 representing

NOTE Confidence: 0.89712554

00:36:27.260 --> 00:36:27.760 thalamocortical

NOTE Confidence: 0.9895256

00:36:28.060 --> 00:36:29.900 connections. So right here, these

NOTE Confidence: 0.9895256

00:36:29.900 --> 00:36:31.580 are all thalamic neurons that

NOTE Confidence: 0.9895256

00:36:31.580 --> 00:36:32.780 must have projected to the

NOTE Confidence: 0.9895256

00:36:32.780 --> 00:36:33.760 frontal cortex.

NOTE Confidence: 0.9764502

00:36:34.985 --> 00:36:35.864 But we also see a

NOTE Confidence: 0.9764502

00:36:35.864 --> 00:36:37.385 variety of other cortical cell

NOTE Confidence: 0.9764502

00:36:37.385 --> 00:36:38.985 types which represent shorter range

NOTE Confidence: 0.9764502

00:36:38.985 --> 00:36:40.425 connections. So those would be,

NOTE Confidence: 0.9764502

00:36:40.425 --> 00:36:41.725 for example, up here,

NOTE Confidence: 0.940426

00:36:42.025 --> 00:36:43.245 excitatory cortex,

NOTE Confidence: 0.992045

00:36:43.864 --> 00:36:45.465 excitatory neurons in the cortex.

NOTE Confidence: 0.992045

00:36:45.465 --> 00:36:46.925 We also have some inhibitory

NOTE Confidence: 0.992045

00:36:47.065 --> 00:36:47.565 neurons.

NOTE Confidence: 0.99755454

00:36:48.099 --> 00:36:49.859 And so we're really able

NOTE Confidence: 0.99755454

00:36:49.859 --> 00:36:51.800 to truly capture widespread dynamics

NOTE Confidence: 0.99755454

00:36:51.859 --> 00:36:52.760 of early connectivity.

NOTE Confidence: 0.9698292

00:36:53.300 --> 00:36:54.599 And I just wanna highlight

NOTE Confidence: 0.9698292

00:36:54.660 --> 00:36:55.859 kind of our confirmation of

NOTE Confidence: 0.9698292

00:36:55.859 --> 00:36:57.800 two smaller cortical neuron populations.

NOTE Confidence: 0.8353892

00:36:58.980 --> 00:37:00.339 So it'd be these. So

NOTE Confidence: 0.8353892

00:37:00.339 --> 00:37:00.839 first,

NOTE Confidence: 0.9494336

00:37:02.625 --> 00:37:04.065 the the yellow cell type

NOTE Confidence: 0.9494336

00:37:04.065 --> 00:37:05.585 here, we've labeled as layer

NOTE Confidence: 0.9494336

00:37:05.585 --> 00:37:06.965 four cortical neurons,

NOTE Confidence: 0.9928006

00:37:07.825 --> 00:37:09.185 and here would be deep

NOTE Confidence: 0.9928006

00:37:09.185 --> 00:37:10.405 layer cortical neurons.

NOTE Confidence: 0.98600304

00:37:10.945 --> 00:37:11.745 So if we were to

NOTE Confidence: 0.98600304

00:37:11.745 --> 00:37:12.705 look at our section, we

NOTE Confidence: 0.98600304

00:37:12.705 --> 00:37:13.905 can see that we see

NOTE Confidence: 0.98600304

00:37:13.905 --> 00:37:15.505 green within the cortex up

NOTE Confidence: 0.98600304

00:37:15.505 --> 00:37:16.005 here.

NOTE Confidence: 0.97728455

00:37:17.280 --> 00:37:18.239 And if we take the

NOTE Confidence: 0.97728455

00:37:18.239 --> 00:37:19.600 gene expression profile of the

NOTE Confidence: 0.97728455

00:37:19.600 --> 00:37:21.040 neurons that we sequenced, we're

NOTE Confidence: 0.97728455

00:37:21.040 --> 00:37:22.239 able to intersect it with

NOTE Confidence: 0.97728455

00:37:22.239 --> 00:37:24.480 existing spatial transcriptomic data from

NOTE Confidence: 0.97728455

00:37:24.480 --> 00:37:25.680 the Allen Institute. This is

NOTE Confidence: 0.97728455

00:37:25.680 --> 00:37:26.800 Mirfisch where they kind of

NOTE Confidence: 0.97728455

00:37:26.800 --> 00:37:28.239 get the gene expression profiles

NOTE Confidence: 0.97728455

00:37:28.239 --> 00:37:29.140 within space

NOTE Confidence: 0.9932104

00:37:29.600 --> 00:37:30.820 of numerous neurons.

NOTE Confidence: 0.999465

00:37:31.745 --> 00:37:33.425 And so that helps us

NOTE Confidence: 0.999465

00:37:33.425 --> 00:37:34.785 identify what the most likely

NOTE Confidence: 0.999465

00:37:34.785 --> 00:37:36.485 location of our neurons are.

NOTE Confidence: 0.9963166

00:37:36.864 --> 00:37:37.665 And so if you look

NOTE Confidence: 0.9963166

00:37:37.665 --> 00:37:38.785 here, this is the spatial

NOTE Confidence: 0.9963166

00:37:38.785 --> 00:37:40.225 mapping. All the blue dots

NOTE Confidence: 0.9963166

00:37:40.225 --> 00:37:41.364 is where we expect

NOTE Confidence: 0.93840927

00:37:42.305 --> 00:37:43.665 the cells or where they

NOTE Confidence: 0.93840927

00:37:43.665 --> 00:37:44.965 potentially would be.

NOTE Confidence: 0.98722

00:37:45.469 --> 00:37:46.269 And if we look just

NOTE Confidence: 0.98722

00:37:46.269 --> 00:37:47.789 at a representative staining, I

NOTE Confidence: 0.98722

00:37:47.789 --> 00:37:48.829 showed this in one of

NOTE Confidence: 0.98722

00:37:48.829 --> 00:37:50.029 the first couple slides, this

NOTE Confidence: 0.98722

00:37:50.029 --> 00:37:51.390 is consistent with those neurons

NOTE Confidence: 0.98722

00:37:51.390 --> 00:37:52.930 being within the upper layers.

