

WEBVTT

NOTE duration:"00:55:47.4560000"

NOTE language:en-us

NOTE Confidence: 0.84646976

00:00:00.000 --> 00:00:03.480 Hello and welcome to grand rounds.

NOTE Confidence: 0.84646976

00:00:03.480 --> 00:00:06.602 Today is the second of three lectures

NOTE Confidence: 0.84646976

00:00:06.602 --> 00:00:09.649 honoring our late director and friend,

NOTE Confidence: 0.84646976

00:00:09.650 --> 00:00:11.186 Doctor Donald J Cohen.

NOTE Confidence: 0.84646976

00:00:11.186 --> 00:00:14.254 Before we go to the main event

NOTE Confidence: 0.84646976

00:00:14.254 --> 00:00:16.279 with Kartik's presentation,

NOTE Confidence: 0.84646976

00:00:16.280 --> 00:00:19.507 I want to share some images and

NOTE Confidence: 0.84646976

00:00:19.507 --> 00:00:21.500 thoughts about Doctor Cohen,

NOTE Confidence: 0.84646976

00:00:21.500 --> 00:00:24.804 recognizing that many of us here today,

NOTE Confidence: 0.84646976

00:00:24.810 --> 00:00:26.974 especially our younger trainees,

NOTE Confidence: 0.84646976

00:00:26.974 --> 00:00:30.810 may not have known Donald Donald Cohen.

NOTE Confidence: 0.84646976

00:00:30.810 --> 00:00:33.354 To remind you who lived between 1940 and

NOTE Confidence: 0.84646976

00:00:33.354 --> 00:00:36.440 2001 was a Sterling professor of child

NOTE Confidence: 0.84646976

00:00:36.440 --> 00:00:38.344 psychiatry psychology in Pediatrics,

NOTE Confidence: 0.84646976

00:00:38.350 --> 00:00:41.414 and he was the director of the Deal

NOTE Confidence: 0.84646976

00:00:41.414 --> 00:00:44.309 Child Study Center from 1983 to 2001.

NOTE Confidence: 0.84646976

00:00:44.310 --> 00:00:47.110 He was one of the most renowned

NOTE Confidence: 0.84646976

00:00:47.110 --> 00:00:49.045 child psychiatrists in the world

NOTE Confidence: 0.84646976

00:00:49.045 --> 00:00:51.653 and those of us who came under his

NOTE Confidence: 0.84646976

00:00:51.734 --> 00:00:54.626 influence remember him not only fondly,

NOTE Confidence: 0.84646976

00:00:54.630 --> 00:00:58.918 but our lives were really changed by him.

NOTE Confidence: 0.84646976

00:00:58.920 --> 00:01:01.447 As I talked the first time during

NOTE Confidence: 0.84646976

00:01:01.447 --> 00:01:02.530 Emily Olsen's presentation,

NOTE Confidence: 0.84646976

00:01:02.530 --> 00:01:04.696 I commented on Donald the builder.

NOTE Confidence: 0.84646976

00:01:04.700 --> 00:01:07.024 And when we talk when we have

NOTE Confidence: 0.84646976

00:01:07.024 --> 00:01:09.388 the third talk by Tom Fernandez,

NOTE Confidence: 0.84646976

00:01:09.390 --> 00:01:12.468 I will focus on Donald Cohen, the mentor.

NOTE Confidence: 0.84646976

00:01:12.468 --> 00:01:14.738 But today with Kartik's presentation,

NOTE Confidence: 0.84646976

00:01:14.740 --> 00:01:16.768 I think it's very fitting that

NOTE Confidence: 0.84646976

00:01:16.768 --> 00:01:18.570 I'll talk about Donald Cohen,
NOTE Confidence: 0.84646976

00:01:18.570 --> 00:01:19.300 the scientist,
NOTE Confidence: 0.84646976

00:01:19.300 --> 00:01:21.490 and one thing that Donald and
NOTE Confidence: 0.84646976

00:01:21.490 --> 00:01:23.918 Kartik had in common is that they
NOTE Confidence: 0.84646976

00:01:23.918 --> 00:01:25.543 both got science early on.
NOTE Confidence: 0.84646976

00:01:25.550 --> 00:01:29.303 They got the bug of science very early on.
NOTE Confidence: 0.84646976

00:01:29.310 --> 00:01:31.686 Karthik is the son of scientists.
NOTE Confidence: 0.84646976

00:01:31.690 --> 00:01:33.410 His early years were marinated
NOTE Confidence: 0.84646976

00:01:33.410 --> 00:01:36.124 in science and he is really the
NOTE Confidence: 0.84646976

00:01:36.124 --> 00:01:38.434 consummate scientist and like Donald,
NOTE Confidence: 0.84646976

00:01:38.440 --> 00:01:42.589 as I say he got the bug early on.
NOTE Confidence: 0.84646976

00:01:42.590 --> 00:01:45.260 Let me share with you how early
NOTE Confidence: 0.84646976

00:01:45.260 --> 00:01:46.780 Donald got this bug.
NOTE Confidence: 0.84646976

00:01:46.780 --> 00:01:49.828 This is an image from Donald in the
NOTE Confidence: 0.84646976

00:01:49.828 --> 00:01:52.050 4th grade, 3rd grade, 2nd grade.
NOTE Confidence: 0.84646976

00:01:52.050 --> 00:01:54.240 I'm sorry and these are words

NOTE Confidence: 0.84646976

00:01:54.314 --> 00:01:57.016 that he wrote maybe a year later

NOTE Confidence: 0.84646976

00:01:57.016 --> 00:01:58.970 after this photograph was taken.

NOTE Confidence: 0.84646976

00:01:58.970 --> 00:02:01.570 So let me quote.

NOTE Confidence: 0.84646976

00:02:01.570 --> 00:02:02.742 Even at age 8,

NOTE Confidence: 0.84646976

00:02:02.742 --> 00:02:04.207 I was curious about relationships

NOTE Confidence: 0.84646976

00:02:04.207 --> 00:02:05.858 and thought about thinking,

NOTE Confidence: 0.84646976

00:02:05.860 --> 00:02:08.170 especially how we think about each other.

NOTE Confidence: 0.84646976

00:02:08.170 --> 00:02:10.558 This was the context of my

NOTE Confidence: 0.84646976

00:02:10.558 --> 00:02:11.752 first formal interview.

NOTE Confidence: 0.84646976

00:02:11.760 --> 00:02:14.076 Michael and I often went to

NOTE Confidence: 0.84646976

00:02:14.076 --> 00:02:15.620 the Garfield Park Conservatory,

NOTE Confidence: 0.84646976

00:02:15.620 --> 00:02:17.164 a wonderful institution available

NOTE Confidence: 0.84646976

00:02:17.164 --> 00:02:18.708 to youngsters in Chicago.

NOTE Confidence: 0.84646976

00:02:18.710 --> 00:02:20.816 We would wander through the rooms

NOTE Confidence: 0.84646976

00:02:20.816 --> 00:02:22.730 filled with the tall tropical

NOTE Confidence: 0.84646976

00:02:22.730 --> 00:02:24.498 trees and exotic Flowers,
NOTE Confidence: 0.84646976

00:02:24.500 --> 00:02:28.404 taking in the beauty and Misty musty smells.
NOTE Confidence: 0.84646976

00:02:28.410 --> 00:02:30.258 I became especially aware of one
NOTE Confidence: 0.84646976

00:02:30.258 --> 00:02:32.288 man who would always be standing
NOTE Confidence: 0.84646976

00:02:32.288 --> 00:02:34.118 quietly and watering the plants.
NOTE Confidence: 0.84646976

00:02:34.120 --> 00:02:36.901 He patiently did his job with a sense of
NOTE Confidence: 0.84646976

00:02:36.901 --> 00:02:39.826 calm and a gentle smile for the newspaper.
NOTE Confidence: 0.84646976

00:02:39.830 --> 00:02:42.091 I thought he would be the ideal
NOTE Confidence: 0.84646976

00:02:42.091 --> 00:02:44.200 person to interview and he consented.
NOTE Confidence: 0.84646976

00:02:44.200 --> 00:02:46.132 The interview was then published in
NOTE Confidence: 0.84646976

00:02:46.132 --> 00:02:47.831 our school newspaper and constitutes
NOTE Confidence: 0.84646976

00:02:47.831 --> 00:02:49.576 one of the earlier reports,
NOTE Confidence: 0.84646976

00:02:49.580 --> 00:02:51.020 though less widely.
NOTE Confidence: 0.84646976

00:02:51.020 --> 00:02:54.380 Circulated than that of Kanner and Asperger,
NOTE Confidence: 0.84646976

00:02:54.380 --> 00:02:56.435 of the central phenomena that
NOTE Confidence: 0.84646976

00:02:56.435 --> 00:02:58.079 still intrigue our field.

NOTE Confidence: 0.84646976
00:02:58.080 --> 00:03:00.135 Let me quote the full
NOTE Confidence: 0.84646976
00:03:00.135 --> 00:03:01.779 article published in 1948,
NOTE Confidence: 0.84646976
00:03:01.780 --> 00:03:05.758 at this time as a historic.
NOTE Confidence: 0.84646976
00:03:05.760 --> 00:03:07.950 And the documentation of the launching
NOTE Confidence: 0.84646976
00:03:07.950 --> 00:03:10.650 of a lifetime career in autism research.
NOTE Confidence: 0.84646976
00:03:10.650 --> 00:03:13.210 This is a verbatim interview.
NOTE Confidence: 0.84646976
00:03:13.210 --> 00:03:16.836 I was a shy and frail child.
NOTE Confidence: 0.84646976
00:03:16.840 --> 00:03:17.525 Therefore,
NOTE Confidence: 0.84646976
00:03:17.525 --> 00:03:21.635 I decided to become a gardener.
NOTE Confidence: 0.84646976
00:03:21.640 --> 00:03:24.180 This early reporting is socially
NOTE Confidence: 0.84646976
00:03:24.180 --> 00:03:24.688 dysfunctional.
NOTE Confidence: 0.84646976
00:03:24.690 --> 00:03:26.730 Adult identifies constitutional factors,
NOTE Confidence: 0.84646976
00:03:26.730 --> 00:03:27.240 shines,
NOTE Confidence: 0.790881
00:03:27.240 --> 00:03:29.560 and possible biological coral.
NOTE Confidence: 0.790881
00:03:29.560 --> 00:03:33.040 Its frailty with long term prognosis
NOTE Confidence: 0.790881

00:03:33.136 --> 00:03:35.890 in a career that was socially isolated,

NOTE Confidence: 0.790881

00:03:35.890 --> 00:03:38.876 the Gardner represents an optimistic

NOTE Confidence: 0.790881

00:03:38.876 --> 00:03:41.352 adaptation to an underlying

NOTE Confidence: 0.790881

00:03:41.352 --> 00:03:44.269 disability in social orientation.

NOTE Confidence: 0.790881

00:03:44.270 --> 00:03:46.448 So that's not. Donald, of course.

NOTE Confidence: 0.790881

00:03:46.450 --> 00:03:49.282 Went on to build a career focus on

NOTE Confidence: 0.790881

00:03:49.282 --> 00:03:51.578 autism work that has continued with

NOTE Confidence: 0.790881

00:03:51.578 --> 00:03:54.459 the likes of Red Oak Mark of Ami,

NOTE Confidence: 0.790881

00:03:54.460 --> 00:03:57.160 Klin of Jane McParland and so

NOTE Confidence: 0.790881

00:03:57.160 --> 00:04:00.110 many other of our colleagues.

NOTE Confidence: 0.790881

00:04:00.110 --> 00:04:02.310 Donna was also a psychoanalyst.

NOTE Confidence: 0.790881

00:04:02.310 --> 00:04:04.310 We're delighted that Phyllis Cohen

NOTE Confidence: 0.790881

00:04:04.310 --> 00:04:07.280 is joining us today and here you see,

NOTE Confidence: 0.790881

00:04:07.280 --> 00:04:09.645 Phyllis and Donald hanging out

NOTE Confidence: 0.790881

00:04:09.645 --> 00:04:11.064 with Anna Freud.

NOTE Confidence: 0.790881

00:04:11.070 --> 00:04:13.458 And this work in psychoanalysis and

NOTE Confidence: 0.790881
00:04:13.458 --> 00:04:15.670 bringing analysis and science together,
NOTE Confidence: 0.790881
00:04:15.670 --> 00:04:17.338 continues thinking of the
NOTE Confidence: 0.790881
00:04:17.338 --> 00:04:19.006 individual and the science,
NOTE Confidence: 0.790881
00:04:19.010 --> 00:04:21.100 not as two separate things,
NOTE Confidence: 0.790881
00:04:21.100 --> 00:04:24.075 but together the importance of
NOTE Confidence: 0.790881
00:04:24.075 --> 00:04:25.860 the lived experience.
NOTE Confidence: 0.790881
00:04:25.860 --> 00:04:28.443 And this is work that also continues
NOTE Confidence: 0.790881
00:04:28.443 --> 00:04:31.230 with Linda and the work at the
NOTE Confidence: 0.790881
00:04:31.230 --> 00:04:33.240 unemployed Center in London today.
NOTE Confidence: 0.790881
00:04:33.240 --> 00:04:35.185 Donald also was a pioneer
NOTE Confidence: 0.790881
00:04:35.185 --> 00:04:37.130 in the use of medication.
NOTE Confidence: 0.790881
00:04:37.130 --> 00:04:39.824 This is the persons of quantity
NOTE Confidence: 0.790881
00:04:39.824 --> 00:04:41.620 1979 for Tourette syndrome.
NOTE Confidence: 0.790881
00:04:41.620 --> 00:04:44.500 And the rest, as we say, is history.
NOTE Confidence: 0.790881
00:04:44.500 --> 00:04:47.380 This is a work that has continued with,
NOTE Confidence: 0.790881

00:04:47.380 --> 00:04:50.244 I mean Amy Arnsten here at Yale with
NOTE Confidence: 0.790881

00:04:50.244 --> 00:04:53.433 Larry Scale now at Emory and medications
NOTE Confidence: 0.790881

00:04:53.433 --> 00:04:55.823 that have really revolutionized the
NOTE Confidence: 0.790881

00:04:55.903 --> 00:04:58.369 way that we treat ADHD Tourettes.
NOTE Confidence: 0.790881

00:04:58.370 --> 00:05:01.513 Here you have Donald in the 1970s
NOTE Confidence: 0.790881

00:05:01.513 --> 00:05:04.930 working on the molecule of quantity.
NOTE Confidence: 0.790881

00:05:04.930 --> 00:05:06.181 And that works.
NOTE Confidence: 0.790881

00:05:06.181 --> 00:05:08.683 That focus on threats continues most
NOTE Confidence: 0.790881

00:05:08.683 --> 00:05:11.561 notably with the work of Jim Lechman
NOTE Confidence: 0.790881

00:05:11.561 --> 00:05:13.602 and the incredible influence that
NOTE Confidence: 0.790881

00:05:13.602 --> 00:05:16.283 Donald had on Jim and the incredible
NOTE Confidence: 0.790881

00:05:16.283 --> 00:05:20.260 influence the gym in turn has had on.
NOTE Confidence: 0.790881

00:05:20.260 --> 00:05:22.708 Like a block on me personally,
NOTE Confidence: 0.790881

00:05:22.710 --> 00:05:26.130 and certainly on our hero of
NOTE Confidence: 0.790881

00:05:26.130 --> 00:05:28.410 the day on Karthik.
NOTE Confidence: 0.790881

00:05:28.410 --> 00:05:29.895 So without further ado,

NOTE Confidence: 0.790881

00:05:29.895 --> 00:05:32.520 let's see what the legacy of Donald

NOTE Confidence: 0.790881

00:05:32.596 --> 00:05:34.661 and the funds from his chair have

NOTE Confidence: 0.790881

00:05:34.661 --> 00:05:37.562 gone to do in the work of wonderful

NOTE Confidence: 0.790881

00:05:37.562 --> 00:05:39.867 young scientists like Emily Olson and

NOTE Confidence: 0.790881

00:05:39.867 --> 00:05:42.009 today Kartick Kartick take it away.

NOTE Confidence: 0.790881

00:05:42.010 --> 00:05:44.212 The grades were dropping and then

NOTE Confidence: 0.790881

00:05:44.212 --> 00:05:46.669 they started to notice that the child

NOTE Confidence: 0.83042085

00:05:46.670 --> 00:05:48.752 was spending more time in their

NOTE Confidence: 0.83042085

00:05:48.752 --> 00:05:50.876 room and eventually the mother was

NOTE Confidence: 0.83042085

00:05:50.876 --> 00:05:52.880 trying to concern and brought him

NOTE Confidence: 0.83042085

00:05:52.880 --> 00:05:55.135 into the emergency room because she

NOTE Confidence: 0.83042085

00:05:55.135 --> 00:05:57.844 noted that this child was talking to.

NOTE Confidence: 0.83042085

00:05:57.844 --> 00:05:59.580 Someone that wasn't there.

NOTE Confidence: 0.83042085

00:05:59.580 --> 00:06:01.638 Eventually the child is diagnosed with

NOTE Confidence: 0.83042085

00:06:01.638 --> 00:06:03.448 schizophrenia and from there schizophrenia

NOTE Confidence: 0.83042085

00:06:03.448 --> 00:06:05.722 is a progressive disorder where there
NOTE Confidence: 0.83042085

00:06:05.722 --> 00:06:07.380 is worsening psychotic symptoms.
NOTE Confidence: 0.83042085

00:06:07.380 --> 00:06:08.860 There's worse than negative
NOTE Confidence: 0.83042085

00:06:08.860 --> 00:06:09.970 and cognitive symptoms.
NOTE Confidence: 0.8149216

00:06:12.630 --> 00:06:14.750 And so I think this is an important
NOTE Confidence: 0.8149216

00:06:14.750 --> 00:06:17.185 point that schizophrenia is not just the
NOTE Confidence: 0.8149216

00:06:17.185 --> 00:06:19.612 psychotic symptoms or the madness, which is,
NOTE Confidence: 0.8149216

00:06:19.612 --> 00:06:22.390 I think is really focused on in a lot
NOTE Confidence: 0.8149216

00:06:22.390 --> 00:06:24.150 of different menu, specifically media.
NOTE Confidence: 0.8149216

00:06:24.150 --> 00:06:25.750 So there are positive symptoms
NOTE Confidence: 0.8149216

00:06:25.750 --> 00:06:26.710 which are hallucinations,
NOTE Confidence: 0.8149216

00:06:26.710 --> 00:06:27.990 delusions, or disorganized thought.
NOTE Confidence: 0.8149216

00:06:27.990 --> 00:06:29.590 But there's also negative symptoms.
NOTE Confidence: 0.8149216

00:06:29.590 --> 00:06:31.510 Which are Anna Donia, a motivation?
NOTE Confidence: 0.8149216

00:06:31.510 --> 00:06:32.164 Social withdrawal?
NOTE Confidence: 0.8149216

00:06:32.164 --> 00:06:34.453 I think that one of the initial

NOTE Confidence: 0.8149216
00:06:34.453 --> 00:06:36.009 terms autoset almost looks like
NOTE Confidence: 0.8149216
00:06:36.009 --> 00:06:38.230 autism as well as a flat affect.
NOTE Confidence: 0.8149216
00:06:38.230 --> 00:06:38.880 And finally,
NOTE Confidence: 0.8149216
00:06:38.880 --> 00:06:40.505 their cognitive symptoms can be
NOTE Confidence: 0.8149216
00:06:40.505 --> 00:06:42.170 quite debilitating for the patients.
NOTE Confidence: 0.8149216
00:06:42.170 --> 00:06:44.078 It's poor short term in working
NOTE Confidence: 0.8149216
00:06:44.078 --> 00:06:46.512 memory as well as difficult and
NOTE Confidence: 0.8149216
00:06:46.512 --> 00:06:48.150 difficulty in communication.
NOTE Confidence: 0.8149216
00:06:48.150 --> 00:06:50.190 And so once this child was
NOTE Confidence: 0.8149216
00:06:50.190 --> 00:06:51.550 admitted to our unit,
NOTE Confidence: 0.8149216
00:06:51.550 --> 00:06:53.590 we decided to start a medication
NOTE Confidence: 0.8149216
00:06:53.590 --> 00:06:55.206 for this child, an antipsychotic.
NOTE Confidence: 0.8149216
00:06:55.206 --> 00:06:56.696 You know everyone has their
NOTE Confidence: 0.8149216
00:06:56.696 --> 00:06:58.445 their choice and despite having
NOTE Confidence: 0.8149216
00:06:58.445 --> 00:07:00.049 medications to treat schizophrenia,
NOTE Confidence: 0.8149216

00:07:00.050 --> 00:07:02.090 the outcomes are still not great.
NOTE Confidence: 0.8149216

00:07:02.090 --> 00:07:02.770 In this.
NOTE Confidence: 0.8149216

00:07:02.770 --> 00:07:05.150 Once they show that 10% of patients
NOTE Confidence: 0.8149216

00:07:05.150 --> 00:07:06.850 with schizophrenia die by sight,
NOTE Confidence: 0.8149216

00:07:06.850 --> 00:07:07.157 suicide,
NOTE Confidence: 0.8149216

00:07:07.157 --> 00:07:08.692 which is greatly elevated from
NOTE Confidence: 0.8149216

00:07:08.692 --> 00:07:10.590 the rest of the population.
NOTE Confidence: 0.8149216

00:07:10.590 --> 00:07:12.290 25% have chronic severe symptoms,
NOTE Confidence: 0.8149216

00:07:12.290 --> 00:07:13.940 while most patients have some
NOTE Confidence: 0.8149216

00:07:13.940 --> 00:07:15.590 level of symptoms and they're
NOTE Confidence: 0.8149216

00:07:15.650 --> 00:07:17.050 just looking at symptoms,
NOTE Confidence: 0.8149216

00:07:17.050 --> 00:07:19.480 functional outcomes are actually much worse.
NOTE Confidence: 0.8149216

00:07:19.480 --> 00:07:22.385 I think part of the issue is that it
NOTE Confidence: 0.8149216

00:07:22.385 --> 00:07:24.590 was kind of highlighted in the Katy
NOTE Confidence: 0.8149216

00:07:24.659 --> 00:07:27.323 trial that was done early in the 2000s,
NOTE Confidence: 0.8149216

00:07:27.330 --> 00:07:29.619 where they showed in two at least.

NOTE Confidence: 0.8149216

00:07:29.620 --> 00:07:30.972 They followed patients with

NOTE Confidence: 0.8149216

00:07:30.972 --> 00:07:33.000 schizophrenia over two years and only

NOTE Confidence: 0.8149216

00:07:33.054 --> 00:07:35.148 26% of them actually stayed on their

NOTE Confidence: 0.8149216

00:07:35.148 --> 00:07:36.810 medication through this whole trial.

NOTE Confidence: 0.8149216

00:07:36.810 --> 00:07:38.424 And due to this progressive illness

NOTE Confidence: 0.8149216

00:07:38.424 --> 00:07:40.766 as well as the difficulty of keeping

NOTE Confidence: 0.8149216

00:07:40.766 --> 00:07:42.370 patients on their medications,

NOTE Confidence: 0.8149216

00:07:42.370 --> 00:07:44.582 the focus has been on prevention and

NOTE Confidence: 0.8149216

00:07:44.582 --> 00:07:47.244 this has been work done starting in the

NOTE Confidence: 0.8149216

00:07:47.244 --> 00:07:49.650 late 80s by various groups instead of.

