WEBVTT

- NOTE duration:"00:55:47.4560000"
- NOTE language:en-us
- NOTE Confidence: 0.84646976
- $00:00:00.000 \rightarrow 00:00:03.480$ Hello and welcome to grand rounds.
- NOTE Confidence: 0.84646976
- $00:00:03.480 \longrightarrow 00:00:06.602$ Today is the second of three lectures
- NOTE Confidence: 0.84646976
- $00:00:06.602 \rightarrow 00:00:09.649$ 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
- $00:00:21.500 \rightarrow 00:00:24.804$ recognizing that many of us here today,
- NOTE Confidence: 0.84646976
- $00:00:24.810 \rightarrow 00:00:26.974$ especially our younger trainees,
- NOTE Confidence: 0.84646976
- $00:00:26.974 \rightarrow 00:00:30.810$ may not have known Donald Donald Cohen.
- NOTE Confidence: 0.84646976
- $00{:}00{:}30{.}810 \dashrightarrow 00{:}00{:}33{.}354$ 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,

 $00:00:38.350 \longrightarrow 00:00:41.414$ 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

 $00{:}00{:}44.310 \dashrightarrow 00{:}00{:}47.110$ 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

 $00{:}00{:}49{.}045 \dashrightarrow 00{:}00{:}51{.}653$ and those of us who came under his

NOTE Confidence: 0.84646976

 $00:00:51.734 \rightarrow 00:00:54.626$ influence remember him not only fondly,

NOTE Confidence: 0.84646976

 $00:00:54.630 \dashrightarrow 00:00:58.918$ but our lives were really changed by him.

NOTE Confidence: 0.84646976

 $00:00:58.920 \rightarrow 00:01:01.447$ 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

 $00:01:02.530 \dashrightarrow 00:01:04.696$ I commented on Donald the builder.

NOTE Confidence: 0.84646976

 $00:01:04.700 \longrightarrow 00:01:07.024$ And when we talk when we have

NOTE Confidence: 0.84646976

 $00{:}01{:}07{.}024 \dashrightarrow 00{:}01{:}09{.}388$ the third talk by Tom Fernandez,

NOTE Confidence: 0.84646976

 $00:01:09.390 \dashrightarrow 00:01:12.468$ I will focus on Donald Cohen, the mentor.

NOTE Confidence: 0.84646976

 $00:01:12.468 \dashrightarrow 00:01:14.738$ But today with Kartik's presentation,

NOTE Confidence: 0.84646976

 $00:01:14.740 \longrightarrow 00:01:16.768$ I think it's very fitting that

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

 $00{:}01{:}19{.}300 \dashrightarrow 00{:}01{:}21{.}490$ 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

 $00:01:23.918 \longrightarrow 00:01:25.543$ both got science early on.

NOTE Confidence: 0.84646976

 $00{:}01{:}25{.}550 \dashrightarrow 00{:}01{:}29{.}303$ They got the bug of science very early on.

NOTE Confidence: 0.84646976

 $00{:}01{:}29{.}310 \dashrightarrow 00{:}01{:}31{.}686$ 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

 $00{:}01{:}33{.}410 \dashrightarrow 00{:}01{:}36{.}124$ in science and he is really the

NOTE Confidence: 0.84646976

 $00:01:36.124 \rightarrow 00:01:38.434$ consummate scientist and like Donald,

NOTE Confidence: 0.84646976

 $00:01:38.440 \longrightarrow 00:01:42.589$ as I say he got the bug early on.

NOTE Confidence: 0.84646976

 $00:01:42.590 \longrightarrow 00:01:45.260$ Let me share with you how early

NOTE Confidence: 0.84646976

 $00:01:45.260 \longrightarrow 00:01:46.780$ Donald got this bug.

NOTE Confidence: 0.84646976

 $00:01:46.780 \dashrightarrow 00:01:49.828$ This is an image from Donald in the

NOTE Confidence: 0.84646976

 $00{:}01{:}49.828 \dashrightarrow 00{:}01{:}52.050$ 4th grade, 3rd grade, 2nd grade.

NOTE Confidence: 0.84646976

 $00{:}01{:}52.050 \dashrightarrow 00{:}01{:}54.240$ I'm sorry and these are words

- NOTE Confidence: 0.84646976
- $00:01:54.314 \longrightarrow 00:01:57.016$ 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
- $00{:}01{:}58{.}970 \dashrightarrow 00{:}02{:}01{.}570$ So let me quote.
- NOTE Confidence: 0.84646976
- $00:02:01.570 \longrightarrow 00:02:02.742$ Even at age 8,
- NOTE Confidence: 0.84646976
- $00:02:02.742 \dashrightarrow 00:02:04.207$ I was curious about relationships
- NOTE Confidence: 0.84646976
- $00:02:04.207 \longrightarrow 00:02:05.858$ and thought about thinking,
- NOTE Confidence: 0.84646976
- $00:02:05.860 \rightarrow 00:02:08.170$ especially how we think about each other.
- NOTE Confidence: 0.84646976
- $00:02:08.170 \longrightarrow 00:02:10.558$ 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
- $00:02:11.760 \longrightarrow 00:02:14.076$ 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
- $00{:}02{:}15.620 \dashrightarrow 00{:}02{:}17.164$ a wonderful institution available
- NOTE Confidence: 0.84646976
- $00:02:17.164 \rightarrow 00:02:18.708$ 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
- $00:02:20.816 \longrightarrow 00:02:22.730$ filled with the tall tropical
- NOTE Confidence: 0.84646976

 $00:02:22.730 \longrightarrow 00:02:24.498$ trees and exotic Flowers,

NOTE Confidence: 0.84646976

 $00:02:24.500 \rightarrow 00:02:28.404$ taking in the beauty and Misty musty smells.

NOTE Confidence: 0.84646976

 $00{:}02{:}28{.}410 \dashrightarrow 00{:}02{:}30{.}258$ I became especially aware of one

NOTE Confidence: 0.84646976

 $00:02:30.258 \rightarrow 00:02:32.288$ man who would always be standing

NOTE Confidence: 0.84646976

 $00:02:32.288 \dashrightarrow 00:02:34.118$ quietly and watering the plants.

NOTE Confidence: 0.84646976

 $00{:}02{:}34{.}120 \dashrightarrow 00{:}02{:}36{.}901$ He patiently did his job with a sense of

NOTE Confidence: 0.84646976

 $00:02:36.901 \rightarrow 00:02:39.826$ calm and a gentle smile for the newspaper.

NOTE Confidence: 0.84646976

 $00:02:39.830 \longrightarrow 00:02:42.091$ I thought he would be the ideal

NOTE Confidence: 0.84646976

 $00{:}02{:}42.091 \dashrightarrow 00{:}02{:}44.200$ person to interview and he consented.

NOTE Confidence: 0.84646976

 $00:02:44.200 \rightarrow 00:02:46.132$ The interview was then published in

NOTE Confidence: 0.84646976

 $00{:}02{:}46.132 \dashrightarrow 00{:}02{:}47.831$ our school newspaper and constitutes

NOTE Confidence: 0.84646976

 $00:02:47.831 \longrightarrow 00:02:49.576$ one of the earlier reports,

NOTE Confidence: 0.84646976

 $00:02:49.580 \longrightarrow 00:02:51.020$ 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

 $00:02:54.380 \longrightarrow 00:02:56.435$ of the central phenomena that

NOTE Confidence: 0.84646976

 $00:02:56.435 \rightarrow 00:02:58.079$ still intrigue our field.

- NOTE Confidence: 0.84646976
- $00:02:58.080 \longrightarrow 00:03:00.135$ 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
- $00{:}03{:}01.780 \dashrightarrow 00{:}03{:}05.758$ at this time as a historic.
- NOTE Confidence: 0.84646976
- $00:03:05.760 \dashrightarrow 00:03:07.950$ And the documentation of the launching
- NOTE Confidence: 0.84646976
- $00{:}03{:}07{.}950 \dashrightarrow 00{:}03{:}10.650$ of a lifetime career in autism research.
- NOTE Confidence: 0.84646976
- $00{:}03{:}10.650 \dashrightarrow 00{:}03{:}13.210$ This is a verbatim interview.
- NOTE Confidence: 0.84646976
- $00:03:13.210 \longrightarrow 00:03:16.836$ I was a shy and frail child.
- NOTE Confidence: 0.84646976
- $00:03:16.840 \longrightarrow 00:03:17.525$ Therefore,
- NOTE Confidence: 0.84646976
- $00:03:17.525 \longrightarrow 00:03:21.635$ I decided to become a gardener.
- NOTE Confidence: 0.84646976
- $00:03:21.640 \rightarrow 00:03:24.180$ This early reporting is socially
- NOTE Confidence: 0.84646976
- $00:03:24.180 \longrightarrow 00:03:24.688$ dysfunctional.
- NOTE Confidence: 0.84646976
- $00{:}03{:}24.690 \dashrightarrow 00{:}03{:}26.730$ Adult identifies constitutional factors,
- NOTE Confidence: 0.84646976
- $00:03:26.730 \longrightarrow 00:03:27.240$ shines,
- NOTE Confidence: 0.790881
- $00{:}03{:}27.240 \dashrightarrow 00{:}03{:}29.560$ and possible biological coral.
- NOTE Confidence: 0.790881
- $00:03:29.560 \rightarrow 00:03:33.040$ Its frailty with long term prognosis
- NOTE Confidence: 0.790881

 $00:03:33.136 \rightarrow 00:03:35.890$ in a career that was socially isolated,

NOTE Confidence: 0.790881

 $00{:}03{:}35{.}890 \dashrightarrow 00{:}03{:}38{.}876$ the Gardner represents an optimistic

NOTE Confidence: 0.790881

 $00:03:38.876 \longrightarrow 00:03:41.352$ adaptation to an underlying

NOTE Confidence: 0.790881

 $00:03:41.352 \rightarrow 00:03:44.269$ disability in social orientation.

NOTE Confidence: 0.790881

 $00:03:44.270 \longrightarrow 00:03:46.448$ So that's not. Donald, of course.

NOTE Confidence: 0.790881

 $00:03:46.450 \rightarrow 00:03:49.282$ 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

 $00{:}03{:}54{.}460 \dashrightarrow 00{:}03{:}57{.}160$ Klin of Jane McParland and so

NOTE Confidence: 0.790881

 $00{:}03{:}57{.}160 \dashrightarrow 00{:}04{:}00{.}110$ many other of our colleagues.

NOTE Confidence: 0.790881

00:04:00.110 $\operatorname{-->}$ 00:04:02.310 Donna was also a psychoanalyst.

NOTE Confidence: 0.790881

 $00:04:02.310 \longrightarrow 00:04:04.310$ 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

 $00{:}04{:}07{.}280 \dashrightarrow 00{:}04{:}09{.}645$ Phyllis and Donald hanging out

NOTE Confidence: 0.790881

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

NOTE Confidence: 0.790881

 $00:04:11.070 \rightarrow 00:04:13.458$ And this work in psychoanalysis and

- NOTE Confidence: 0.790881
- $00:04:13.458 \rightarrow 00:04:15.670$ bringing analysis and science together,

 $00{:}04{:}15.670 \dashrightarrow 00{:}04{:}17.338$ continues thinking of the

NOTE Confidence: 0.790881

00:04:17.338 --> 00:04:19.006 individual and the science,

NOTE Confidence: 0.790881

 $00:04:19.010 \rightarrow 00:04:21.100$ not as two separate things,

NOTE Confidence: 0.790881

 $00{:}04{:}21{.}100 \dashrightarrow 00{:}04{:}24{.}075$ but together the importance of

NOTE Confidence: 0.790881

 $00:04:24.075 \longrightarrow 00:04:25.860$ the lived experience.

NOTE Confidence: 0.790881

 $00{:}04{:}25{.}860 \dashrightarrow 00{:}04{:}28{.}443$ And this is work that also continues

NOTE Confidence: 0.790881

 $00{:}04{:}28{.}443 \dashrightarrow 00{:}04{:}31{.}230$ with Linda and the work at the

NOTE Confidence: 0.790881

 $00:04:31.230 \longrightarrow 00:04:33.240$ unemployed Center in London today.

NOTE Confidence: 0.790881

 $00:04:33.240 \longrightarrow 00:04:35.185$ Donald also was a pioneer

NOTE Confidence: 0.790881

 $00:04:35.185 \longrightarrow 00:04:37.130$ in the use of medication.

NOTE Confidence: 0.790881

 $00{:}04{:}37{.}130 \dashrightarrow 00{:}04{:}39{.}824$ This is the persons of quantity

NOTE Confidence: 0.790881

 $00:04:39.824 \longrightarrow 00:04:41.620$ 1979 for Tourette syndrome.

NOTE Confidence: 0.790881

 $00{:}04{:}41.620 \dashrightarrow 00{:}04{:}44.500$ And the rest, as we say, is history.