NOTE Confidence: 0.9847375

00:37:54.829 --> 00:37:56.589 In addition, cluster fourteen, which

NOTE Confidence: 0.9847375

00:37:56.589 --> 00:37:58.369 was that purplish cluster,

NOTE Confidence: 0.9720928

00:37:59.925 --> 00:38:00.885 seems to be only in

NOTE Confidence: 0.9720928

00:38:00.885 --> 00:38:02.005 the deepest parts of the

NOTE Confidence: 0.9720928

00:38:02.005 --> 00:38:03.844 cortex right here. This is

NOTE Confidence: 0.9720928

00:38:03.844 --> 00:38:05.125 a little bit of layer

NOTE Confidence: 0.9720928

00:38:05.125 --> 00:38:06.725 six a and mostly layer

NOTE Confidence: 0.9720928

00:38:06.725 --> 00:38:07.864 six b. So

NOTE Confidence: 0.97397333

00:38:10.085 --> 00:38:11.364 this is what the mouse

NOTE Confidence: 0.97397333

00:38:11.364 --> 00:38:12.270 cortex looks like at that

NOTE Confidence: 0.97397333

00:38:12.270 --> 00:38:13.390 point, and this purple would

NOTE Confidence: 0.97397333

00:38:13.390 --> 00:38:14.350 be those cells that we

NOTE Confidence: 0.97397333

00:38:14.350 --> 00:38:14.850 see.

NOTE Confidence: 0.98950154

00:38:15.230 --> 00:38:16.050 And so

NOTE Confidence: 0.98349977

00:38:17.150 --> 00:38:18.270 one reason we find this

NOTE Confidence: 0.98349977

00:38:18.270 --> 00:38:19.469 really cool is that layer

NOTE Confidence: 0.98349977

00:38:19.469 --> 00:38:20.850 six b is a remnant

NOTE Confidence: 0.98349977

00:38:20.989 --> 00:38:22.430 of the subplate, which is

NOTE Confidence: 0.98349977

00:38:22.430 --> 00:38:24.030 a transient zone during development,

NOTE Confidence: 0.98349977

00:38:24.030 --> 00:38:24.915 and we find this

NOTE Confidence: 0.9910965

00:38:25.395 --> 00:38:26.995 really cool because subplate neurons

NOTE Confidence: 0.9910965

00:38:26.995 --> 00:38:28.435 sit in the subplate beneath

NOTE Confidence: 0.9910965

00:38:28.435 --> 00:38:29.955 the cortical plate at the

NOTE Confidence: 0.9910965

00:38:29.955 --> 00:38:31.555 interface of cortical gray and

NOTE Confidence: 0.9910965

00:38:31.555 --> 00:38:32.835 white matter. So it sits

NOTE Confidence: 0.9910965

00:38:32.835 --> 00:38:33.795 between the rest of the

NOTE Confidence: 0.9910965

00:38:33.795 --> 00:38:34.295 neurons

NOTE Confidence: 0.9720949

00:38:34.594 --> 00:38:35.875 and all the projections that

NOTE Confidence: 0.9720949

00:38:35.875 --> 00:38:37.895 are growing, extending everything else.

NOTE Confidence: 0.98765093

00:38:38.300 --> 00:38:39.260 And so here on the

NOTE Confidence: 0.98765093

00:38:39.260 --> 00:38:40.140 left, you can see an

NOTE Confidence: 0.98765093

00:38:40.140 --> 00:38:41.500 example of a subplate neuron

NOTE Confidence: 0.98765093

00:38:41.500 --> 00:38:43.500 in green and typical pyramidal

NOTE Confidence: 0.98765093

00:38:43.500 --> 00:38:45.599 neurons in magenta. They're actually

NOTE Confidence: 0.98765093

00:38:45.660 --> 00:38:47.200 pretty distinct in their morphology,

NOTE Confidence: 0.98765093

00:38:47.260 --> 00:38:48.780 and they're really widespread in

NOTE Confidence: 0.98765093

00:38:48.780 --> 00:38:49.680 what they do.

NOTE Confidence: 0.9983046

00:38:49.980 --> 00:38:50.480 But

NOTE Confidence: 0.98946124

00:38:51.094 --> 00:38:51.974 what we think is so

NOTE Confidence: 0.98946124

00:38:51.974 --> 00:38:53.015 cool about this group and

NOTE Confidence: 0.98946124

00:38:53.015 --> 00:38:54.135 why we think it's interesting

NOTE Confidence: 0.98946124

00:38:54.135 --> 00:38:55.255 that we've traced them from

NOTE Confidence: 0.98946124

00:38:55.255 --> 00:38:55.755 early

NOTE Confidence: 0.9746155

00:38:56.214 --> 00:38:58.315 frontal cortex connections is that

NOTE Confidence: 0.9746155

00:38:58.375 --> 00:38:59.654 they're the firstborn neurons from

NOTE Confidence: 0.9746155

00:38:59.654 --> 00:39:00.635 the dorsal cortex,

NOTE Confidence: 0.8975778

00:39:01.174 --> 00:39:02.614 and they perform kind of

NOTE Confidence: 0.8975778

00:39:02.614 --> 00:39:04.154 diverse function throughout development.

NOTE Confidence: 0.9622796

00:39:04.560 --> 00:39:05.280 They make some of the

NOTE Confidence: 0.9622796

00:39:05.280 --> 00:39:06.800 earliest synapses. So, okay, it

NOTE Confidence: 0.9622796

00:39:06.800 --> 00:39:08.000 makes sense. We see some

NOTE Confidence: 0.9622796

00:39:08.000 --> 00:39:10.000 tracing very early on. But

NOTE Confidence: 0.9622796

00:39:10.000 --> 00:39:11.380 typically, this is not,

NOTE Confidence: 0.9994711

00:39:12.000 --> 00:39:13.120 that well studied in the

NOTE Confidence: 0.9994711

00:39:13.120 --> 00:39:14.500 context of frontal cortex.

NOTE Confidence: 0.985078

00:39:16.160 --> 00:39:17.280 Additionally, they're some of the

NOTE Confidence: 0.985078

00:39:17.280 --> 00:39:18.340 first to have activity,

NOTE Confidence: 0.9069065

00:39:19.125 --> 00:39:20.565 and they perform many non

NOTE Confidence: 0.9069065

00:39:20.565 --> 00:39:21.225 cell autonomous

NOTE Confidence: 0.98501635

00:39:21.765 --> 00:39:23.285 axon guidance functions. So they

NOTE Confidence: 0.98501635

00:39:23.285 --> 00:39:24.885 basically tell everything else where

NOTE Confidence: 0.98501635

00:39:24.885 --> 00:39:26.085 to go. They set the

NOTE Confidence: 0.98501635

00:39:26.085 --> 00:39:27.685 stage for how do we

NOTE Confidence: 0.98501635

00:39:27.685 --> 00:39:29.225 make these circuits functional.