NOTE Confidence: 0.8149216

00:07:49.650 --> 00:07:51.410 Anything including a strong group

NOTE Confidence: 0.8149216

00:07:51.410 --> 00:07:53.556 here in adult psychiatry with the

NOTE Confidence: 0.8149216

00:07:53.556 --> 00:07:55.500 focus has been as is intervening

NOTE Confidence: 0.8149216

00:07:55.500 --> 00:07:56.870 during this prodromal stage.

NOTE Confidence: 0.8149216

00:07:56.870 --> 00:07:59.173 So when our honor student is slowly

NOTE Confidence: 0.8149216

00:07:59.173 --> 00:08:00.660 starting to academically decline,
NOTE Confidence: 0.8149216

00:08:00.660 --> 00:08:03.068 can we interview at that point intervene?
NOTE Confidence: 0.8149216

00:08:03.070 --> 00:08:05.373 Sorry at that point to change the
NOTE Confidence: 0.8149216

00:08:05.373 --> 00:08:07.133 trajectory of schizophrenia and maybe
NOTE Confidence: 0.8149216

00:08:07.133 --> 00:08:08.908 prevent the transition to psychosis.
NOTE Confidence: 0.8149216

00:08:08.910 --> 00:08:10.890 And there's been a lot of
NOTE Confidence: 0.8149216

00:08:10.890 --> 00:08:13.039 great work done in that area,
NOTE Confidence: 0.8149216

00:08:13.040 --> 00:08:14.730 especially the focus on psychoeducation
NOTE Confidence: 0.8149216

00:08:14.730 --> 00:08:16.830 teaching the family what to expect,
NOTE Confidence: 0.8149216

00:08:16.830 --> 00:08:18.936 as well as reducing the stress
NOTE Confidence: 0.8149216

00:08:18.936 --> 00:08:20.340 that the child experiences
NOTE Confidence: 0.8149216

00:08:20.411 --> 00:08:22.136 as it's thought that stress.
NOTE Confidence: 0.8149216

00:08:22.140 --> 00:08:24.597 Can worsen the trajectory of the disorder
NOTE Confidence: 0.8149216

00:08:24.597 --> 00:08:26.950 and despite all these great studies,
NOTE Confidence: 0.8149216

00:08:26.950 --> 00:08:28.930 kinda bleak meta analysis came out
NOTE Confidence: 0.8149216

00:08:28.930 --> 00:08:31.570 July of 2020 and then I'll just

NOTE Confidence: 0.8149216

00:08:31.570 --> 00:08:33.234 highlight that first sentence.

NOTE Confidence: 0.8149216

00:08:33.240 --> 00:08:35.802 No evidence was found that that favored

NOTE Confidence: 0.8149216

00:08:35.802 --> 00:08:37.679 any indicated intervention over another,

NOTE Confidence: 0.8149216

00:08:37.680 --> 00:08:38.790 including control conditions.

NOTE Confidence: 0.8149216

00:08:38.790 --> 00:08:40.640 So despite all this work,

NOTE Confidence: 0.8149216

00:08:40.640 --> 00:08:43.010 we're not really preventing the transition

NOTE Confidence: 0.8149216

00:08:43.010 --> 00:08:45.450 to psychosis and later on they talk.

NOTE Confidence: 0.8149216

00:08:45.450 --> 00:08:47.400 There's actually no real obvious improvement

NOTE Confidence: 0.8149216

00:08:47.400 --> 00:08:50.628 in a lot of these other functional measures,

NOTE Confidence: 0.8149216

00:08:50.630 --> 00:08:51.980 So what gives?

NOTE Confidence: 0.8149216

00:08:51.980 --> 00:08:54.230 How can we prevent schizophrenia?

NOTE Confidence: 0.8149216

00:08:54.230 --> 00:08:56.120 And I think part of the issue

NOTE Confidence: 0.8149216

00:08:56.120 --> 00:08:57.784 has been this psychosis driven

NOTE Confidence: 0.8149216

00:08:57.784 --> 00:08:59.759 formulation of the disorder that

NOTE Confidence: 0.8149216

00:08:59.759 --> 00:09:01.830 prior to this prodromal phase

NOTE Confidence: 0.8149216

00:09:01.830 --> 00:09:04.278 there's no symptoms or few symptoms,
NOTE Confidence: 0.8149216

00:09:04.280 --> 00:09:07.502 and so the focus has been on the prodrome.
NOTE Confidence: 0.8357679

00:09:07.510 --> 00:09:10.618 But actually data shows something different.
NOTE Confidence: 0.8357679

00:09:10.620 --> 00:09:12.514 This was one of the seminal
NOTE Confidence: 0.8357679

00:09:12.514 --> 00:09:14.410 works that came out in 1994,
NOTE Confidence: 0.8357679

00:09:14.410 --> 00:09:17.114 led by Doctor Elaine Walker and what she
NOTE Confidence: 0.8357679

00:09:17.114 --> 00:09:19.780 showed along with when it came out in 1994.
NOTE Confidence: 0.8357679

00:09:19.780 --> 00:09:21.999 I thought it was kind of funny.
NOTE Confidence: 0.8357679

00:09:22.000 --> 00:09:23.580 Was that this is correlated.
NOTE Confidence: 0.8357679

00:09:23.580 --> 00:09:25.785 But 20 years after like home video
NOTE Confidence: 0.8357679

00:09:25.785 --> 00:09:27.679 cameras became popular with this study,
NOTE Confidence: 0.8357679

00:09:27.680 --> 00:09:29.920 did was they looked at the life they
NOTE Confidence: 0.8357679

00:09:29.920 --> 00:09:31.144 recruited patients with schizophrenia
NOTE Confidence: 0.8357679

00:09:31.144 --> 00:09:33.279 and then looked at their home videos
NOTE Confidence: 0.8357679

00:09:33.279 --> 00:09:35.749 from their childhood and they looked for
NOTE Confidence: 0.8357679

00:09:35.749 --> 00:09:37.477 neuromotor abnormalities and what they

NOTE Confidence: 0.8357679

00:09:37.477 --> 00:09:39.379 found specifically in infants is that.

NOTE Confidence: 0.8357679

00:09:39.380 --> 00:09:41.010 And so this population that

NOTE Confidence: 0.8357679

00:09:41.010 --> 00:09:41.988 later developed schizophrenia.

NOTE Confidence: 0.8357679

00:09:41.990 --> 00:09:44.188 Has schizophrenia as a child they showed

NOTE Confidence: 0.8357679

00:09:44.188 --> 00:09:45.510 increased abnormal motor movements

NOTE Confidence: 0.8357679

00:09:45.510 --> 00:09:47.460 while their healthy siblings did not.

NOTE Confidence: 0.8357679

00:09:47.460 --> 00:09:49.170 Just things that did not have

NOTE Confidence: 0.8357679

00:09:49.170 --> 00:09:50.310 schizophrenia and patients with

NOTE Confidence: 0.8357679

00:09:50.365 --> 00:09:51.713 other affective disorders also

NOTE Confidence: 0.8357679

00:09:51.713 --> 00:09:53.398 didn't have a significant difference

NOTE Confidence: 0.8357679

00:09:53.398 --> 00:09:55.189 from the patients of schizophrenia.

NOTE Confidence: 0.803379103000001

00:09:58.190 --> 00:09:59.339 Later, Lin walked.

NOTE Confidence: 0.803379103000001

00:09:59.339 --> 00:10:02.020 Walker was part of this other study

NOTE Confidence: 0.803379103000001

00:10:02.096 --> 00:10:03.976 that was more thoughtful 'cause

NOTE Confidence: 0.803379103000001

00:10:03.976 --> 00:10:06.598 they had no more time to design

NOTE Confidence: 0.803379103000001

00:10:06.598 --> 00:10:08.929 this study and what they did was
NOTE Confidence: 0.803379103000001

00:10:08.929 --> 00:10:10.530 they videotaped 1311 through 13
NOTE Confidence: 0.803379103000001

00:10:10.530 --> 00:10:12.420 year olds in Scandinavia that have
NOTE Confidence: 0.803379103000001

00:10:12.472 --> 00:10:14.277 an increased risk of schizophrenia.
NOTE Confidence: 0.803379103000001

00:10:14.280 --> 00:10:15.680 Specifically a parent with
NOTE Confidence: 0.803379103000001

00:10:15.680 --> 00:10:17.430 schizophrenia and they found that
NOTE Confidence: 0.803379103000001

00:10:17.430 --> 00:10:19.290 when they went and then waited to
NOTE Confidence: 0.803379103000001

00:10:19.290 --> 00:10:21.198 see which one of these children
NOTE Confidence: 0.803379103000001

00:10:21.198 --> 00:10:22.958 would later develop schizophrenia,
NOTE Confidence: 0.803379103000001

00:10:22.960 --> 00:10:24.886 they found that the children that
NOTE Confidence: 0.803379103000001

00:10:24.886 --> 00:10:26.170 later developed schizophrenia show
NOTE Confidence: 0.803379103000001

00:10:26.222 --> 00:10:27.638 deficits and social behaviors.
NOTE Confidence: 0.803379103000001

00:10:27.640 --> 00:10:29.710 Around 11:13 there wasn't an obviously
NOTE Confidence: 0.803379103000001

00:10:29.710 --> 00:10:31.090 significant different in motor.
NOTE Confidence: 0.803379103000001

00:10:31.090 --> 00:10:33.100 Even though it trended in boys
NOTE Confidence: 0.803379103000001

00:10:33.100 --> 00:10:35.040 towards having some motor atypical,

NOTE Confidence: 0.803379103000001
00:10:35.040 --> 00:10:36.249 atypical motor behaviors,
NOTE Confidence: 0.803379103000001
00:10:36.249 --> 00:10:38.667 and this more recent paper was
NOTE Confidence: 0.803379103000001
00:10:38.667 --> 00:10:40.775 something that I was really drawn to,
NOTE Confidence: 0.803379103000001
00:10:40.780 --> 00:10:43.314 and this was part of the Avon
NOTE Confidence: 0.803379103000001
00:10:43.314 --> 00:10:45.205 Perspective study where they just
NOTE Confidence: 0.803379103000001
00:10:45.205 --> 00:10:47.781 tracked children that were born in two
NOTE Confidence: 0.803379103000001
00:10:47.781 --> 00:10:50.480 years in this city of Avon and England,
NOTE Confidence: 0.803379103000001
00:10:50.480 --> 00:10:52.829 and then just did a bunch of like just
NOTE Confidence: 0.803379103000001
00:10:52.829 --> 00:10:54.648 neuro psychological battery on them
NOTE Confidence: 0.803379103000001
00:10:54.648 --> 00:10:56.892 and they found that children that
NOTE Confidence: 0.803379103000001
00:10:56.952 --> 00:10:59.088 later developed psychotic disorders,
NOTE Confidence: 0.803379103000001
00:10:59.090 --> 00:11:02.026 that's that red line around the age of.
NOTE Confidence: 0.803379103000001
00:11:02.030 --> 00:11:04.058 18 months somewhere to 18 months
NOTE Confidence: 0.803379103000001
00:11:04.058 --> 00:11:06.591 in four years start to show a
NOTE Confidence: 0.803379103000001
00:11:06.591 --> 00:11:08.075 decline in cognitive function.
NOTE Confidence: 0.803379103000001

00:11:08.080 --> 00:11:10.565 This is seen in full scale IQ,
NOTE Confidence: 0.8033791030000001

00:11:10.570 --> 00:11:12.214 verbal IQ and nonverbal IQ and
NOTE Confidence: 0.8033791030000001

00:11:12.214 --> 00:11:14.181 so I think these findings along
NOTE Confidence: 0.8033791030000001

00:11:14.181 --> 00:11:16.196 with various other studies suggest
NOTE Confidence: 0.8033791030000001

00:11:16.196 --> 00:11:18.050 maybe we're missing something.
NOTE Confidence: 0.8033791030000001

00:11:18.050 --> 00:11:19.805 Maybe schizophrenia actually
NOTE Confidence: 0.8033791030000001

00:11:19.805 --> 00:11:22.730 starts earlier than we thought.
NOTE Confidence: 0.8033791030000001

00:11:22.730 --> 00:11:25.066 And so this has been led to kind
NOTE Confidence: 0.8033791030000001

00:11:25.066 --> 00:11:28.018 of a new version of schizophrenia,
NOTE Confidence: 0.8033791030000001

00:11:28.020 --> 00:11:31.044 which I feel is much more child psychiatry.
NOTE Confidence: 0.8033791030000001

00:11:31.050 --> 00:11:32.446 Child psychology focused where
NOTE Confidence: 0.8033791030000001

00:11:32.446 --> 00:11:33.842 initially their cognitive motor
NOTE Confidence: 0.8033791030000001

00:11:33.842 --> 00:11:35.825 and social impairments and these
NOTE Confidence: 0.8033791030000001

00:11:35.825 --> 00:11:37.465 progressively moved towards psychosis,
NOTE Confidence: 0.8033791030000001

00:11:37.470 --> 00:11:40.319 and I think this is a really
NOTE Confidence: 0.8033791030000001

00:11:40.319 --> 00:11:42.281 interesting theory because it kind

NOTE Confidence: 0.803379103000001
00:11:42.281 --> 00:11:44.626 of gives us a longer runway, right?
NOTE Confidence: 0.803379103000001
00:11:44.626 --> 00:11:47.048 Can we intervene much earlier and to
NOTE Confidence: 0.803379103000001
00:11:47.048 --> 00:11:49.567 later prevent this transition to psychosis?
NOTE Confidence: 0.803379103000001
00:11:49.570 --> 00:11:49.956 However,
NOTE Confidence: 0.803379103000001
00:11:49.956 --> 00:11:53.044 in order to turn this model into real?
NOTE Confidence: 0.803379103000001
00:11:53.050 --> 00:11:53.902 Real clinical intervention.
NOTE Confidence: 0.803379103000001
00:11:53.902 --> 00:11:55.890 We have to kind of understand the
NOTE Confidence: 0.803379103000001
00:11:55.937 --> 00:11:57.937 neurobiological underpinnings of this data.
NOTE Confidence: 0.803379103000001
00:11:57.940 --> 00:11:59.495 So what are the neurobiological
NOTE Confidence: 0.803379103000001
00:11:59.495 --> 00:12:01.050 correlates of the neuro developmental
NOTE Confidence: 0.803379103000001
00:12:01.097 --> 00:12:02.180 theory of schizophrenia?
NOTE Confidence: 0.803379103000001
00:12:02.180 --> 00:12:04.430 Which is something that I'm very
NOTE Confidence: 0.803379103000001
00:12:04.430 --> 00:12:06.982 interested and so the first thing we
NOTE Confidence: 0.803379103000001
00:12:06.982 --> 00:12:09.750 can do is look to our colleagues in
NOTE Confidence: 0.803379103000001
00:12:09.750 --> 00:12:12.606 psychiatric genetics such as my good friend.
NOTE Confidence: 0.803379103000001

00:12:12.610 --> 00:12:13.262 Emily Olson,
NOTE Confidence: 0.803379103000001

00:12:13.262 --> 00:12:13.914 who's like,
NOTE Confidence: 0.803379103000001

00:12:13.914 --> 00:12:16.310 does a brilliant work and gave an
NOTE Confidence: 0.803379103000001

00:12:16.310 --> 00:12:18.190 amazing presentation two weeks ago.
NOTE Confidence: 0.803379103000001

00:12:18.190 --> 00:12:20.092 As Doctor Martin mentioned and what
NOTE Confidence: 0.803379103000001

00:12:20.092 --> 00:12:22.569 she kind of talked about was the
NOTE Confidence: 0.803379103000001

00:12:22.569 --> 00:12:24.479 current state of psychiatric genetics,
NOTE Confidence: 0.803379103000001

00:12:24.480 --> 00:12:26.993 and in the last 10 years there's
NOTE Confidence: 0.803379103000001

00:12:26.993 --> 00:12:29.008 been amazing progress in the field,
NOTE Confidence: 0.803379103000001

00:12:29.010 --> 00:12:30.750 and schizophrenia is also seen
NOTE Confidence: 0.803379103000001

00:12:30.750 --> 00:12:32.142 great progress in schizophrenia,
NOTE Confidence: 0.803379103000001

00:12:32.150 --> 00:12:32.492 genetics,
NOTE Confidence: 0.803379103000001

00:12:32.492 --> 00:12:34.202 where they have identified several
NOTE Confidence: 0.803379103000001

00:12:34.202 --> 00:12:35.570 genes associated or enriched
NOTE Confidence: 0.803379103000001

00:12:35.624 --> 00:12:37.384 in mutations in several genes
NOTE Confidence: 0.803379103000001

00:12:37.384 --> 00:12:38.440 associated with schizophrenia,

NOTE Confidence: 0.803379103000001

00:12:38.440 --> 00:12:40.876 and what a recent study has done.

NOTE Confidence: 0.803379103000001

00:12:40.880 --> 00:12:42.700 And this is kind of.

NOTE Confidence: 0.803379103000001

00:12:42.700 --> 00:12:44.494 Where several labs are doing this

NOTE Confidence: 0.803379103000001

00:12:44.494 --> 00:12:46.400 where you have so many genes,

NOTE Confidence: 0.803379103000001

00:12:46.400 --> 00:12:48.395 how can we turn these jeans into

NOTE Confidence: 0.803379103000001

00:12:48.395 --> 00:12:50.294 specific targets or regions or time

NOTE Confidence: 0.803379103000001

00:12:50.294 --> 00:12:51.939 periods of development to study?

NOTE Confidence: 0.803379103000001

00:12:51.940 --> 00:12:54.005 And what this study did was they

NOTE Confidence: 0.803379103000001

00:12:54.005 --> 00:12:55.913 looked for regions in the brain

NOTE Confidence: 0.803379103000001

00:12:55.913 --> 00:12:56.870 in specific periods.

NOTE Confidence: 0.8552168

00:12:56.870 --> 00:12:58.410 They looked at fetal infancy,

NOTE Confidence: 0.8552168

00:12:58.410 --> 00:13:00.522 an adult adolescent stages and they

NOTE Confidence: 0.8552168

00:13:00.522 --> 00:13:02.486 looked at different regions of the

NOTE Confidence: 0.8552168

00:13:02.486 --> 00:13:04.827 brain and they looked for a place and a

NOTE Confidence: 0.8552168

00:13:04.827 --> 00:13:07.018 time where there was an enrichment of

NOTE Confidence: 0.8552168

00:13:07.018 --> 00:13:08.258 genes associated with schizophrenia.

NOTE Confidence: 0.8552168

00:13:08.258 --> 00:13:09.778 Almost like you have people

NOTE Confidence: 0.8552168

00:13:09.778 --> 00:13:11.040 involved in a crime.

NOTE Confidence: 0.8552168

00:13:11.040 --> 00:13:13.294 Are they in the same place together?

NOTE Confidence: 0.8552168

00:13:13.300 --> 00:13:15.838 As a way of maybe giving you a time

NOTE Confidence: 0.8552168

00:13:15.838 --> 00:13:18.114 point in an area to specifically

NOTE Confidence: 0.8552168

00:13:18.114 --> 00:13:20.500 dig deeper into to understand what

NOTE Confidence: 0.8552168

00:13:20.500 --> 00:13:22.445 they found was an enrichment.

NOTE Confidence: 0.8552168

00:13:22.450 --> 00:13:24.556 These alleles in the fetal cortex,

NOTE Confidence: 0.8552168

00:13:24.560 --> 00:13:26.320 specifically in the frontal lobe,

NOTE Confidence: 0.8552168

00:13:26.320 --> 00:13:28.497 and this is very similar findings to

NOTE Confidence: 0.8552168

00:13:28.497 --> 00:13:30.617 work done by Matt States Group and

NOTE Confidence: 0.8552168

00:13:30.617 --> 00:13:33.265 he was here at Yale in autism and

NOTE Confidence: 0.8552168

00:13:33.265 --> 00:13:35.971 this also coincides really well with

NOTE Confidence: 0.8552168

00:13:35.971 --> 00:13:37.584 earlier epidemiological data that

NOTE Confidence: 0.8552168

00:13:37.584 --> 00:13:39.344 shows that stress during pregnancy,

NOTE Confidence: 0.8552168

00:13:39.350 --> 00:13:41.235 specifically during the 2nd trimester

NOTE Confidence: 0.8552168

00:13:41.235 --> 00:13:43.629 increase the chance of having a child.

NOTE Confidence: 0.8552168

00:13:43.630 --> 00:13:47.299 That develops schizophrenia.

NOTE Confidence: 0.8552168

00:13:47.300 --> 00:13:49.043 So this led to our more focused

NOTE Confidence: 0.8552168

00:13:49.043 --> 00:13:50.570 question how does disruption of

NOTE Confidence: 0.8552168

00:13:50.570 --> 00:13:52.375 neurodevelopmental events in the mid

NOTE Confidence: 0.8552168

00:13:52.375 --> 00:13:54.518 fetal frontal cortex lead to the

NOTE Confidence: 0.8552168

00:13:54.518 --> 00:13:55.854 complex symptoms of schizophrenia?

NOTE Confidence: 0.8552168

00:13:55.860 --> 00:13:59.828 And so this is where the story starts.

NOTE Confidence: 0.8552168

00:13:59.830 --> 00:14:02.008 And So what we did is we use that

NOTE Confidence: 0.8552168

00:14:02.008 --> 00:14:04.068 same data set that these previous

NOTE Confidence: 0.8552168

00:14:04.068 --> 00:14:06.400 groups use is called psych encoder.

NOTE Confidence: 0.8552168

00:14:06.400 --> 00:14:07.830 Brain sandwiches generated in this

NOTE Confidence: 0.8552168

00:14:07.830 --> 00:14:10.216 test in lab to look for genes that

NOTE Confidence: 0.8552168

00:14:10.216 --> 00:14:12.022 were uniquely enriched in the frontal

NOTE Confidence: 0.8552168

00:14:12.022 --> 00:14:13.920 lobe during mid field development.
NOTE Confidence: 0.8552168

00:14:13.920 --> 00:14:15.480 We're looking for something specific
NOTE Confidence: 0.8552168

00:14:15.480 --> 00:14:16.728 to the mid function.
NOTE Confidence: 0.8552168

00:14:16.730 --> 00:14:18.524 The midfielder frontal lobe and that's
NOTE Confidence: 0.8552168

00:14:18.524 --> 00:14:21.107 why we looked for genes are enriched there.
NOTE Confidence: 0.8552168

00:14:21.110 --> 00:14:23.231 And so we identified 125 genes enriched
NOTE Confidence: 0.8552168

00:14:23.231 --> 00:14:24.870 specifically in the frontal lobe.
NOTE Confidence: 0.8552168

00:14:24.870 --> 00:14:25.809 During this period,
NOTE Confidence: 0.8552168

00:14:25.809 --> 00:14:28.000 Anna's Emily showed in her previous talk.
NOTE Confidence: 0.8552168

00:14:28.000 --> 00:14:30.324 We looked at what do these jeans?
NOTE Confidence: 0.8552168

00:14:30.330 --> 00:14:32.696 Share this click gene ontogeny analysis and
NOTE Confidence: 0.8552168

00:14:32.696 --> 00:14:35.426 what we found was that these genes are in.
NOTE Confidence: 0.8552168

00:14:35.430 --> 00:14:37.341 This list is enriched for genes that
NOTE Confidence: 0.8552168

00:14:37.341 --> 00:14:39.314 are involved in circuit formation so
NOTE Confidence: 0.8552168

00:14:39.314 --> 00:14:41.149 synapse assembly Axon development in
NOTE Confidence: 0.8552168

00:14:41.149 --> 00:14:43.410 circuits are kind of the functional unit.