NOTE Confidence: 0.790881

 $00:04:44.500 \dashrightarrow 00:04:47.380$ This is a work that has continued with,

 $00:04:47.380 \rightarrow 00:04:50.244$ 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 $00:04:53.433 \longrightarrow 00:04:55.823$ that have really revolutionized the NOTE Confidence: 0.790881 $00:04:55.903 \rightarrow 00:04:58.369$ way that we treat ADHD Tourettes. NOTE Confidence: 0.790881 $00:04:58.370 \longrightarrow 00:05:01.513$ Here you have Donald in the 1970s NOTE Confidence: 0.790881 $00:05:01.513 \rightarrow 00:05:04.930$ working on the molecule of quantity. NOTE Confidence: 0.790881 $00:05:04.930 \longrightarrow 00:05:06.181$ And that works. NOTE Confidence: 0.790881 $00:05:06.181 \rightarrow 00:05:08.683$ That focus on threats continues most NOTE Confidence: 0.790881 $00:05:08.683 \dashrightarrow 00:05:11.561$ notably with the work of Jim Lechman NOTE Confidence: 0.790881 $00:05:11.561 \rightarrow 00:05:13.602$ and the incredible influence that NOTE Confidence: 0.790881 $00:05:13.602 \rightarrow 00:05:16.283$ Donald had on Jim and the incredible NOTE Confidence: 0.790881 $00:05:16.283 \rightarrow 00:05:20.260$ 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 $00{:}05{:}22{.}710 \dashrightarrow 00{:}05{:}26{.}130$ and certainly on our hero of NOTE Confidence: 0.790881 $00:05:26.130 \longrightarrow 00:05:28.410$ the day on Karthik. NOTE Confidence: 0.790881 $00:05:28.410 \longrightarrow 00:05:29.895$ So without further ado, 9

 $00:05:29.895 \rightarrow 00:05:32.520$ let's see what the legacy of Donald

NOTE Confidence: 0.790881

 $00{:}05{:}32{.}596 \dashrightarrow 00{:}05{:}34{.}661$ and the funds from his chair have

NOTE Confidence: 0.790881

 $00:05:34.661 \dashrightarrow 00:05:37.562$ gone to do in the work of wonderful NOTE Confidence: 0.790881

 $00{:}05{:}37{.}562 \dashrightarrow 00{:}05{:}39{.}867$ young scientists like Emily Olson and NOTE Confidence: 0.790881

 $00{:}05{:}39{.}867 \dashrightarrow 00{:}05{:}42{.}009$ 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

 $00{:}05{:}44.212 \dashrightarrow 00{:}05{:}46.669$ 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

 $00{:}05{:}50.876 \dashrightarrow 00{:}05{:}52.880$ trying to concern and brought him

NOTE Confidence: 0.83042085

 $00{:}05{:}52.880 \dashrightarrow 00{:}05{:}55.135$ into the emergency room because she

NOTE Confidence: 0.83042085

 $00{:}05{:}55{.}135 \dashrightarrow 00{:}05{:}57{.}844$ noted that this child was talking to.

NOTE Confidence: 0.83042085

 $00{:}05{:}57{.}844 \dashrightarrow 00{:}05{:}59{.}580$ Someone that wasn't there.

NOTE Confidence: 0.83042085

 $00{:}05{:}59{.}580 \dashrightarrow 00{:}06{:}01{.}638$ 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

 $00:06:03.448 \rightarrow 00:06:05.722$ is a progressive disorder where there

NOTE Confidence: 0.83042085

 $00{:}06{:}05{.}722 \dashrightarrow 00{:}06{:}07{.}380$ is worsening psychotic symptoms.

NOTE Confidence: 0.83042085

 $00{:}06{:}07{.}380 \dashrightarrow 00{:}06{:}08{.}860$ There's worse than negative

NOTE Confidence: 0.83042085

 $00:06:08.860 \longrightarrow 00:06:09.970$ and cognitive symptoms.

NOTE Confidence: 0.8149216

 $00{:}06{:}12.630 \dashrightarrow 00{:}06{:}14.750$ And so I think this is an important

NOTE Confidence: 0.8149216

 $00{:}06{:}14.750 \dashrightarrow 00{:}06{:}17.185$ 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

 $00:06:19.612 \rightarrow 00:06:22.390$ I think is really focused on in a lot

NOTE Confidence: 0.8149216

 $00{:}06{:}22.390 \dashrightarrow 00{:}06{:}24.150$ of different menu, specifically media.

NOTE Confidence: 0.8149216

 $00{:}06{:}24.150 \dashrightarrow 00{:}06{:}25.750$ So there are positive symptoms

NOTE Confidence: 0.8149216

 $00:06:25.750 \longrightarrow 00:06:26.710$ which are hallucinations,

NOTE Confidence: 0.8149216

 $00:06:26.710 \dashrightarrow 00:06:27.990$ delusions, or disorganized thought.

NOTE Confidence: 0.8149216

 $00:06:27.990 \longrightarrow 00:06:29.590$ 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

 $00:06:31.510 \longrightarrow 00:06:32.164$ Social withdrawal?

NOTE Confidence: 0.8149216

 $00:06:32.164 \longrightarrow 00:06:34.453$ I think that one of the initial

- NOTE Confidence: 0.8149216
- $00:06:34.453 \rightarrow 00:06:36.009$ terms autoset almost looks like

 $00{:}06{:}36{.}009 \dashrightarrow 00{:}06{:}38{.}230$ 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

 $00:06:38.880 \dashrightarrow 00:06:40.505$ their cognitive symptoms can be

NOTE Confidence: 0.8149216

 $00:06:40.505 \rightarrow 00:06:42.170$ quite debilitating for the patients.

NOTE Confidence: 0.8149216

 $00{:}06{:}42.170 \dashrightarrow 00{:}06{:}44.078$ It's poor short term in working

NOTE Confidence: 0.8149216

 $00:06:44.078 \longrightarrow 00:06:46.512$ 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 $\operatorname{-->}$ 00:06:50.190 And so once this child was

NOTE Confidence: 0.8149216

 $00:06:50.190 \longrightarrow 00:06:51.550$ admitted to our unit,

NOTE Confidence: 0.8149216

 $00{:}06{:}51{.}550 \dashrightarrow 00{:}06{:}53{.}590$ we decided to start a medication

NOTE Confidence: 0.8149216

 $00{:}06{:}53.590 \dashrightarrow 00{:}06{:}55.206$ 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

 $00{:}06{:}56.696 \dashrightarrow 00{:}06{:}58.445$ their choice and despite having

NOTE Confidence: 0.8149216

 $00:06:58.445 \rightarrow 00:07:00.049$ medications to treat schizophrenia,

- $00:07:00.050 \dashrightarrow 00:07:02.090$ the outcomes are still not great.
- NOTE Confidence: 0.8149216
- $00{:}07{:}02.090 \dashrightarrow 00{:}07{:}02.770$ In this.

 $00{:}07{:}02.770 \dashrightarrow 00{:}07{:}05.150$ 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

 $00:07:06.850 \longrightarrow 00:07:07.157$ suicide,

NOTE Confidence: 0.8149216

 $00{:}07{:}07{.}157 \dashrightarrow 00{:}07{:}08.692$ which is greatly elevated from

NOTE Confidence: 0.8149216

 $00{:}07{:}08.692 \dashrightarrow 00{:}07{:}10.590$ the rest of the population.

NOTE Confidence: 0.8149216

 $00:07:10.590 \longrightarrow 00:07:12.290 25\%$ have chronic severe symptoms,

NOTE Confidence: 0.8149216

 $00{:}07{:}12.290 \dashrightarrow 00{:}07{:}13.940$ while most patients have some

NOTE Confidence: 0.8149216

 $00:07:13.940 \longrightarrow 00:07:15.590$ level of symptoms and they're

NOTE Confidence: 0.8149216

 $00:07:15.650 \longrightarrow 00:07:17.050$ just looking at symptoms,

NOTE Confidence: 0.8149216

 $00:07:17.050 \longrightarrow 00:07:19.480$ 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

 $00{:}07{:}22.385 \dashrightarrow 00{:}07{:}24.590$ was kind of highlighted in the Katy

NOTE Confidence: 0.8149216

 $00:07:24.659 \longrightarrow 00:07:27.323$ trial that was done early in the 2000s,

NOTE Confidence: 0.8149216

 $00:07:27.330 \longrightarrow 00:07:29.619$ where they showed in two at least.

 $00:07:29.620 \longrightarrow 00:07:30.972$ They followed patients with

NOTE Confidence: 0.8149216

 $00:07:30.972 \dashrightarrow 00:07:33.000$ 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

 $00{:}07{:}35.148 \dashrightarrow 00{:}07{:}36.810$ medication through this whole trial.

NOTE Confidence: 0.8149216

 $00{:}07{:}36{.}810 \dashrightarrow 00{:}07{:}38{.}424$ And due to this progressive illness

NOTE Confidence: 0.8149216

 $00{:}07{:}38{.}424 \dashrightarrow 00{:}07{:}40{.}766$ as well as the difficulty of keeping

NOTE Confidence: 0.8149216

 $00:07:40.766 \longrightarrow 00:07:42.370$ patients on their medications,

NOTE Confidence: 0.8149216

 $00{:}07{:}42.370 \dashrightarrow 00{:}07{:}44.582$ the focus has been on prevention and

NOTE Confidence: 0.8149216

 $00{:}07{:}44.582 \dashrightarrow 00{:}07{:}47.244$ this has been work done starting in the

NOTE Confidence: 0.8149216

 $00{:}07{:}47{.}244 \dashrightarrow 00{:}07{:}49{.}650$ late 80s by various groups instead of.

NOTE Confidence: 0.8149216

 $00{:}07{:}49.650 \dashrightarrow 00{:}07{:}51.410$ Anything including a strong group

NOTE Confidence: 0.8149216

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

NOTE Confidence: 0.8149216

 $00{:}07{:}53.556 \dashrightarrow 00{:}07{:}55.500$ focus has been as is intervening

NOTE Confidence: 0.8149216

 $00{:}07{:}55{.}500 \dashrightarrow 00{:}07{:}56{.}870$ during this prodromal stage.

NOTE Confidence: 0.8149216

 $00{:}07{:}56.870 \dashrightarrow 00{:}07{:}59.173$ So when our honor student is slowly

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

NOTE Confidence: 0.8149216

 $00:08:00.660 \rightarrow 00:08:03.068$ can we interview at that point intervene?

NOTE Confidence: 0.8149216

 $00:08:03.070 \longrightarrow 00:08:05.373$ Sorry at that point to change the

NOTE Confidence: 0.8149216

 $00:08:05.373 \rightarrow 00:08:07.133$ trajectory of schizophrenia and maybe

NOTE Confidence: 0.8149216

 $00:08:07.133 \longrightarrow 00:08:08.908$ prevent the transition to psychosis.

NOTE Confidence: 0.8149216

 $00{:}08{:}08{.}910 \dashrightarrow 00{:}08{:}10{.}890$ And there's been a lot of

NOTE Confidence: 0.8149216

 $00{:}08{:}10.890 \dashrightarrow 00{:}08{:}13.039$ great work done in that area,

NOTE Confidence: 0.8149216

 $00:08:13.040 \rightarrow 00:08:14.730$ especially the focus on psychoeducation

NOTE Confidence: 0.8149216

 $00{:}08{:}14.730 \dashrightarrow 00{:}08{:}16.830$ teaching the family what to expect,

NOTE Confidence: 0.8149216

 $00{:}08{:}16.830 \dashrightarrow 00{:}08{:}18.936$ as well as reducing the stress

NOTE Confidence: 0.8149216

 $00:08:18.936 \longrightarrow 00:08:20.340$ that the child experiences

NOTE Confidence: 0.8149216

 $00:08:20.411 \rightarrow 00:08:22.136$ as it's thought that stress.

NOTE Confidence: 0.8149216

 $00{:}08{:}22.140 \dashrightarrow 00{:}08{:}24.597$ Can worsen the trajectory of the disorder

NOTE Confidence: 0.8149216

 $00:08:24.597 \rightarrow 00:08:26.950$ 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

 $00:08:28.930 \longrightarrow 00:08:31.570$ July of 2020 and then I'll just

- NOTE Confidence: 0.8149216
- 00:08:31.570 00:08:33.234 highlight that first sentence.

 $00:08:33.240 \longrightarrow 00:08:35.802$ No evidence was found that that favored

NOTE Confidence: 0.8149216

 $00:08:35.802 \rightarrow 00:08:37.679$ any indicated intervention over another,

NOTE Confidence: 0.8149216

 $00:08:37.680 \rightarrow 00:08:38.790$ including control conditions.

NOTE Confidence: 0.8149216

 $00:08:38.790 \longrightarrow 00:08:40.640$ So despite all this work,

NOTE Confidence: 0.8149216

 $00{:}08{:}40{.}640 \dashrightarrow 00{:}08{:}43{.}010$ we're not really preventing the transition

NOTE Confidence: 0.8149216

 $00:08:43.010 \rightarrow 00:08:45.450$ to psychosis and later on they talk.

NOTE Confidence: 0.8149216

 $00:08:45.450 \rightarrow 00:08:47.400$ There's actually no real obvious improvement

NOTE Confidence: 0.8149216

 $00:08:47.400 \rightarrow 00:08:50.628$ in a lot of these other functional measures,

NOTE Confidence: 0.8149216

 $00:08:50.630 \longrightarrow 00:08:51.980$ So what gives?

NOTE Confidence: 0.8149216

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

NOTE Confidence: 0.8149216

 $00{:}08{:}54{.}230 \dashrightarrow 00{:}08{:}56{.}120$ And I think part of the issue

NOTE Confidence: 0.8149216

 $00:08:56.120 \longrightarrow 00:08:57.784$ has been this psychosis driven

NOTE Confidence: 0.8149216

 $00{:}08{:}57{.}784 \dashrightarrow 00{:}08{:}59{.}759$ formulation of the disorder that

NOTE Confidence: 0.8149216

 $00:08:59.759 \longrightarrow 00:09:01.830$ prior to this prodromal phase

 $00:09:01.830 \longrightarrow 00:09:04.278$ there's no symptoms or few symptoms,

NOTE Confidence: 0.8149216

 $00{:}09{:}04{.}280 \dashrightarrow 00{:}09{:}07{.}502$ and so the focus has been on the prodrome.

NOTE Confidence: 0.8357679

 $00{:}09{:}07{.}510 \dashrightarrow 00{:}09{:}10.618$ But actually data shows something different.