NOTE Confidence: 0.99744284

00:39:29.925 --> 00:39:30.665 And so

NOTE Confidence: 0.9903313

00:39:31.160 --> 00:39:32.520 one of the most well

NOTE Confidence: 0.9903313

00:39:32.520 --> 00:39:34.280 known functions of the subplate

NOTE Confidence: 0.9903313

00:39:34.280 --> 00:39:35.660 is to help thalamocortical

NOTE Confidence: 0.98885727

00:39:36.040 --> 00:39:37.100 projections develop.

NOTE Confidence: 0.9897892

00:39:37.480 --> 00:39:38.520 So how do we bring

NOTE Confidence: 0.9897892

00:39:38.520 --> 00:39:39.719 information from the thalamus to

NOTE Confidence: 0.9897892

00:39:39.719 --> 00:39:41.160 the cortex? The subplate helps

NOTE Confidence: 0.9897892

00:39:41.160 --> 00:39:42.380 sets all of that up.

NOTE Confidence: 0.9571851

00:39:43.485 --> 00:39:44.605 So importantly, we can see

NOTE Confidence: 0.9571851

00:39:44.605 --> 00:39:45.805 in many mouse models that

NOTE Confidence: 0.9571851

00:39:45.805 --> 00:39:47.405 disruption of subplate can impair

NOTE Confidence: 0.9571851

00:39:47.405 --> 00:39:49.165 initial wiring of the lamina

NOTE Confidence: 0.9571851

00:39:49.165 --> 00:39:50.625 cortical circuit. So here

NOTE Confidence: 0.9507405

00:39:50.925 --> 00:39:52.045 in green on the top,

NOTE Confidence: 0.9507405

00:39:52.045 --> 00:39:53.965 again, in brown, you can

NOTE Confidence: 0.9507405

00:39:53.965 --> 00:39:55.165 see all of the whisker

NOTE Confidence: 0.9507405

00:39:55.165 --> 00:39:56.580 barrels of a control mouse.

NOTE Confidence: 0.9507405

00:39:56.660 --> 00:39:57.940 So again, this is sensory

NOTE Confidence: 0.9507405

00:39:57.940 --> 00:39:59.380 information from one whisker of

NOTE Confidence: 0.9507405

00:39:59.380 --> 00:40:01.140 the mouse is each whisker

NOTE Confidence: 0.9507405

00:40:01.140 --> 00:40:01.640 barrel.

NOTE Confidence: 0.99764633

00:40:02.900 --> 00:40:04.260 But in a scenario where

NOTE Confidence: 0.99764633

00:40:04.260 --> 00:40:04.760 we

NOTE Confidence: 0.99477744

00:40:05.060 --> 00:40:06.360 disrupt subplate development,

NOTE Confidence: 0.95995045

00:40:06.739 --> 00:40:07.540 you can see that there

NOTE Confidence: 0.95995045

00:40:07.540 --> 00:40:09.060 is no longer stereotyped and

NOTE Confidence: 0.95995045

00:40:09.060 --> 00:40:10.760 organized sensory input.

NOTE Confidence: 0.99772114

00:40:11.140 --> 00:40:11.640 So

NOTE Confidence: 0.98266506

00:40:12.855 --> 00:40:14.614 while we investigate early cortical

NOTE Confidence: 0.98266506

00:40:14.614 --> 00:40:16.295 connectivity, the subplate is likely

NOTE Confidence: 0.98266506

00:40:16.295 --> 00:40:17.655 crucial to mediating that, and

NOTE Confidence: 0.98266506

00:40:17.655 --> 00:40:18.775 we can kind of piece

NOTE Confidence: 0.98266506

00:40:18.775 --> 00:40:19.895 the two parts together and

NOTE Confidence: 0.98266506

00:40:19.895 --> 00:40:21.335 say, okay. These are the

NOTE Confidence: 0.98266506

00:40:21.335 --> 00:40:22.795 early circuits that are made.

NOTE Confidence: 0.98266506

00:40:22.855 --> 00:40:24.535 What's really directing them to

NOTE Confidence: 0.98266506

00:40:24.535 --> 00:40:25.815 make those connections in the

NOTE Confidence: 0.98266506

00:40:25.815 --> 00:40:26.555 first place?

NOTE Confidence: 0.98110676

00:40:27.469 --> 00:40:28.349 But at the end of

NOTE Confidence: 0.98110676

00:40:28.349 --> 00:40:29.150 the day, it's kind of

NOTE Confidence: 0.98110676

00:40:29.150 --> 00:40:30.029 why do we care? Why

NOTE Confidence: 0.98110676

00:40:30.029 --> 00:40:31.650 is this relevant for us?

NOTE Confidence: 0.99869967

00:40:31.950 --> 00:40:32.690 And so

NOTE Confidence: 0.99187714

00:40:33.150 --> 00:40:34.829 subplate neurons are also altered

NOTE Confidence: 0.99187714

00:40:34.829 --> 00:40:35.890 in cases of neurodevelopmental

NOTE Confidence: 0.89982826

00:40:36.349 --> 00:40:38.049 disorders. So for example,

NOTE Confidence: 0.98116267

00:40:38.829 --> 00:40:40.349 postmortem brains of patients with

NOTE Confidence: 0.98116267

00:40:40.349 --> 00:40:41.410 autism and schizophrenia

NOTE Confidence: 0.983816

00:40:42.065 --> 00:40:43.265 been reported to have increased

NOTE Confidence: 0.983816

00:40:43.265 --> 00:40:44.785 subplate remnants. Right? This is

NOTE Confidence: 0.983816

00:40:44.785 --> 00:40:46.465 a transient population that's supposed

NOTE Confidence: 0.983816

00:40:46.465 --> 00:40:48.225 to die off really early

NOTE Confidence: 0.983816

00:40:48.225 --> 00:40:48.725 postnatally.

NOTE Confidence: 0.99906707

00:40:49.585 --> 00:40:50.864 But in cases of autism

NOTE Confidence: 0.99906707

00:40:50.864 --> 00:40:52.225 and schizophrenia, we've seen an

NOTE Confidence: 0.99906707

00:40:52.225 --> 00:40:53.345 increase in the number of

NOTE Confidence: 0.99906707

00:40:53.345 --> 00:40:54.485 neurons that remain.