NOTE Confidence: 0.8552168

00:14:43.410 --> 00:14:44.682 I think I, uh,

NOTE Confidence: 0.8552168

00:14:44.682 --> 00:14:45.954 I guess eventually unit.

NOTE Confidence: 0.8552168

00:14:45.960 --> 00:14:48.504 That's like high truly focuses on the brain,

NOTE Confidence: 0.8552168

00:14:48.510 --> 00:14:50.382 but we also saw something that

NOTE Confidence: 0.8552168

00:14:50.382 --> 00:14:52.011 was unexpected which was jeans

NOTE Confidence: 0.8552168

00:14:52.011 --> 00:14:53.616 that are responsive to rent.

NOTE Confidence: 0.8552168

00:14:53.620 --> 00:14:55.867 No gas or jeans that are regulated

NOTE Confidence: 0.8552168

00:14:55.867 --> 00:14:58.121 by retinoic acid and this was very

NOTE Confidence: 0.8552168

00:14:58.121 --> 00:15:00.039 exciting for us. For several reasons.

NOTE Confidence: 0.8552168

00:15:00.039 --> 00:15:01.704 There was a basic science.

NOTE Confidence: 0.8552168

00:15:01.710 --> 00:15:03.635 Perspective which I want talking

NOTE Confidence: 0.8552168

00:15:03.635 --> 00:15:05.175 or evolutionary perspective that

NOTE Confidence: 0.8552168

00:15:05.175 --> 00:15:06.718 I want to talk about.

NOTE Confidence: 0.8552168

00:15:06.720 --> 00:15:08.868 But there was a very interesting

NOTE Confidence: 0.8552168

00:15:08.868 --> 00:15:09.584 clinical perspective.

NOTE Confidence: 0.8552168

00:15:09.590 --> 00:15:11.492 So disruption of retinoic acid signaling
NOTE Confidence: 0.8552168

00:15:11.492 --> 00:15:13.520 has been implicated in schizophrenia.
NOTE Confidence: 0.8552168

00:15:13.520 --> 00:15:15.515 And it seems that the your polygenic
NOTE Confidence: 0.8552168

00:15:15.515 --> 00:15:17.894 risk score or how many genes associated
NOTE Confidence: 0.8552168

00:15:17.894 --> 00:15:20.084 with retinoic acid's are affected seem
NOTE Confidence: 0.8552168

00:15:20.147 --> 00:15:22.613 to be elevated in patients schizophrenia
NOTE Confidence: 0.8552168

00:15:22.613 --> 00:15:24.257 with severe cognitive symptoms.
NOTE Confidence: 0.8552168

00:15:24.260 --> 00:15:26.105 So this was something very
NOTE Confidence: 0.8552168

00:15:26.105 --> 00:15:28.200 interesting and very exciting to us,
NOTE Confidence: 0.8552168

00:15:28.200 --> 00:15:29.985 so we postulated that disruption
NOTE Confidence: 0.8552168

00:15:29.985 --> 00:15:32.200 of RA regulated or related genes.
NOTE Confidence: 0.8552168

00:15:32.200 --> 00:15:34.276 Causes some change in brain development.
NOTE Confidence: 0.8552168

00:15:34.280 --> 00:15:35.668 Likely circuit formation as
NOTE Confidence: 0.8552168

00:15:35.668 --> 00:15:37.750 those are what those genes are.
NOTE Confidence: 0.8552168

00:15:37.750 --> 00:15:40.116 Also enriched and and that can lead
NOTE Confidence: 0.8552168

00:15:40.116 --> 00:15:42.479 to the early cognitive symptoms

NOTE Confidence: 0.8552168

00:15:42.479 --> 00:15:43.749 of schizophrenia.

NOTE Confidence: 0.8552168

00:15:43.750 --> 00:15:44.854 So to study this,

NOTE Confidence: 0.8552168

00:15:44.854 --> 00:15:46.951 we turn to a mouse model and

NOTE Confidence: 0.8552168

00:15:46.951 --> 00:15:49.159 we asked what is retinoic acid

NOTE Confidence: 0.8552168

00:15:49.159 --> 00:15:50.263 doing specifically in

NOTE Confidence: 0.8393542

00:15:50.338 --> 00:15:51.589 the frontal cortex.

NOTE Confidence: 0.8393542

00:15:51.590 --> 00:15:53.557 So we generated a mutant mouse line

NOTE Confidence: 0.8393542

00:15:53.557 --> 00:15:55.299 where we're able to specifically

NOTE Confidence: 0.8393542

00:15:55.299 --> 00:15:57.389 reduce retinoic acid signaling Justin,

NOTE Confidence: 0.8393542

00:15:57.390 --> 00:15:58.754 the mouse equivalent of

NOTE Confidence: 0.8393542

00:15:58.754 --> 00:15:59.777 the prefrontal cortex,

NOTE Confidence: 0.8393542

00:15:59.780 --> 00:16:02.174 and So what you see here is a PO

NOTE Confidence: 0.8393542

00:16:02.174 --> 00:16:04.613 mouse brain which is equivalent to

NOTE Confidence: 0.8393542

00:16:04.613 --> 00:16:07.109 mid fetal about post Conception Week

NOTE Confidence: 0.8393542

00:16:07.109 --> 00:16:09.363 24 in the human and these purple

NOTE Confidence: 0.8393542

00:16:09.363 --> 00:16:11.374 dots are cells where there's active

NOTE Confidence: 0.8393542

00:16:11.374 --> 00:16:13.079 retinoic acid signaling going on,

NOTE Confidence: 0.8393542

00:16:13.080 --> 00:16:15.198 and so this is the control.

NOTE Confidence: 0.8393542

00:16:15.200 --> 00:16:17.062 And this is the mutant where we've

NOTE Confidence: 0.8393542

00:16:17.062 --> 00:16:18.380 modified retinoic acid signaling,

NOTE Confidence: 0.8393542

00:16:18.380 --> 00:16:20.060 and you can see a dramatic

NOTE Confidence: 0.8393542

00:16:20.060 --> 00:16:21.532 reduction in purple cells which

NOTE Confidence: 0.8393542

00:16:21.532 --> 00:16:23.284 is quantified here on the right.

NOTE Confidence: 0.8393542

00:16:23.290 --> 00:16:24.880 And so now that we've reduced

NOTE Confidence: 0.8393542

00:16:24.880 --> 00:16:26.576 retinoic acid saying we looked at

NOTE Confidence: 0.8393542

00:16:26.576 --> 00:16:28.316 what happens to circuit formation in

NOTE Confidence: 0.8393542

00:16:28.316 --> 00:16:30.153 the frontal cortex or specific middle

NOTE Confidence: 0.8393542

00:16:30.153 --> 00:16:31.953 prefrontal cortex in the mouse and

NOTE Confidence: 0.8393542

00:16:31.960 --> 00:16:33.990 what we found was a couple things.

NOTE Confidence: 0.8393542

00:16:33.990 --> 00:16:36.006 But I'll highlight just a few phenotypes.

NOTE Confidence: 0.8393542

00:16:36.010 --> 00:16:36.282 First,

NOTE Confidence: 0.8393542

00:16:36.282 --> 00:16:38.186 we found a reduction in dendritic spines

NOTE Confidence: 0.8393542

00:16:38.186 --> 00:16:39.986 which are kind of excitatory connections

NOTE Confidence: 0.8393542

00:16:39.986 --> 00:16:42.080 in the brain which is quantified here.

NOTE Confidence: 0.8393542

00:16:42.080 --> 00:16:43.808 This is done in the adult,

NOTE Confidence: 0.8393542

00:16:43.810 --> 00:16:45.598 and so you can see a

NOTE Confidence: 0.8393542

00:16:45.598 --> 00:16:46.790 reduction in total spines.

NOTE Confidence: 0.8393542

00:16:46.790 --> 00:16:47.450 But also,

NOTE Confidence: 0.8393542

00:16:47.450 --> 00:16:48.770 reduction in mushroom bodies,

NOTE Confidence: 0.8393542

00:16:48.770 --> 00:16:51.038 which are mature spines and we replicate

NOTE Confidence: 0.8393542

00:16:51.038 --> 00:16:53.427 this finding both during the equivalent of

NOTE Confidence: 0.8393542

00:16:53.427 --> 00:16:55.700 midfied development in the human at PO.

NOTE Confidence: 0.8393542

00:16:55.700 --> 00:16:57.350 So this occurs very early.

NOTE Confidence: 0.8393542

00:16:57.350 --> 00:16:59.000 But we also saw this

NOTE Confidence: 0.8393542

00:16:59.000 --> 00:17:00.650 finding in adults as well,

NOTE Confidence: 0.8393542

00:17:00.650 --> 00:17:02.981 so this seems like this deficit in

NOTE Confidence: 0.8393542

00:17:02.981 --> 00:17:04.609 excitatory connections starts very early,
NOTE Confidence: 0.8393542

00:17:04.610 --> 00:17:06.802 but the finding that I want to focus
NOTE Confidence: 0.8393542

00:17:06.802 --> 00:17:08.858 on is this very interesting deficit
NOTE Confidence: 0.8393542

00:17:08.858 --> 00:17:11.869 that we found that got us all excited.
NOTE Confidence: 0.8393542

00:17:11.870 --> 00:17:13.520 We first found this data,
NOTE Confidence: 0.8393542

00:17:13.520 --> 00:17:16.112 so this is a study using this mutant
NOTE Confidence: 0.8393542

00:17:16.112 --> 00:17:18.420 mouse line using diffusion tensor.
NOTE Confidence: 0.8393542

00:17:18.420 --> 00:17:20.716 Which looks at connectivity in the brain,
NOTE Confidence: 0.8393542

00:17:20.720 --> 00:17:23.176 and so this is a five day old
NOTE Confidence: 0.8393542

00:17:23.176 --> 00:17:25.103 mouse brain which you can see
NOTE Confidence: 0.8393542

00:17:25.103 --> 00:17:27.630 kind of as a Gray fuzzy outline,
NOTE Confidence: 0.8393542

00:17:27.630 --> 00:17:29.667 and so about five days equivalent to
NOTE Confidence: 0.8393542

00:17:29.667 --> 00:17:32.262 birth in the human and what we found
NOTE Confidence: 0.8393542

00:17:32.262 --> 00:17:33.922 was a dramatic reduction between
NOTE Confidence: 0.8393542

00:17:33.991 --> 00:17:36.187 connections which are shown by these.
NOTE Confidence: 0.8393542

00:17:36.190 --> 00:17:37.980 These red lines between the

NOTE Confidence: 0.8393542

00:17:37.980 --> 00:17:39.770 prefrontal cortex and the thalamus

NOTE Confidence: 0.8393542

00:17:39.832 --> 00:17:41.446 on the right is the control,

NOTE Confidence: 0.8393542

00:17:41.450 --> 00:17:43.319 so you can see this thick bundle

NOTE Confidence: 0.8393542

00:17:43.319 --> 00:17:45.842 and on the left is the mutant where

NOTE Confidence: 0.8393542

00:17:45.842 --> 00:17:48.005 you see a dramatic reduction in

NOTE Confidence: 0.8393542

00:17:48.005 --> 00:17:49.797 connectivity which is quantified.

NOTE Confidence: 0.8393542

00:17:49.800 --> 00:17:50.980 Here on the left,

NOTE Confidence: 0.8393542

00:17:50.980 --> 00:17:53.520 and so we found this deficit very early,

NOTE Confidence: 0.8393542

00:17:53.520 --> 00:17:55.380 but it seems like this may.

NOTE Confidence: 0.8393542

00:17:55.380 --> 00:17:56.930 This deficit is maintained during

NOTE Confidence: 0.8393542

00:17:56.930 --> 00:17:58.790 adolescence, so we checked it P.

NOTE Confidence: 0.8393542

00:17:58.790 --> 00:18:00.960 21 but we also checked it P.

NOTE Confidence: 0.8393542

00:18:00.960 --> 00:18:01.890 16 The adult.

NOTE Confidence: 0.8393542

00:18:01.890 --> 00:18:03.440 So this isn't, you know,

NOTE Confidence: 0.8393542

00:18:03.440 --> 00:18:04.680 a delay in development.

NOTE Confidence: 0.8393542

00:18:04.680 --> 00:18:06.456 This is a complete disruption of
NOTE Confidence: 0.8393542

00:18:06.456 --> 00:18:08.399 the circuit in our mouse model.
NOTE Confidence: 0.81007785

00:18:10.520 --> 00:18:12.508 And this was kind of fits what
NOTE Confidence: 0.81007785

00:18:12.508 --> 00:18:14.365 we've been thinking about with
NOTE Confidence: 0.81007785

00:18:14.365 --> 00:18:15.875 schizophrenia, so this connection,
NOTE Confidence: 0.81007785

00:18:15.875 --> 00:18:17.600 the connection between the medial
NOTE Confidence: 0.81007785

00:18:17.600 --> 00:18:19.256 prefrontal cortex and the thalamus
NOTE Confidence: 0.81007785

00:18:19.256 --> 00:18:20.476 is essential for cognition,
NOTE Confidence: 0.81007785

00:18:20.480 --> 00:18:21.473 specifically working memory.
NOTE Confidence: 0.81007785

00:18:21.473 --> 00:18:22.797 This is a study.
NOTE Confidence: 0.81007785

00:18:22.800 --> 00:18:24.792 This is a reviewed written by
NOTE Confidence: 0.81007785

00:18:24.792 --> 00:18:26.120 Doctor Gordon Josh Gordon,
NOTE Confidence: 0.81007785

00:18:26.120 --> 00:18:28.776 who is now the head of the MH,
NOTE Confidence: 0.81007785

00:18:28.780 --> 00:18:30.385 who showed that the connection
NOTE Confidence: 0.81007785

00:18:30.385 --> 00:18:31.669 between the mediodorsal thalamus
NOTE Confidence: 0.81007785

00:18:31.669 --> 00:18:33.100 and the prefrontal cortex,

NOTE Confidence: 0.81007785
00:18:33.100 --> 00:18:34.484 and there's typical connection
NOTE Confidence: 0.81007785
00:18:34.484 --> 00:18:35.868 between the prefrontal cortex
NOTE Confidence: 0.81007785
00:18:35.868 --> 00:18:37.586 and the mediodorsal thalamus is
NOTE Confidence: 0.81007785
00:18:37.586 --> 00:18:39.536 essential for the delay in the
NOTE Confidence: 0.81007785
00:18:39.536 --> 00:18:41.139 retrieval steps of working memory.
NOTE Confidence: 0.81007785
00:18:41.140 --> 00:18:43.088 The circuits also been
NOTE Confidence: 0.81007785
00:18:43.088 --> 00:18:45.036 implicated in social behavior,
NOTE Confidence: 0.81007785
00:18:45.040 --> 00:18:47.959 so it's a circuit that's very it's
NOTE Confidence: 0.81007785
00:18:47.959 --> 00:18:50.899 highly studied in psychiatric biology.
NOTE Confidence: 0.8224325
00:18:53.740 --> 00:18:56.351 And so our proposed model is that
NOTE Confidence: 0.8224325
00:18:56.351 --> 00:18:57.880 disruption of retinoic acid,
NOTE Confidence: 0.8224325
00:18:57.880 --> 00:18:59.825 associated and regulated genes lead
NOTE Confidence: 0.8224325
00:18:59.825 --> 00:19:01.770 to reduce connectivity between the
NOTE Confidence: 0.8224325
00:19:01.829 --> 00:19:03.354 prefrontal cortex in the thalamus
NOTE Confidence: 0.8224325
00:19:03.354 --> 00:19:05.411 and that leads to the early
NOTE Confidence: 0.8224325

00:19:05.411 --> 00:19:07.279 cognitive symptoms of schizophrenia.

NOTE Confidence: 0.8224325

00:19:07.280 --> 00:19:10.346 This deficit occurs during the 2nd

NOTE Confidence: 0.8224325

00:19:10.346 --> 00:19:12.891 trimester of development in scene

NOTE Confidence: 0.8224325

00:19:12.891 --> 00:19:15.775 right at birth in our mouse model.

NOTE Confidence: 0.8224325

00:19:15.780 --> 00:19:17.836 So this led to a lot of important

NOTE Confidence: 0.8224325

00:19:17.836 --> 00:19:19.420 questions of future directions,

NOTE Confidence: 0.8224325

00:19:19.420 --> 00:19:20.584 which I'll talk about.

NOTE Confidence: 0.8224325

00:19:20.584 --> 00:19:22.750 So first this is the mouse model.

NOTE Confidence: 0.8224325

00:19:22.750 --> 00:19:24.568 This is have any relevance to

NOTE Confidence: 0.8224325

00:19:24.568 --> 00:19:25.477 patients with schizophrenia?

NOTE Confidence: 0.8224325

00:19:25.480 --> 00:19:27.664 And so this in this case we turn

NOTE Confidence: 0.8224325

00:19:27.664 --> 00:19:29.419 to another set of colleagues,

NOTE Confidence: 0.8224325

00:19:29.420 --> 00:19:30.628 colleagues that are involved

NOTE Confidence: 0.8224325

00:19:30.628 --> 00:19:31.534 in functional imaging,

NOTE Confidence: 0.8224325

00:19:31.540 --> 00:19:33.184 functional neural humanit,

NOTE Confidence: 0.8224325

00:19:33.184 --> 00:19:34.280 functional imaging.

NOTE Confidence: 0.8224325

00:19:34.280 --> 00:19:36.323 And this is a study done in 2015 and

NOTE Confidence: 0.8224325

00:19:36.323 --> 00:19:38.380 what they found they were specifically

NOTE Confidence: 0.8224325

00:19:38.380 --> 00:19:40.150 looking at the limbic cortical

NOTE Confidence: 0.8224325

00:19:40.215 --> 00:19:42.015 networks in healthy subjects that

NOTE Confidence: 0.8224325

00:19:42.015 --> 00:19:44.138 compare them to patients within four

NOTE Confidence: 0.8224325

00:19:44.138 --> 00:19:46.046 weeks of their diagnosis of schizophrenia.

NOTE Confidence: 0.8224325

00:19:46.050 --> 00:19:47.635 And then patients with chronic

NOTE Confidence: 0.8224325

00:19:47.635 --> 00:19:48.586 schizophrenia chronic psychosis.

NOTE Confidence: 0.8224325

00:19:48.590 --> 00:19:52.574 So this has been over a couple years.

NOTE Confidence: 0.8224325

00:19:52.580 --> 00:19:54.135 Of being diagnosed with schizophrenia

NOTE Confidence: 0.8224325

00:19:54.135 --> 00:19:56.488 and we can see in the blue bar,

NOTE Confidence: 0.8224325

00:19:56.490 --> 00:19:58.134 so this is functional connectivity so

NOTE Confidence: 0.8224325

00:19:58.134 --> 00:20:00.179 it's looking at just connection between.

NOTE Confidence: 0.8224325

00:20:00.180 --> 00:20:00.808 Different regions,

NOTE Confidence: 0.8224325

00:20:00.808 --> 00:20:02.064 specifically the limbic regions

NOTE Confidence: 0.8224325

00:20:02.064 --> 00:20:03.006 of the cortex,
NOTE Confidence: 0.8224325

00:20:03.010 --> 00:20:04.942 and they showed that compared to
NOTE Confidence: 0.8224325

00:20:04.942 --> 00:20:07.090 the control which is the blue bar,
NOTE Confidence: 0.8224325

00:20:07.090 --> 00:20:08.346 there is reduced connectivity
NOTE Confidence: 0.8224325

00:20:08.346 --> 00:20:09.288 both at diagnosis,
NOTE Confidence: 0.8224325

00:20:09.290 --> 00:20:11.285 which is shown at the yellow bar
NOTE Confidence: 0.8224325

00:20:11.285 --> 00:20:13.368 and both in the chronic stage.
NOTE Confidence: 0.8224325

00:20:13.370 --> 00:20:15.248 So that seems like this disruption
NOTE Confidence: 0.8224325

00:20:15.248 --> 00:20:15.874 is present,
NOTE Confidence: 0.8224325

00:20:15.880 --> 00:20:17.450 and at least this population
NOTE Confidence: 0.8224325

00:20:17.450 --> 00:20:18.706 of patients with schizophrenia,
NOTE Confidence: 0.8224325

00:20:18.710 --> 00:20:20.714 something else that was really interesting
NOTE Confidence: 0.8224325

00:20:20.714 --> 00:20:23.420 was a study done by Alan and Tisha Vich,
NOTE Confidence: 0.8224325

00:20:23.420 --> 00:20:25.932 who is in I guess now apiai in
NOTE Confidence: 0.8224325

00:20:25.932 --> 00:20:26.560 adult psychiatry.
NOTE Confidence: 0.8224325

00:20:26.560 --> 00:20:28.786 But this is when he was working

NOTE Confidence: 0.8224325

00:20:28.786 --> 00:20:30.609 in Doctor Tyrone Cannons Lab.

NOTE Confidence: 0.8224325

00:20:30.610 --> 00:20:32.752 And they looked at patients with high

NOTE Confidence: 0.8224325

00:20:32.752 --> 00:20:34.490 risk of developing schizophrenia.

NOTE Confidence: 0.8224325

00:20:34.490 --> 00:20:36.380 They had a certain set of criteria

NOTE Confidence: 0.8224325

00:20:36.380 --> 00:20:38.467 to kind of identify these patients

NOTE Confidence: 0.8224325

00:20:38.467 --> 00:20:40.885 and what they showed was this

NOTE Confidence: 0.8224325

00:20:40.885 --> 00:20:42.468 disconnection between Hypo connection

NOTE Confidence: 0.8224325

00:20:42.468 --> 00:20:45.079 with they called it between the medial

NOTE Confidence: 0.8224325

00:20:45.080 --> 00:20:47.198 frontal cortex or the frontal cortex,

NOTE Confidence: 0.8224325

00:20:47.200 --> 00:20:49.204 and the thalamus was present even

NOTE Confidence: 0.8224325

00:20:49.204 --> 00:20:51.440 prior to conversion in two psychosis.