NOTE Confidence: 0.8357679

 $00:09:10.620 \longrightarrow 00:09:12.514$ This was one of the seminal

NOTE Confidence: 0.8357679

 $00:09:12.514 \longrightarrow 00:09:14.410$ works that came out in 1994,

NOTE Confidence: 0.8357679

 $00{:}09{:}14.410 \dashrightarrow 00{:}09{:}17.114$ led by Doctor Elaine Walker and what she

NOTE Confidence: 0.8357679

 $00:09:17.114 \rightarrow 00:09:19.780$ showed along with when it came out in 1994.

NOTE Confidence: 0.8357679

 $00:09:19.780 \rightarrow 00:09:21.999$ I thought it was kind of funny.

NOTE Confidence: 0.8357679

 $00{:}09{:}22{.}000 \dashrightarrow 00{:}09{:}23{.}580$ 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

 $00:09:25.785 \dashrightarrow 00:09:27.679$ cameras became popular with this study,

NOTE Confidence: 0.8357679

 $00:09:27.680 \dashrightarrow 00:09:29.920$ did was they looked at the life they

NOTE Confidence: 0.8357679

 $00{:}09{:}29{.}920 \dashrightarrow 00{:}09{:}31{.}144$ recruited patients with schizophrenia

NOTE Confidence: 0.8357679

 $00{:}09{:}31{.}144 \dashrightarrow 00{:}09{:}33{.}279$ 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

 $00:09:35.749 \longrightarrow 00:09:37.477$ neuromotor abnormalities and what they

- NOTE Confidence: 0.8357679
- $00:09:37.477 \rightarrow 00:09:39.379$ found specifically in infants is that.

 $00{:}09{:}39{.}380 \dashrightarrow 00{:}09{:}41{.}010$ And so this population that

NOTE Confidence: 0.8357679

 $00:09:41.010 \longrightarrow 00:09:41.988$ later developed schizophrenia.

NOTE Confidence: 0.8357679

 $00{:}09{:}41{.}990 \dashrightarrow 00{:}09{:}44{.}188$ Has schizophrenia as a child they showed

NOTE Confidence: 0.8357679

 $00{:}09{:}44.188 \dashrightarrow 00{:}09{:}45.510$ increased abnormal motor movements

NOTE Confidence: 0.8357679

 $00:09:45.510 \dashrightarrow 00:09:47.460$ while their healthy siblings did not.

NOTE Confidence: 0.8357679

 $00:09:47.460 \longrightarrow 00:09:49.170$ Just things that did not have

NOTE Confidence: 0.8357679

 $00:09:49.170 \dashrightarrow 00:09:50.310$ schizophrenia and patients with

NOTE Confidence: 0.8357679

 $00{:}09{:}50{.}365 \dashrightarrow 00{:}09{:}51{.}713$ other affective disorders also

NOTE Confidence: 0.8357679

 $00{:}09{:}51{.}713 \dashrightarrow 00{:}09{:}53{.}398$ didn't have a significant difference

NOTE Confidence: 0.8357679

 $00:09:53.398 \longrightarrow 00:09:55.189$ from the patients of schizophrenia.

NOTE Confidence: 0.803379103000001

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

NOTE Confidence: 0.803379103000001

 $00:09:59.339 \rightarrow 00:10:02.020$ Walker was part of this other study

NOTE Confidence: 0.803379103000001

 $00{:}10{:}02{.}096 \dashrightarrow 00{:}10{:}03{.}976$ that was more thoughtful 'cause

NOTE Confidence: 0.803379103000001

 $00:10:03.976 \longrightarrow 00:10:06.598$ they had no more time to design

 $00{:}10{:}06{.}598 \dashrightarrow 00{:}10{:}08{.}929$ this study and what they did was

NOTE Confidence: 0.803379103000001

 $00:10:08.929 \longrightarrow 00:10:10.530$ they videotaped 1311 through 13

NOTE Confidence: 0.803379103000001

 $00:10:10.530 \longrightarrow 00:10:12.420$ year olds in Scandinavia that have NOTE Confidence: 0.803379103000001

 $00:10:12.472 \longrightarrow 00:10:14.277$ an increased risk of schizophrenia.

NOTE Confidence: 0.803379103000001

 $00{:}10{:}14.280 \dashrightarrow 00{:}10{:}15.680$ Specifically a parent with

NOTE Confidence: 0.803379103000001

 $00{:}10{:}15{.}680 \dashrightarrow 00{:}10{:}17{.}430$ schizophrenia and they found that

NOTE Confidence: 0.803379103000001

 $00{:}10{:}17{.}430 \dashrightarrow 00{:}10{:}19{.}290$ when they went and then waited to

NOTE Confidence: 0.803379103000001

 $00{:}10{:}19{.}290 \dashrightarrow 00{:}10{:}21{.}198$ 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

 $00:10:22.960 \longrightarrow 00:10:24.886$ they found that the children that

NOTE Confidence: 0.803379103000001

 $00{:}10{:}24.886 \dashrightarrow 00{:}10{:}26.170$ later developed schizophrenia show

NOTE Confidence: 0.803379103000001

 $00{:}10{:}26.222 \dashrightarrow 00{:}10{:}27.638$ deficits and social behaviors.

NOTE Confidence: 0.803379103000001

 $00:10:27.640 \longrightarrow 00:10:29.710$ Around 11:13 there wasn't an obviously

NOTE Confidence: 0.803379103000001

 $00{:}10{:}29{.}710 \dashrightarrow 00{:}10{:}31.090$ significant different in motor.

NOTE Confidence: 0.803379103000001

 $00:10:31.090 \rightarrow 00:10:33.100$ Even though it trended in boys

NOTE Confidence: 0.803379103000001

 $00:10:33.100 \rightarrow 00:10:35.040$ towards having some motor atypical,

- NOTE Confidence: 0.803379103000001
- 00:10:35.040 --> 00:10:36.249 atypical motor behaviors,
- NOTE Confidence: 0.803379103000001
- $00:10:36.249 \longrightarrow 00:10:38.667$ and this more recent paper was
- NOTE Confidence: 0.803379103000001
- $00{:}10{:}38.667 \dashrightarrow 00{:}10{:}40.775$ something that I was really drawn to,
- NOTE Confidence: 0.803379103000001
- $00:10:40.780 \longrightarrow 00:10:43.314$ and this was part of the Avon
- NOTE Confidence: 0.803379103000001
- $00:10:43.314 \rightarrow 00:10:45.205$ Perspective study where they just
- NOTE Confidence: 0.803379103000001
- $00{:}10{:}45{.}205 \dashrightarrow 00{:}10{:}47{.}781$ 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
- $00{:}10{:}50{.}480 \dashrightarrow 00{:}10{:}52{.}829$ and then just did a bunch of like just
- NOTE Confidence: 0.803379103000001
- $00{:}10{:}52.829 \dashrightarrow 00{:}10{:}54.648$ neuro psychological battery on them
- NOTE Confidence: 0.803379103000001
- $00{:}10{:}54.648 \dashrightarrow 00{:}10{:}56.892$ and they found that children that
- NOTE Confidence: 0.803379103000001
- $00:10:56.952 \rightarrow 00:10:59.088$ later developed psychotic disorders,
- NOTE Confidence: 0.803379103000001
- $00{:}10{:}59{.}090 \dashrightarrow 00{:}11{:}02{.}026$ that's that red line around the age of.
- NOTE Confidence: 0.803379103000001
- $00:11:02.030 \longrightarrow 00:11:04.058$ 18 months somewhere to 18 months
- NOTE Confidence: 0.803379103000001
- $00:11:04.058 \longrightarrow 00:11:06.591$ 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: 0.803379103000001

 $00{:}11{:}10.570 \dashrightarrow 00{:}11{:}12.214$ verbal IQ and nonverbal IQ and

NOTE Confidence: 0.803379103000001

 $00:11:12.214 \rightarrow 00:11:14.181$ so I think these findings along

NOTE Confidence: 0.803379103000001

 $00:11:14.181 \rightarrow 00:11:16.196$ with various other studies suggest

NOTE Confidence: 0.803379103000001

 $00:11:16.196 \rightarrow 00:11:18.050$ maybe we're missing something.

NOTE Confidence: 0.803379103000001

00:11:18.050 --> 00:11:19.805 Maybe schizophrenia actually

NOTE Confidence: 0.803379103000001

00:11:19.805 - 00:11:22.730 starts earlier than we thought.

NOTE Confidence: 0.803379103000001

 $00:11:22.730 \longrightarrow 00:11:25.066$ And so this has been led to kind

NOTE Confidence: 0.803379103000001

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

NOTE Confidence: 0.803379103000001

 $00:11:28.020 \rightarrow 00:11:31.044$ which I feel is much more child psychiatry.

NOTE Confidence: 0.803379103000001

 $00:11:31.050 \rightarrow 00:11:32.446$ Child psychology focused where

NOTE Confidence: 0.803379103000001

 $00{:}11{:}32.446 \dashrightarrow 00{:}11{:}33.842$ initially their cognitive motor

NOTE Confidence: 0.803379103000001

 $00:11:33.842 \rightarrow 00:11:35.825$ and social impairments and these

NOTE Confidence: 0.803379103000001

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

NOTE Confidence: 0.803379103000001

 $00:11:37.470 \longrightarrow 00:11:40.319$ and I think this is a really

NOTE Confidence: 0.803379103000001

 $00:11:40.319 \rightarrow 00:11:42.281$ interesting theory because it kind

00:11:42.281 --> 00:11:44.626 of gives us a longer runway, right?

NOTE Confidence: 0.803379103000001

 $00{:}11{:}44.626 \dashrightarrow 00{:}11{:}47.048$ Can we intervene much earlier and to

NOTE Confidence: 0.803379103000001

 $00:11:47.048 \rightarrow 00:11:49.567$ later prevent this transition to psychosis?

NOTE Confidence: 0.803379103000001

 $00:11:49.570 \rightarrow 00:11:49.956$ 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

 $00{:}11{:}53.050 \dashrightarrow 00{:}11{:}53.902$ Real clinical intervention.

NOTE Confidence: 0.803379103000001

 $00{:}11{:}53{.}902 \dashrightarrow 00{:}11{:}55{.}890$ We have to kind of understand the

NOTE Confidence: 0.803379103000001

 $00:11:55.937 \rightarrow 00:11:57.937$ neurobiological underpinnings of this data.

NOTE Confidence: 0.803379103000001

 $00{:}11{:}57{.}940 \dashrightarrow 00{:}11{:}59{.}495$ So what are the neurobiological

NOTE Confidence: 0.803379103000001

 $00:11:59.495 \longrightarrow 00:12:01.050$ correlates of the neuro developmental

NOTE Confidence: 0.803379103000001

 $00:12:01.097 \rightarrow 00:12:02.180$ theory of schizophrenia?

NOTE Confidence: 0.803379103000001

 $00{:}12{:}02{.}180 \dashrightarrow 00{:}12{:}04{.}430$ Which is something that I'm very

NOTE Confidence: 0.803379103000001

 $00{:}12{:}04{.}430 \dashrightarrow 00{:}12{:}06{.}982$ 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

 $00:12:09.750 \rightarrow 00:12:12.606$ psychiatric genetics such as my good friend.

- 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
- $00:12:13.914 \longrightarrow 00:12:16.310$ does a brilliant work and gave an
- NOTE Confidence: 0.803379103000001
- $00:12:16.310 \rightarrow 00:12:18.190$ amazing presentation two weeks ago.
- NOTE Confidence: 0.803379103000001
- $00{:}12{:}18.190 \dashrightarrow 00{:}12{:}20.092$ As Doctor Martin mentioned and what
- NOTE Confidence: 0.803379103000001
- $00{:}12{:}20.092 \dashrightarrow 00{:}12{:}22.569$ 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
- $00:12:24.480 \longrightarrow 00:12:26.993$ and in the last 10 years there's
- NOTE Confidence: 0.803379103000001
- $00{:}12{:}26{.}993 \dashrightarrow 00{:}12{:}29{.}008$ been a mazing progress in the field,
- NOTE Confidence: 0.803379103000001
- $00:12:29.010 \longrightarrow 00:12:30.750$ and schizophrenia is also seen
- NOTE Confidence: 0.803379103000001
- $00{:}12{:}30{.}750 \dashrightarrow 00{:}12{:}32{.}142$ great progress in schizophrenia,
- NOTE Confidence: 0.803379103000001
- $00{:}12{:}32{.}150 \dashrightarrow 00{:}12{:}32{.}492$ genetics,
- NOTE Confidence: 0.803379103000001
- $00:12:32.492 \rightarrow 00:12:34.202$ where they have identified several
- NOTE Confidence: 0.803379103000001
- $00:12:34.202 \longrightarrow 00:12:35.570$ genes associated or enriched
- NOTE Confidence: 0.803379103000001
- $00:12:35.624 \rightarrow 00:12:37.384$ in mutations in several genes
- NOTE Confidence: 0.803379103000001
- $00:12:37.384 \rightarrow 00:12:38.440$ associated with schizophrenia,

- NOTE Confidence: 0.803379103000001
- $00:12:38.440 \longrightarrow 00:12:40.876$ 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
- $00:12:42.700 \rightarrow 00:12:44.494$ Where several labs are doing this
- NOTE Confidence: 0.803379103000001
- $00:12:44.494 \rightarrow 00:12:46.400$ 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
- $00:12:48.395 \rightarrow 00:12:50.294$ specific targets or regions or time
- NOTE Confidence: 0.803379103000001
- $00:12:50.294 \rightarrow 00:12:51.939$ periods of development to study?
- NOTE Confidence: 0.803379103000001
- $00:12:51.940 \longrightarrow 00:12:54.005$ And what this study did was they
- NOTE Confidence: 0.803379103000001
- $00{:}12{:}54.005 \dashrightarrow 00{:}12{:}55.913$ looked for regions in the brain
- NOTE Confidence: 0.803379103000001
- $00:12:55.913 \rightarrow 00:12:56.870$ in specific periods.
- NOTE Confidence: 0.8552168
- 00:12:56.870 --> 00:12:58.410 They looked at fetal infancy,
- NOTE Confidence: 0.8552168
- $00:12:58.410 \longrightarrow 00:13:00.522$ an adult adolescent stages and they
- NOTE Confidence: 0.8552168
- $00:13:00.522 \rightarrow 00:13:02.486$ looked at different regions of the
- NOTE Confidence: 0.8552168
- $00:13:02.486 \rightarrow 00:13:04.827$ brain and they looked for a place and a
- NOTE Confidence: 0.8552168
- $00:13:04.827 \rightarrow 00:13:07.018$ time where there was an enrichment of NOTE Confidence: 0.8552168

 $00:13:07.018 \rightarrow 00:13:08.258$ 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

 $00:13:09.778 \longrightarrow 00:13:11.040$ involved in a crime.