NOTE Confidence: 0.93237215

00:40:55.859 --> 00:40:57.000 They've also been

NOTE Confidence: 0.9928217

00:40:57.460 --> 00:40:58.980 reported at a different density

NOTE Confidence: 0.9928217

00:40:58.980 --> 00:40:59.960 and different localization.

NOTE Confidence: 0.92903394

00:41:00.660 --> 00:41:02.039 So there's more,

NOTE Confidence: 0.9972641

00:41:02.339 --> 00:41:03.619 they're in places they shouldn't

NOTE Confidence: 0.9972641

00:41:03.619 --> 00:41:04.119 be,

NOTE Confidence: 0.99459

00:41:04.819 --> 00:41:06.260 and they're too close or

NOTE Confidence: 0.99459

00:41:06.260 --> 00:41:07.559 too far from each other.

NOTE Confidence: 0.99459

00:41:07.715 --> 00:41:08.675 So all this to say

NOTE Confidence: 0.99459

00:41:08.675 --> 00:41:09.955 that by mapping the early

NOTE Confidence: 0.99459

00:41:09.955 --> 00:41:11.875 developmental connectivity of the cortex,

NOTE Confidence: 0.99459

00:41:11.875 --> 00:41:12.855 we're able to get

NOTE Confidence: 0.9306314

00:41:13.395 --> 00:41:14.675 both after the cell types

NOTE Confidence: 0.9306314

00:41:14.675 --> 00:41:16.215 and gene expression that orchestrate

NOTE Confidence: 0.9306314

00:41:16.275 --> 00:41:18.275 brain circuits and ultimately how

NOTE Confidence: 0.9306314

00:41:18.275 --> 00:41:19.495 altering these processes

NOTE Confidence: 0.9304377

00:41:20.049 --> 00:41:21.569 can change circuit wiring in

NOTE Confidence: 0.9304377

00:41:21.569 --> 00:41:22.630 different brain disorders.

NOTE Confidence: 0.9638787

00:41:23.089 --> 00:41:24.130 So when we mess something

NOTE Confidence: 0.9638787

00:41:24.130 --> 00:41:24.630 up,

NOTE Confidence: 0.9860984

00:41:25.010 --> 00:41:26.210 when we change something, what

NOTE Confidence: 0.9860984

00:41:26.210 --> 00:41:27.489 does that really do, and

NOTE Confidence: 0.9860984

00:41:27.489 --> 00:41:29.010 should we expect something different

NOTE Confidence: 0.9860984

00:41:29.010 --> 00:41:30.049 when we look at imaging

NOTE Confidence: 0.9860984

00:41:30.049 --> 00:41:30.549 data?

NOTE Confidence: 0.8953267

00:41:31.089 --> 00:41:31.829 So overall,

NOTE Confidence: 0.99293673

00:41:32.289 --> 00:41:34.035 just a general summary is

NOTE Confidence: 0.99293673

00:41:34.035 --> 00:41:35.635 that we know genetic mutations

NOTE Confidence: 0.99293673

00:41:35.635 --> 00:41:36.835 can affect the development of

NOTE Confidence: 0.99293673

00:41:36.835 --> 00:41:38.315 brain circuits, but mice are

NOTE Confidence: 0.99293673

00:41:38.315 --> 00:41:39.555 a really crucial tool for

NOTE Confidence: 0.99293673

00:41:39.555 --> 00:41:40.435 us to be able to

NOTE Confidence: 0.99293673

00:41:40.435 --> 00:41:42.214 assess what's truly going on.

NOTE Confidence: 0.97396934

00:41:44.275 --> 00:41:46.195 Fine resolution tracing of early

NOTE Confidence: 0.97396934

00:41:46.195 --> 00:41:48.560 functional developmental circuits is possible

NOTE Confidence: 0.9176718

00:41:49.020 --> 00:41:50.620 using rabies virus three d

NOTE Confidence: 0.9176718

00:41:50.620 --> 00:41:51.980 brain imaging and single cell

NOTE Confidence: 0.9176718

00:41:51.980 --> 00:41:53.280 RNA seq to

NOTE Confidence: 0.98584855

00:41:53.580 --> 00:41:55.180 kind of integrate what cells

NOTE Confidence: 0.98584855

00:41:55.180 --> 00:41:56.460 these are, where they're connecting

NOTE Confidence: 0.98584855

00:41:56.460 --> 00:41:57.500 to, and do it across

NOTE Confidence: 0.98584855

00:41:57.500 --> 00:41:58.000 time.

NOTE Confidence: 0.99912137

00:41:58.620 --> 00:42:00.160 And then by using these

NOTE Confidence: 0.99912137

00:42:00.300 --> 00:42:00.800 more

NOTE Confidence: 0.98529893

00:42:02.835 --> 00:42:04.515 cross species comparisons, it may

NOTE Confidence: 0.98529893

00:42:04.515 --> 00:42:06.455 reveal conserved features that underlie

NOTE Confidence: 0.9991442

00:42:06.835 --> 00:42:08.695 developmental circuit wiring that's

NOTE Confidence: 0.9940275

00:42:09.155 --> 00:42:10.594 relevant to brain disorders and

NOTE Confidence: 0.9940275

00:42:10.594 --> 00:42:11.555 may also lead us in

NOTE Confidence: 0.9940275

00:42:11.555 --> 00:42:12.055 avenues

NOTE Confidence: 0.9794122

00:42:12.594 --> 00:42:14.114 where something is not present

NOTE Confidence: 0.9794122

00:42:14.114 --> 00:42:14.994 in mice, but may be

NOTE Confidence: 0.9794122

00:42:14.994 --> 00:42:16.675 present in human. And this

NOTE Confidence: 0.9794122

00:42:16.675 --> 00:42:17.175 advancement

NOTE Confidence: 0.96585816

00:42:17.700 --> 00:42:18.500 may kind of be at

NOTE Confidence: 0.96585816

00:42:18.500 --> 00:42:19.880 the heart of of

NOTE Confidence: 0.98533213

00:42:24.339 --> 00:42:25.400 possible disruption.