NOTE Confidence: 0.8224325

00:20:51.440 --> 00:20:51.779 Specifically,

NOTE Confidence: 0.8224325

00:20:51.779 --> 00:20:53.813 that then I guess in addition

NOTE Confidence: 0.8224325

00:20:53.813 --> 00:20:55.320 to what they showed,

NOTE Confidence: 0.8224325

00:20:55.320 --> 00:20:57.784 was that the worst the psychotic symptoms,

NOTE Confidence: 0.8224325

00:20:57.790 --> 00:20:59.620 the more the reduced connectivity
NOTE Confidence: 0.8224325

00:20:59.620 --> 00:21:00.718 there was between.
NOTE Confidence: 0.8224325

00:21:00.720 --> 00:21:01.494 These two regions,
NOTE Confidence: 0.8224325

00:21:01.494 --> 00:21:03.940 so it seems like even prior to conversion,
NOTE Confidence: 0.8224325

00:21:03.940 --> 00:21:05.698 there seems to be this disconnection
NOTE Confidence: 0.8224325

00:21:05.698 --> 00:21:07.460 between the thalamus in the cortex,
NOTE Confidence: 0.8224325

00:21:07.460 --> 00:21:09.708 and so I think this is an interesting
NOTE Confidence: 0.8224325

00:21:09.708 --> 00:21:12.145 circuit to study in and further work from.
NOTE Confidence: 0.8224325

00:21:12.150 --> 00:21:13.254 Functional neurology is important
NOTE Confidence: 0.8224325

00:21:13.254 --> 00:21:15.900 to kind of see if this is a much
NOTE Confidence: 0.8224325

00:21:15.900 --> 00:21:16.836 more generalizable etiology.
NOTE Confidence: 0.8224325

00:21:16.840 --> 00:21:19.983 We also plan to study this in
NOTE Confidence: 0.8224325

00:21:19.983 --> 00:21:22.139 various mouse models as well.
NOTE Confidence: 0.8224325

00:21:22.140 --> 00:21:23.386 So the second question,
NOTE Confidence: 0.8224325

00:21:23.386 --> 00:21:25.174 which I think is something that
NOTE Confidence: 0.8224325

00:21:25.174 --> 00:21:27.215 I'm very excited about and I think

NOTE Confidence: 0.8224325

00:21:27.215 --> 00:21:29.048 is an essential question to really

NOTE Confidence: 0.8224325

00:21:29.048 --> 00:21:30.983 understand how to understand the

NOTE Confidence: 0.8224325

00:21:30.983 --> 00:21:32.531 complex symptoms of schizophrenia,

NOTE Confidence: 0.8224325

00:21:32.540 --> 00:21:34.472 is how can a specific deficit in

NOTE Confidence: 0.8224325

00:21:34.472 --> 00:21:36.093 one circuit that's involved in

NOTE Confidence: 0.8224325

00:21:36.093 --> 00:21:37.933 cognition lead to the complex

NOTE Confidence: 0.8224325

00:21:37.933 --> 00:21:39.037 symptoms of schizophrenia?

NOTE Confidence: 0.8224325

00:21:39.040 --> 00:21:41.049 Just as a quick refresher we talk

NOTE Confidence: 0.8224325

00:21:41.049 --> 00:21:42.955 about we're talking about a circuit

NOTE Confidence: 0.8224325

00:21:42.955 --> 00:21:44.275 that's important for cognition

NOTE Confidence: 0.8224325

00:21:44.275 --> 00:21:45.265 and maybe some

NOTE Confidence: 0.8407046

00:21:45.323 --> 00:21:46.189 social behavior,

NOTE Confidence: 0.8407046

00:21:46.190 --> 00:21:47.820 but there's also the hallucinations,

NOTE Confidence: 0.8407046

00:21:47.820 --> 00:21:49.116 delusions, the various other

NOTE Confidence: 0.8407046

00:21:49.116 --> 00:21:50.088 symptoms of schizophrenia,

NOTE Confidence: 0.8407046

00:21:50.090 --> 00:21:52.258 so we turn back to those studies that
NOTE Confidence: 0.8407046

00:21:52.258 --> 00:21:54.468 I just mentioned from functional.
NOTE Confidence: 0.8407046

00:21:54.470 --> 00:21:57.846 Human neuroimaging and what we see is in,
NOTE Confidence: 0.8407046

00:21:57.850 --> 00:22:00.797 so I showed you this panel here,
NOTE Confidence: 0.8407046

00:22:00.800 --> 00:22:02.685 which is the connectivity between
NOTE Confidence: 0.8407046

00:22:02.685 --> 00:22:05.091 the prefrontal cortex and the family
NOTE Confidence: 0.8407046

00:22:05.091 --> 00:22:06.931 showed reduced connectivity during
NOTE Confidence: 0.8407046

00:22:06.931 --> 00:22:09.231 chronic psychosis and early stages,
NOTE Confidence: 0.8407046

00:22:09.240 --> 00:22:11.922 but we actually see a commensurate
NOTE Confidence: 0.8407046

00:22:11.922 --> 00:22:13.710 hyper connectivity between the
NOTE Confidence: 0.8407046

00:22:13.785 --> 00:22:16.291 thalamus in the motor cortex and the
NOTE Confidence: 0.8407046

00:22:16.291 --> 00:22:18.950 thalamus in the somato sensory cortex.
NOTE Confidence: 0.8407046

00:22:18.950 --> 00:22:21.326 What's interesting is that that the
NOTE Confidence: 0.8407046

00:22:21.326 --> 00:22:23.948 study done by Allen Tiffin Teacher
NOTE Confidence: 0.8407046

00:22:23.948 --> 00:22:26.078 ***** so that same hyperconnectivity
NOTE Confidence: 0.8407046

00:22:26.078 --> 00:22:28.550 as well in these prodromal patients.

NOTE Confidence: 0.81973433

00:22:30.930 --> 00:22:33.621 And so that in this kind of I turned

NOTE Confidence: 0.81973433

00:22:33.621 --> 00:22:36.547 back to kind of some of our mouse works.

NOTE Confidence: 0.81973433

00:22:36.550 --> 00:22:38.776 So we not only looked at connections

NOTE Confidence: 0.81973433

00:22:38.776 --> 00:22:40.680 between the thalamus and the frontal

NOTE Confidence: 0.81973433

00:22:40.680 --> 00:22:42.462 cortex in our mutant mouse time,

NOTE Confidence: 0.81973433

00:22:42.470 --> 00:22:44.030 we looked at various other

NOTE Confidence: 0.81973433

00:22:44.030 --> 00:22:45.590 connectivity at specifically at P4,

NOTE Confidence: 0.81973433

00:22:45.590 --> 00:22:47.150 which is equivalent to birth,

NOTE Confidence: 0.81973433

00:22:47.150 --> 00:22:49.246 and at this stage the only deficit that

NOTE Confidence: 0.81973433

00:22:49.246 --> 00:22:51.549 we found was a connection between the

NOTE Confidence: 0.81973433

00:22:51.549 --> 00:22:53.710 thalamus and the medial prefrontal cortex,

NOTE Confidence: 0.81973433

00:22:53.710 --> 00:22:56.069 and we did not see reduced connectivity

NOTE Confidence: 0.81973433

00:22:56.069 --> 00:22:58.706 between the thalamus in the motor cortex or

NOTE Confidence: 0.81973433

00:22:58.706 --> 00:23:00.730 the thalamus in the somatosensory cortex.

NOTE Confidence: 0.81973433

00:23:00.730 --> 00:23:02.886 So what we're interested in doing is

NOTE Confidence: 0.81973433

00:23:02.886 --> 00:23:04.720 seeing whether there's a change in
NOTE Confidence: 0.81973433

00:23:04.720 --> 00:23:06.424 this kind of diagram in connectivity.
NOTE Confidence: 0.81973433

00:23:06.430 --> 00:23:07.930 As the mouse gets older,
NOTE Confidence: 0.81973433

00:23:07.930 --> 00:23:10.030 do we see a change in adolescence,
NOTE Confidence: 0.81973433

00:23:10.030 --> 00:23:12.430 and do we see a change in adulthood?
NOTE Confidence: 0.81973433

00:23:12.430 --> 00:23:14.230 We know that the connection between
NOTE Confidence: 0.81973433

00:23:14.230 --> 00:23:15.430 the medial prefrontal cortex,
NOTE Confidence: 0.81973433

00:23:15.430 --> 00:23:17.230 the prefrontal cortex in the thalamus,
NOTE Confidence: 0.81973433

00:23:17.230 --> 00:23:19.030 is lost all the way through.
NOTE Confidence: 0.81973433

00:23:19.030 --> 00:23:20.830 But what happens to other circuits?
NOTE Confidence: 0.81973433

00:23:20.830 --> 00:23:22.310 Are there progressive change and
NOTE Confidence: 0.81973433

00:23:22.310 --> 00:23:24.430 so kind of fleshing out this model,
NOTE Confidence: 0.81973433

00:23:24.430 --> 00:23:26.206 which is something that we need
NOTE Confidence: 0.81973433

00:23:26.206 --> 00:23:28.029 to continue to test and study?
NOTE Confidence: 0.81973433

00:23:28.030 --> 00:23:29.600 Is that retinoic acid associated
NOTE Confidence: 0.81973433

00:23:29.600 --> 00:23:31.170 genes disruption in these genes

NOTE Confidence: 0.81973433

00:23:31.221 --> 00:23:32.349 lead to reduced medial?

NOTE Confidence: 0.81973433

00:23:32.350 --> 00:23:33.439 The frontal cortex,

NOTE Confidence: 0.81973433

00:23:33.439 --> 00:23:35.617 medial dorsal thalamus and medial prefrontal

NOTE Confidence: 0.81973433

00:23:35.617 --> 00:23:37.605 cortex connectivity and that leads

NOTE Confidence: 0.81973433

00:23:37.605 --> 00:23:39.565 specifically to early cognitive symptoms.

NOTE Confidence: 0.81973433

00:23:39.570 --> 00:23:39.926 However,

NOTE Confidence: 0.81973433

00:23:39.926 --> 00:23:43.130 the brain now has to compensate so this this

NOTE Confidence: 0.81973433

00:23:43.204 --> 00:23:46.025 disruption of a circuit occurs very early.

NOTE Confidence: 0.81973433

00:23:46.030 --> 00:23:48.226 So during childhood the brain is

NOTE Confidence: 0.81973433

00:23:48.226 --> 00:23:50.589 trying to compensate for this deficit.

NOTE Confidence: 0.81973433

00:23:50.590 --> 00:23:51.730 As we know,

NOTE Confidence: 0.81973433

00:23:51.730 --> 00:23:54.010 the brain can do through neuroplasticity,

NOTE Confidence: 0.81973433

00:23:54.010 --> 00:23:55.700 and maybe these secondary changes

NOTE Confidence: 0.81973433

00:23:55.700 --> 00:23:57.390 may underlie the positive and

NOTE Confidence: 0.81973433

00:23:57.449 --> 00:23:59.329 negative symptoms of schizophrenia.

NOTE Confidence: 0.81973433

00:23:59.330 --> 00:24:00.894 Abig critique of the
NOTE Confidence: 0.81973433

00:24:00.894 --> 00:24:02.458 neurodevelopmental theory is what?
NOTE Confidence: 0.81973433

00:24:02.460 --> 00:24:04.134 Explains that big gap between what's
NOTE Confidence: 0.81973433

00:24:04.134 --> 00:24:06.059 supposed to be the deficit during
NOTE Confidence: 0.81973433

00:24:06.059 --> 00:24:08.309 development and the positive symptoms later,
NOTE Confidence: 0.81973433

00:24:08.310 --> 00:24:10.586 and what what it could be is
NOTE Confidence: 0.81973433

00:24:10.586 --> 00:24:12.210 that the brain is compensating
NOTE Confidence: 0.81973433

00:24:12.210 --> 00:24:13.510 it's compensating it's working.
NOTE Confidence: 0.81973433

00:24:13.510 --> 00:24:15.926 It's kind of figuring out different ways to
NOTE Confidence: 0.81973433

00:24:15.926 --> 00:24:18.706 try to make up for this cognitive deficit,
NOTE Confidence: 0.81973433

00:24:18.710 --> 00:24:20.660 and eventually as expectations get higher,
NOTE Confidence: 0.81973433

00:24:20.660 --> 00:24:22.610 there's a breakdown in the system,
NOTE Confidence: 0.81973433

00:24:22.610 --> 00:24:24.885 and that leads to the psychotic symptoms.
NOTE Confidence: 0.81973433

00:24:24.890 --> 00:24:26.946 This can also kind of dovetail well with
NOTE Confidence: 0.81973433

00:24:26.946 --> 00:24:29.447 kind of the current driving force kind
NOTE Confidence: 0.81973433

00:24:29.447 --> 00:24:31.377 of driving neurodevelopmental theory that

NOTE Confidence: 0.81973433

00:24:31.432 --> 00:24:33.628 it's a specific synaptic pruning deficit.

NOTE Confidence: 0.81973433

00:24:33.630 --> 00:24:34.204 During adolescence,

NOTE Confidence: 0.81973433

00:24:34.204 --> 00:24:36.500 and that's where you see the break then.

NOTE Confidence: 0.81973433

00:24:36.500 --> 00:24:38.216 So maybe as you prune more,

NOTE Confidence: 0.81973433

00:24:38.220 --> 00:24:39.655 you've lost some of these

NOTE Confidence: 0.81973433

00:24:39.655 --> 00:24:40.516 compensatory mechanisms,

NOTE Confidence: 0.81973433

00:24:40.520 --> 00:24:41.950 leading to a psychotic break.

NOTE Confidence: 0.81973433

00:24:41.950 --> 00:24:44.106 And this is something that I'm really

NOTE Confidence: 0.81973433

00:24:44.106 --> 00:24:45.970 interested in testing in a mouse model.

NOTE Confidence: 0.81973433

00:24:45.970 --> 00:24:47.754 What happens to our mouse when we have

NOTE Confidence: 0.81973433

00:24:47.754 --> 00:24:49.734 a specific deficit in this mediodorsal

NOTE Confidence: 0.81973433

00:24:49.734 --> 00:24:50.847 prefrontal cortex connection,

NOTE Confidence: 0.81973433

00:24:50.850 --> 00:24:53.720 and how does it change the rest of the brain?

NOTE Confidence: 0.81973433

00:24:53.720 --> 00:24:56.420 And how does it change behavior

NOTE Confidence: 0.81973433

00:24:56.420 --> 00:24:57.770 progressively through time?

NOTE Confidence: 0.81973433

00:24:57.770 --> 00:24:59.723 And I think this also gives us
NOTE Confidence: 0.81973433

00:24:59.723 --> 00:25:01.589 an opportunity to think about
NOTE Confidence: 0.81973433

00:25:01.589 --> 00:25:03.525 interventions or future interventions.
NOTE Confidence: 0.81973433

00:25:03.530 --> 00:25:05.690 If this is the primary insult,
NOTE Confidence: 0.81973433

00:25:05.690 --> 00:25:07.490 a connection between the mediodorsal
NOTE Confidence: 0.81973433

00:25:07.490 --> 00:25:09.290 down in the prefrontal cortex,
NOTE Confidence: 0.81973433

00:25:09.290 --> 00:25:11.456 can we try to strengthen this
NOTE Confidence: 0.81973433

00:25:11.456 --> 00:25:13.250 connection using in the few?
NOTE Confidence: 0.81973433

00:25:13.250 --> 00:25:15.410 It's very futuristic at this point,
NOTE Confidence: 0.83900446

00:25:15.410 --> 00:25:17.210 but maybe deep brain stimulation
NOTE Confidence: 0.83900446

00:25:17.210 --> 00:25:19.010 or TMS or other processes.
NOTE Confidence: 0.83900446

00:25:19.010 --> 00:25:21.890 Or we could just work on cognitive skills.
NOTE Confidence: 0.83900446

00:25:21.890 --> 00:25:24.056 Could we do brain training apps
NOTE Confidence: 0.83900446

00:25:24.056 --> 00:25:26.209 almost like a burst to three?
NOTE Confidence: 0.83900446

00:25:26.210 --> 00:25:29.194 However, for patients that are at high risk?
NOTE Confidence: 0.83900446

00:25:29.200 --> 00:25:31.180 Of schizophrenia and the thought is

NOTE Confidence: 0.83900446

00:25:31.180 --> 00:25:33.797 by not only by treating this trying

NOTE Confidence: 0.83900446

00:25:33.797 --> 00:25:36.251 to strengthen this circuit can we

NOTE Confidence: 0.83900446

00:25:36.251 --> 00:25:38.780 improve these early cognitive symptoms?

NOTE Confidence: 0.83900446

00:25:38.780 --> 00:25:40.976 We can altogether prevent the secondary

NOTE Confidence: 0.83900446

00:25:40.976 --> 00:25:42.954 circuit changes and maybe prevent

NOTE Confidence: 0.83900446

00:25:42.954 --> 00:25:44.758 positive and negatives symptoms.

NOTE Confidence: 0.83900446

00:25:44.760 --> 00:25:47.154 And this is something I'm just

NOTE Confidence: 0.83900446

00:25:47.154 --> 00:25:48.750 generally interested in studying.

NOTE Confidence: 0.83900446

00:25:48.750 --> 00:25:49.950 Currently circuits neuroscience,

NOTE Confidence: 0.83900446

00:25:49.950 --> 00:25:51.532 which is, I think,

NOTE Confidence: 0.83900446

00:25:51.532 --> 00:25:54.269 a big crux of adult psychiatry has

NOTE Confidence: 0.83900446

00:25:54.269 --> 00:25:57.130 an adult focus of what they do.

NOTE Confidence: 0.83900446

00:25:57.130 --> 00:25:59.330 Is they disrupt relevant circuits?

NOTE Confidence: 0.83900446

00:25:59.330 --> 00:26:01.010 Like the study I showed that

NOTE Confidence: 0.83900446

00:26:01.010 --> 00:26:03.009 was done by Josh Gordon's lab.

NOTE Confidence: 0.83900446

00:26:03.010 --> 00:26:04.430 They just daily disrupt these
NOTE Confidence: 0.83900446

00:26:04.430 --> 00:26:06.241 circuits during adult in adults or
NOTE Confidence: 0.83900446

00:26:06.241 --> 00:26:07.617 they disrupted during adolescence.
NOTE Confidence: 0.83900446

00:26:07.620 --> 00:26:10.076 And then they look, went to disrupt it.
NOTE Confidence: 0.83900446

00:26:10.080 --> 00:26:11.610 How does that affect behavior?
NOTE Confidence: 0.83900446

00:26:11.610 --> 00:26:13.882 But what I'm interested in is I think
NOTE Confidence: 0.83900446

00:26:13.882 --> 00:26:15.910 more relevant to disorders like autism,
NOTE Confidence: 0.83900446

00:26:15.910 --> 00:26:16.249 schizophrenia,
NOTE Confidence: 0.83900446

00:26:16.249 --> 00:26:18.283 where we see this disruption occurs
NOTE Confidence: 0.83900446

00:26:18.283 --> 00:26:20.419 very early and so we can then study
NOTE Confidence: 0.83900446

00:26:20.419 --> 00:26:21.952 if we disrupt in the development
NOTE Confidence: 0.83900446

00:26:21.952 --> 00:26:23.580 of specific circuits early.
NOTE Confidence: 0.83900446

00:26:23.580 --> 00:26:25.422 How does that affect the rest
NOTE Confidence: 0.83900446

00:26:25.422 --> 00:26:26.650 of brain dump development?
NOTE Confidence: 0.83900446

00:26:26.650 --> 00:26:30.220 I think this could generate a more.
NOTE Confidence: 0.83900446

00:26:30.220 --> 00:26:34.105 A better version or better model of

NOTE Confidence: 0.83900446

00:26:34.105 --> 00:26:36.850 neuro psychiatric disease in our

NOTE Confidence: 0.83900446

00:26:36.850 --> 00:26:39.320 model systems to further study.

NOTE Confidence: 0.83900446

00:26:39.320 --> 00:26:42.120 So this is a summary of the talk.

NOTE Confidence: 0.83900446

00:26:42.120 --> 00:26:44.199 I think the main points I want

NOTE Confidence: 0.83900446

00:26:44.199 --> 00:26:46.140 everyone to take away within some

NOTE Confidence: 0.83900446

00:26:46.140 --> 00:26:48.436 that we can further discuss is that

NOTE Confidence: 0.83900446

00:26:48.509 --> 00:26:50.564 the cognitive and motor symptoms

NOTE Confidence: 0.83900446

00:26:50.564 --> 00:26:52.619 of schizophrenia may precede the

NOTE Confidence: 0.83900446

00:26:52.620 --> 00:26:54.060 positive symptoms in schizophrenia.

NOTE Confidence: 0.83900446

00:26:54.060 --> 00:26:55.860 This is underlying the neuro

NOTE Confidence: 0.83900446

00:26:55.860 --> 00:26:57.310 developmental theory of schizophrenia

NOTE Confidence: 0.83900446

00:26:57.310 --> 00:26:59.040 and disruption of frontal cortex

NOTE Confidence: 0.83900446

00:26:59.040 --> 00:27:00.772 development during the 2nd trimester

NOTE Confidence: 0.83900446

00:27:00.772 --> 00:27:02.417 has been associated with schizophrenia,

NOTE Confidence: 0.83900446

00:27:02.420 --> 00:27:04.322 both genetically as well as from

NOTE Confidence: 0.83900446

00:27:04.322 --> 00:27:05.590 epidemiological data and then
NOTE Confidence: 0.83900446

00:27:05.641 --> 00:27:06.970 finally prefrontal cortex,
NOTE Confidence: 0.83900446

00:27:06.970 --> 00:27:07.744 Islamic connectivity.
NOTE Confidence: 0.83900446

00:27:07.744 --> 00:27:09.292 Maybe the underlying developmental
NOTE Confidence: 0.83900446

00:27:09.292 --> 00:27:11.300 etiology of schizophrenia and a target.
NOTE Confidence: 0.83900446

00:27:11.300 --> 00:27:13.799 For early intervention.
NOTE Confidence: 0.83900446

00:27:13.800 --> 00:27:16.280 So this was the data that I showed
NOTE Confidence: 0.83900446

00:27:16.280 --> 00:27:18.057 was part of a as netted,
NOTE Confidence: 0.83900446

00:27:18.060 --> 00:27:19.492 mentioned a large collaborative
NOTE Confidence: 0.83900446

00:27:19.492 --> 00:27:21.640 effort at specifically like to thank
NOTE Confidence: 0.83900446

00:27:21.697 --> 00:27:23.527 men and who's been an excellent
NOTE Confidence: 0.83900446

00:27:23.527 --> 00:27:25.282 mentoring is really giving me a
NOTE Confidence: 0.83900446

00:27:25.282 --> 00:27:26.704 great opportunity in the lab and
NOTE Confidence: 0.83900446

00:27:26.704 --> 00:27:28.700 as well as a Mickey to Shibata,
NOTE Confidence: 0.83900446

00:27:28.700 --> 00:27:30.518 who we worked very closely in
NOTE Confidence: 0.83900446

00:27:30.518 --> 00:27:31.427 leading this project.

NOTE Confidence: 0.83900446

00:27:31.430 --> 00:27:32.618 But as I said,

NOTE Confidence: 0.83900446

00:27:32.618 --> 00:27:34.773 there were so many different people in

NOTE Confidence: 0.83900446

00:27:34.773 --> 00:27:37.205 the lab that were involved in this project.

NOTE Confidence: 0.83900446

00:27:37.210 --> 00:27:38.426 Doing experiments giving feedback.

NOTE Confidence: 0.83900446

00:27:38.426 --> 00:27:40.250 It's just been really amazing process,

NOTE Confidence: 0.83900446

00:27:40.250 --> 00:27:42.679 but I also like to thank all

NOTE Confidence: 0.83900446

00:27:42.679 --> 00:27:43.720 of our collaborators.

NOTE Confidence: 0.83900446

00:27:43.720 --> 00:27:45.764 They helped us with both the generating

NOTE Confidence: 0.83900446

00:27:45.764 --> 00:27:48.130 the mice as well as the neuroimaging.