NOTE Confidence: 0.8552168

 $00:13:11.040 \longrightarrow 00:13:13.294$ 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

 $00{:}13{:}15{.}838 \dashrightarrow 00{:}13{:}18{.}114$ point in an area to specifically

NOTE Confidence: 0.8552168

 $00{:}13{:}18{.}114 \dashrightarrow 00{:}13{:}20{.}500$ dig deeper into to understand what

NOTE Confidence: 0.8552168

 $00:13:20.500 \longrightarrow 00:13:22.445$ 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

 $00:13:24.560 \longrightarrow 00:13:26.320$ specifically in the frontal lobe,

NOTE Confidence: 0.8552168

 $00{:}13{:}26{.}320 \dashrightarrow 00{:}13{:}28{.}497$ and this is very similar findings to

NOTE Confidence: 0.8552168

 $00{:}13{:}28{.}497 \dashrightarrow 00{:}13{:}30{.}617$ work done by Matt States Group and NOTE Confidence: 0.8552168

 $00{:}13{:}30{.}617 \dashrightarrow 00{:}13{:}33{.}265$ he was here at Yale in autism and

NOTE Confidence: 0.8552168

 $00{:}13{:}33{.}265 \dashrightarrow 00{:}13{:}35{.}971$ this also coincides really well with

NOTE Confidence: 0.8552168

 $00{:}13{:}35{.}971 \dashrightarrow 00{:}13{:}37{.}584$ earlier epidemiological data that

NOTE Confidence: 0.8552168

 $00:13:37.584 \rightarrow 00:13:39.344$ shows that stress during pregnancy,

- NOTE Confidence: 0.8552168
- $00:13:39.350 \rightarrow 00:13:41.235$ specifically during the 2nd trimester

 $00{:}13{:}41.235 \dashrightarrow 00{:}13{:}43.629$ increase the chance of having a child.

NOTE Confidence: 0.8552168

 $00:13:43.630 \dashrightarrow 00:13:47.299$ That develops schizophrenia.

NOTE Confidence: 0.8552168

 $00:13:47.300 \longrightarrow 00:13:49.043$ So this led to our more focused

NOTE Confidence: 0.8552168

 $00{:}13{:}49{.}043 \dashrightarrow 00{:}13{:}50{.}570$ 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

 $00{:}13{:}52{.}375 \dashrightarrow 00{:}13{:}54{.}518$ fet al frontal cortex lead to the

NOTE Confidence: 0.8552168

 $00:13:54.518 \rightarrow 00:13:55.854$ complex symptoms of schizophrenia?

NOTE Confidence: 0.8552168

 $00{:}13{:}55{.}860 \dashrightarrow 00{:}13{:}59{.}828$ 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

 $00{:}14{:}02.008 \dashrightarrow 00{:}14{:}04.068$ same data set that these previous

NOTE Confidence: 0.8552168

 $00{:}14{:}04.068 \dashrightarrow 00{:}14{:}06.400$ groups use is called psych encoder.

NOTE Confidence: 0.8552168

 $00{:}14{:}06{.}400 \dashrightarrow 00{:}14{:}07{.}830$ 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

 $00:14:10.216 \rightarrow 00:14:12.022$ were uniquely enriched in the frontal

 $00:14:12.022 \rightarrow 00:14:13.920$ 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

 $00{:}14{:}15{.}480 \dashrightarrow 00{:}14{:}16{.}728$ to the mid function.

NOTE Confidence: 0.8552168

 $00{:}14{:}16.730 \dashrightarrow 00{:}14{:}18.524$ The midfielder frontal lobe and that's

NOTE Confidence: 0.8552168

 $00:14:18.524 \rightarrow 00:14:21.107$ why we looked for genes are enriched there.

NOTE Confidence: 0.8552168

 $00{:}14{:}21{.}110 \dashrightarrow 00{:}14{:}23{.}231$ And so we identified 125 genes enriched

NOTE Confidence: 0.8552168

 $00:14:23.231 \longrightarrow 00:14:24.870$ specifically in the frontal lobe.

NOTE Confidence: 0.8552168

 $00:14:24.870 \rightarrow 00:14:25.809$ During this period,

NOTE Confidence: 0.8552168

 $00{:}14{:}25{.}809 \dashrightarrow 00{:}14{:}28{.}000$ Anna's Emily showed in her previous talk.

NOTE Confidence: 0.8552168

 $00:14:28.000 \rightarrow 00:14:30.324$ We looked at what do these jeans?

NOTE Confidence: 0.8552168

 $00{:}14{:}30{.}330 \dashrightarrow 00{:}14{:}32{.}696$ Share this click gene onto geny analysis and NOTE Confidence: 0.8552168

 $00:14:32.696 \rightarrow 00:14:35.426$ what we found was that these genes are in.

NOTE Confidence: 0.8552168

 $00{:}14{:}35{.}430 \dashrightarrow 00{:}14{:}37{.}341$ This list is enriched for genes that

NOTE Confidence: 0.8552168

 $00{:}14{:}37{.}341 \dashrightarrow 00{:}14{:}39{.}314$ are involved in circuit formation so

NOTE Confidence: 0.8552168

 $00:14:39.314 \rightarrow 00:14:41.149$ synapse assembly Axon development in

NOTE Confidence: 0.8552168

 $00{:}14{:}41{.}149 \dashrightarrow 00{:}14{:}43{.}410$ 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
- $00:14:48.510 \longrightarrow 00:14:50.382$ but we also saw something that
- NOTE Confidence: 0.8552168
- $00{:}14{:}50{.}382 \dashrightarrow 00{:}14{:}52{.}011$ was unexpected which was jeans
- NOTE Confidence: 0.8552168
- $00:14:52.011 \longrightarrow 00:14:53.616$ that are responsive to rent.
- NOTE Confidence: 0.8552168
- $00:14:53.620 \rightarrow 00:14:55.867$ No gas or jeans that are regulated
- NOTE Confidence: 0.8552168
- $00:14:55.867 \rightarrow 00:14:58.121$ by retinoic acid and this was very
- NOTE Confidence: 0.8552168
- $00{:}14{:}58{.}121 \dashrightarrow 00{:}15{:}00{.}039$ exciting for us. For several reasons.
- NOTE Confidence: 0.8552168
- $00:15:00.039 \longrightarrow 00:15:01.704$ 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
- $00{:}15{:}03.635 \dashrightarrow 00{:}15{:}05.175$ 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
- $00{:}15{:}06{.}720 \dashrightarrow 00{:}15{:}08{.}868$ But there was a very interesting
- NOTE Confidence: 0.8552168
- $00:15:08.868 \rightarrow 00:15:09.584$ clinical perspective.
- NOTE Confidence: 0.8552168

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

NOTE Confidence: 0.8552168

 $00{:}15{:}11.492 \dashrightarrow 00{:}15{:}13.520$ has been implicated in schizophrenia.

NOTE Confidence: 0.8552168

 $00{:}15{:}13.520 \dashrightarrow 00{:}15{:}15.515$ 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

 $00{:}15{:}17.894 \dashrightarrow 00{:}15{:}20.084$ with retinoic acid's are affected seem

NOTE Confidence: 0.8552168

 $00{:}15{:}20{.}147 \dashrightarrow 00{:}15{:}22{.}613$ to be elevated in patients schizophrenia NOTE Confidence: 0.8552168

 $00:15:22.613 \rightarrow 00:15:24.257$ with severe cognitive symptoms.

NOTE Confidence: 0.8552168

 $00:15:24.260 \longrightarrow 00:15:26.105$ So this was something very

NOTE Confidence: 0.8552168

 $00{:}15{:}26.105 \dashrightarrow 00{:}15{:}28.200$ interesting and very exciting to us,

NOTE Confidence: 0.8552168

 $00{:}15{:}28{.}200 \dashrightarrow 00{:}15{:}29{.}985$ so we postulated that disruption

NOTE Confidence: 0.8552168

 $00{:}15{:}29{.}985 \dashrightarrow 00{:}15{:}32{.}200$ of RA regulated or related genes.

NOTE Confidence: 0.8552168

 $00:15:32.200 \rightarrow 00:15:34.276$ 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

 $00{:}15{:}35{.}668 \dashrightarrow 00{:}15{:}37{.}750$ those are what those genes are.

NOTE Confidence: 0.8552168

 $00{:}15{:}37{.}750 \dashrightarrow 00{:}15{:}40{.}116$ Also enriched and that can lead

NOTE Confidence: 0.8552168

 $00:15:40.116 \longrightarrow 00:15:42.479$ 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
- $00{:}15{:}44.854 \dashrightarrow 00{:}15{:}46.951$ we turn to a mouse model and
- NOTE Confidence: 0.8552168
- $00{:}15{:}46{.}951 \dashrightarrow 00{:}15{:}49{.}159$ we asked what is retinoic acid
- NOTE Confidence: 0.8552168
- $00:15:49.159 \longrightarrow 00:15:50.263$ doing specifically in
- NOTE Confidence: 0.8393542
- $00{:}15{:}50{.}338 \dashrightarrow 00{:}15{:}51{.}589$ the frontal cortex.
- NOTE Confidence: 0.8393542
- $00:15:51.590 \rightarrow 00:15:53.557$ So we generated a mutant mouse line
- NOTE Confidence: 0.8393542
- $00:15:53.557 \rightarrow 00:15:55.299$ where we're able to specifically
- NOTE Confidence: 0.8393542
- $00{:}15{:}55{.}299 \dashrightarrow 00{:}15{:}57{.}389$ reduce retinoic acid signaling Justin,
- NOTE Confidence: 0.8393542
- $00:15:57.390 \longrightarrow 00:15:58.754$ the mouse equivalent of
- NOTE Confidence: 0.8393542
- $00:15:58.754 \longrightarrow 00:15:59.777$ the prefrontal cortex,
- NOTE Confidence: 0.8393542
- $00{:}15{:}59{.}780 \dashrightarrow 00{:}16{:}02{.}174$ and So what you see here is a PO
- NOTE Confidence: 0.8393542
- $00:16:02.174 \rightarrow 00:16:04.613$ 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
- $00{:}16{:}07{.}109 \dashrightarrow 00{:}16{:}09{.}363$ 24 in the human and these purple
- NOTE Confidence: 0.8393542

 $00{:}16{:}09{.}363 \dashrightarrow 00{:}16{:}11{.}374$ 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

 $00:16:13.080 \longrightarrow 00:16:15.198$ and so this is the control.

NOTE Confidence: 0.8393542

 $00:16:15.200 \longrightarrow 00:16:17.062$ 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

 $00{:}16{:}18{.}380 \dashrightarrow 00{:}16{:}20{.}060$ and you can see a dramatic

NOTE Confidence: 0.8393542

 $00:16:20.060 \longrightarrow 00:16:21.532$ reduction in purple cells which

NOTE Confidence: 0.8393542

 $00:16:21.532 \rightarrow 00:16:23.284$ 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

 $00{:}16{:}24.880 \dashrightarrow 00{:}16{:}26.576$ 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

 $00:16:28.316 \rightarrow 00:16:30.153$ the frontal cortex or specific middle

NOTE Confidence: 0.8393542

 $00{:}16{:}30{.}153 \dashrightarrow 00{:}16{:}31{.}953$ prefrontal cortex in the mouse and

NOTE Confidence: 0.8393542

 $00{:}16{:}31{.}960 \dashrightarrow 00{:}16{:}33{.}990$ 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
- $00:16:36.282 \rightarrow 00:16:38.186$ we found a reduction in dendritic spines

 $00:16:38.186 \longrightarrow 00:16:39.986$ which are kind of excitatory connections

NOTE Confidence: 0.8393542

 $00:16:39.986 \longrightarrow 00:16:42.080$ in the brain which is quantified here.

NOTE Confidence: 0.8393542

 $00:16:42.080 \rightarrow 00:16:43.808$ This is done in the adult,

NOTE Confidence: 0.8393542

 $00:16:43.810 \longrightarrow 00:16:45.598$ and so you can see a

NOTE Confidence: 0.8393542

 $00:16:45.598 \longrightarrow 00:16:46.790$ 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

 $00{:}16{:}48.770 \dashrightarrow 00{:}16{:}51.038$ which are mature spines and we replicate

NOTE Confidence: 0.8393542

 $00{:}16{:}51{.}038 \dashrightarrow 00{:}16{:}53{.}427$ this finding both during the equivalent of

NOTE Confidence: 0.8393542

 $00{:}16{:}53{.}427 \dashrightarrow 00{:}16{:}55{.}700$ midfield development in the human at PO.