NOTE Confidence: 0.9981386

00:42:26.339 --> 00:42:27.560 And so with that,

NOTE Confidence: 0.91810817

00:42:28.180 --> 00:42:29.940 both Nanad and Karthik's labs

NOTE Confidence: 0.91810817

00:42:29.940 --> 00:42:31.219 as well as Christian's lab

NOTE Confidence: 0.91810817

00:42:31.219 --> 00:42:32.820 have been integral in setting

NOTE Confidence: 0.91810817

00:42:32.820 --> 00:42:33.480 this up,

NOTE Confidence: 0.99969167

00:42:34.075 --> 00:42:35.275 and I'd be happy to

NOTE Confidence: 0.99969167

00:42:35.275 --> 00:42:36.175 take any questions.

NOTE Confidence: 0.98093486

00:42:53.289 --> 00:42:54.089 I mean, how can you

NOTE Confidence: 0.98093486

00:42:54.089 --> 00:42:54.969 not be impressed by those

NOTE Confidence: 0.98093486

00:42:54.969 --> 00:42:56.089 images of the brain? They're

NOTE Confidence: 0.98093486

00:42:56.089 --> 00:42:57.369 just so, so cool.

NOTE Confidence: 0.8630459

00:42:57.690 --> 00:42:58.890 I was just wondering, maybe

NOTE Confidence: 0.8630459

00:42:58.890 --> 00:43:00.250 I missed is there a

NOTE Confidence: 0.8630459

00:43:00.250 --> 00:43:02.009 parallel sets of experiments going

NOTE Confidence: 0.8630459

00:43:02.009 --> 00:43:04.005 on with, maternal immune activation

NOTE Confidence: 0.8630459

00:43:04.145 --> 00:43:04.864 to look at,

NOTE Confidence: 0.9996532

00:43:05.585 --> 00:43:06.085 connectivity

NOTE Confidence: 0.9814948

00:43:06.625 --> 00:43:07.985 in in the postnatal period

NOTE Confidence: 0.9814948

00:43:07.985 --> 00:43:09.905 as well? So we haven't

NOTE Confidence: 0.9814948

00:43:09.905 --> 00:43:11.344 really considered doing that, but

NOTE Confidence: 0.9814948

00:43:11.344 --> 00:43:12.545 it's a good idea. Right

NOTE Confidence: 0.9814948

00:43:12.545 --> 00:43:14.864 now, our initial focus is

NOTE Confidence: 0.9814948

00:43:14.864 --> 00:43:15.905 to kind of stick with,

NOTE Confidence: 0.9814948

00:43:16.225 --> 00:43:18.325 the genetic mutations and see

NOTE Confidence: 0.9814948

00:43:18.520 --> 00:43:19.020 That's

NOTE Confidence: 0.99931943

00:43:19.400 --> 00:43:20.620 a bit more of

NOTE Confidence: 0.9839178

00:43:21.800 --> 00:43:23.400 a straightforward approach for us.

NOTE Confidence: 0.9839178

00:43:23.400 --> 00:43:24.520 Right? It's more of a

NOTE Confidence: 0.9839178

00:43:24.520 --> 00:43:26.120 binary. And so it's a

NOTE Confidence: 0.9839178

00:43:26.120 --> 00:43:26.780 good question,

NOTE Confidence: 0.9625282

00:43:27.160 --> 00:43:28.680 and maybe something for for

NOTE Confidence: 0.9625282

00:43:28.680 --> 00:43:30.280 future postdocs down the road.

NOTE Confidence: 0.9625282

00:43:30.280 --> 00:43:30.780 Thanks.

NOTE Confidence: 0.8809403

00:43:37.465 --> 00:43:39.165 Oh yeah, so I was

NOTE Confidence: 0.4907947

00:43:39.945 --> 00:43:40.445 asking,

NOTE Confidence: 0.92586905

00:43:41.625 --> 00:43:42.745 so Dan was presenting work

NOTE Confidence: 0.92586905

00:43:42.745 --> 00:43:43.885 on genetic manipulations

NOTE Confidence: 0.99560916

00:43:44.585 --> 00:43:45.645 and how that alters

NOTE Confidence: 0.9742807

00:43:46.025 --> 00:43:47.085 cortical connectivity

NOTE Confidence: 0.9639218

00:43:47.719 --> 00:43:49.079 And, I know in Karthik's

NOTE Confidence: 0.9639218

00:43:49.079 --> 00:43:50.440 lab, they're very interested in

NOTE Confidence: 0.9639218

00:43:50.440 --> 00:43:52.619 maternal immune activation, so infection,

NOTE Confidence: 0.98159516

00:43:52.920 --> 00:43:54.219 and how that can also

NOTE Confidence: 0.98159516

00:43:54.279 --> 00:43:55.819 alter kind of brain wiring.

NOTE Confidence: 0.9946747

00:43:56.279 --> 00:43:57.079 And so I was just

NOTE Confidence: 0.9946747

00:43:57.079 --> 00:43:58.440 wondering if they'd use that

NOTE Confidence: 0.9946747

00:43:58.440 --> 00:43:59.799 rabies tool to look at

NOTE Confidence: 0.9946747

00:43:59.799 --> 00:44:00.460 the connectivity

NOTE Confidence: 0.99980307

00:44:01.005 --> 00:44:01.744 following maternal

NOTE Confidence: 0.9964956

00:44:02.125 --> 00:44:03.904 infection or immune activation

NOTE Confidence: 0.93795335

00:44:04.285 --> 00:44:05.164 to see how that could

NOTE Confidence: 0.93795335

00:44:05.164 --> 00:44:06.765 alter connectivity because there's at

NOTE Confidence: 0.93795335

00:44:06.765 --> 00:44:07.265 least

NOTE Confidence: 0.94758105

00:44:07.964 --> 00:44:09.164 in the offspring in the

NOTE Confidence: 0.94758105

00:44:09.164 --> 00:44:10.525 offspring. Yeah. With this kind

NOTE Confidence: 0.94758105

00:44:10.525 --> 00:44:11.805 of idea that maternal immune

NOTE Confidence: 0.94758105

00:44:11.805 --> 00:44:13.469 activation has been associated with

NOTE Confidence: 0.94758105

00:44:13.630 --> 00:44:15.230 increased risk for psychiatric disorders,

NOTE Confidence: 0.94758105

00:44:15.230 --> 00:44:17.310 including schizophrenia that are associated

NOTE Confidence: 0.94758105

00:44:17.310 --> 00:44:18.290 with ultra connectivity.