NOTE Confidence: 0.83900446

00:27:48.130 --> 00:27:49.390 The diffusion tensor imaging

NOTE Confidence: 0.83900446

00:27:49.390 --> 00:27:50.650 in the mouse model,

NOTE Confidence: 0.83900446

00:27:50.650 --> 00:27:52.540 as well as our funding sources

NOTE Confidence: 0.83900446

00:27:52.540 --> 00:27:53.800 there retinoic acid choice,

NOTE Confidence: 0.83900446

00:27:53.800 --> 00:27:55.375 specifically was funded by Safari

NOTE Confidence: 0.83900446

00:27:55.375 --> 00:27:56.950 Assignments Foundation for Autism Research,

NOTE Confidence: 0.83900446

00:27:56.950 --> 00:27:59.470 and then it is funded by the NIH,
NOTE Confidence: 0.83900446

00:27:59.470 --> 00:28:01.192 and I received some money from
NOTE Confidence: 0.83900446

00:28:01.192 --> 00:28:02.940 the Riva Ariella Ritvo endowment,
NOTE Confidence: 0.83900446

00:28:02.940 --> 00:28:04.884 which I'm using towards kind of
NOTE Confidence: 0.83900446

00:28:04.884 --> 00:28:06.816 answering that last question that I'm
NOTE Confidence: 0.83900446

00:28:06.816 --> 00:28:08.562 really interested to and then finally
NOTE Confidence: 0.83900446

00:28:08.562 --> 00:28:10.500 like to thank the Solar Program.
NOTE Confidence: 0.78569424

00:28:10.500 --> 00:28:12.498 The Child Study Center this other
NOTE Confidence: 0.78569424

00:28:12.498 --> 00:28:14.205 program has been really amazing
NOTE Confidence: 0.78569424

00:28:14.205 --> 00:28:16.095 opportunity to really kind of get
NOTE Confidence: 0.78569424

00:28:16.095 --> 00:28:18.388 into lab and really kind of bridge.
NOTE Confidence: 0.78569424

00:28:18.390 --> 00:28:20.340 The clinic as well as my
NOTE Confidence: 0.78569424

00:28:20.340 --> 00:28:21.315 basic science interests,
NOTE Confidence: 0.78569424

00:28:21.320 --> 00:28:23.609 so I'm really thankful to doctor Block,
NOTE Confidence: 0.78569424

00:28:23.610 --> 00:28:25.140 Doctor Stube and Tiny Cologne
NOTE Confidence: 0.78569424

00:28:25.140 --> 00:28:27.190 who really do the heavy lifting.

NOTE Confidence: 0.78569424

00:28:27.190 --> 00:28:30.124 The program as well as the T 32 fellowship,

NOTE Confidence: 0.78569424

00:28:30.130 --> 00:28:33.055 which funds my last two years in the program.

NOTE Confidence: 0.81864005

00:28:35.430 --> 00:28:36.889 And that's the talk.

NOTE Confidence: 0.8971473

00:28:45.710 --> 00:28:48.170 I have a question if I can

NOTE Confidence: 0.8971473

00:28:48.170 --> 00:28:50.739 jump in and it's amazing data,

NOTE Confidence: 0.8971473

00:28:50.740 --> 00:28:54.650 I just think it's so important.

NOTE Confidence: 0.8971473

00:28:54.650 --> 00:28:56.930 I had a question about connectivity.

NOTE Confidence: 0.8971473

00:28:56.930 --> 00:28:59.150 Were you able to see reduced

NOTE Confidence: 0.8971473

00:28:59.150 --> 00:29:00.810 connectivity and other pathways,

NOTE Confidence: 0.8971473

00:29:00.810 --> 00:29:02.350 either longranger or local?

NOTE Confidence: 0.8971473

00:29:02.350 --> 00:29:04.275 I know it's very challenging

NOTE Confidence: 0.8971473

00:29:04.275 --> 00:29:06.586 in the mouse where there isn't

NOTE Confidence: 0.8971473

00:29:06.586 --> 00:29:08.128 that much cortical cortical,

NOTE Confidence: 0.8971473

00:29:08.128 --> 00:29:10.822 but I'm guessing that this is and

NOTE Confidence: 0.8971473

00:29:10.822 --> 00:29:12.706 the the thalamic mouse prefrontal

NOTE Confidence: 0.8971473

00:29:12.706 --> 00:29:14.576 connection is extra important in
NOTE Confidence: 0.8971473

00:29:14.576 --> 00:29:16.985 a mouse compared to a primate.
NOTE Confidence: 0.8971473

00:29:16.985 --> 00:29:19.250 I think 'cause of that were
NOTE Confidence: 0.8971473

00:29:19.250 --> 00:29:21.600 you able to see others here,
NOTE Confidence: 0.8971473

00:29:21.600 --> 00:29:23.140 so we definitely looked
NOTE Confidence: 0.81684583

00:29:23.140 --> 00:29:25.926 at that. We wanted to make sure.
NOTE Confidence: 0.81684583

00:29:25.930 --> 00:29:27.410 Whether this was a specific
NOTE Confidence: 0.81684583

00:29:27.410 --> 00:29:28.890 lesion and before we started,
NOTE Confidence: 0.81684583

00:29:28.890 --> 00:29:30.766 we were kind of agnostic about the
NOTE Confidence: 0.81684583

00:29:30.766 --> 00:29:32.439 circuit that we were expecting,
NOTE Confidence: 0.81684583

00:29:32.440 --> 00:29:34.216 so we did a couple things.
NOTE Confidence: 0.81684583

00:29:34.220 --> 00:29:36.875 First, I kind of went quickly to this side,
NOTE Confidence: 0.81684583

00:29:36.880 --> 00:29:38.360 so this is very diffusion
NOTE Confidence: 0.81684583

00:29:38.360 --> 00:29:39.840 tensor imaging data from P5.
NOTE Confidence: 0.81684583

00:29:39.840 --> 00:29:41.320 So we kind of basically
NOTE Confidence: 0.81684583

00:29:41.320 --> 00:29:42.800 parcel atede using an Atlas.

NOTE Confidence: 0.81684583
00:29:42.800 --> 00:29:44.280 Different regions of the brain,
NOTE Confidence: 0.81684583
00:29:44.280 --> 00:29:46.023 and so we didn't see any deficits
NOTE Confidence: 0.81684583
00:29:46.023 --> 00:29:47.161 in inflamma cortical connections
NOTE Confidence: 0.81684583
00:29:47.161 --> 00:29:48.876 besides the connection to the
NOTE Confidence: 0.81684583
00:29:48.876 --> 00:29:49.905 medial prefrontal cortex.
NOTE Confidence: 0.81684583
00:29:49.910 --> 00:29:51.750 We did see a little bit of a
NOTE Confidence: 0.81684583
00:29:51.750 --> 00:29:53.749 deficit in the orbitofrontal cortex,
NOTE Confidence: 0.81684583
00:29:53.750 --> 00:29:55.938 which isn't shown here.
NOTE Confidence: 0.81684583
00:29:55.940 --> 00:29:56.740 What was really interesting
NOTE Confidence: 0.81684583
00:29:56.740 --> 00:29:58.021 is that it seems like both of
NOTE Confidence: 0.81684583
00:29:58.021 --> 00:29:58.960 these tracks ride together,
NOTE Confidence: 0.81684583
00:29:58.960 --> 00:30:00.250 and so we were one day.
NOTE Confidence: 0.81684583
00:30:00.250 --> 00:30:02.044 Weather DTI was aimed really had
NOTE Confidence: 0.81684583
00:30:02.044 --> 00:30:03.240 some issues separating them,
NOTE Confidence: 0.81684583
00:30:03.240 --> 00:30:05.168 but we didn't see any and I'll show
NOTE Confidence: 0.81684583

00:30:05.168 --> 00:30:06.605 some later date a couple slides
NOTE Confidence: 0.81684583

00:30:06.605 --> 00:30:08.433 down but we shot so no deficits
NOTE Confidence: 0.81684583

00:30:08.433 --> 00:30:10.109 in cortical cortical connectivity
NOTE Confidence: 0.81684583

00:30:10.109 --> 00:30:11.785 between the somatosensory cortex
NOTE Confidence: 0.81684583

00:30:11.785 --> 00:30:13.700 with the motor cortex as well
NOTE Confidence: 0.81684583

00:30:13.700 --> 00:30:14.892 as the prefrontal cortex,
NOTE Confidence: 0.81684583

00:30:14.900 --> 00:30:16.694 and we didn't see any changes
NOTE Confidence: 0.81684583

00:30:16.694 --> 00:30:17.890 in cortical amic tracks.
NOTE Confidence: 0.81684583

00:30:17.890 --> 00:30:19.690 We also looked at dopaminergic input.
NOTE Confidence: 0.81684583

00:30:19.690 --> 00:30:21.358 We actually initially thought we would
NOTE Confidence: 0.81684583

00:30:21.358 --> 00:30:23.206 see a deficit in dopaminergic input
NOTE Confidence: 0.81684583

00:30:23.206 --> 00:30:25.240 and made that underlies the positive
NOTE Confidence: 0.81684583

00:30:25.240 --> 00:30:26.778 symptoms of schizophrenia and at
NOTE Confidence: 0.81684583

00:30:26.778 --> 00:30:28.986 least at the ages that we looked at,
NOTE Confidence: 0.81684583

00:30:28.986 --> 00:30:30.290 we didn't see any.
NOTE Confidence: 0.81684583

00:30:30.290 --> 00:30:32.150 Gross abnormalities in dopaminergic input,

NOTE Confidence: 0.81684583

00:30:32.150 --> 00:30:34.298 and I know times aren't senior

NOTE Confidence: 0.81684583

00:30:34.298 --> 00:30:36.240 interest in the prefrontal cortex,

NOTE Confidence: 0.81684583

00:30:36.240 --> 00:30:37.728 so we also did.

NOTE Confidence: 0.8246989

00:30:40.330 --> 00:30:42.986 Yeah, so we also didn't show this slide,

NOTE Confidence: 0.8246989

00:30:42.990 --> 00:30:45.342 but we also did viral tracing

NOTE Confidence: 0.8246989

00:30:45.342 --> 00:30:47.236 from the prefrontal cortex and

NOTE Confidence: 0.8246989

00:30:47.236 --> 00:30:49.284 so this was in the so we did.

NOTE Confidence: 0.8246989

00:30:49.290 --> 00:30:51.156 This was in the adult where

NOTE Confidence: 0.8246989

00:30:51.156 --> 00:30:53.280 we and this was nabbed car.

NOTE Confidence: 0.8246989

00:30:53.280 --> 00:30:55.184 Doctor Carr was a postdoc in the

NOTE Confidence: 0.8246989

00:30:55.184 --> 00:30:57.448 lab who did an injection in the

NOTE Confidence: 0.8246989

00:30:57.448 --> 00:30:59.178 prefrontal cortex and then we

NOTE Confidence: 0.8246989

00:30:59.178 --> 00:31:01.415 looked at just inputs into the

NOTE Confidence: 0.8246989

00:31:01.415 --> 00:31:02.875 prefrontal cortex and whether

NOTE Confidence: 0.8246989

00:31:02.875 --> 00:31:04.332 there are any specific deficits.

NOTE Confidence: 0.8246989

00:31:04.332 --> 00:31:06.454 We saw a little bit of reduction
NOTE Confidence: 0.8246989

00:31:06.454 --> 00:31:08.549 connectivity between in the insula,
NOTE Confidence: 0.8246989

00:31:08.550 --> 00:31:11.318 but still once again the primary deficit was.
NOTE Confidence: 0.8246989

00:31:11.320 --> 00:31:13.108 The mediodorsal doubtful amic
NOTE Confidence: 0.8246989

00:31:13.108 --> 00:31:15.343 input into the prefrontal cortex.
NOTE Confidence: 0.803034

00:31:18.370 --> 00:31:19.550 And I'm copying
NOTE Confidence: 0.803034

00:31:19.550 --> 00:31:23.089 that slide so I can look at it is.
NOTE Confidence: 0.803034

00:31:23.090 --> 00:31:25.316 Is that also a reduced connectivity
NOTE Confidence: 0.803034

00:31:25.316 --> 00:31:27.410 with is that medial orbital?
NOTE Confidence: 0.8113074

00:31:30.450 --> 00:31:31.260 We didn't see
NOTE Confidence: 0.8113074

00:31:31.260 --> 00:31:33.150 that much, so I called that date.
NOTE Confidence: 0.8113074

00:31:33.150 --> 00:31:35.920 We call that the insula.
NOTE Confidence: 0.8113074

00:31:35.920 --> 00:31:37.324 There wasn't much connectivity that we
NOTE Confidence: 0.8113074

00:31:37.324 --> 00:31:39.119 could see in our tracing experiment,
NOTE Confidence: 0.8113074

00:31:39.120 --> 00:31:41.523 but I can look more closely over the data.
NOTE Confidence: 0.8113074

00:31:41.530 --> 00:31:43.078 I can definitely email you some

NOTE Confidence: 0.8113074
00:31:43.078 --> 00:31:44.980 of the slides so we can look
NOTE Confidence: 0.8113074
00:31:44.980 --> 00:31:46.325 at it more closely together.
NOTE Confidence: 0.8113074
00:31:46.330 --> 00:31:47.670 Great if I may interject.
NOTE Confidence: 0.8113074
00:31:47.670 --> 00:31:49.266 Amy, I think you are right.
NOTE Confidence: 0.8113074
00:31:49.270 --> 00:31:50.606 Actually, we do suspended that,
NOTE Confidence: 0.8113074
00:31:50.606 --> 00:31:53.602 but you know, the problem is that we just.
NOTE Confidence: 0.8113074
00:31:53.602 --> 00:31:57.875 Our goal for us not to claim too much.
NOTE Confidence: 0.8113074
00:31:57.875 --> 00:31:59.270 I totally understand
NOTE Confidence: 0.8259022
00:31:59.270 --> 00:32:03.630 that for publication in particular, but.
NOTE Confidence: 0.8259022
00:32:03.630 --> 00:32:07.626 Especially, you know, given the cortical
NOTE Confidence: 0.8259022
00:32:07.626 --> 00:32:10.780 cortical connections and and the.
NOTE Confidence: 0.8259022
00:32:10.780 --> 00:32:13.140 Between hemispheres was that one
NOTE Confidence: 0.828859
00:32:13.140 --> 00:32:15.500 also not affected that was
NOTE Confidence: 0.828859
00:32:15.500 --> 00:32:18.326 not affected as well. The closel.
NOTE Confidence: 0.828859
00:32:18.330 --> 00:32:21.161 I just imagine that if it's
NOTE Confidence: 0.828859

00:32:21.161 --> 00:32:23.516 more general than the thalamic,
NOTE Confidence: 0.828859

00:32:23.520 --> 00:32:27.299 we really see that in the human, and
NOTE Confidence: 0.828859

00:32:27.300 --> 00:32:30.126 that it would be tremendously important.
NOTE Confidence: 0.8823768

00:32:32.200 --> 00:32:33.829 Ask your question.
NOTE Confidence: 0.8823768

00:32:33.830 --> 00:32:38.316 Kept up or you know about 30 years ago,
NOTE Confidence: 0.8823768

00:32:38.320 --> 00:32:40.818 Danny Weinberger at NIMH had
NOTE Confidence: 0.8823768

00:32:40.818 --> 00:32:42.810 a developmental theory about
NOTE Confidence: 0.8823768

00:32:42.810 --> 00:32:44.810 schizophrenia and that the
NOTE Confidence: 0.8823768

00:32:44.810 --> 00:32:47.805 reason that it sort of showed
NOTE Confidence: 0.8823768

00:32:47.805 --> 00:32:51.300 up at around age 20 or so.
NOTE Confidence: 0.8823768

00:32:51.300 --> 00:32:53.288 Why is that? The
NOTE Confidence: 0.85358673

00:32:53.290 --> 00:32:55.282 kind of prefrontal inhibitory
NOTE Confidence: 0.85358673

00:32:55.282 --> 00:32:56.776 functions that usually
NOTE Confidence: 0.85358673

00:32:56.780 --> 00:33:00.780 began to come online it around that time?
NOTE Confidence: 0.85358673

00:33:00.780 --> 00:33:05.169 Somehow words and I was just curious.
NOTE Confidence: 0.85358673

00:33:05.170 --> 00:33:08.840 This is a naive question in terms of

NOTE Confidence: 0.85358673

00:33:08.840 --> 00:33:12.056 my understanding of DTI and maybe this

NOTE Confidence: 0.85358673

00:33:12.056 --> 00:33:13.890 retrograde study shows something.

NOTE Confidence: 0.85358673

00:33:13.890 --> 00:33:16.190 But what is the directionality?

NOTE Confidence: 0.85358673

00:33:16.190 --> 00:33:18.480 You talk about defects in

NOTE Confidence: 0.81070876

00:33:18.480 --> 00:33:19.860 connectivity between the

NOTE Confidence: 0.81070876

00:33:19.860 --> 00:33:22.151 prefrontal cortex and the thalamus?

NOTE Confidence: 0.81070876

00:33:22.151 --> 00:33:23.990 Are those simply reciprocal,

NOTE Confidence: 0.81070876

00:33:23.990 --> 00:33:29.670 or are they mostly kind of top down? And

NOTE Confidence: 0.8552397

00:33:29.670 --> 00:33:32.005 then the other question is

NOTE Confidence: 0.8552397

00:33:32.005 --> 00:33:34.807 that you know going way back

NOTE Confidence: 0.8552397

00:33:34.807 --> 00:33:38.540 to the 70s and 80s with work by

NOTE Confidence: 0.8552397

00:33:38.540 --> 00:33:40.880 Barbara Fish and Kornblatt and

NOTE Confidence: 0.8552397

00:33:40.880 --> 00:33:43.210 other people who are studying

NOTE Confidence: 0.8552397

00:33:43.210 --> 00:33:45.546 children of skits, high risk

NOTE Confidence: 0.8552397

00:33:45.546 --> 00:33:47.410 offspring of schizophrenic patients.

NOTE Confidence: 0.8552397

00:33:47.410 --> 00:33:50.678 I mean they showed a lot of
NOTE Confidence: 0.8552397

00:33:50.680 --> 00:33:53.010 early kind of minor ADHD
NOTE Confidence: 0.8552397

00:33:53.010 --> 00:33:53.950 inhibitory difficulties,
NOTE Confidence: 0.8552397

00:33:53.950 --> 00:33:55.354 subtle neuropsychological deficits,
NOTE Confidence: 0.8552397

00:33:55.354 --> 00:33:57.689 and I was wondering if
NOTE Confidence: 0.8552397

00:33:57.690 --> 00:34:00.020 you had thoughts about what
NOTE Confidence: 0.786532095

00:34:00.020 --> 00:34:02.320 the? Underlying neural correlate's
NOTE Confidence: 0.786532095

00:34:02.320 --> 00:34:05.706 of those are. Definitely yeah,
NOTE Confidence: 0.786532095

00:34:05.706 --> 00:34:07.862 and I think that Danny Weinberger's work.
NOTE Confidence: 0.786532095

00:34:07.870 --> 00:34:10.642 I have a Erica. That's a slide from his.
NOTE Confidence: 0.786532095

00:34:10.650 --> 00:34:12.690 So he really was the creator of this
NOTE Confidence: 0.786532095

00:34:12.690 --> 00:34:14.979 theory of the neuro developmental theory.
NOTE Confidence: 0.786532095

00:34:14.980 --> 00:34:16.835 And this is actually from one of
NOTE Confidence: 0.786532095

00:34:16.835 --> 00:34:18.777 his more recent reviews and I
NOTE Confidence: 0.786532095

00:34:18.777 --> 00:34:20.229 think that's really interesting.
NOTE Confidence: 0.786532095

00:34:20.230 --> 00:34:22.057 And so I think the focus has

NOTE Confidence: 0.786532095

00:34:22.057 --> 00:34:23.940 been really in that adolescence,

NOTE Confidence: 0.786532095

00:34:23.940 --> 00:34:25.480 and it makes sense, right?

NOTE Confidence: 0.786532095

00:34:25.480 --> 00:34:26.100 Maybe there.

NOTE Confidence: 0.786532095

00:34:26.100 --> 00:34:28.270 I think it combines two theories together.

NOTE Confidence: 0.786532095

00:34:28.270 --> 00:34:30.547 I tried to touch on that and that what

NOTE Confidence: 0.786532095

00:34:30.547 --> 00:34:33.279 we see is that the brain is trying to

NOTE Confidence: 0.786532095

00:34:33.279 --> 00:34:35.679 compensate the brains trying to compensate.

NOTE Confidence: 0.786532095

00:34:35.680 --> 00:34:36.610 As I mentioned.

NOTE Confidence: 0.786532095

00:34:36.610 --> 00:34:37.914 And then, once the.

NOTE Confidence: 0.786532095

00:34:37.914 --> 00:34:39.624 The normal processes of development

NOTE Confidence: 0.786532095

00:34:39.624 --> 00:34:41.360 that occur during adolescence,

NOTE Confidence: 0.786532095

00:34:41.360 --> 00:34:42.880 which strips away these

NOTE Confidence: 0.786532095

00:34:42.880 --> 00:34:44.400 connections at reduced plasticity.

NOTE Confidence: 0.786532095

00:34:44.400 --> 00:34:47.060 With the closure of these neural Nets,

NOTE Confidence: 0.786532095

00:34:47.060 --> 00:34:49.340 you lose that compensatory mechanisms,

NOTE Confidence: 0.786532095

00:34:49.340 --> 00:34:52.364 and then that kind of breaks
NOTE Confidence: 0.786532095

00:34:52.364 --> 00:34:55.819 through and leads to the symptoms.
NOTE Confidence: 0.786532095

00:34:55.820 --> 00:34:57.170 Maybe that's something that needs
NOTE Confidence: 0.786532095

00:34:57.170 --> 00:34:58.522 to be really studied, right?
NOTE Confidence: 0.786532095

00:34:58.522 --> 00:35:00.698 I mean, I think this is still something
NOTE Confidence: 0.786532095

00:35:00.698 --> 00:35:02.838 that we're looking at in a mouse model.
NOTE Confidence: 0.786532095

00:35:02.840 --> 00:35:04.840 I kind of pull on a little adult
NOTE Confidence: 0.786532095

00:35:04.840 --> 00:35:07.159 data to try to give it some support.
NOTE Confidence: 0.786532095

00:35:07.160 --> 00:35:07.700 You're actually,
NOTE Confidence: 0.786532095

00:35:07.700 --> 00:35:09.860 I'm not familiar with the papers like ADHD,
NOTE Confidence: 0.786532095

00:35:09.860 --> 00:35:11.480 so definitely to look those up,
NOTE Confidence: 0.786532095

00:35:11.480 --> 00:35:13.100 but they kind of make sense.
NOTE Confidence: 0.786532095

00:35:13.100 --> 00:35:14.180 ADHD is also distorted.
NOTE Confidence: 0.786532095

00:35:14.180 --> 00:35:14.990 The frontal cortex,
NOTE Confidence: 0.786532095

00:35:14.990 --> 00:35:17.150 something that I have been interested in is,
NOTE Confidence: 0.786532095

00:35:17.150 --> 00:35:17.698 you know,

NOTE Confidence: 0.786532095

00:35:17.698 --> 00:35:19.616 it's thought to be like a dopaminergic

NOTE Confidence: 0.786532095

00:35:19.616 --> 00:35:20.928 deficit that occurs in ADHD.

NOTE Confidence: 0.786532095

00:35:20.930 --> 00:35:22.550 That's why stimulant works so well.

NOTE Confidence: 0.786532095

00:35:22.550 --> 00:35:23.888 And so I wonder what would

NOTE Confidence: 0.786532095

00:35:23.888 --> 00:35:25.240 be the secondary changes in

NOTE Confidence: 0.786532095

00:35:25.240 --> 00:35:26.058 dopaminergic innervation?

NOTE Confidence: 0.786532095

00:35:26.060 --> 00:35:27.236 We looked kinda early,

NOTE Confidence: 0.786532095

00:35:27.236 --> 00:35:27.530 but.