NOTE Confidence: 0.8393542

 $00:16:55.700 \longrightarrow 00:16:57.350$ So this occurs very early.

NOTE Confidence: 0.8393542

 $00:16:57.350 \longrightarrow 00:16:59.000$ But we also saw this

NOTE Confidence: 0.8393542

 $00{:}16{:}59{.}000 \dashrightarrow 00{:}17{:}00{.}650$ finding in a dults as well,

NOTE Confidence: 0.8393542

 $00{:}17{:}00{.}650 \dashrightarrow 00{:}17{:}02{.}981$ so this seems like this deficit in

 $00:17:02.981 \rightarrow 00:17:04.609$ excitatory connections starts very early,

NOTE Confidence: 0.8393542

 $00{:}17{:}04.610 \dashrightarrow 00{:}17{:}06.802$ but the finding that I want to focus

NOTE Confidence: 0.8393542

 $00:17:06.802 \rightarrow 00:17:08.858$ on is this very interesting deficit

NOTE Confidence: 0.8393542

 $00:17:08.858 \rightarrow 00:17:11.869$ that we found that got us all excited.

NOTE Confidence: 0.8393542

 $00:17:11.870 \longrightarrow 00:17:13.520$ We first found this data,

NOTE Confidence: 0.8393542

 $00:17:13.520 \rightarrow 00:17:16.112$ so this is a study using this mutant

NOTE Confidence: 0.8393542

 $00:17:16.112 \rightarrow 00:17:18.420$ mouse line using diffusion tensor.

NOTE Confidence: 0.8393542

 $00:17:18.420 \rightarrow 00:17:20.716$ Which looks at connectivity in the brain,

NOTE Confidence: 0.8393542

 $00{:}17{:}20.720 \dashrightarrow 00{:}17{:}23.176$ and so this is a five day old

NOTE Confidence: 0.8393542

 $00:17:23.176 \longrightarrow 00:17:25.103$ 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

 $00{:}17{:}27.630 \dashrightarrow 00{:}17{:}29.667$ and so about five days equivalent to

NOTE Confidence: 0.8393542

 $00{:}17{:}29.667 \dashrightarrow 00{:}17{:}32.262$ birth in the human and what we found

NOTE Confidence: 0.8393542

 $00{:}17{:}32.262 \dashrightarrow 00{:}17{:}33.922$ was a dramatic reduction between

NOTE Confidence: 0.8393542

 $00:17:33.991 \rightarrow 00:17:36.187$ connections which are shown by these.

NOTE Confidence: 0.8393542

 $00:17:36.190 \longrightarrow 00:17:37.980$ These red lines between the

- NOTE Confidence: 0.8393542
- $00:17:37.980 \rightarrow 00:17:39.770$ prefrontal cortex and the thalamus

 $00{:}17{:}39{.}832 \dashrightarrow 00{:}17{:}41{.}446$ on the right is the control,

NOTE Confidence: 0.8393542

 $00:17:41.450 \longrightarrow 00:17:43.319$ so you can see this thick bundle

NOTE Confidence: 0.8393542

 $00{:}17{:}43{.}319 \dashrightarrow 00{:}17{:}45{.}842$ and on the left is the mutant where

NOTE Confidence: 0.8393542

 $00:17:45.842 \longrightarrow 00:17:48.005$ you see a dramatic reduction in

NOTE Confidence: 0.8393542

 $00:17:48.005 \rightarrow 00:17:49.797$ connectivity which is quantified.

NOTE Confidence: 0.8393542

 $00:17:49.800 \longrightarrow 00:17:50.980$ Here on the left,

NOTE Confidence: 0.8393542

 $00:17:50.980 \rightarrow 00:17:53.520$ and so we found this deficit very early,

NOTE Confidence: 0.8393542

 $00{:}17{:}53{.}520 \dashrightarrow 00{:}17{:}55{.}380$ but it seems like this may.

NOTE Confidence: 0.8393542

 $00:17:55.380 \rightarrow 00:17:56.930$ This deficit is maintained during

NOTE Confidence: 0.8393542

 $00:17:56.930 \longrightarrow 00:17:58.790$ adolescence, so we checked it P.

NOTE Confidence: 0.8393542

 $00{:}17{:}58{.}790 \dashrightarrow 00{:}18{:}00{.}960$ 21 but we also checked it P.

NOTE Confidence: 0.8393542

 $00{:}18{:}00{.}960 \dashrightarrow 00{:}18{:}01{.}890$ 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

 $00{:}18{:}03{.}440 \dashrightarrow 00{:}18{:}04{.}680$ a delay in development.

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

NOTE Confidence: 0.8393542

 $00{:}18{:}06{.}456 \dashrightarrow 00{:}18{:}08{.}399$ the circuit in our mouse model.

NOTE Confidence: 0.81007785

 $00:18:10.520 \longrightarrow 00:18:12.508$ 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

 $00{:}18{:}15{.}875 \dashrightarrow 00{:}18{:}17{.}600$ 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

 $00:18:19.256 \longrightarrow 00:18:20.476$ is essential for cognition,

NOTE Confidence: 0.81007785

 $00{:}18{:}20{.}480 \dashrightarrow 00{:}18{:}21{.}473$ specifically working memory.

NOTE Confidence: 0.81007785

 $00:18:21.473 \longrightarrow 00:18:22.797$ This is a study.

NOTE Confidence: 0.81007785

 $00:18:22.800 \longrightarrow 00:18:24.792$ 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

 $00:18:26.120 \longrightarrow 00:18:28.776$ who is now the head of the MH,

NOTE Confidence: 0.81007785

 $00{:}18{:}28{.}780 \dashrightarrow 00{:}18{:}30{.}385$ who showed that the connection

NOTE Confidence: 0.81007785

 $00{:}18{:}30{.}385 \dashrightarrow 00{:}18{:}31{.}669$ between the mediodorsal thal amus

NOTE Confidence: 0.81007785

 $00:18:31.669 \longrightarrow 00:18:33.100$ and the prefrontal cortex,

 $00:18:33.100 \longrightarrow 00:18:34.484$ and there's typical connection

NOTE Confidence: 0.81007785

 $00{:}18{:}34{.}484 \dashrightarrow 00{:}18{:}35{.}868$ between the prefrontal cortex

NOTE Confidence: 0.81007785

 $00{:}18{:}35{.}868 \dashrightarrow 00{:}18{:}37{.}586$ and the mediodorsal thalamus is

NOTE Confidence: 0.81007785

 $00:18:37.586 \longrightarrow 00:18:39.536$ 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

 $00:18:45.040 \longrightarrow 00:18:47.959$ so it's a circuit that's very it's

NOTE Confidence: 0.81007785

 $00:18:47.959 \rightarrow 00:18:50.899$ highly studied in psychiatric biology.

NOTE Confidence: 0.8224325

 $00:18:53.740 \longrightarrow 00:18:56.351$ And so our proposed model is that

NOTE Confidence: 0.8224325

 $00:18:56.351 \longrightarrow 00:18:57.880$ disruption of retinoic acid,

NOTE Confidence: 0.8224325

 $00{:}18{:}57{.}880 \dashrightarrow 00{:}18{:}59{.}825$ associated and regulated genes lead

NOTE Confidence: 0.8224325

 $00{:}18{:}59{.}825 \dashrightarrow 00{:}19{:}01{.}770$ 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

 $00:19:03.354 \longrightarrow 00:19:05.411$ and that leads to the early
$00:19:05.411 \rightarrow 00:19:07.279$ 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

 $00:19:12.891 \rightarrow 00:19:15.775$ right at birth in our mouse model.

NOTE Confidence: 0.8224325

 $00:19:15.780 \longrightarrow 00:19:17.836$ 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

 $00{:}19{:}19{.}420 \dashrightarrow 00{:}19{:}20{.}584$ which I'll talk about.

NOTE Confidence: 0.8224325

 $00:19:20.584 \rightarrow 00:19:22.750$ So first this is the mouse model.

NOTE Confidence: 0.8224325

 $00{:}19{:}22{.}750 \dashrightarrow 00{:}19{:}24{.}568$ This is have any relevance to

NOTE Confidence: 0.8224325

 $00:19:24.568 \rightarrow 00:19:25.477$ patients with schizophrenia?

NOTE Confidence: 0.8224325

 $00{:}19{:}25{.}480 \dashrightarrow 00{:}19{:}27{.}664$ And so this in this case we turn

NOTE Confidence: 0.8224325

 $00:19:27.664 \longrightarrow 00:19:29.419$ to another set of colleagues,

NOTE Confidence: 0.8224325

 $00:19:29.420 \longrightarrow 00:19:30.628$ colleagues that are involved

NOTE Confidence: 0.8224325

 $00:19:30.628 \rightarrow 00:19:31.534$ in functional imaging,

NOTE Confidence: 0.8224325

 $00:19:31.540 \rightarrow 00:19:33.184$ functional neural humanit,

NOTE Confidence: 0.8224325

 $00:19:33.184 \rightarrow 00:19:34.280$ functional imaging.

- NOTE Confidence: 0.8224325
- $00:19:34.280 \longrightarrow 00:19:36.323$ And this is a study done in 2015 and

 $00:19:36.323 \rightarrow 00:19:38.380$ what they found they were specifically

NOTE Confidence: 0.8224325

 $00{:}19{:}38{.}380 \dashrightarrow 00{:}19{:}40{.}150$ looking at the lambic cortical

NOTE Confidence: 0.8224325

 $00:19:40.215 \rightarrow 00:19:42.015$ networks in healthy subjects that

NOTE Confidence: 0.8224325

 $00{:}19{:}42.015 \dashrightarrow 00{:}19{:}44.138$ compare them to patients within four

NOTE Confidence: 0.8224325

 $00{:}19{:}44{.}138 \dashrightarrow 00{:}19{:}46{.}046$ weeks of their diagnosis of schizophrenia.

NOTE Confidence: 0.8224325

 $00{:}19{:}46.050 \dashrightarrow 00{:}19{:}47.635$ And then patients with chronic

NOTE Confidence: 0.8224325

 $00:19:47.635 \rightarrow 00:19:48.586$ schizophrenia chronic psychosis.

NOTE Confidence: 0.8224325

 $00:19:48.590 \dashrightarrow 00:19:52.574$ So this has been over a couple years.

NOTE Confidence: 0.8224325

 $00{:}19{:}52{.}580 \dashrightarrow 00{:}19{:}54{.}135$ Of being diagnosed with schizophrenia

NOTE Confidence: 0.8224325

 $00:19:54.135 \rightarrow 00:19:56.488$ and we can see in the blue bar,

NOTE Confidence: 0.8224325

 $00:19:56.490 \longrightarrow 00:19:58.134$ so this is functional connectivity so

NOTE Confidence: 0.8224325

 $00:19:58.134 \rightarrow 00:20:00.179$ it's looking at just connection between.

NOTE Confidence: 0.8224325

 $00:20:00.180 \longrightarrow 00:20:00.808$ Different regions,

NOTE Confidence: 0.8224325

 $00:20:00.808 \rightarrow 00:20:02.064$ specifically the almacen regions

- $00:20:02.064 \rightarrow 00:20:03.006$ of the cortex,
- NOTE Confidence: 0.8224325
- $00{:}20{:}03.010 \dashrightarrow 00{:}20{:}04.942$ and they showed that compared to
- NOTE Confidence: 0.8224325
- $00:20:04.942 \longrightarrow 00:20:07.090$ the control which is the blue bar,
- NOTE Confidence: 0.8224325
- $00:20:07.090 \rightarrow 00:20:08.346$ there is reduced connectivity
- NOTE Confidence: 0.8224325
- $00:20:08.346 \longrightarrow 00:20:09.288$ both at diagnosis,
- NOTE Confidence: 0.8224325
- $00{:}20{:}09{.}290 \dashrightarrow 00{:}20{:}11{.}285$ which is shown at the yellow bar
- NOTE Confidence: 0.8224325
- $00:20:11.285 \longrightarrow 00:20:13.368$ and both in the chronic stage.
- NOTE Confidence: 0.8224325
- $00:20:13.370 \longrightarrow 00:20:15.248$ So that seems like this disruption
- NOTE Confidence: 0.8224325
- $00:20:15.248 \longrightarrow 00:20:15.874$ is present,
- NOTE Confidence: 0.8224325
- $00:20:15.880 \longrightarrow 00:20:17.450$ and at least this population
- NOTE Confidence: 0.8224325
- $00{:}20{:}17.450 \dashrightarrow 00{:}20{:}18.706$ of patients with schizophrenia,
- NOTE Confidence: 0.8224325
- $00:20:18.710 \rightarrow 00:20:20.714$ 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
- $00:20:23.420 \longrightarrow 00:20:25.932$ 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.

 $00:20:30.610 \longrightarrow 00:20:32.752$ 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

 $00:20:34.490 \longrightarrow 00:20:36.380$ They had a certain set of criteria

NOTE Confidence: 0.8224325

 $00:20:36.380 \longrightarrow 00:20:38.467$ to kind of identify these patients

NOTE Confidence: 0.8224325

 $00:20:38.467 \longrightarrow 00:20:40.885$ and what they showed was this

NOTE Confidence: 0.8224325

 $00:20:40.885 \rightarrow 00:20:42.468$ disconnection between Hypo connection

NOTE Confidence: 0.8224325

 $00:20:42.468 \longrightarrow 00:20:45.079$ 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

 $00{:}20{:}47{.}200 \dashrightarrow 00{:}20{:}49{.}204$ and the thalamus was present even

NOTE Confidence: 0.8224325

 $00:20:49.204 \rightarrow 00:20:51.440$ prior to conversion in two psychosis.