NOTE Confidence: 0.98510456

00:44:25.725 --> 00:44:27.565 Impressive. This is completely outside

NOTE Confidence: 0.98510456

00:44:27.565 --> 00:44:28.605 of my wheelhouse. I'm a

NOTE Confidence: 0.98510456

00:44:28.605 --> 00:44:30.364 clinical, you know, scientist for

NOTE Confidence: 0.98510456

00:44:30.445 --> 00:44:31.725 that does therapy work. But

NOTE Confidence: 0.98510456

00:44:31.725 --> 00:44:33.485 I'm wondering if I'm thinking

NOTE Confidence: 0.98510456

00:44:33.485 --> 00:44:34.525 about this as it might

NOTE Confidence: 0.98510456

00:44:34.525 --> 00:44:35.425 apply to,

NOTE Confidence: 0.9916501

00:44:36.765 --> 00:44:38.945 aggressive behavior or impulsivity.

NOTE Confidence: 0.9274268

00:44:39.325 --> 00:44:40.560 And so if if thinking

NOTE Confidence: 0.9274268

00:44:40.560 --> 00:44:42.000 about cortical connections, and do

NOTE Confidence: 0.9274268

00:44:42.000 --> 00:44:43.040 you think there is some

NOTE Confidence: 0.9274268

00:44:43.040 --> 00:44:44.320 relevance to this kind of

NOTE Confidence: 0.9274268

00:44:44.320 --> 00:44:45.380 work to studying

NOTE Confidence: 0.8927509

00:44:45.760 --> 00:44:47.400 that down the road in

NOTE Confidence: 0.9561564

00:44:47.840 --> 00:44:49.040 Yeah. I think so. It

NOTE Confidence: 0.9561564

00:44:49.040 --> 00:44:50.580 impacts humans and their impulsivity.

NOTE Confidence: 0.99309886

00:44:51.120 --> 00:44:51.620 Mhmm.

NOTE Confidence: 0.9745261

00:44:51.920 --> 00:44:52.900 So impulsivity,

NOTE Confidence: 0.9446003

00:44:54.255 --> 00:44:55.375 unsure because I don't know

NOTE Confidence: 0.9446003

00:44:55.375 --> 00:44:56.654 how you study that in

NOTE Confidence: 0.9446003

00:44:56.654 --> 00:44:57.694 mice. I don't have a

NOTE Confidence: 0.9446003

00:44:57.694 --> 00:44:59.474 a behavioral background, so,

NOTE Confidence: 0.96615905

00:45:00.255 --> 00:45:01.875 not my area either. But

NOTE Confidence: 0.9085844

00:45:03.694 --> 00:45:05.214 different types of behavior. So

NOTE Confidence: 0.9085844

00:45:05.214 --> 00:45:05.875 let's say

NOTE Confidence: 0.9564282

00:45:06.255 --> 00:45:07.154 there's altered

NOTE Confidence: 0.9864134

00:45:07.830 --> 00:45:10.010 connections between between the amygdala

NOTE Confidence: 0.9864134

00:45:10.150 --> 00:45:11.370 and the frontal cortex,

NOTE Confidence: 0.92197794

00:45:11.670 --> 00:45:12.710 but we may see difference

NOTE Confidence: 0.92197794

00:45:12.710 --> 00:45:14.310 in anxiety or fear or

NOTE Confidence: 0.92197794

00:45:14.310 --> 00:45:15.130 something else.

NOTE Confidence: 0.92899233

00:45:15.910 --> 00:45:17.370 And, typically, we use,

NOTE Confidence: 0.9843089

00:45:18.710 --> 00:45:20.650 just different retrograde or anterograde

NOTE Confidence: 0.9843089

00:45:20.790 --> 00:45:21.290 tracers.

NOTE Confidence: 0.974368

00:45:22.185 --> 00:45:23.625 But this may be useful

NOTE Confidence: 0.974368

00:45:23.625 --> 00:45:24.825 to see where they're actually

NOTE Confidence: 0.974368

00:45:24.825 --> 00:45:27.325 forming functional synapses as opposed

NOTE Confidence: 0.99702847

00:45:27.785 --> 00:45:29.085 to the typical location.

NOTE Confidence: 0.94410664

00:45:29.545 --> 00:45:30.665 And so seeing, okay. They're

NOTE Confidence: 0.94410664

00:45:30.665 --> 00:45:32.265 not going to prefrontal cortex,

NOTE Confidence: 0.94410664

00:45:32.265 --> 00:45:32.765 but

NOTE Confidence: 0.9876213

00:45:33.065 --> 00:45:34.185 what are they connecting to

NOTE Confidence: 0.9876213

00:45:34.185 --> 00:45:35.145 now that may make a

NOTE Confidence: 0.9876213

00:45:35.145 --> 00:45:36.825 difference? Maybe it's not simply

NOTE Confidence: 0.9876213

00:45:36.825 --> 00:45:38.550 the loss of connections, but

NOTE Confidence: 0.9876213

00:45:38.550 --> 00:45:40.410 the alteration of those connections

NOTE Confidence: 0.9876213

00:45:40.470 --> 00:45:42.150 instead. So I think yes.

NOTE Confidence: 0.9862455

00:45:43.110 --> 00:45:43.610 And

NOTE Confidence: 0.9378421

00:45:43.989 --> 00:45:45.750 Nanad's lab has Nanad's lab

NOTE Confidence: 0.9378421

00:45:45.750 --> 00:45:46.550 has done a little bit

NOTE Confidence: 0.9378421

00:45:46.550 --> 00:45:48.970 of behavior on altered circuits,

NOTE Confidence: 0.9765606

00:45:51.344 --> 00:45:52.945 but we hadn't applied the

NOTE Confidence: 0.9765606

00:45:52.945 --> 00:45:54.805 the rabies virus approach. So

NOTE Confidence: 0.9975033

00:45:55.105 --> 00:45:57.445 we haven't truly identified the

NOTE Confidence: 0.9975033

00:45:57.505 --> 00:45:59.525 individual connections at that level.

NOTE Confidence: 0.98502004

00:46:00.465 --> 00:46:01.285 Thank you.

NOTE Confidence: 0.99441576

00:46:02.545 --> 00:46:03.525 Any other questions?

NOTE Confidence: 0.8594992

00:46:04.950 --> 00:46:05.930 I have two.