NOTE Confidence: 0.786532095

00:35:27.530 --> 00:35:29.258 Is there some subtle change and

NOTE Confidence: 0.786532095

00:35:29.258 --> 00:35:30.854 that's why antipsychotics work in

NOTE Confidence: 0.786532095

00:35:30.854 --> 00:35:32.039 schizophrenia despite focusing?

NOTE Confidence: 0.786532095

00:35:32.040 --> 00:35:34.287 I'm focusing on a non dopaminergic circuit,

NOTE Confidence: 0.786532095

00:35:34.290 --> 00:35:36.336 so that's something that I probably

NOTE Confidence: 0.786532095

00:35:36.336 --> 00:35:38.479 have to read into a lot more,

NOTE Confidence: 0.786532095

00:35:38.480 --> 00:35:40.268 but it's really interesting

NOTE Confidence: 0.786532095

00:35:40.268 --> 00:35:42.503 of like 80s ADHD symptoms.
NOTE Confidence: 0.786532095

00:35:42.510 --> 00:35:44.900 There's a lot of evidence
NOTE Confidence: 0.8132778

00:35:44.900 --> 00:35:47.280 out of Judie Rapoport's group,
NOTE Confidence: 0.8132778

00:35:47.280 --> 00:35:49.666 that ADHD involves impaired development
NOTE Confidence: 0.8132778

00:35:49.666 --> 00:35:52.051 of the right inferior frontal,
NOTE Confidence: 0.8132778

00:35:52.051 --> 00:35:54.916 and one wonders if somehow that's
NOTE Confidence: 0.8132778

00:35:54.916 --> 00:35:56.820 associated with reduced retinoic
NOTE Confidence: 0.8132778

00:35:56.820 --> 00:36:00.158 acid in a mosaic sort of way.
NOTE Confidence: 0.8132778

00:36:00.160 --> 00:36:03.498 I also wonder if is there any
NOTE Confidence: 0.8132778

00:36:03.498 --> 00:36:05.402 evidence that inflammation reduces
NOTE Confidence: 0.8132778

00:36:05.402 --> 00:36:07.788 retinoic acid since there's so
NOTE Confidence: 0.8132778

00:36:07.790 --> 00:36:09.698 many ties between inflammatory
NOTE Confidence: 0.8132778

00:36:09.700 --> 00:36:12.630 insults in utero and schizophrenia.
NOTE Confidence: 0.8132778

00:36:12.630 --> 00:36:13.302 Definitely. I mean,
NOTE Confidence: 0.8132778

00:36:13.302 --> 00:36:14.422 I think the inflammation thing
NOTE Confidence: 0.8132778

00:36:14.422 --> 00:36:15.891 is is quite interesting, right?

NOTE Confidence: 0.8132778

00:36:15.891 --> 00:36:17.146 How can we coincide both?

NOTE Confidence: 0.8132778

00:36:17.150 --> 00:36:19.103 I mean, I just read a recent paper by

NOTE Confidence: 0.8132778

00:36:19.103 --> 00:36:21.160 archive of more about the compliment pathway,

NOTE Confidence: 0.8132778

00:36:21.160 --> 00:36:22.415 so that's something that could

NOTE Confidence: 0.8132778

00:36:22.415 --> 00:36:23.168 be quite interesting.

NOTE Confidence: 0.8132778

00:36:23.170 --> 00:36:24.676 And what I didn't touch it.

NOTE Confidence: 0.8132778

00:36:24.680 --> 00:36:26.186 I think we talked a little

NOTE Confidence: 0.8132778

00:36:26.186 --> 00:36:27.190 bit before awhile ago.

NOTE Confidence: 0.8132778

00:36:27.190 --> 00:36:28.912 We were talking about the RA paper

NOTE Confidence: 0.8132778

00:36:28.912 --> 00:36:30.697 is what we show in the human,

NOTE Confidence: 0.8132778

00:36:30.700 --> 00:36:32.206 at least compared to the mouse.

NOTE Confidence: 0.8132778

00:36:32.210 --> 00:36:33.911 And there's a great expansion of retinoic

NOTE Confidence: 0.8132778

00:36:33.911 --> 00:36:35.469 acid signaling in the frontal cortex,

NOTE Confidence: 0.8132778

00:36:35.470 --> 00:36:36.996 so you could see similar deficits may

NOTE Confidence: 0.8132778

00:36:36.996 --> 00:36:38.766 be in the human that you don't see

NOTE Confidence: 0.8132778

00:36:38.766 --> 00:36:40.197 in the mouse of these connectivity
NOTE Confidence: 0.8132778

00:36:40.197 --> 00:36:42.063 changes in other regions of the
NOTE Confidence: 0.8132778

00:36:42.063 --> 00:36:45.508 Association aspects of the frontal lobe.
NOTE Confidence: 0.8132778

00:36:45.510 --> 00:36:46.668 Arctic, this was real.
NOTE Confidence: 0.8132778

00:36:46.668 --> 00:36:47.244 Thank you.
NOTE Confidence: 0.8132778

00:36:47.244 --> 00:36:48.980 This was really great and one
NOTE Confidence: 0.8132778

00:36:48.980 --> 00:36:51.006 of the things I love when you
NOTE Confidence: 0.8132778

00:36:51.006 --> 00:36:53.026 talk is that you always get us
NOTE Confidence: 0.8132778

00:36:53.026 --> 00:36:54.760 to think about things in a
NOTE Confidence: 0.82324153

00:36:54.760 --> 00:36:57.064 very different way. So I just had a
NOTE Confidence: 0.82324153

00:36:57.070 --> 00:36:58.510 question about your idea about
NOTE Confidence: 0.82324153

00:36:58.510 --> 00:37:00.830 stress and if you think of you know,
NOTE Confidence: 0.82324153

00:37:00.830 --> 00:37:02.558 as you suggested, that you know
NOTE Confidence: 0.82324153

00:37:02.560 --> 00:37:05.885 later around the skirts of the brain.
NOTE Confidence: 0.82324153

00:37:05.890 --> 00:37:06.988 Of the schizophrenic,
NOTE Confidence: 0.82324153

00:37:06.988 --> 00:37:09.178 you know just can't manage all

NOTE Confidence: 0.82324153

00:37:09.178 --> 00:37:12.100 the all the stress and all the the

NOTE Confidence: 0.82324153

00:37:12.100 --> 00:37:14.290 the bombardment of demands on it.

NOTE Confidence: 0.82324153

00:37:14.290 --> 00:37:15.379 Could you think

NOTE Confidence: 0.8423583

00:37:15.380 --> 00:37:18.640 of those you know? Individuals early

NOTE Confidence: 0.8423583

00:37:18.640 --> 00:37:20.940 on in childhood who are doing better

NOTE Confidence: 0.81314194

00:37:20.940 --> 00:37:23.236 not being exposed to as much stress

NOTE Confidence: 0.81314194

00:37:23.236 --> 00:37:25.217 and having much more early supports.

NOTE Confidence: 0.81314194

00:37:25.217 --> 00:37:28.160 You know the the work of us in the

NOTE Confidence: 0.81314194

00:37:28.244 --> 00:37:30.152 field of child psychiatry that would

NOTE Confidence: 0.81314194

00:37:30.152 --> 00:37:32.790 somehow prepare them in a way to have

NOTE Confidence: 0.81314194

00:37:32.790 --> 00:37:35.030 kind of a more resilient brain for

NOTE Confidence: 0.81314194

00:37:35.030 --> 00:37:37.390 later on and hopes of doing better.

NOTE Confidence: 0.81314194

00:37:37.390 --> 00:37:38.710 Does that make any

NOTE Confidence: 0.81314194

00:37:38.710 --> 00:37:40.018 sense to you? I

NOTE Confidence: 0.81314194

00:37:40.020 --> 00:37:41.340 really like that approach.

NOTE Confidence: 0.81314194

00:37:41.340 --> 00:37:43.647 I think you know, it's really easy
NOTE Confidence: 0.81314194

00:37:43.647 --> 00:37:45.950 to get very sized by in science.
NOTE Confidence: 0.81314194

00:37:45.950 --> 00:37:48.078 You know, like we're going to virally
NOTE Confidence: 0.81314194

00:37:48.078 --> 00:37:49.764 infect the brain changes gene
NOTE Confidence: 0.81314194

00:37:49.764 --> 00:37:51.851 expression on this other thing, but.
NOTE Confidence: 0.81314194

00:37:51.851 --> 00:37:54.028 I think we're quite far from that,
NOTE Confidence: 0.81314194

00:37:54.030 --> 00:37:55.405 so building these skills very
NOTE Confidence: 0.81314194

00:37:55.405 --> 00:37:57.300 early in these high risk children,
NOTE Confidence: 0.81314194

00:37:57.300 --> 00:37:58.780 especially something like you know
NOTE Confidence: 0.81314194

00:37:58.780 --> 00:38:00.240 resilience, skills or cognitive skills.
NOTE Confidence: 0.81314194

00:38:00.240 --> 00:38:02.342 Now what I like about these types
NOTE Confidence: 0.81314194

00:38:02.342 --> 00:38:04.148 of interventions is that the risk
NOTE Confidence: 0.81314194

00:38:04.148 --> 00:38:05.616 profile is really low, right?
NOTE Confidence: 0.81314194

00:38:05.616 --> 00:38:07.096 If we're stimulating a circuit,
NOTE Confidence: 0.81314194

00:38:07.100 --> 00:38:09.137 or we're giving retinoic acid or work
NOTE Confidence: 0.81314194

00:38:09.137 --> 00:38:10.668 virally infecting the brain, right?

NOTE Confidence: 0.81314194

00:38:10.668 --> 00:38:12.516 You have to be pretty confident

NOTE Confidence: 0.81314194

00:38:12.516 --> 00:38:14.615 that this child is going to develop

NOTE Confidence: 0.81314194

00:38:14.615 --> 00:38:16.602 a disorder that will be, you know,

NOTE Confidence: 0.81314194

00:38:16.602 --> 00:38:17.786 quite dramatically, life altering.

NOTE Confidence: 0.81314194

00:38:17.790 --> 00:38:19.942 And so I like building on these skills

NOTE Confidence: 0.81314194

00:38:19.942 --> 00:38:21.888 because if this child doesn't convert

NOTE Confidence: 0.81314194

00:38:21.888 --> 00:38:24.290 to psychosis even in the prodromal stage.

NOTE Confidence: 0.81314194

00:38:24.290 --> 00:38:26.586 Data about a third of these high risk

NOTE Confidence: 0.81314194

00:38:26.586 --> 00:38:28.360 patients actually develop schizophrenia,

NOTE Confidence: 0.81314194

00:38:28.360 --> 00:38:30.551 and so building skills that I think

NOTE Confidence: 0.81314194

00:38:30.551 --> 00:38:32.605 could help this child leaders and

NOTE Confidence: 0.81314194

00:38:32.605 --> 00:38:34.705 help manage the stress which is

NOTE Confidence: 0.81314194

00:38:34.705 --> 00:38:36.823 clearly been shown to affect kind

NOTE Confidence: 0.81314194

00:38:36.823 --> 00:38:38.187 of severity of symptoms.

NOTE Confidence: 0.81314194

00:38:38.190 --> 00:38:42.168 I think it just makes a ton of sense.

NOTE Confidence: 0.81314194

00:38:42.170 --> 00:38:43.019 It just fits
NOTE Confidence: 0.8538997

00:38:43.020 --> 00:38:44.987 so nicely with her model of lowering.
NOTE Confidence: 0.8538997

00:38:44.990 --> 00:38:46.118 You know inflammatory insult
NOTE Confidence: 0.8538997

00:38:46.118 --> 00:38:47.246 from stress and things.
NOTE Confidence: 0.8538997

00:38:47.250 --> 00:38:48.656 So thank you very much.
NOTE Confidence: 0.8538997

00:38:48.656 --> 00:38:52.050 I really enjoyed this very much.
NOTE Confidence: 0.8538997

00:38:52.050 --> 00:38:52.738 Hi Christine.
NOTE Confidence: 0.8538997

00:38:52.738 --> 00:38:54.458 Hi, this is Flora vaccarino.
NOTE Confidence: 0.8538997

00:38:54.460 --> 00:38:57.060 I have a question very interesting so can
NOTE Confidence: 0.8538997

00:38:57.060 --> 00:38:59.959 you go a little bit into the mechanism?
NOTE Confidence: 0.8538997

00:38:59.960 --> 00:39:02.368 What do you think is happening here?
NOTE Confidence: 0.8538997

00:39:02.370 --> 00:39:05.706 Do you think that there is a relative
NOTE Confidence: 0.8538997

00:39:05.706 --> 00:39:08.050 deficit over 18 OIC acid that?
NOTE Confidence: 0.8538997

00:39:08.050 --> 00:39:09.542 Somehow, directly or indirectly
NOTE Confidence: 0.8538997

00:39:09.542 --> 00:39:11.780 stunts the growth of this connection
NOTE Confidence: 0.8538997

00:39:11.838 --> 00:39:13.868 downstream connection to that Alamos.

NOTE Confidence: 0.8538997

00:39:13.870 --> 00:39:16.600 Do you think there is a chemoattractant

NOTE Confidence: 0.8538997

00:39:16.600 --> 00:39:19.685 role for 18 OIC acid in attracting

NOTE Confidence: 0.8538997

00:39:19.685 --> 00:39:22.439 those connections in that alamaze or?

NOTE Confidence: 0.8538997

00:39:22.440 --> 00:39:25.120 Or what do you think is going on?

NOTE Confidence: 0.8538997

00:39:25.120 --> 00:39:27.160 Because retinoic acid is thought to

NOTE Confidence: 0.8538997

00:39:27.160 --> 00:39:29.552 be a very important more for John

NOTE Confidence: 0.8538997

00:39:29.552 --> 00:39:31.490 earlier on to write much earlier,

NOTE Confidence: 0.8538997

00:39:31.490 --> 00:39:33.765 but it seems to be more in

NOTE Confidence: 0.8538997

00:39:33.765 --> 00:39:35.509 posterior regions of the brain,

NOTE Confidence: 0.8538997

00:39:35.510 --> 00:39:37.520 where here you're talking about something

NOTE Confidence: 0.8538997

00:39:37.520 --> 00:39:38.860 specific for prefrontal cortex,

NOTE Confidence: 0.8538997

00:39:38.860 --> 00:39:41.540 yeah, is that right? I mean can you?

NOTE Confidence: 0.78017604

00:39:43.020 --> 00:39:45.516 Something that netted an in the lab is

NOTE Confidence: 0.78017604

00:39:45.516 --> 00:39:47.392 talked about, kind of retinoic acid.

NOTE Confidence: 0.78017604

00:39:47.392 --> 00:39:48.957 Historically we have been thought

NOTE Confidence: 0.78017604

00:39:48.957 --> 00:39:50.816 of as a post theorizing factor,
NOTE Confidence: 0.78017604

00:39:50.820 --> 00:39:52.116 especially in the hindbrain,
NOTE Confidence: 0.78017604

00:39:52.116 --> 00:39:54.706 but I think then it has a more
NOTE Confidence: 0.78017604

00:39:54.706 --> 00:39:56.434 complex theory of how it goes,
NOTE Confidence: 0.78017604

00:39:56.440 --> 00:39:59.239 but I think your point is well taken overall,
NOTE Confidence: 0.78017604

00:39:59.240 --> 00:40:00.266 that retinoic acid.
NOTE Confidence: 0.78017604

00:40:00.266 --> 00:40:00.950 Is pleiotropic.
NOTE Confidence: 0.78017604

00:40:00.950 --> 00:40:02.685 It's involved in almost every
NOTE Confidence: 0.78017604

00:40:02.685 --> 00:40:04.420 process of brain development and
NOTE Confidence: 0.78017604

00:40:04.483 --> 00:40:06.331 development overall and so I guess
NOTE Confidence: 0.78017604

00:40:06.331 --> 00:40:08.171 to answer the couple questions and
NOTE Confidence: 0.78017604

00:40:08.171 --> 00:40:10.363 remind me if I missed some of this.
NOTE Confidence: 0.78017604

00:40:10.370 --> 00:40:12.466 First, what we show in the paper is
NOTE Confidence: 0.78017604

00:40:12.466 --> 00:40:14.368 that retinoic acid during mid field
NOTE Confidence: 0.78017604

00:40:14.368 --> 00:40:15.692 development is tightly regulated
NOTE Confidence: 0.78017604

00:40:15.692 --> 00:40:17.589 to just the prefrontal cortex.

NOTE Confidence: 0.78017604

00:40:17.590 --> 00:40:19.160 So there's actually the sink,

NOTE Confidence: 0.78017604

00:40:19.160 --> 00:40:21.393 so there's 626B1 which is a retinoic

NOTE Confidence: 0.78017604

00:40:21.393 --> 00:40:23.006 acid degrading enzyme which is

NOTE Confidence: 0.78017604

00:40:23.006 --> 00:40:24.788 great enriched in the medial pre

NOTE Confidence: 0.78017604

00:40:24.788 --> 00:40:26.379 installed in the motor cortex.

NOTE Confidence: 0.78017604

00:40:26.380 --> 00:40:28.088 So that kind of restricts it to

NOTE Confidence: 0.78017604

00:40:28.088 --> 00:40:30.195 and then we also showed various

NOTE Confidence: 0.78017604

00:40:30.195 --> 00:40:31.947 different sources of synthesizing.

NOTE Confidence: 0.78017604

00:40:31.950 --> 00:40:33.984 AXA of genes of both intrinsic

NOTE Confidence: 0.78017604

00:40:33.984 --> 00:40:35.988 to the parenchyma itself as well

NOTE Confidence: 0.78017604

00:40:35.988 --> 00:40:38.018 as inputs that are coming in from

NOTE Confidence: 0.78017604

00:40:38.018 --> 00:40:39.912 other regions of the cortex that

NOTE Confidence: 0.78017604

00:40:39.912 --> 00:40:41.795 seem to be expressing a retinoic

NOTE Confidence: 0.78017604

00:40:41.795 --> 00:40:42.800 acid synthesizing enzyme.

NOTE Confidence: 0.78017604

00:40:42.800 --> 00:40:44.810 So it seems to tightly restrict

NOTE Confidence: 0.78017604

00:40:44.866 --> 00:40:46.391 it that mechanism that first
NOTE Confidence: 0.78017604

00:40:46.391 --> 00:40:47.916 question you asked is something
NOTE Confidence: 0.78017604

00:40:47.967 --> 00:40:49.387 that I'm very interested in.
NOTE Confidence: 0.78017604

00:40:49.390 --> 00:40:51.178 So what is retinoic acid actually
NOTE Confidence: 0.78017604

00:40:51.178 --> 00:40:52.870 doing in making this circuit?
NOTE Confidence: 0.78017604

00:40:52.870 --> 00:40:55.200 And So what we looked at is so we have
NOTE Confidence: 0.78017604

00:40:55.263 --> 00:40:57.630 we did RNA seq in our mouse model where
NOTE Confidence: 0.78017604

00:40:57.630 --> 00:41:00.167 we reduced retinoic acid signaling a
NOTE Confidence: 0.78017604

00:41:00.167 --> 00:41:02.372 specific the medial prefrontal cortex.
NOTE Confidence: 0.78017604

00:41:02.380 --> 00:41:03.772 So we microdissected the
NOTE Confidence: 0.78017604

00:41:03.772 --> 00:41:04.816 medial prefrontal cortex.
NOTE Confidence: 0.78017604

00:41:04.820 --> 00:41:06.512 Orbital frontal cortex in the motor
NOTE Confidence: 0.78017604

00:41:06.512 --> 00:41:08.304 cortex and looked at what's different
NOTE Confidence: 0.78017604

00:41:08.304 --> 00:41:10.453 between the control and the wild type.
NOTE Confidence: 0.78017604

00:41:10.460 --> 00:41:12.836 And we found a lot of target genes,
NOTE Confidence: 0.78017604

00:41:12.840 --> 00:41:13.869 specifically adhesion molecules

NOTE Confidence: 0.78017604

00:41:13.869 --> 00:41:15.584 instead of chemo attractants that

NOTE Confidence: 0.78017604

00:41:15.584 --> 00:41:17.287 are seem to be at the synapse.

NOTE Confidence: 0.78017604

00:41:17.290 --> 00:41:19.450 And so we're thinking that my kind of

NOTE Confidence: 0.78017604

00:41:19.450 --> 00:41:21.447 general interest is in cortical connectivity,

NOTE Confidence: 0.78017604

00:41:21.450 --> 00:41:22.822 especially long range connectivity,

NOTE Confidence: 0.78017604

00:41:22.822 --> 00:41:25.228 and so we're I'm thinking is that

NOTE Confidence: 0.78017604

00:41:25.228 --> 00:41:27.251 these axons are able to navigate the

NOTE Confidence: 0.78017604

00:41:27.251 --> 00:41:29.121 striatum and all these cues there to

NOTE Confidence: 0.78017604

00:41:29.121 --> 00:41:30.908 get to the doorstep of the cortex,

NOTE Confidence: 0.78017604

00:41:30.908 --> 00:41:32.552 but they're not getting that final

NOTE Confidence: 0.78017604

00:41:32.552 --> 00:41:33.477 chemoattractant that retinoic

NOTE Confidence: 0.78017604

00:41:33.477 --> 00:41:34.817 acid is specifically regulating,

NOTE Confidence: 0.78017604

00:41:34.820 --> 00:41:37.298 and so it's getting there and not.

NOTE Confidence: 0.78017604

00:41:37.300 --> 00:41:39.478 To form the connection and then

NOTE Confidence: 0.78017604

00:41:39.478 --> 00:41:42.298 actually kind of loses it and I forgot

NOTE Confidence: 0.78017604

00:41:42.298 --> 00:41:44.780 something that Doctor King as it we see.

NOTE Confidence: 0.78017604

00:41:44.780 --> 00:41:46.140 Reciprocal loss of glamo,

NOTE Confidence: 0.78017604

00:41:46.140 --> 00:41:47.160 cortical prefrontal connections,

NOTE Confidence: 0.78017604

00:41:47.160 --> 00:41:49.200 both Pfc to Mia dorsal thalamus

NOTE Confidence: 0.78017604

00:41:49.200 --> 00:41:50.560 about Mr prefrontal cortex.

NOTE Confidence: 0.78017604

00:41:50.560 --> 00:41:52.260 Yeah doctrina, that's a vacuum.

NOTE Confidence: 0.78017604

00:41:52.260 --> 00:41:53.808 That's a great question,

NOTE Confidence: 0.78017604

00:41:53.808 --> 00:41:55.743 and that's something that we're

NOTE Confidence: 0.78017604

00:41:55.743 --> 00:41:58.107 really careful to show in the paper

NOTE Confidence: 0.78017604

00:41:58.107 --> 00:42:00.051 that we're not altering cell number

NOTE Confidence: 0.78017604

00:42:00.051 --> 00:42:02.158 or brain size or all these other

NOTE Confidence: 0.78017604

00:42:02.158 --> 00:42:04.065 kind of factors that retinoic acid

NOTE Confidence: 0.78017604

00:42:04.065 --> 00:42:06.458 is involved in seems to be very

NOTE Confidence: 0.78017604

00:42:06.458 --> 00:42:08.636 selectively involved in kind of circuit.

NOTE Confidence: 0.78017604

00:42:08.640 --> 00:42:11.056 Formation if you reduce it just to that

NOTE Confidence: 0.79421383

00:42:11.060 --> 00:42:13.083 period, I'm just asking how you doing

NOTE Confidence: 0.79421383

00:42:13.083 --> 00:42:15.120 there asking the obvious question.