NOTE Confidence: 0.8224325

 $00:20:51.440 \longrightarrow 00:20:51.779$ Specifically,

NOTE Confidence: 0.8224325

 $00{:}20{:}51.779 \dashrightarrow 00{:}20{:}53.813$ that then I guess in addition

NOTE Confidence: 0.8224325

 $00{:}20{:}53.813 \dashrightarrow 00{:}20{:}55.320$ to what they showed,

NOTE Confidence: 0.8224325

 $00:20:55.320 \rightarrow 00:20:57.784$ was that the worst the psychotic symptoms,

 $00:20:57.790 \rightarrow 00:20:59.620$ the more the reduced connectivity

NOTE Confidence: 0.8224325

 $00{:}20{:}59{.}620 \dashrightarrow 00{:}21{:}00{.}718$ there was between.

NOTE Confidence: 0.8224325

 $00:21:00.720 \longrightarrow 00:21:01.494$ These two regions,

NOTE Confidence: 0.8224325

 $00:21:01.494 \rightarrow 00:21:03.940$ so it seems like even prior to conversion,

NOTE Confidence: 0.8224325

 $00{:}21{:}03{.}940 \dashrightarrow 00{:}21{:}05{.}698$ there seems to be this disconnection

NOTE Confidence: 0.8224325

 $00{:}21{:}05.698 \dashrightarrow 00{:}21{:}07.460$ between the thalamus in the cortex,

NOTE Confidence: 0.8224325

 $00{:}21{:}07{.}460 \dashrightarrow 00{:}21{:}09{.}708$ and so I think this is an interesting

NOTE Confidence: 0.8224325

 $00:21:09.708 \rightarrow 00:21:12.145$ 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

 $00:21:13.254 \longrightarrow 00:21:15.900$ to kind of see if this is a much

NOTE Confidence: 0.8224325

 $00{:}21{:}15{.}900 \dashrightarrow 00{:}21{:}16{.}836$ more generalizable etiology.

NOTE Confidence: 0.8224325

 $00:21:16.840 \longrightarrow 00:21:19.983$ We also plan to study this in

NOTE Confidence: 0.8224325

 $00{:}21{:}19{.}983 \dashrightarrow 00{:}21{:}22{.}139$ various mouse models as well.

NOTE Confidence: 0.8224325

 $00:21:22.140 \longrightarrow 00:21:23.386$ So the second question,

NOTE Confidence: 0.8224325

 $00{:}21{:}23.386 \dashrightarrow 00{:}21{:}25.174$ 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
- $00:21:27.215 \rightarrow 00:21:29.048$ is an essential question to really

 $00{:}21{:}29.048 \dashrightarrow 00{:}21{:}30.983$ understand how to understand the

NOTE Confidence: 0.8224325

 $00:21:30.983 \rightarrow 00:21:32.531$ complex symptoms of schizophrenia,

NOTE Confidence: 0.8224325

 $00:21:32.540 \longrightarrow 00:21:34.472$ is how can a specific deficit in

NOTE Confidence: 0.8224325

 $00{:}21{:}34{.}472 \dashrightarrow 00{:}21{:}36{.}093$ one circuit that's involved in

NOTE Confidence: 0.8224325

 $00{:}21{:}36.093 \dashrightarrow 00{:}21{:}37.933$ cognition lead to the complex

NOTE Confidence: 0.8224325

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

NOTE Confidence: 0.8224325

 $00{:}21{:}39{.}040 \dashrightarrow 00{:}21{:}41{.}049$ Just as a quick refresher we talk

NOTE Confidence: 0.8224325

 $00{:}21{:}41.049 \dashrightarrow 00{:}21{:}42.955$ about we're talking about a circuit

NOTE Confidence: 0.8224325

 $00{:}21{:}42.955 \dashrightarrow 00{:}21{:}44.275$ that's important for cognition

NOTE Confidence: 0.8224325

 $00:21:44.275 \longrightarrow 00:21:45.265$ and maybe some

NOTE Confidence: 0.8407046

 $00:21:45.323 \longrightarrow 00:21:46.189$ social behavior,

NOTE Confidence: 0.8407046

 $00{:}21{:}46.190 \dashrightarrow 00{:}21{:}47.820$ but there's also the hall ucinations,

NOTE Confidence: 0.8407046

 $00{:}21{:}47.820 \dashrightarrow 00{:}21{:}49.116$ delusions, the various other

NOTE Confidence: 0.8407046

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

 $00{:}21{:}50{.}090 \dashrightarrow 00{:}21{:}52{.}258$ 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

 $00:21:54.470 \rightarrow 00:21:57.846$ Human neuroimaging and what we see is in,

NOTE Confidence: 0.8407046

 $00:21:57.850 \longrightarrow 00:22:00.797$ so I showed you this panel here,

NOTE Confidence: 0.8407046

 $00{:}22{:}00{.}800 \dashrightarrow 00{:}22{:}02{.}685$ which is the connectivity between

NOTE Confidence: 0.8407046

 $00{:}22{:}02.685 \dashrightarrow 00{:}22{:}05.091$ the prefrontal cortex and the family NOTE Confidence: 0.8407046

 $00:22:05.091 \rightarrow 00:22:06.931$ showed reduced connectivity during

NOTE Confidence: 0.8407046

 $00:22:06.931 \rightarrow 00:22:09.231$ 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

 $00{:}22{:}11{.}922 \dashrightarrow 00{:}22{:}13{.}710$ hyper connectivity between the

NOTE Confidence: 0.8407046

 $00{:}22{:}13.785 \dashrightarrow 00{:}22{:}16.291$ thalamus in the motor cortex and the NOTE Confidence: 0.8407046

 $00:22:16.291 \rightarrow 00:22:18.950$ thalamus in the somato sensory cortex.

NOTE Confidence: 0.8407046

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

NOTE Confidence: 0.8407046

 $00{:}22{:}21{.}326 \dashrightarrow 00{:}22{:}23{.}948$ study done by Allen Tiffin Teacher

NOTE Confidence: 0.8407046

 $00:22:23.948 \longrightarrow 00:22:26.078$ ***** so that same hyperconnectivity

NOTE Confidence: 0.8407046

 $00:22:26.078 \rightarrow 00:22:28.550$ as well in these prodromal patients.

 $00{:}22{:}30{.}930 \dashrightarrow 00{:}22{:}33{.}621$ And so that in this kind of I turned

NOTE Confidence: 0.81973433

 $00{:}22{:}33{.}621 \dashrightarrow 00{:}22{:}36{.}547$ back to kind of some of our mouse works.

NOTE Confidence: 0.81973433

 $00{:}22{:}36{.}550 \dashrightarrow 00{:}22{:}38{.}776$ So we not only looked at connections

NOTE Confidence: 0.81973433

 $00{:}22{:}38.776 \dashrightarrow 00{:}22{:}40.680$ 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

 $00{:}22{:}42.470 \dashrightarrow 00{:}22{:}44.030$ 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

 $00:22:45.590 \longrightarrow 00:22:47.150$ which is equivalent to birth,

NOTE Confidence: 0.81973433

 $00{:}22{:}47.150 \dashrightarrow 00{:}22{:}49.246$ and at this stage the only deficit that

NOTE Confidence: 0.81973433

 $00{:}22{:}49{.}246 \dashrightarrow 00{:}22{:}51{.}549$ 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

 $00{:}22{:}56.069 \dashrightarrow 00{:}22{:}58.706$ between the thal amus in the motor cortex or

NOTE Confidence: 0.81973433

 $00{:}22{:}58.706 \dashrightarrow 00{:}23{:}00.730$ the thalamus in the somatos ensory cortex.

NOTE Confidence: 0.81973433

 $00{:}23{:}00{.}730 \dashrightarrow 00{:}23{:}02{.}886$ So what we're interested in doing is

 $00:23:02.886 \rightarrow 00:23:04.720$ seeing whether there's a change in

NOTE Confidence: 0.81973433

 $00{:}23{:}04.720 \dashrightarrow 00{:}23{:}06.424$ this kind of diagram in connectivity.

NOTE Confidence: 0.81973433

 $00:23:06.430 \longrightarrow 00:23:07.930$ 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

 $00{:}23{:}10{.}030 \dashrightarrow 00{:}23{:}12{.}430$ and do we see a change in a dulthood?

NOTE Confidence: 0.81973433

 $00{:}23{:}12{.}430 \dashrightarrow 00{:}23{:}14{.}230$ 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

 $00:23:15.430 \rightarrow 00:23:17.230$ the prefrontal cortex in the thalamus,

NOTE Confidence: 0.81973433

 $00{:}23{:}17{.}230 \dashrightarrow 00{:}23{:}19{.}030$ is lossed 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

 $00{:}23{:}20{.}830 \dashrightarrow 00{:}23{:}22{.}310$ Are there progressive change and

NOTE Confidence: 0.81973433

 $00{:}23{:}22{.}310 \dashrightarrow 00{:}23{:}24{.}430$ so kind of fleshing out this model,

NOTE Confidence: 0.81973433

 $00{:}23{:}24{.}430 \dashrightarrow 00{:}23{:}26{.}206$ which is something that we need

NOTE Confidence: 0.81973433

 $00:23:26.206 \longrightarrow 00:23:28.029$ to continue to test and study?

NOTE Confidence: 0.81973433

 $00{:}23{:}28{.}030 \dashrightarrow 00{:}23{:}29{.}600$ 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
- $00:23:31.221 \longrightarrow 00:23:32.349$ lead to reduced medial?

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

NOTE Confidence: 0.81973433

 $00:23:33.439 \longrightarrow 00:23:35.617$ medial dorsal thalamus and medial prefrontal

NOTE Confidence: 0.81973433

 $00:23:35.617 \rightarrow 00:23:37.605$ 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

 $00:23:39.926 \rightarrow 00:23:43.130$ the brain now has to compensate so this this

NOTE Confidence: 0.81973433

 $00{:}23{:}43{.}204 \dashrightarrow 00{:}23{:}46{.}025$ disruption of a circuit occurs very early.

NOTE Confidence: 0.81973433

 $00{:}23{:}46{.}030 \dashrightarrow 00{:}23{:}48{.}226$ So during childhood the brain is

NOTE Confidence: 0.81973433

 $00:23:48.226 \rightarrow 00:23:50.589$ trying to compensate for this deficit.

NOTE Confidence: 0.81973433

 $00{:}23{:}50{.}590 \dashrightarrow 00{:}23{:}51{.}730$ As we know,

NOTE Confidence: 0.81973433

 $00{:}23{:}51{.}730 \dashrightarrow 00{:}23{:}54{.}010$ the brain can do through neuroplasticity,

NOTE Confidence: 0.81973433

 $00:23:54.010 \rightarrow 00:23:55.700$ and maybe these secondary changes

NOTE Confidence: 0.81973433

 $00:23:55.700 \longrightarrow 00:23:57.390$ may underlie the positive and

NOTE Confidence: 0.81973433

 $00{:}23{:}57{.}449 \dashrightarrow 00{:}23{:}59{.}329$ negative symptoms of schizophrenia.

 $00:23:59.330 \longrightarrow 00:24:00.894$ Abig critique of the

NOTE Confidence: 0.81973433

 $00:24:00.894 \rightarrow 00:24:02.458$ neurodevelopmental theory is what?

NOTE Confidence: 0.81973433

 $00:24:02.460 \longrightarrow 00:24:04.134$ Explains that big gap between what's

NOTE Confidence: 0.81973433

 $00:24:04.134 \rightarrow 00:24:06.059$ supposed to be the deficit during

NOTE Confidence: 0.81973433

 $00{:}24{:}06{.}059 \dashrightarrow 00{:}24{:}08{.}309$ development and the positive symptoms later,

NOTE Confidence: 0.81973433

 $00{:}24{:}08{.}310 \dashrightarrow 00{:}24{:}10{.}586$ and what what it could be is

NOTE Confidence: 0.81973433

 $00:24:10.586 \rightarrow 00:24:12.210$ 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

 $00:24:15.926 \rightarrow 00:24:18.706$ try to make up for this cognitive deficit,

NOTE Confidence: 0.81973433

 $00{:}24{:}18.710 \dashrightarrow 00{:}24{:}20.660$ and eventually as expectations get higher,

NOTE Confidence: 0.81973433

 $00{:}24{:}20.660 \dashrightarrow 00{:}24{:}22.610$ there's a breakdown in the system,

NOTE Confidence: 0.81973433

 $00{:}24{:}22.610 \dashrightarrow 00{:}24{:}24.885$ and that leads to the psychotic symptoms.

NOTE Confidence: 0.81973433

 $00{:}24{:}24{.}890 \dashrightarrow 00{:}24{:}26{.}946$ This can also kind of dovetail well with

NOTE Confidence: 0.81973433

 $00:24:26.946 \rightarrow 00:24:29.447$ kind of the current driving force kind

NOTE Confidence: 0.81973433

 $00:24:29.447 \rightarrow 00:24:31.377$ of driving neurodevelopmental theory that

- NOTE Confidence: 0.81973433
- $00:24:31.432 \rightarrow 00:24:33.628$ it's a specific synaptic pruning deficit.

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

NOTE Confidence: 0.81973433

 $00{:}24{:}34{.}204 \dashrightarrow 00{:}24{:}36{.}500$ and that's where you see the break then.

NOTE Confidence: 0.81973433

 $00:24:36.500 \longrightarrow 00:24:38.216$ So maybe as you prune more,

NOTE Confidence: 0.81973433

 $00:24:38.220 \longrightarrow 00:24:39.655$ you've lost some of these

NOTE Confidence: 0.81973433

00:24:39.655 --> 00:24:40.516 compens atory mechanisms,

NOTE Confidence: 0.81973433

 $00:24:40.520 \longrightarrow 00:24:41.950$ leading to a psychotic break.