NOTE Confidence: 0.9630273

00:46:06.310 --> 00:46:08.089 So the first question is,

NOTE Confidence: 0.8982446

00:46:08.950 --> 00:46:09.910 we study EEG in the

NOTE Confidence: 0.8982446

00:46:09.910 --> 00:46:11.050 lab. We use EEG.

NOTE Confidence: 0.9971213

00:46:11.430 --> 00:46:11.930 And

NOTE Confidence: 0.9438063

00:46:12.230 --> 00:46:14.070 lamina cortical connectivity is known

NOTE Confidence: 0.9438063

00:46:14.070 --> 00:46:15.430 to be a major driver

NOTE Confidence: 0.9438063

00:46:15.430 --> 00:46:16.630 of the EEG that we

NOTE Confidence: 0.9438063

00:46:16.630 --> 00:46:17.130 measure.

NOTE Confidence: 0.98550093

00:46:17.585 --> 00:46:18.884 And you're able to,

NOTE Confidence: 0.9422782

00:46:19.344 --> 00:46:20.384 it sounds like to me,

NOTE Confidence: 0.9422782

00:46:20.384 --> 00:46:21.444 although I'm novice

NOTE Confidence: 0.96753275

00:46:21.744 --> 00:46:22.884 at your level of neuroscience,

NOTE Confidence: 0.8913983

00:46:23.825 --> 00:46:24.565 able to,

NOTE Confidence: 0.9953675

00:46:25.825 --> 00:46:27.045 affect the laminar

NOTE Confidence: 0.99410236

00:46:27.344 --> 00:46:29.444 development of, in the cortex.

NOTE Confidence: 0.9724778

00:46:29.960 --> 00:46:30.859 And so I'm wondering,

NOTE Confidence: 0.9803634

00:46:31.239 --> 00:46:31.960 and I know that people

NOTE Confidence: 0.9803634

00:46:31.960 --> 00:46:33.339 do EEG in mice,

NOTE Confidence: 0.6864597

00:46:33.960 --> 00:46:34.779 little caps.

NOTE Confidence: 0.96876717

00:46:35.880 --> 00:46:37.019 Are they able to,

NOTE Confidence: 0.9930538

00:46:38.119 --> 00:46:39.099 affect those,

NOTE Confidence: 0.9410862

00:46:39.719 --> 00:46:41.719 laminar structures and then be

NOTE Confidence: 0.92041284

00:46:42.545 --> 00:46:43.425 have some sense of how

NOTE Confidence: 0.92041284

00:46:43.505 --> 00:46:44.645 what that does to EEG.

NOTE Confidence: 0.92041284

00:46:44.705 --> 00:46:45.665 Right? Right now, it's a

NOTE Confidence: 0.92041284

00:46:45.665 --> 00:46:46.545 black box for us. So

NOTE Confidence: 0.92041284

00:46:46.545 --> 00:46:47.105 I'm wondering

NOTE Confidence: 0.9915763

00:46:47.505 --> 00:46:48.245 Yeah. What

NOTE Confidence: 0.9679114

00:46:48.785 --> 00:46:50.864 I'm not a hundred percent

NOTE Confidence: 0.9679114

00:46:50.864 --> 00:46:52.325 sure. I imagine yes.

NOTE Confidence: 0.8701792

00:46:54.640 --> 00:46:55.780 So for example

NOTE Confidence: 0.9768018

00:46:56.560 --> 00:46:57.760 oh, the sharing is gone.

NOTE Confidence: 0.9768018

00:46:57.760 --> 00:46:58.239 But,

NOTE Confidence: 0.99206173

00:46:58.800 --> 00:47:00.260 if we disrupt the barrels,

NOTE Confidence: 0.99206173

00:47:00.400 --> 00:47:01.520 let's say, even if we

NOTE Confidence: 0.99206173

00:47:01.520 --> 00:47:03.119 don't affect the lamination, if

NOTE Confidence: 0.99206173

00:47:03.119 --> 00:47:04.480 we just disrupt where those

NOTE Confidence: 0.99206173

00:47:04.480 --> 00:47:06.320 projections are going, we should

NOTE Confidence: 0.99206173

00:47:06.320 --> 00:47:07.280 see a shift in the

NOTE Confidence: 0.99206173

00:47:07.280 --> 00:47:07.755 input

NOTE Confidence: 0.97775745

00:47:08.234 --> 00:47:09.434 activity. So if there's no

NOTE Confidence: 0.97775745

00:47:09.434 --> 00:47:11.194 longer stereotyped whisker barrels, we

NOTE Confidence: 0.97775745

00:47:11.194 --> 00:47:12.234 would expect that in the

NOTE Confidence: 0.97775745

00:47:12.234 --> 00:47:12.734 EEG,

NOTE Confidence: 0.9673903

00:47:13.114 --> 00:47:14.154 you would no longer get

NOTE Confidence: 0.9673903

00:47:14.154 --> 00:47:14.974 kind of those,

NOTE Confidence: 0.9942673

00:47:15.914 --> 00:47:17.934 robust signals where the somatosensory

NOTE Confidence: 0.8323959

00:47:18.234 --> 00:47:20.255 cortex is and maybe more

NOTE Confidence: 0.9935359

00:47:20.634 --> 00:47:21.134 widespread

NOTE Confidence: 0.91198516

00:47:21.434 --> 00:47:22.494 but lower level.

NOTE Confidence: 0.9535627

00:47:22.969 --> 00:47:24.170 So EEG relies on the

NOTE Confidence: 0.9535627

00:47:24.170 --> 00:47:25.930 columnar structure of the of

NOTE Confidence: 0.9535627

00:47:25.930 --> 00:47:27.130 the cortex, and you're disrupting

NOTE Confidence: 0.9535627

00:47:27.130 --> 00:47:28.010 that, and that would affect

NOTE Confidence: 0.9535627

00:47:28.010 --> 00:47:29.549 the EEG. Okay. Yeah.

NOTE Confidence: 0.98064053

00:47:29.930 --> 00:47:31.369 And my second question, this

NOTE Confidence: 0.98064053

00:47:31.369 --> 00:47:32.670 is a colleague of mine.

NOTE Confidence: 0.9972717

00:47:34.650 --> 00:47:36.029 A colleague of mine studies,

NOTE Confidence: 0.88989353

00:47:36.410 --> 00:47:37.549 premature babies.