NOTE Confidence: 0.79421383

00:42:15.120 --> 00:42:16.600 Organize stuff.

NOTE Confidence: 0.79421383

00:42:16.600 --> 00:42:18.301 You can easily test this in organoids

NOTE Confidence: 0.79421383

00:42:18.301 --> 00:42:19.670 from Cortex entoloma schizophrenic,

NOTE Confidence: 0.79421383

00:42:19.670 --> 00:42:20.226 personally definitely.

NOTE Confidence: 0.79421383

00:42:20.226 --> 00:42:21.616 So this is something that

NOTE Confidence: 0.78806835

00:42:21.620 --> 00:42:22.748 we're really interested in.

NOTE Confidence: 0.78806835

00:42:22.748 --> 00:42:25.283 I I know that you're so far ahead in

NOTE Confidence: 0.78806835

00:42:25.283 --> 00:42:27.103 the field and we've been reading a

NOTE Confidence: 0.78806835

00:42:27.164 --> 00:42:29.159 lot of assembly papers in the paper.

NOTE Confidence: 0.78806835

00:42:29.160 --> 00:42:30.833 I was really like the Pasco paper

NOTE Confidence: 0.78806835

00:42:30.833 --> 00:42:32.611 that showed kind of like this

NOTE Confidence: 0.78806835

00:42:32.611 --> 00:42:33.616 cortical striatal connection.

NOTE Confidence: 0.78806835

00:42:33.620 --> 00:42:34.700 It's really interesting that

NOTE Confidence: 0.78806835

00:42:34.700 --> 00:42:36.050 that connectivity can then maybe

NOTE Confidence: 0.78806835

00:42:36.050 --> 00:42:36.969 alter the properties,
NOTE Confidence: 0.78806835

00:42:36.970 --> 00:42:39.077 so I think that's a great mechanism
NOTE Confidence: 0.78806835

00:42:39.077 --> 00:42:40.523 to study specifically human if
NOTE Confidence: 0.78806835

00:42:40.523 --> 00:42:41.987 this is relevant in a human.
NOTE Confidence: 0.78806835

00:42:41.990 --> 00:42:43.106 So I agree, yeah,
NOTE Confidence: 0.78806835

00:42:43.106 --> 00:42:45.060 I should have actually figured it out.
NOTE Confidence: 0.8024582

00:42:46.600 --> 00:42:49.617 Find the results and the way we're
NOTE Confidence: 0.8024582

00:42:49.617 --> 00:42:52.749 developing a system where you can develop,
NOTE Confidence: 0.8024582

00:42:52.750 --> 00:42:54.940 organize from different brain regions
NOTE Confidence: 0.8024582

00:42:54.940 --> 00:42:56.692 using gradients of morphogens,
NOTE Confidence: 0.8024582

00:42:56.700 --> 00:43:00.092 so that could be also used to actually
NOTE Confidence: 0.8024582

00:43:00.092 --> 00:43:02.362 specifically do at Alamo Alamo
NOTE Confidence: 0.8024582

00:43:02.362 --> 00:43:05.032 particles system that you could use.
NOTE Confidence: 0.8024582

00:43:05.040 --> 00:43:06.351 That sounds great.
NOTE Confidence: 0.8024582

00:43:06.351 --> 00:43:08.550 Yeah, 'cause it is. Great
NOTE Confidence: 0.8024582

00:43:08.550 --> 00:43:09.870 idea. Yeah thank

NOTE Confidence: 0.8024582

00:43:09.870 --> 00:43:14.385 can I can I? I'm delighted to see how

NOTE Confidence: 0.8024582

00:43:14.385 --> 00:43:16.697 much interest your talk has taken and

NOTE Confidence: 0.8024582

00:43:16.697 --> 00:43:18.846 I want to go in another direction.

NOTE Confidence: 0.8024582

00:43:18.850 --> 00:43:21.413 I want to go from organoid to humanoid

NOTE Confidence: 0.8024582

00:43:21.413 --> 00:43:23.660 because one of the things then Karthik.

NOTE Confidence: 0.8024582

00:43:23.660 --> 00:43:25.646 We've had the pleasure of working

NOTE Confidence: 0.8024582

00:43:25.646 --> 00:43:27.942 together and I've seen you as a

NOTE Confidence: 0.8024582

00:43:27.942 --> 00:43:29.754 clinician and your clinician as well.

NOTE Confidence: 0.8024582

00:43:29.760 --> 00:43:32.007 And you know the the experience of

NOTE Confidence: 0.8024582

00:43:32.007 --> 00:43:32.970 individuals with schizophrenia,

NOTE Confidence: 0.8024582

00:43:32.970 --> 00:43:34.896 which is something that we see

NOTE Confidence: 0.8024582

00:43:34.896 --> 00:43:37.470 and I just want to in the chat,

NOTE Confidence: 0.8024582

00:43:37.470 --> 00:43:39.391 which has been very active. Angie,

NOTE Confidence: 0.8024582

00:43:39.391 --> 00:43:41.317 thank you for mentioning gating systems.

NOTE Confidence: 0.8024582

00:43:41.320 --> 00:43:43.735 You know there's a question about gating.

NOTE Confidence: 0.8024582

00:43:43.740 --> 00:43:46.372 I want to call your attention and to
NOTE Confidence: 0.8024582

00:43:46.372 --> 00:43:48.333 everyone and there's this wonderful
NOTE Confidence: 0.8024582

00:43:48.333 --> 00:43:50.793 book called Hidden Valley Rd that
NOTE Confidence: 0.8024582

00:43:50.793 --> 00:43:53.198 came out last year about a family that
NOTE Confidence: 0.8024582

00:43:53.198 --> 00:43:55.402 had 7 / 12 siblings had schizophrenia
NOTE Confidence: 0.8024582

00:43:55.402 --> 00:43:57.117 and what's interesting is both
NOTE Confidence: 0.8024582

00:43:57.117 --> 00:43:58.492 the experience of schizophrenia.
NOTE Confidence: 0.8024582

00:43:58.492 --> 00:44:01.574 But this is a family that was followed very,
NOTE Confidence: 0.8024582

00:44:01.580 --> 00:44:03.290 very closely by Robert Friedman.
NOTE Confidence: 0.8024582

00:44:03.290 --> 00:44:03.922 You know,
NOTE Confidence: 0.8024582

00:44:03.922 --> 00:44:05.502 the great psychiatrist in Colorado
NOTE Confidence: 0.8024582

00:44:05.502 --> 00:44:07.647 who was the pioneer of gating
NOTE Confidence: 0.8024582

00:44:07.647 --> 00:44:08.778 so highly recommended.
NOTE Confidence: 0.8024582

00:44:08.780 --> 00:44:10.834 But if you could comment something
NOTE Confidence: 0.8024582

00:44:10.834 --> 00:44:12.554 about gating and then moving
NOTE Confidence: 0.8024582

00:44:12.554 --> 00:44:14.208 in the humanoid direction.

NOTE Confidence: 0.8024582

00:44:14.210 --> 00:44:16.091 I wanna after you answer that I want to

NOTE Confidence: 0.8024582

00:44:16.091 --> 00:44:18.158 call our attention to Doctor Yankee Yazgan,

NOTE Confidence: 0.8024582

00:44:18.160 --> 00:44:19.684 who is our colleague from Turkey

NOTE Confidence: 0.8024582

00:44:19.684 --> 00:44:21.459 who is joining us here and he

NOTE Confidence: 0.8024582

00:44:21.459 --> 00:44:23.097 will have a comment after you met.

NOTE Confidence: 0.8024582

00:44:23.100 --> 00:44:24.285 Maybe you mentioned that thank

NOTE Confidence: 0.8024582

00:44:24.285 --> 00:44:25.820 you for great great talk Arctic.

NOTE Confidence: 0.8024582

00:44:25.820 --> 00:44:26.067 Yeah,

NOTE Confidence: 0.8024582

00:44:26.067 --> 00:44:26.808 I think getting

NOTE Confidence: 0.8396991999999999

00:44:26.810 --> 00:44:28.448 it first before I actually reflect on

NOTE Confidence: 0.8396991999999999

00:44:28.448 --> 00:44:30.747 some of my time back on when he wanted

NOTE Confidence: 0.8396991999999999

00:44:30.747 --> 00:44:32.545 something that did strike me when I

NOTE Confidence: 0.8396991999999999

00:44:32.545 --> 00:44:34.211 was there 'cause we were actually doing

NOTE Confidence: 0.8396991999999999

00:44:34.220 --> 00:44:36.434 the work while I was on when he won.

NOTE Confidence: 0.8396991999999999

00:44:36.440 --> 00:44:38.501 My last run. Was that some of the kids

NOTE Confidence: 0.8396991999999999

00:44:38.501 --> 00:44:40.357 that come in with early onset psychosis

NOTE Confidence: 0.8396991999999999

00:44:40.357 --> 00:44:42.370 or a couple of stick in my head.

NOTE Confidence: 0.8396991999999999

00:44:42.370 --> 00:44:44.236 I won't give the names obviously.

NOTE Confidence: 0.8396991999999999

00:44:44.240 --> 00:44:45.950 But they showed distinct low IQ's.

NOTE Confidence: 0.8396991999999999

00:44:45.950 --> 00:44:47.882 I think they were running in the

NOTE Confidence: 0.8396991999999999

00:44:47.882 --> 00:44:50.549 60s and 70s and so that kind of was

NOTE Confidence: 0.8396991999999999

00:44:50.549 --> 00:44:52.607 something that I always kind of brewing

NOTE Confidence: 0.8396991999999999

00:44:52.607 --> 00:44:54.785 that idea as as I was going there.

NOTE Confidence: 0.8396991999999999

00:44:54.785 --> 00:44:56.495 Yet gaining is a really interesting

NOTE Confidence: 0.8396991999999999

00:44:56.495 --> 00:44:57.065 question right?

NOTE Confidence: 0.8396991999999999

00:44:57.070 --> 00:44:58.490 Especially for positive symptoms, right?

NOTE Confidence: 0.8396991999999999

00:44:58.490 --> 00:44:59.920 Can you gate sensory information?

NOTE Confidence: 0.8396991999999999

00:44:59.920 --> 00:45:01.630 That's going into the cortex right?

NOTE Confidence: 0.8396991999999999

00:45:01.630 --> 00:45:03.910 And and there's great work by Al Powers.

NOTE Confidence: 0.8396991999999999

00:45:03.910 --> 00:45:05.330 Who's in the adult Department?

NOTE Confidence: 0.8396991999999999

00:45:05.330 --> 00:45:07.325 He's a young faculty of the question.

NOTE Confidence: 0.8396991999999999
00:45:07.330 --> 00:45:09.171 It is actually the information that's going
NOTE Confidence: 0.8396991999999999
00:45:09.171 --> 00:45:11.597 in from the founders of the cortex incorrect?
NOTE Confidence: 0.8396991999999999
00:45:11.600 --> 00:45:13.025 Or is the cortex processing
NOTE Confidence: 0.8396991999999999
00:45:13.025 --> 00:45:13.880 that information incorrectly?
NOTE Confidence: 0.8396991999999999
00:45:13.880 --> 00:45:15.806 And I think that kind of.
NOTE Confidence: 0.8396991999999999
00:45:15.810 --> 00:45:18.082 Really eludes to kind of what I was
NOTE Confidence: 0.8396991999999999
00:45:18.082 --> 00:45:19.996 saying without trying to put my foot
NOTE Confidence: 0.8396991999999999
00:45:19.996 --> 00:45:22.157 down that as the you're getting abnormal
NOTE Confidence: 0.8396991999999999
00:45:22.157 --> 00:45:24.207 extra connectivity with these sensory
NOTE Confidence: 0.8396991999999999
00:45:24.207 --> 00:45:26.724 areas between the thalamus in the cortex,
NOTE Confidence: 0.8396991999999999
00:45:26.724 --> 00:45:28.650 so maybe you're getting too much
NOTE Confidence: 0.8396991999999999
00:45:28.707 --> 00:45:30.954 information going in and you're not able
NOTE Confidence: 0.8396991999999999
00:45:30.954 --> 00:45:32.902 to really parse what's truly occurring
NOTE Confidence: 0.8396991999999999
00:45:32.902 --> 00:45:35.391 as well as a kind of background noise,
NOTE Confidence: 0.8396991999999999
00:45:35.391 --> 00:45:38.280 and that could be a nice kind of circuit.
NOTE Confidence: 0.8396991999999999

00:45:38.280 --> 00:45:40.122 Kind of psychobiology kind of thought
NOTE Confidence: 0.8396991999999999

00:45:40.122 --> 00:45:42.726 about how you create a hallucination or a
NOTE Confidence: 0.8396991999999999

00:45:42.726 --> 00:45:44.700 delusion or disorganized thought as well.
NOTE Confidence: 0.8396991999999999

00:45:44.700 --> 00:45:46.390 Any of the positive symptoms.
NOTE Confidence: 0.8396991999999999

00:45:46.390 --> 00:45:47.368 To be honest,
NOTE Confidence: 0.7796665

00:45:47.370 --> 00:45:48.990 so on an international angle,
NOTE Confidence: 0.7796665

00:45:48.990 --> 00:45:50.940 we're going first to Turkey and
NOTE Confidence: 0.7796665

00:45:50.940 --> 00:45:52.895 then to France. So Yankee asking,
NOTE Confidence: 0.7796665

00:45:52.895 --> 00:45:54.840 and then Lilia Benoit Yankee, please.
NOTE Confidence: 0.86525387

00:45:57.210 --> 00:45:58.760 Just hi there everybody.
NOTE Confidence: 0.86525387

00:45:58.760 --> 00:46:01.478 So glad to be back in New
NOTE Confidence: 0.86525387

00:46:01.480 --> 00:46:03.808 Haven, at least for a couple
NOTE Confidence: 0.86525387

00:46:03.810 --> 00:46:05.750 of weeks after 25 years.
NOTE Confidence: 0.86525387

00:46:05.750 --> 00:46:07.686 So I've been following what's
NOTE Confidence: 0.86525387

00:46:07.686 --> 00:46:10.012 going on at child study closely,
NOTE Confidence: 0.86525387

00:46:10.012 --> 00:46:13.120 but haven't had the chance to be in

NOTE Confidence: 0.86525387

00:46:13.120 --> 00:46:16.848 grand rounds for awhile. Thanks for.

NOTE Confidence: 0.86525387

00:46:16.850 --> 00:46:19.703 Including me and great to see

NOTE Confidence: 0.86525387

00:46:19.703 --> 00:46:22.075 friend friendly faces and friends.

NOTE Confidence: 0.86525387

00:46:22.075 --> 00:46:24.450 I'm really impressed by the

NOTE Confidence: 0.86525387

00:46:24.450 --> 00:46:27.775 quality of the work that says that

NOTE Confidence: 0.86525387

00:46:27.775 --> 00:46:30.626 seemed to that will be changing

NOTE Confidence: 0.86525387

00:46:30.626 --> 00:46:33.950 the way we deal with these cases,

NOTE Confidence: 0.86525387

00:46:33.950 --> 00:46:36.802 but so if you questions or

NOTE Confidence: 0.86525387

00:46:36.802 --> 00:46:38.230 minor questions probably.

NOTE Confidence: 0.86525387

00:46:38.230 --> 00:46:41.080 I'm also I have been interested

NOTE Confidence: 0.86525387

00:46:41.080 --> 00:46:43.930 in the neuromotor signs as an

NOTE Confidence: 0.86525387

00:46:43.930 --> 00:46:45.830 indicator of future psychopathology

NOTE Confidence: 0.86525387

00:46:45.830 --> 00:46:49.448 an my my question would be.

NOTE Confidence: 0.86525387

00:46:49.450 --> 00:46:53.272 How would how is the the diagnostic

NOTE Confidence: 0.86525387

00:46:53.272 --> 00:46:54.910 specifity established either

NOTE Confidence: 0.86525387

00:46:54.997 --> 00:46:57.589 schizophrenia or aspergers or
NOTE Confidence: 0.86525387

00:46:57.589 --> 00:47:00.580 whatever based on these findings?
NOTE Confidence: 0.86525387

00:47:00.580 --> 00:47:04.044 I mean can we replace schizophrenia
NOTE Confidence: 0.86525387

00:47:04.044 --> 00:47:06.884 with ASD or with another
NOTE Confidence: 0.86525387

00:47:06.884 --> 00:47:08.790 new developmental disorder
NOTE Confidence: 0.8256377

00:47:08.790 --> 00:47:12.890 on neurological terms? Thank you party, nice
NOTE Confidence: 0.8256377

00:47:12.890 --> 00:47:17.786 nice meeting you by the way.
NOTE Confidence: 0.8256377

00:47:17.790 --> 00:47:19.050 That's a great question.
NOTE Confidence: 0.8256377

00:47:19.050 --> 00:47:20.940 Even the initial paper by Elaine
NOTE Confidence: 0.8256377

00:47:20.999 --> 00:47:22.407 Walker specifically said that
NOTE Confidence: 0.8256377

00:47:22.407 --> 00:47:24.165 this is not specific, right?
NOTE Confidence: 0.8256377

00:47:24.165 --> 00:47:26.235 Like there, other disorders ASD that
NOTE Confidence: 0.8256377

00:47:26.235 --> 00:47:28.180 showed these same type of things.
NOTE Confidence: 0.8256377

00:47:28.180 --> 00:47:31.350 So I think the diagnostic.
NOTE Confidence: 0.8256377

00:47:31.350 --> 00:47:32.558 Capacity of these things
NOTE Confidence: 0.8256377

00:47:32.558 --> 00:47:33.766 is probably quite for,

NOTE Confidence: 0.8256377

00:47:33.770 --> 00:47:35.290 I think, over all right.

NOTE Confidence: 0.8256377

00:47:35.290 --> 00:47:36.805 I think there might be

NOTE Confidence: 0.8256377

00:47:36.805 --> 00:47:38.017 something subtle I mean,

NOTE Confidence: 0.8256377

00:47:38.020 --> 00:47:41.350 and so if you look at the kind of the listed,

NOTE Confidence: 0.8256377

00:47:41.350 --> 00:47:42.865 all the criteria they looked

NOTE Confidence: 0.8256377

00:47:42.865 --> 00:47:44.077 at through motor right?

NOTE Confidence: 0.8256377

00:47:44.080 --> 00:47:45.898 So it was like increased tone

NOTE Confidence: 0.8256377

00:47:45.898 --> 00:47:47.110 like abnormal hand movements.

NOTE Confidence: 0.8256377

00:47:47.110 --> 00:47:49.808 All these things that we could see in a

NOTE Confidence: 0.8256377

00:47:49.808 --> 00:47:51.253 lot of developmental disorders because

NOTE Confidence: 0.8256377

00:47:51.253 --> 00:47:53.470 they if we think of cerebral palsy,

NOTE Confidence: 0.8256377

00:47:53.470 --> 00:47:55.288 is like the classic developmental disorder.

NOTE Confidence: 0.8256377

00:47:55.290 --> 00:47:56.800 Some sort of deficit in

NOTE Confidence: 0.8256377

00:47:56.800 --> 00:47:57.706 circuit formation early.

NOTE Confidence: 0.8256377

00:47:57.710 --> 00:47:59.528 They show these signs very distinctly,

NOTE Confidence: 0.8256377

00:47:59.530 --> 00:48:00.898 so I think the.
NOTE Confidence: 0.8256377

00:48:00.898 --> 00:48:02.266 Specificity is probably extremely
NOTE Confidence: 0.8256377

00:48:02.266 --> 00:48:04.337 low for these types of things,
NOTE Confidence: 0.8256377

00:48:04.340 --> 00:48:06.876 but I think that as we start turning
NOTE Confidence: 0.8256377

00:48:06.876 --> 00:48:09.439 our focus to early in earlier stages,
NOTE Confidence: 0.8256377

00:48:09.440 --> 00:48:11.185 which is what these perspective
NOTE Confidence: 0.8256377

00:48:11.185 --> 00:48:13.180 studies are so exciting to me,
NOTE Confidence: 0.8256377

00:48:13.180 --> 00:48:15.343 I think maybe we can narrow it
NOTE Confidence: 0.8256377

00:48:15.343 --> 00:48:16.920 down to something specific.
NOTE Confidence: 0.8256377

00:48:16.920 --> 00:48:18.775 One thing I didn't know in these
NOTE Confidence: 0.8256377

00:48:18.775 --> 00:48:20.725 studies is that patients that later
NOTE Confidence: 0.8256377

00:48:20.725 --> 00:48:22.185 developed bipolar disorder which
NOTE Confidence: 0.8256377

00:48:22.185 --> 00:48:24.520 have you know a similar psychotic
NOTE Confidence: 0.8256377

00:48:24.520 --> 00:48:26.100 E type presentation untreated,
NOTE Confidence: 0.8256377

00:48:26.100 --> 00:48:27.800 those time control don't show
NOTE Confidence: 0.8256377

00:48:27.800 --> 00:48:28.820 these motor signs,

NOTE Confidence: 0.8256377

00:48:28.820 --> 00:48:31.347 and so that's I thought quite interesting.

NOTE Confidence: 0.8256377

00:48:31.350 --> 00:48:33.234 But I think ASD and Sara

NOTE Confidence: 0.8256377

00:48:33.234 --> 00:48:34.176 Palsy and schizophrenic.

NOTE Confidence: 0.8256377

00:48:34.180 --> 00:48:36.064 There's a lot of overlap and

NOTE Confidence: 0.8256377

00:48:36.064 --> 00:48:37.320 I think disease pathology.

NOTE Confidence: 0.8256377

00:48:37.320 --> 00:48:37.958 You know,

NOTE Confidence: 0.8256377

00:48:37.958 --> 00:48:40.191 both in the time period that specifically

NOTE Confidence: 0.8256377

00:48:40.191 --> 00:48:42.030 sensitive the cells that are affected,

NOTE Confidence: 0.8256377

00:48:42.030 --> 00:48:43.600 the jeans that are effective.

NOTE Confidence: 0.8256377

00:48:43.600 --> 00:48:45.322 There seems to be similar processes

NOTE Confidence: 0.8256377

00:48:45.322 --> 00:48:47.548 that are affected or altered and why

NOTE Confidence: 0.8256377

00:48:47.548 --> 00:48:49.248 they manifest is different disorders.

NOTE Confidence: 0.8256377

00:48:49.250 --> 00:48:51.754 I think that's still a long way away,

NOTE Confidence: 0.8256377

00:48:51.760 --> 00:48:54.268 and it needs a lot of research to

NOTE Confidence: 0.8256377

00:48:54.268 --> 00:48:57.709 make sense that thanks very much.