NOTE Confidence: 0.81973433

 $00:24:41.950 \rightarrow 00:24:44.106$ And this is something that I'm really

NOTE Confidence: 0.81973433

 $00:24:44.106 \rightarrow 00:24:45.970$ interested in testing in a mouse model.

NOTE Confidence: 0.81973433

 $00{:}24{:}45{.}970 \dashrightarrow 00{:}24{:}47{.}754$ What happens to our mouse when we have

NOTE Confidence: 0.81973433

 $00{:}24{:}47.754 \dashrightarrow 00{:}24{:}49.734$ a specific deficit in this mediodorsal

NOTE Confidence: 0.81973433

 $00{:}24{:}49{.}734 \dashrightarrow 00{:}24{:}50{.}847$ prefrontal cortex connection,

NOTE Confidence: 0.81973433

 $00:24:50.850 \rightarrow 00:24:53.720$ and how does it change the rest of the brain?

NOTE Confidence: 0.81973433

 $00:24:53.720 \longrightarrow 00:24:56.420$ And how does it change behavior

NOTE Confidence: 0.81973433

 $00:24:56.420 \rightarrow 00:24:57.770$ progressively through time?

 $00:24:57.770 \longrightarrow 00:24:59.723$ And I think this also gives us

NOTE Confidence: 0.81973433

 $00{:}24{:}59{.}723 \dashrightarrow 00{:}25{:}01{.}589$ an opportunity to think about

NOTE Confidence: 0.81973433

 $00:25:01.589 \rightarrow 00:25:03.525$ interventions or future interventions.

NOTE Confidence: 0.81973433

 $00:25:03.530 \longrightarrow 00:25:05.690$ If this is the primary insult,

NOTE Confidence: 0.81973433

 $00{:}25{:}05.690 \dashrightarrow 00{:}25{:}07.490$ a connection between the mediodorsal

NOTE Confidence: 0.81973433

 $00{:}25{:}07{.}490 \dashrightarrow 00{:}25{:}09{.}290$ down in the prefrontal cortex,

NOTE Confidence: 0.81973433

 $00:25:09.290 \longrightarrow 00:25:11.456$ can we try to strengthen this

NOTE Confidence: 0.81973433

 $00:25:11.456 \rightarrow 00:25:13.250$ 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

 $00:25:15.410 \rightarrow 00:25:17.210$ but maybe deep brain stimulation

NOTE Confidence: 0.83900446

 $00{:}25{:}17{.}210 \dashrightarrow 00{:}25{:}19{.}010$ or TMS or other processes.

NOTE Confidence: 0.83900446

 $00:25:19.010 \rightarrow 00:25:21.890$ Or we could just work on cognitive skills.

NOTE Confidence: 0.83900446

 $00{:}25{:}21.890 \dashrightarrow 00{:}25{:}24.056$ Could we do brain training apps

NOTE Confidence: 0.83900446

 $00:25:24.056 \rightarrow 00:25:26.209$ 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

 $00:25:29.200 \rightarrow 00:25:31.180$ Of schizophrenia and the thought is

- NOTE Confidence: 0.83900446
- $00:25:31.180 \rightarrow 00:25:33.797$ by not only by treating this trying

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

NOTE Confidence: 0.83900446

 $00:25:36.251 \rightarrow 00:25:38.780$ improve these early cognitive symptoms?

NOTE Confidence: 0.83900446

 $00{:}25{:}38.780 \dashrightarrow 00{:}25{:}40.976$ We can altogether prevent the secondary

NOTE Confidence: 0.83900446

 $00:25:40.976 \longrightarrow 00:25:42.954$ circuit changes and maybe prevent

NOTE Confidence: 0.83900446

 $00{:}25{:}42{.}954 \dashrightarrow 00{:}25{:}44{.}758$ positive and negatives symptoms.

NOTE Confidence: 0.83900446

 $00:25:44.760 \longrightarrow 00:25:47.154$ And this is something I'm just

NOTE Confidence: 0.83900446

 $00:25:47.154 \rightarrow 00:25:48.750$ generally interested in studying.

NOTE Confidence: 0.83900446

 $00{:}25{:}48.750 \dashrightarrow 00{:}25{:}49.950$ Currently circuits neuroscience,

NOTE Confidence: 0.83900446

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

NOTE Confidence: 0.83900446

 $00{:}25{:}51{.}532 \dashrightarrow 00{:}25{:}54{.}269$ a big crux of a dult psychiatry has

NOTE Confidence: 0.83900446

 $00{:}25{:}54{.}269 \dashrightarrow 00{:}25{:}57{.}130$ an adult focus of what they do.

NOTE Confidence: 0.83900446

 $00{:}25{:}57{.}130 \dashrightarrow 00{:}25{:}59{.}330$ Is they disrupt relevant circuits?

NOTE Confidence: 0.83900446

 $00{:}25{:}59{.}330 \dashrightarrow 00{:}26{:}01{.}010$ Like the study I showed that

NOTE Confidence: 0.83900446

 $00:26:01.010 \longrightarrow 00:26:03.009$ was done by Josh Gordon's lab.

00:26:03.010 - 00:26:04.430 They just daily disrupt these

NOTE Confidence: 0.83900446

 $00{:}26{:}04{.}430 \dashrightarrow 00{:}26{:}06{.}241$ circuits during adult in adults or

NOTE Confidence: 0.83900446

 $00:26:06.241 \rightarrow 00:26:07.617$ they disrupted during adolescence.

NOTE Confidence: 0.83900446

 $00:26:07.620 \longrightarrow 00:26:10.076$ And then they look, went to disrupt it.

NOTE Confidence: 0.83900446

 $00:26:10.080 \longrightarrow 00:26:11.610$ 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

 $00{:}26{:}18.283 \dashrightarrow 00{:}26{:}20.419$ very early and so we can then study

NOTE Confidence: 0.83900446

 $00:26:20.419 \rightarrow 00:26:21.952$ 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

 $00{:}26{:}23.580 \dashrightarrow 00{:}26{:}25.422$ How does that affect the rest

NOTE Confidence: 0.83900446

 $00:26:25.422 \rightarrow 00:26:26.650$ of brain dump development?

NOTE Confidence: 0.83900446

 $00{:}26{:}26{.}650 \dashrightarrow 00{:}26{:}30{.}220$ I think this could generate a more.

NOTE Confidence: 0.83900446

 $00{:}26{:}30{.}220 \dashrightarrow 00{:}26{:}34{.}105$ A better version or better model of

 $00:26:34.105 \rightarrow 00:26:36.850$ neuro psychiatric disease in our

NOTE Confidence: 0.83900446

 $00{:}26{:}36.850 \dashrightarrow 00{:}26{:}39.320$ model systems to further study.

NOTE Confidence: 0.83900446

 $00:26:39.320 \longrightarrow 00:26:42.120$ So this is a summary of the talk.

NOTE Confidence: 0.83900446

 $00:26:42.120 \longrightarrow 00:26:44.199$ I think the main points I want

NOTE Confidence: 0.83900446

 $00{:}26{:}44.199 \dashrightarrow 00{:}26{:}46.140$ every one 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

 $00{:}26{:}48.509 \dashrightarrow 00{:}26{:}50.564$ the cognitive and motor symptoms

NOTE Confidence: 0.83900446

 $00:26:50.564 \rightarrow 00:26:52.619$ of schizophrenia may precede the

NOTE Confidence: 0.83900446

 $00{:}26{:}52.620 \dashrightarrow 00{:}26{:}54.060$ positive symptoms in schizophrenia.

NOTE Confidence: 0.83900446

 $00:26:54.060 \rightarrow 00:26:55.860$ This is underlying the neuro

NOTE Confidence: 0.83900446

 $00{:}26{:}55{.}860 \dashrightarrow 00{:}26{:}57{.}310$ developmental theory of schizophrenia

NOTE Confidence: 0.83900446

 $00{:}26{:}57{.}310 \dashrightarrow 00{:}26{:}59{.}040$ and disruption of frontal cortex

NOTE Confidence: 0.83900446

 $00{:}26{:}59{.}040 \dashrightarrow 00{:}27{:}00{.}772$ development during the 2nd trimester

NOTE Confidence: 0.83900446

 $00{:}27{:}00.772 \dashrightarrow 00{:}27{:}02.417$ has been associated with schizophrenia,

NOTE Confidence: 0.83900446

 $00{:}27{:}02{.}420 \dashrightarrow 00{:}27{:}04{.}322$ both genetically as well as from

 $00:27:04.322 \longrightarrow 00:27:05.590$ 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

 $00:27:07.744 \longrightarrow 00:27:09.292$ Maybe the underlying developmental

NOTE Confidence: 0.83900446

 $00:27:09.292 \rightarrow 00:27:11.300$ etiology of schizophrenia and a target.

NOTE Confidence: 0.83900446

 $00:27:11.300 \longrightarrow 00:27:13.799$ For early intervention.

NOTE Confidence: 0.83900446

 $00{:}27{:}13.800 \dashrightarrow 00{:}27{:}16.280$ So this was the data that I showed

NOTE Confidence: 0.83900446

 $00:27:16.280 \longrightarrow 00:27:18.057$ 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

 $00{:}27{:}19{.}492 \dashrightarrow 00{:}27{:}21{.}640$ effort at specifically like to thank

NOTE Confidence: 0.83900446

 $00{:}27{:}21.697 \dashrightarrow 00{:}27{:}23.527$ men and who's been an excellent NOTE Confidence: 0.83900446

 $00:27:23.527 \rightarrow 00:27:25.282$ mentoring is really giving me a

NOTE Confidence: 0.83900446

 $00{:}27{:}25{.}282 \dashrightarrow 00{:}27{:}26{.}704$ 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

 $00:27:28.700 \longrightarrow 00:27:30.518$ who we worked very closely in

NOTE Confidence: 0.83900446

 $00:27:30.518 \rightarrow 00:27:31.427$ leading this project.

- NOTE Confidence: 0.83900446
- 00:27:31.430 --> 00:27:32.618 But as I said,
- NOTE Confidence: 0.83900446
- $00:27:32.618 \rightarrow 00:27:34.773$ there were so many different people in
- NOTE Confidence: 0.83900446
- $00:27:34.773 \rightarrow 00:27:37.205$ the lab that were involved in this project.
- NOTE Confidence: 0.83900446
- $00:27:37.210 \rightarrow 00:27:38.426$ 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
- $00:27:42.679 \longrightarrow 00:27:43.720$ of our collaborators.
- NOTE Confidence: 0.83900446
- $00:27:43.720 \rightarrow 00:27:45.764$ They helped us with both the generating
- NOTE Confidence: 0.83900446
- $00{:}27{:}45.764 \dashrightarrow 00{:}27{:}48.130$ 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
- $00:27:49.390 \longrightarrow 00:27:50.650$ in the mouse model,
- NOTE Confidence: 0.83900446
- $00{:}27{:}50{.}650 \dashrightarrow 00{:}27{:}52{.}540$ as well as our funding sources
- NOTE Confidence: 0.83900446
- $00:27:52.540 \longrightarrow 00:27:53.800$ there retinoic acid choice,
- NOTE Confidence: 0.83900446
- $00{:}27{:}53{.}800 \dashrightarrow 00{:}27{:}55{.}375$ 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

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 $00:28:04.884 \rightarrow 00:28:06.816$ answering that last question that I'm NOTE Confidence: 0.83900446 $00:28:06.816 \rightarrow 00:28:08.562$ really interested to and then finally NOTE Confidence: 0.83900446 $00:28:08.562 \longrightarrow 00:28:10.500$ 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 $00:28:18.390 \rightarrow 00:28:20.340$ 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 $00:28:25.140 \longrightarrow 00:28:27.190$ who really do the heavy lifting. 55

 $00:27:56.950 \longrightarrow 00:27:59.470$ and then it is funded by the NIH,

 $00{:}27{:}59{.}470 \dashrightarrow 00{:}28{:}01{.}192$ and I received some money from

- NOTE Confidence: 0.78569424
- $00:28:27.190 \rightarrow 00:28:30.124$ The program as well as the T 32 fellowship,
- NOTE Confidence: 0.78569424
- $00{:}28{:}30{.}130 \dashrightarrow 00{:}28{:}33{.}055$ which funds my last two years in the program.
- NOTE Confidence: 0.81864005
- $00:28:35.430 \longrightarrow 00:28:36.889$ And that's the talk.
- NOTE Confidence: 0.8971473
- $00:28:45.710 \longrightarrow 00:28:48.170$ 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
- $00:28:50.740 \longrightarrow 00:28:54.650$ 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
- $00:28:56.930 \longrightarrow 00:28:59.150$ Were you able to see reduced
- NOTE Confidence: 0.8971473
- $00{:}28{:}59{.}150 \dashrightarrow 00{:}29{:}00{.}810$ connectivity and other pathways,
- NOTE Confidence: 0.8971473
- $00:29:00.810 \longrightarrow 00:29:02.350$ 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
- $00{:}29{:}04{.}275 \dashrightarrow 00{:}29{:}06{.}586$ in the mouse where there isn't
- NOTE Confidence: 0.8971473
- $00:29:06.586 \longrightarrow 00:29:08.128$ 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
- $00{:}29{:}10.822 \dashrightarrow 00{:}29{:}12.706$ the the thalamic mouse prefrontal
- NOTE Confidence: 0.8971473

 $00:29:12.706 \longrightarrow 00:29:14.576$ 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

 $00:29:19.250 \longrightarrow 00:29:21.600$ you able to see others here,

NOTE Confidence: 0.8971473

 $00:29:21.600 \longrightarrow 00:29:23.140$ so we definitely looked

NOTE Confidence: 0.81684583

 $00{:}29{:}23.140 \dashrightarrow 00{:}29{:}25.926$ 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

 $00:29:32.440 \longrightarrow 00:29:34.216$ 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

 $00:29:36.880 \longrightarrow 00:29:38.360$ 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

 $00:29:39.840 \longrightarrow 00:29:41.320$ So we kind of basically

NOTE Confidence: 0.81684583

 $00:29:41.320 \rightarrow 00:29:42.800$ parcel atede using an Atlas.