NOTE Confidence: 0.99313515

00:47:38.025 --> 00:47:39.545 And he's following them into

NOTE Confidence: 0.99313515

00:47:39.545 --> 00:47:41.305 adulthood. And what he's noticing

NOTE Confidence: 0.99313515

00:47:41.305 --> 00:47:42.664 is that they are more

NOTE Confidence: 0.99313515

00:47:42.664 --> 00:47:43.944 avoidant, so bridging the two

NOTE Confidence: 0.99313515

00:47:43.944 --> 00:47:44.444 talks.

NOTE Confidence: 0.9969374

00:47:44.744 --> 00:47:45.484 And so,

NOTE Confidence: 0.9588673

00:47:46.424 --> 00:47:47.224 you know, I know there's

NOTE Confidence: 0.9588673

00:47:47.224 --> 00:47:48.844 some disruption in in terms

NOTE Confidence: 0.9588673

00:47:48.905 --> 00:47:50.285 of lamocortical connectivity

NOTE Confidence: 0.96920586

00:47:50.585 --> 00:47:51.325 with prematurity.

NOTE Confidence: 0.9934708

00:47:51.944 --> 00:47:53.484 And I'm wondering, you know,

NOTE Confidence: 0.99956334

00:47:54.239 --> 00:47:55.700 do people do animal studies

NOTE Confidence: 0.99956334

00:47:55.840 --> 00:47:56.580 on prematurity

NOTE Confidence: 0.9452109

00:47:56.880 --> 00:47:58.719 and looking at avoidance as

NOTE Confidence: 0.9452109

00:47:58.719 --> 00:47:59.620 a as an outcome?

NOTE Confidence: 0.8122528

00:48:01.200 --> 00:48:02.020 A good question.

NOTE Confidence: 0.9805244

00:48:02.400 --> 00:48:04.000 Again, not one hundred percent

NOTE Confidence: 0.9805244

00:48:04.000 --> 00:48:04.960 sure, but I'm

NOTE Confidence: 0.9719695

00:48:07.445 --> 00:48:07.945 prematurity,

NOTE Confidence: 0.97073686

00:48:08.965 --> 00:48:10.325 I would imagine the max

NOTE Confidence: 0.97073686

00:48:10.325 --> 00:48:12.005 is only one day or

NOTE Confidence: 0.97073686

00:48:12.005 --> 00:48:13.205 so in the mouse. So

NOTE Confidence: 0.97073686

00:48:13.205 --> 00:48:14.344 we can we can

NOTE Confidence: 0.98817015

00:48:15.045 --> 00:48:16.405 have the mice delivered one

NOTE Confidence: 0.98817015

00:48:16.405 --> 00:48:18.245 day early, so eighteen days

NOTE Confidence: 0.98817015

00:48:18.245 --> 00:48:20.380 instead of nineteen. But the

NOTE Confidence: 0.98817015

00:48:20.380 --> 00:48:21.660 earlier you go, they won't

NOTE Confidence: 0.98817015

00:48:21.660 --> 00:48:23.040 survive outside the womb.

NOTE Confidence: 0.992386

00:48:24.460 --> 00:48:25.580 Like I said, the the

NOTE Confidence: 0.992386

00:48:25.580 --> 00:48:27.200 p zero stage is about

NOTE Confidence: 0.9638419

00:48:28.540 --> 00:48:29.680 late mid fetal.

NOTE Confidence: 0.9883375

00:48:30.219 --> 00:48:31.340 So if we try to

NOTE Confidence: 0.9883375

00:48:31.340 --> 00:48:32.940 deliver earlier than that, it's

NOTE Confidence: 0.9883375

00:48:32.940 --> 00:48:34.719 gonna be really, really difficult.

NOTE Confidence: 0.9836814

00:48:40.474 --> 00:48:41.375 There are ways

NOTE Confidence: 0.9352204

00:48:42.234 --> 00:48:43.835 aside from disrupting the cortex

NOTE Confidence: 0.9352204

00:48:43.835 --> 00:48:45.055 to disrupt thalamocortical

NOTE Confidence: 0.91375303

00:48:45.435 --> 00:48:46.815 innervation, though. If we,

NOTE Confidence: 0.98186374

00:48:47.915 --> 00:48:49.035 mess with the thalamus a

NOTE Confidence: 0.98186374

00:48:49.035 --> 00:48:49.835 little bit, we're able to

NOTE Confidence: 0.98186374

00:48:49.835 --> 00:48:51.035 affect where their axons go

NOTE Confidence: 0.98186374

00:48:51.035 --> 00:48:52.140 as well or their projections

NOTE Confidence: 0.98186374

00:48:52.140 --> 00:48:53.819 go. So that's maybe an

NOTE Confidence: 0.98186374

00:48:53.819 --> 00:48:54.319 alternative

NOTE Confidence: 0.9984369

00:48:54.940 --> 00:48:56.539 to if you see something

NOTE Confidence: 0.9984369

00:48:56.539 --> 00:48:57.039 in

NOTE Confidence: 0.9174435

00:48:59.099 --> 00:49:00.799 imaging data from premature

NOTE Confidence: 0.9906752

00:49:01.819 --> 00:49:02.719 human births,

NOTE Confidence: 0.98945767

00:49:03.500 --> 00:49:04.299 then we may be able

NOTE Confidence: 0.98945767

00:49:04.299 --> 00:49:05.579 to model that back into

NOTE Confidence: 0.98945767

00:49:05.579 --> 00:49:06.705 the mice and say, okay.

NOTE Confidence: 0.98945767

00:49:06.864 --> 00:49:08.385 Now let's direct the circuits

NOTE Confidence: 0.98945767

00:49:08.385 --> 00:49:10.065 to form elsewhere. What really

NOTE Confidence: 0.98945767

00:49:10.065 --> 00:49:11.285 happens with the mice?

NOTE Confidence: 0.94265926

00:49:11.665 --> 00:49:13.265 I see. It's a diffuse

NOTE Confidence: 0.94265926

00:49:13.265 --> 00:49:14.864 insult, really. So it's Mhmm.

NOTE Confidence: 0.94265926

00:49:14.864 --> 00:49:16.385 It's yeah. Yeah. Okay. Well,

NOTE Confidence: 0.94265926

00:49:16.385 --> 00:49:17.525 thank you for your your

NOTE Confidence: 0.94265926

00:49:17.585 --> 00:49:19.025 answer and for this wonderful

NOTE Confidence: 0.94265926

00:49:19.025 --> 00:49:20.245 talk. Any other questions?