NOTE Confidence: 0.8256377

00:48:57.710 --> 00:48:59.000 Paid Lilia and
NOTE Confidence: 0.8062014

00:48:59.000 --> 00:49:01.150 then Ellen Hoffman. High thank
NOTE Confidence: 0.8062014

00:49:01.150 --> 00:49:03.300 you very much. Much chaotic.
NOTE Confidence: 0.8062014

00:49:03.300 --> 00:49:04.660 So just a comment.
NOTE Confidence: 0.8062014

00:49:04.660 --> 00:49:07.630 We had just seeing that the 30 years
NOTE Confidence: 0.8062014

00:49:07.630 --> 00:49:09.770 of research carried on clinical
NOTE Confidence: 0.8062014

00:49:09.770 --> 00:49:12.760 transition by our Australian colleagues,
NOTE Confidence: 0.8062014

00:49:12.760 --> 00:49:15.610 for instance, Patrick McGorry trying to
NOTE Confidence: 0.8062014

00:49:15.610 --> 00:49:18.878 to build clinical tools like the cars
NOTE Confidence: 0.8062014

00:49:18.878 --> 00:49:21.028 and following clinical subjects like
NOTE Confidence: 0.8062014

00:49:21.028 --> 00:49:24.178 we see with the drama that it's not
NOTE Confidence: 0.8062014

00:49:24.178 --> 00:49:27.890 really working as as we would have reached 2.
NOTE Confidence: 0.8062014

00:49:27.890 --> 00:49:30.011 Because it was a great hope to
NOTE Confidence: 0.8062014

00:49:30.011 --> 00:49:32.491 to have those clinical tools and
NOTE Confidence: 0.8062014

00:49:32.491 --> 00:49:34.495 psychoeducation and omega-3 etc.
NOTE Confidence: 0.8062014

00:49:34.500 --> 00:49:37.108 So I mean, it's really important to see

NOTE Confidence: 0.8062014

00:49:37.108 --> 00:49:40.337 that we still need the fundamental research,

NOTE Confidence: 0.8062014

00:49:40.340 --> 00:49:42.668 so that's still very much needed,

NOTE Confidence: 0.8062014

00:49:42.670 --> 00:49:46.045 so it's interesting.

NOTE Confidence: 0.8062014

00:49:46.045 --> 00:49:49.504 But I think that's something that was

NOTE Confidence: 0.8062014

00:49:49.504 --> 00:49:51.555 also interesting in this clinical

NOTE Confidence: 0.8062014

00:49:51.555 --> 00:49:54.544 assessment was to build strong cohorts an,

NOTE Confidence: 0.8062014

00:49:54.550 --> 00:49:56.600 so that's something that they

NOTE Confidence: 0.8062014

00:49:56.600 --> 00:49:58.650 they really managed to do,

NOTE Confidence: 0.8062014

00:49:58.650 --> 00:50:00.470 and I'm wondering because.

NOTE Confidence: 0.8062014

00:50:00.470 --> 00:50:02.745 Cohorts that you cited include

NOTE Confidence: 0.8062014

00:50:02.745 --> 00:50:04.230 very few children.

NOTE Confidence: 0.8062014

00:50:04.230 --> 00:50:07.692 So do you know of ongoing

NOTE Confidence: 0.8062014

00:50:07.692 --> 00:50:10.000 cohort that would maybe?

NOTE Confidence: 0.8062014

00:50:10.000 --> 00:50:12.280 Gather better data on neuromuscular skills,

NOTE Confidence: 0.8062014

00:50:12.280 --> 00:50:12.660 etc.

NOTE Confidence: 0.8062014

00:50:12.660 --> 00:50:13.420 Yeah yeah,
NOTE Confidence: 0.8062014

00:50:13.420 --> 00:50:14.180 yeah yeah,
NOTE Confidence: 0.8062014

00:50:14.180 --> 00:50:15.320 I'm new to
NOTE Confidence: 0.81124085

00:50:15.320 --> 00:50:18.050 them or the clinical world as I
NOTE Confidence: 0.81124085

00:50:18.050 --> 00:50:20.012 actually recently talked to one
NOTE Confidence: 0.81124085

00:50:20.012 --> 00:50:22.154 of our graduates from our program,
NOTE Confidence: 0.81124085

00:50:22.160 --> 00:50:23.300 Jerome Doctor Taylor,
NOTE Confidence: 0.81124085

00:50:23.300 --> 00:50:25.200 who's now faculty at Penn,
NOTE Confidence: 0.81124085

00:50:25.200 --> 00:50:27.874 and he's working as part of the
NOTE Confidence: 0.81124085

00:50:27.874 --> 00:50:30.140 lifespan lifespan group with the girls,
NOTE Confidence: 0.81124085

00:50:30.140 --> 00:50:32.800 and so they have this larger study.
NOTE Confidence: 0.81124085

00:50:32.800 --> 00:50:35.080 I don't know the exact things
NOTE Confidence: 0.81124085

00:50:35.080 --> 00:50:36.220 like Philadelphia, children,
NOTE Confidence: 0.81124085

00:50:36.220 --> 00:50:37.740 something where they're really
NOTE Confidence: 0.81124085

00:50:37.740 --> 00:50:38.880 deeply profiling children,
NOTE Confidence: 0.81124085

00:50:38.880 --> 00:50:40.648 just agnostically kids that.

NOTE Confidence: 0.81124085

00:50:40.648 --> 00:50:42.440 Initially, like a lot of the

NOTE Confidence: 0.81124085

00:50:42.440 --> 00:50:44.173 work was focused on stress and

NOTE Confidence: 0.81124085

00:50:44.173 --> 00:50:46.069 like kind of exposure to trauma.

NOTE Confidence: 0.81124085

00:50:46.070 --> 00:50:48.184 We heard like a presentation from we

NOTE Confidence: 0.81124085

00:50:48.184 --> 00:50:50.759 went there for a treat a couple years ago,

NOTE Confidence: 0.81124085

00:50:50.760 --> 00:50:52.220 but they are actually interested

NOTE Confidence: 0.81124085

00:50:52.220 --> 00:50:54.024 in psychosis and so they are

NOTE Confidence: 0.81124085

00:50:54.024 --> 00:50:55.740 looking more closely at that group.

NOTE Confidence: 0.81124085

00:50:55.740 --> 00:50:57.320 That same group actually does

NOTE Confidence: 0.81124085

00:50:57.320 --> 00:50:59.260 looks at patients of 22 Q 11,

NOTE Confidence: 0.81124085

00:50:59.260 --> 00:51:01.018 which is a genetic deletion that

NOTE Confidence: 0.81124085

00:51:01.018 --> 00:51:02.716 has a 30% increase chance of

NOTE Confidence: 0.81124085

00:51:02.716 --> 00:51:03.804 developing schizophrenia is way

NOTE Confidence: 0.81124085

00:51:03.804 --> 00:51:05.409 higher than the normal population.

NOTE Confidence: 0.81124085

00:51:05.410 --> 00:51:07.258 So there are also carefully built a

NOTE Confidence: 0.81124085

00:51:07.258 --> 00:51:09.090 large cohort of these patients because
NOTE Confidence: 0.81124085

00:51:09.090 --> 00:51:11.379 the issue is schizophrenia as it's rare.
NOTE Confidence: 0.81124085

00:51:11.380 --> 00:51:11.687 Right?
NOTE Confidence: 0.81124085

00:51:11.687 --> 00:51:13.222 Like even in highly focused
NOTE Confidence: 0.81124085

00:51:13.222 --> 00:51:14.750 clinical populations of high risk,
NOTE Confidence: 0.81124085

00:51:14.750 --> 00:51:15.360 30% convert.
NOTE Confidence: 0.81124085

00:51:15.360 --> 00:51:17.495 And so if you're taking all takers,
NOTE Confidence: 0.81124085

00:51:17.500 --> 00:51:19.408 you're going to get the population
NOTE Confidence: 0.81124085

00:51:19.408 --> 00:51:21.829 rate and so something like 22 Q 11
NOTE Confidence: 0.81124085

00:51:21.829 --> 00:51:23.461 are some of these genetic disorders
NOTE Confidence: 0.81124085

00:51:23.527 --> 00:51:25.459 that you can pick out immediately.
NOTE Confidence: 0.81124085

00:51:25.460 --> 00:51:28.205 Who has these, and you can really trace them.
NOTE Confidence: 0.81124085

00:51:28.210 --> 00:51:29.450 Could be, I think,
NOTE Confidence: 0.81124085

00:51:29.450 --> 00:51:31.880 a fruitful way of making sense of this.
NOTE Confidence: 0.81124085

00:51:31.880 --> 00:51:32.747 But yeah, numbers,
NOTE Confidence: 0.81124085

00:51:32.747 --> 00:51:35.250 you just gotta get higher and higher numbers.

NOTE Confidence: 0.81124085

00:51:35.250 --> 00:51:36.830 But I think the Philadelphia

NOTE Confidence: 0.81124085

00:51:36.830 --> 00:51:38.750 size actually is really cool work

NOTE Confidence: 0.81124085

00:51:38.750 --> 00:51:40.135 in the garage slab there.

NOTE Confidence: 0.8354016

00:51:41.170 --> 00:51:43.218 Can I just say before LL and will

NOTE Confidence: 0.8354016

00:51:43.218 --> 00:51:44.970 have one last question and then

NOTE Confidence: 0.8354016

00:51:44.970 --> 00:51:47.220 we can hang out with with Kartik?

NOTE Confidence: 0.8354016

00:51:47.220 --> 00:51:49.356 We won't close a room but if people

NOTE Confidence: 0.8354016

00:51:49.356 --> 00:51:51.707 need to leave but I just want to

NOTE Confidence: 0.8354016

00:51:51.707 --> 00:51:53.523 call your attention to next week's

NOTE Confidence: 0.8354016

00:51:53.523 --> 00:51:55.567 grand rounds which is going to be

NOTE Confidence: 0.8354016

00:51:55.567 --> 00:51:57.300 a little bit continuing and some

NOTE Confidence: 0.8354016

00:51:57.300 --> 00:51:58.740 related way so Kieran O'Donnell,

NOTE Confidence: 0.8354016

00:51:58.740 --> 00:52:00.924 one of our newest faculty members is going

NOTE Confidence: 0.8354016

00:52:00.924 --> 00:52:03.347 to be talking to us about early early,

NOTE Confidence: 0.8354016

00:52:03.350 --> 00:52:05.036 early, early early years and the

NOTE Confidence: 0.8354016

00:52:05.036 --> 00:52:06.510 impact on the developing brain.

NOTE Confidence: 0.8354016

00:52:06.510 --> 00:52:08.590 So I think it's going to be very

NOTE Confidence: 0.8354016

00:52:08.590 --> 00:52:10.260 in keeping with today's talk.

NOTE Confidence: 0.8354016

00:52:10.260 --> 00:52:13.008 So Ellen last question for Karthik.

NOTE Confidence: 0.8354016

00:52:13.010 --> 00:52:13.390 Carter

NOTE Confidence: 0.78803855

00:52:13.390 --> 00:52:16.029 great great talk, I really enjoyed it.

NOTE Confidence: 0.78803855

00:52:16.030 --> 00:52:19.180 You know, I guess as we think about a lot

NOTE Confidence: 0.78803855

00:52:19.262 --> 00:52:21.890 of different questions that one question

NOTE Confidence: 0.78803855

00:52:21.890 --> 00:52:25.109 which I wrote in the chat with you.

NOTE Confidence: 0.78803855

00:52:25.110 --> 00:52:26.995 Sorry you arrived at the

NOTE Confidence: 0.78803855

00:52:26.995 --> 00:52:28.126 retinoic acid pathway.

NOTE Confidence: 0.78803855

00:52:28.130 --> 00:52:30.344 Sort of thinking about risk genes

NOTE Confidence: 0.78803855

00:52:30.344 --> 00:52:32.290 or following the genes there.

NOTE Confidence: 0.78803855

00:52:32.290 --> 00:52:34.906 So to what extent do you think that

NOTE Confidence: 0.78803855

00:52:34.906 --> 00:52:37.431 this pathway and the thalamus to

NOTE Confidence: 0.78803855

00:52:37.431 --> 00:52:39.231 prefrontal cortex connection might

NOTE Confidence: 0.78803855

00:52:39.231 --> 00:52:41.700 represent a common pathway across?

NOTE Confidence: 0.78803855

00:52:41.700 --> 00:52:43.700 Schizophrenia risk genes versus one

NOTE Confidence: 0.78803855

00:52:43.700 --> 00:52:46.429 of several routes there and the sort

NOTE Confidence: 0.78803855

00:52:46.429 --> 00:52:48.427 of related to the other question.

NOTE Confidence: 0.78803855

00:52:48.430 --> 00:52:49.050 Previous question,

NOTE Confidence: 0.78803855

00:52:49.050 --> 00:52:50.910 to what extent might this represent

NOTE Confidence: 0.78803855

00:52:50.910 --> 00:52:53.055 a common pathway across other

NOTE Confidence: 0.78803855

00:52:53.055 --> 00:52:54.039 neurodevelopmental disorders?

NOTE Confidence: 0.78803855

00:52:54.040 --> 00:52:55.910 And that's such an important

NOTE Confidence: 0.78803855

00:52:55.910 --> 00:52:57.406 question for us to

NOTE Confidence: 0.81150025

00:52:57.410 --> 00:52:59.275 really be able to transition

NOTE Confidence: 0.81150025

00:52:59.275 --> 00:53:00.394 this intervention right?

NOTE Confidence: 0.81150025

00:53:00.400 --> 00:53:03.393 Because as this was a mouse model, right?

NOTE Confidence: 0.81150025

00:53:03.393 --> 00:53:04.885 And we actually weren't

NOTE Confidence: 0.81150025

00:53:04.885 --> 00:53:06.004 looking at schizophrenia,

NOTE Confidence: 0.81150025

00:53:06.010 --> 00:53:07.726 we were really interesting.

NOTE Confidence: 0.81150025

00:53:07.726 --> 00:53:09.442 Just prefrontal cortex evolution

NOTE Confidence: 0.81150025

00:53:09.442 --> 00:53:11.329 and development when we initially

NOTE Confidence: 0.81150025

00:53:11.329 --> 00:53:13.261 started this study and so retinoic

NOTE Confidence: 0.81150025

00:53:13.261 --> 00:53:15.449 acid actually agnostically popped up.

NOTE Confidence: 0.81150025

00:53:15.450 --> 00:53:16.854 There was some data before from

NOTE Confidence: 0.81150025

00:53:16.854 --> 00:53:18.380 an earlier study in this testing

NOTE Confidence: 0.81150025

00:53:18.380 --> 00:53:20.000 lab that pointed at retinoic acid,

NOTE Confidence: 0.81150025

00:53:20.000 --> 00:53:22.586 and then we kind of reconfirmed

NOTE Confidence: 0.81150025

00:53:22.586 --> 00:53:24.650 it and then analyzed it.

NOTE Confidence: 0.81150025

00:53:24.650 --> 00:53:25.649 Retinoic acid specific.

NOTE Confidence: 0.81150025

00:53:25.649 --> 00:53:27.647 There's a couple of papers that

NOTE Confidence: 0.81150025

00:53:27.647 --> 00:53:29.542 have really kind of focused on

NOTE Confidence: 0.81150025

00:53:29.542 --> 00:53:31.456 retinoic acid as as possible as

NOTE Confidence: 0.81150025

00:53:31.456 --> 00:53:32.876 a possible signaling pathway.

NOTE Confidence: 0.81150025

00:53:32.880 --> 00:53:35.183 I still I'm kind of wary about

NOTE Confidence: 0.81150025

00:53:35.183 --> 00:53:36.170 specifically retinoic acid.

NOTE Confidence: 0.81150025

00:53:36.170 --> 00:53:38.246 I think as Doctor Vaccarino mentioned

NOTE Confidence: 0.81150025

00:53:38.246 --> 00:53:40.063 is I think something downstream

NOTE Confidence: 0.81150025

00:53:40.063 --> 00:53:42.247 and also kind of putting together

NOTE Confidence: 0.81150025

00:53:42.247 --> 00:53:43.934 with our current knowledge that

NOTE Confidence: 0.81150025

00:53:43.934 --> 00:53:46.038 seems to be like a lot of the

NOTE Confidence: 0.81150025

00:53:46.040 --> 00:53:47.027 schizophrenia associations an

NOTE Confidence: 0.81150025

00:53:47.027 --> 00:53:49.330 autism will soon be at the synapse.

NOTE Confidence: 0.81150025

00:53:49.330 --> 00:53:50.798 Maybe it's something specifically

NOTE Confidence: 0.81150025

00:53:50.798 --> 00:53:52.633 about Synapse connectivity and we

NOTE Confidence: 0.81150025

00:53:52.633 --> 00:53:54.635 just happened to stumble upon it by.

NOTE Confidence: 0.81150025

00:53:54.640 --> 00:53:56.330 Going the retinoic acid path,

NOTE Confidence: 0.81150025

00:53:56.330 --> 00:53:58.696 I do though to you later point.

NOTE Confidence: 0.81150025

00:53:58.700 --> 00:54:00.905 I do think plasma cortical dysfunction may

NOTE Confidence: 0.81150025

00:54:00.905 --> 00:54:03.428 be some core pathology in the disorder,

NOTE Confidence: 0.81150025

00:54:03.430 --> 00:54:05.614 and that I like that circuit based
NOTE Confidence: 0.81150025

00:54:05.614 --> 00:54:07.820 focus versus like a signaling pathway,
NOTE Confidence: 0.81150025

00:54:07.820 --> 00:54:09.172 because I feel like,
NOTE Confidence: 0.81150025

00:54:09.172 --> 00:54:10.524 as I mentioned before,
NOTE Confidence: 0.81150025

00:54:10.530 --> 00:54:12.546 like retinoic acid involved in everything.
NOTE Confidence: 0.81150025

00:54:12.550 --> 00:54:15.592 So it would be really hard to target it,
NOTE Confidence: 0.81150025

00:54:15.600 --> 00:54:17.958 and so I think there is some data that's
NOTE Confidence: 0.81150025

00:54:17.958 --> 00:54:19.940 coming together that Flamel cortical
NOTE Confidence: 0.81150025

00:54:19.940 --> 00:54:22.015 dysfunction is specifically an issue,
NOTE Confidence: 0.81150025

00:54:22.020 --> 00:54:23.031 whether it's specifically
NOTE Confidence: 0.81150025

00:54:23.031 --> 00:54:24.379 thalamic to prefrontal cortex.
NOTE Confidence: 0.81150025

00:54:24.380 --> 00:54:26.516 I think that might be at
NOTE Confidence: 0.81150025

00:54:26.516 --> 00:54:27.584 least a subpopulation.
NOTE Confidence: 0.81150025

00:54:27.590 --> 00:54:29.050 Of it will be interesting,
NOTE Confidence: 0.81150025

00:54:29.050 --> 00:54:30.500 kind of the gating question.
NOTE Confidence: 0.81150025

00:54:30.500 --> 00:54:31.684 Maybe other Islamic deficits,

NOTE Confidence: 0.81150025

00:54:31.684 --> 00:54:32.868 Lima cortical connectivity deficits

NOTE Confidence: 0.81150025

00:54:32.868 --> 00:54:33.990 could explain other things.

NOTE Confidence: 0.81150025

00:54:33.990 --> 00:54:36.240 And if you kind of read I I spent

NOTE Confidence: 0.81150025

00:54:36.240 --> 00:54:38.647 a lot of time before this talk,

NOTE Confidence: 0.81150025

00:54:38.650 --> 00:54:40.660 like kind of reading through all

NOTE Confidence: 0.81150025

00:54:40.660 --> 00:54:41.665 this schizophrenia literature

NOTE Confidence: 0.81150025

00:54:41.665 --> 00:54:43.393 because I spend more time reading

NOTE Confidence: 0.81150025

00:54:43.393 --> 00:54:45.031 like gene regulation stuff and one

NOTE Confidence: 0.81150025

00:54:45.031 --> 00:54:46.507 of the theories has put forward.

NOTE Confidence: 0.81150025

00:54:46.510 --> 00:54:48.250 There's almost two types of schizophrenia.

NOTE Confidence: 0.81150025

00:54:48.250 --> 00:54:49.705 There's like a classic honor

NOTE Confidence: 0.81150025

00:54:49.705 --> 00:54:50.869 student type of schizophrenia,

NOTE Confidence: 0.81150025

00:54:50.870 --> 00:54:51.671 word, psychotic symptoms,

NOTE Confidence: 0.81150025

00:54:51.671 --> 00:54:53.540 1st and then you kind of progressives

NOTE Confidence: 0.81150025

00:54:53.585 --> 00:54:55.240 are very responsive to antipsychotic's.

NOTE Confidence: 0.81150025

00:54:55.240 --> 00:54:56.770 But there's also the second
NOTE Confidence: 0.81150025

00:54:56.770 --> 00:54:58.300 type which is very driven.
NOTE Confidence: 0.81150025

00:54:58.300 --> 00:54:59.672 This cognitive negative symptoms,
NOTE Confidence: 0.81150025

00:54:59.672 --> 00:55:01.995 so I wonder if, like you know,
NOTE Confidence: 0.81150025

00:55:01.995 --> 00:55:03.570 one population is specifically shows
NOTE Confidence: 0.81150025

00:55:03.570 --> 00:55:05.518 this Pfc Flamel cortical deficit,
NOTE Confidence: 0.81150025

00:55:05.520 --> 00:55:07.590 and while his other population doesn't.
NOTE Confidence: 0.81150025

00:55:07.590 --> 00:55:08.278 You know,
NOTE Confidence: 0.81150025

00:55:08.278 --> 00:55:09.998 kind of phenotyping versus maybe
NOTE Confidence: 0.81150025

00:55:09.998 --> 00:55:11.030 thalamic cortical connectivity.
NOTE Confidence: 0.81150025

00:55:11.030 --> 00:55:12.745 Maybe something that spans across
NOTE Confidence: 0.81150025

00:55:12.745 --> 00:55:14.117 these different endo phenotypes,
NOTE Confidence: 0.81150025

00:55:14.120 --> 00:55:16.880 but I think we just need more close,
NOTE Confidence: 0.81150025

00:55:16.880 --> 00:55:17.568 thoughtful thinking.
NOTE Confidence: 0.81150025

00:55:17.568 --> 00:55:18.600 Like I guess,
NOTE Confidence: 0.81150025

00:55:18.600 --> 00:55:20.116 characterization of these patients

NOTE Confidence: 0.81150025
00:55:20.116 --> 00:55:21.632 of patients schizophrenia to
NOTE Confidence: 0.81150025
00:55:21.632 --> 00:55:23.408 really kind of link a disorder.
NOTE Confidence: 0.81150025
00:55:23.410 --> 00:55:23.986 But yeah,
NOTE Confidence: 0.81150025
00:55:23.986 --> 00:55:25.714 I do think there's something with
NOTE Confidence: 0.81150025
00:55:25.714 --> 00:55:27.540 the llama cortical connectivity.
NOTE Confidence: 0.81150025
00:55:27.540 --> 00:55:28.580 It's always in some.
NOTE Confidence: 0.81150025
00:55:28.580 --> 00:55:30.140 I've been interested in that may
NOTE Confidence: 0.81150025
00:55:30.194 --> 00:55:32.159 underlie schizophrenia across the board.
NOTE Confidence: 0.8470596
00:55:34.470 --> 00:55:36.138 Well Kartik, thank you for a
NOTE Confidence: 0.8470596
00:55:36.138 --> 00:55:37.250 really magnificent grand rounds.
NOTE Confidence: 0.8470596
00:55:37.250 --> 00:55:38.948 We're going to leave the room
NOTE Confidence: 0.8470596
00:55:38.948 --> 00:55:40.589 open if anyone wants to join,
NOTE Confidence: 0.8470596
00:55:40.590 --> 00:55:42.246 but I want to thank you.
NOTE Confidence: 0.8470596
00:55:42.250 --> 00:55:44.231 And you've taught us a lot of
NOTE Confidence: 0.8470596
00:55:44.231 --> 00:55:45.589 science science with a heart,
NOTE Confidence: 0.8470596

00:55:45.590 --> 00:55:47.455 so that's that's really good.