- NOTE Confidence: 0.81684583
- 00:29:42.800 --> 00:29:44.280 Different regions of the brain,

 $00{:}29{:}44{.}280 \dashrightarrow 00{:}29{:}46{.}023$ and so we didn't see any deficits

NOTE Confidence: 0.81684583

 $00{:}29{:}46.023 \dashrightarrow 00{:}29{:}47.161$ in inflamma cortical connections

NOTE Confidence: 0.81684583

 $00:29:47.161 \longrightarrow 00:29:48.876$ besides the connection to the

NOTE Confidence: 0.81684583

00:29:48.876 --> 00:29:49.905 medial prefrontal cortex.

NOTE Confidence: 0.81684583

 $00:29:49.910 \longrightarrow 00:29:51.750$ We did see a little bit of a

NOTE Confidence: 0.81684583

 $00:29:51.750 \rightarrow 00:29:53.749$ deficit in the orbitofrontal cortex,

NOTE Confidence: 0.81684583

 $00{:}29{:}53.750 \dashrightarrow 00{:}29{:}55.938$ which isn't shown here.

NOTE Confidence: 0.81684583

 $00:29:55.940 \longrightarrow 00:29:56.740$ What was really interesting

NOTE Confidence: 0.81684583

 $00:29:56.740 \longrightarrow 00:29:58.021$ is that it seems like both of

NOTE Confidence: 0.81684583

 $00:29:58.021 \longrightarrow 00:29:58.960$ these tracks ride together,

NOTE Confidence: 0.81684583

 $00:29:58.960 \longrightarrow 00:30:00.250$ 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

 $00:30:02.044 \rightarrow 00:30:03.240$ some issues separating them,

NOTE Confidence: 0.81684583

 $00:30:03.240 \longrightarrow 00:30:05.168$ but we didn't see any and I'll show

 $00:30:05.168 \rightarrow 00:30:06.605$ 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

 $00:30:08.433 \rightarrow 00:30:10.109$ in cortical connectivity

NOTE Confidence: 0.81684583

 $00:30:10.109 \rightarrow 00:30:11.785$ between the somatosensory cortex

NOTE Confidence: 0.81684583

 $00{:}30{:}11.785 \dashrightarrow 00{:}30{:}13.700$ with the motor cortex as well

NOTE Confidence: 0.81684583

 $00:30:13.700 \longrightarrow 00:30:14.892$ 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

 $00{:}30{:}16.694 \dashrightarrow 00{:}30{:}17.890$ in cortical amic tracks.

NOTE Confidence: 0.81684583

 $00{:}30{:}17.890 \dashrightarrow 00{:}30{:}19.690$ We also looked at dopaminergic input.

NOTE Confidence: 0.81684583

 $00{:}30{:}19.690 \dashrightarrow 00{:}30{:}21.358$ We actually initially thought we would

NOTE Confidence: 0.81684583

 $00{:}30{:}21.358 \dashrightarrow 00{:}30{:}23.206$ see a deficit in dopaminergic input

NOTE Confidence: 0.81684583

 $00{:}30{:}23.206 \dashrightarrow 00{:}30{:}25.240$ and made that underlies the positive

NOTE Confidence: 0.81684583

 $00:30:25.240 \rightarrow 00:30:26.778$ symptoms of schizophrenia and at

NOTE Confidence: 0.81684583

 $00:30:26.778 \rightarrow 00:30:28.986$ least at the ages that we looked at,

NOTE Confidence: 0.81684583

 $00:30:28.986 \longrightarrow 00:30:30.290$ 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
- $00{:}30{:}32{.}150 \dashrightarrow 00{:}30{:}34{.}298$ and I know times aren't senior

 $00{:}30{:}34.298 \dashrightarrow 00{:}30{:}36.240$ interest in the prefrontal cortex,

NOTE Confidence: 0.81684583

 $00:30:36.240 \longrightarrow 00:30:37.728$ so we also did.

NOTE Confidence: 0.8246989

 $00:30:40.330 \longrightarrow 00:30:42.986$ Yeah, so we also didn't show this slide,

NOTE Confidence: 0.8246989

 $00:30:42.990 \longrightarrow 00:30:45.342$ but we also did viral tracing

NOTE Confidence: 0.8246989

 $00:30:45.342 \longrightarrow 00:30:47.236$ from the prefrontal cortex and

NOTE Confidence: 0.8246989

 $00:30:47.236 \longrightarrow 00:30:49.284$ so this was in the so we did.

NOTE Confidence: 0.8246989

 $00:30:49.290 \longrightarrow 00:30:51.156$ This was in the adult where

NOTE Confidence: 0.8246989

 $00{:}30{:}51{.}156 \dashrightarrow 00{:}30{:}53{.}280$ we and this was nabbed car.

NOTE Confidence: 0.8246989

 $00{:}30{:}53.280 \dashrightarrow 00{:}30{:}55.184$ Doctor Carr was a postdoc in the

NOTE Confidence: 0.8246989

 $00:30:55.184 \longrightarrow 00:30:57.448$ 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

 $00{:}31{:}01{.}415 \dashrightarrow 00{:}31{:}02{.}875$ prefrontal cortex and whether

NOTE Confidence: 0.8246989

 $00:31:02.875 \dashrightarrow 00:31:04.332$ there are any specific deficits.

- $00{:}31{:}04{.}332 \dashrightarrow 00{:}31{:}06{.}454$ We saw a little bit of reduction
- NOTE Confidence: 0.8246989
- $00{:}31{:}06{.}454 \dashrightarrow 00{:}31{:}08{.}549$ connectivity between in the insula,
- NOTE Confidence: 0.8246989
- $00{:}31{:}08{.}550 \dashrightarrow 00{:}31{:}11{.}318$ but still once again the primary deficit was.
- NOTE Confidence: 0.8246989
- $00{:}31{:}11{.}320 \dashrightarrow 00{:}31{:}13{.}108$ The mediodorsal doubtful amic
- NOTE Confidence: 0.8246989
- $00{:}31{:}13.108 \dashrightarrow 00{:}31{:}15.343$ 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
- $00:31:19.550 \longrightarrow 00:31:23.089$ that slide so I can look at it is.
- NOTE Confidence: 0.803034
- $00:31:23.090 \rightarrow 00:31:25.316$ Is that also a reduced connectivity
- NOTE Confidence: 0.803034
- $00:31:25.316 \longrightarrow 00:31:27.410$ 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
- $00{:}31{:}31{.}260 \dashrightarrow 00{:}31{:}33{.}150$ that much, so I called that date.
- NOTE Confidence: 0.8113074
- $00:31:33.150 \longrightarrow 00:31:35.920$ We call that the insula.
- NOTE Confidence: 0.8113074
- $00:31:35.920 \longrightarrow 00:31:37.324$ There wasn't much connectivity that we
- NOTE Confidence: 0.8113074
- $00{:}31{:}37{.}324 \dashrightarrow 00{:}31{:}39{.}119$ could see in our tracing experiment,
- NOTE Confidence: 0.8113074
- $00:31:39.120 \rightarrow 00:31:41.523$ 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
- $00{:}31{:}43.078 \dashrightarrow 00{:}31{:}44.980$ of the slides so we can look

 $00:31:44.980 \longrightarrow 00:31:46.325$ at it more closely together.

NOTE Confidence: 0.8113074

 $00{:}31{:}46{.}330 \dashrightarrow 00{:}31{:}47{.}670$ 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

 $00:31:50.606 \dashrightarrow 00:31:53.602$ but you know, the problem is that we just.

NOTE Confidence: 0.8113074

 $00{:}31{:}53.602 \dashrightarrow 00{:}31{:}57.875$ 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

 $00:31:59.270 \rightarrow 00:32:03.630$ that for publication in particular, but.

NOTE Confidence: 0.8259022

 $00:32:03.630 \dashrightarrow 00:32:07.626$ Especially, you know, given the cortical

NOTE Confidence: 0.8259022

 $00{:}32{:}07.626$ --> $00{:}32{:}10.780$ cortical connections and 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

 $00{:}32{:}15{.}500 \dashrightarrow 00{:}32{:}18{.}326$ 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

 $00:32:21.161 \rightarrow 00:32:23.516$ more general than the thalamic,

NOTE Confidence: 0.828859

 $00{:}32{:}23.520 \dashrightarrow 00{:}32{:}27.299$ we really see that in the human, and

NOTE Confidence: 0.828859

 $00:32:27.300 \longrightarrow 00:32:30.126$ 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

 $00{:}32{:}38{.}320 \dashrightarrow 00{:}32{:}40{.}818$ Danny Weinberger at NIMH had

NOTE Confidence: 0.8823768

 $00:32:40.818 \longrightarrow 00:32:42.810$ a developmental theory about

NOTE Confidence: 0.8823768

 $00:32:42.810 \longrightarrow 00:32:44.810$ schizophrenia and that the

NOTE Confidence: 0.8823768

 $00{:}32{:}44{.}810 \dashrightarrow 00{:}32{:}47{.}805$ reason that it sort of showed

NOTE Confidence: 0.8823768

 $00:32:47.805 \longrightarrow 00:32:51.300$ up at around age 20 or so.

NOTE Confidence: 0.8823768

 $00:32:51.300 \longrightarrow 00:32:53.288$ Why is that? The

NOTE Confidence: 0.85358673

00:32:53.290 --> 00:32:55.282 kind of prefrontal inhibitory

NOTE Confidence: 0.85358673

 $00:32:55.282 \longrightarrow 00:32:56.776$ functions that usually

NOTE Confidence: 0.85358673

 $00:32:56.780 \rightarrow 00:33:00.780$ began to come online it around that time?

NOTE Confidence: 0.85358673

 $00:33:00.780 \dashrightarrow 00:33:05.169$ Somehow words and I was just curious.

NOTE Confidence: 0.85358673

 $00:33:05.170 \longrightarrow 00:33:08.840$ This is a naive question in terms of

 $00:33:08.840 \rightarrow 00:33:12.056$ my understanding of DTI and maybe this

NOTE Confidence: 0.85358673

 $00{:}33{:}12.056 \dashrightarrow 00{:}33{:}13.890$ 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

 $00:33:18.480 \longrightarrow 00:33:19.860$ connectivity between the

NOTE Confidence: 0.81070876

 $00:33:19.860 \dashrightarrow 00:33:22.151$ 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

 $00:33:23.990 \rightarrow 00:33:29.670$ or are they mostly kind of top down? And

NOTE Confidence: 0.8552397

 $00:33:29.670 \longrightarrow 00:33:32.005$ 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

 $00:33:34.807 \longrightarrow 00:33:38.540$ to the 70s and 80s with work by

NOTE Confidence: 0.8552397

 $00{:}33{:}38{.}540 \dashrightarrow 00{:}33{:}40{.}880$ Barbara Fish and Kornblatt and

NOTE Confidence: 0.8552397

 $00{:}33{:}40.880 \dashrightarrow 00{:}33{:}43.210$ 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

 $00{:}33{:}45{.}546 \dashrightarrow 00{:}33{:}47{.}410$ offspring of schizophrenic patients.

 $00:33:47.410 \longrightarrow 00:33:50.678$ 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

 $00:33:53.950 \rightarrow 00:33:55.354$ subtle neuropsychological deficits,

NOTE Confidence: 0.8552397

 $00{:}33{:}55{.}354 \dashrightarrow 00{:}33{:}57{.}689$ and I was wondering if

NOTE Confidence: 0.8552397

 $00:33:57.690 \longrightarrow 00:34:00.020$ you had thoughts about what

NOTE Confidence: 0.786532095

 $00:34:00.020 \rightarrow 00:34:02.320$ the? Underlying neural correlate's

NOTE Confidence: 0.786532095

 $00:34:02.320 \longrightarrow 00:34:05.706$ of those are. Definitely yeah,

NOTE Confidence: 0.786532095

 $00:34:05.706 \dashrightarrow 00:34:07.862$ and I think that Danny Weinberger's work.

NOTE Confidence: 0.786532095

 $00{:}34{:}07{.}870 \dashrightarrow 00{:}34{:}10.642$ I have a Erica. That's a slide from his.

NOTE Confidence: 0.786532095

 $00{:}34{:}10.650 \dashrightarrow 00{:}34{:}12.690$ So he really was the creator of this

NOTE Confidence: 0.786532095

 $00:34:12.690 \rightarrow 00:34:14.979$ theory of the neuro developmental theory.

NOTE Confidence: 0.786532095

 $00{:}34{:}14{.}980 \dashrightarrow 00{:}34{:}16{.}835$ And this is actually from one of

NOTE Confidence: 0.786532095

 $00{:}34{:}16.835 \dashrightarrow 00{:}34{:}18.777$ his more recent reviews and I

NOTE Confidence: 0.786532095

 $00:34{:}18.777 \dashrightarrow 00{:}34{:}20.229$ think that's really interesting.

NOTE Confidence: 0.786532095

 $00{:}34{:}20{.}230 \dashrightarrow 00{:}34{:}22{.}057$ And so I think the focus has

- NOTE Confidence: 0.786532095
- $00:34:22.057 \rightarrow 00:34:23.940$ been really in that adolescence,
- NOTE Confidence: 0.786532095
- $00:34:23.940 \longrightarrow 00:34:25.480$ and it makes sense, right?
- NOTE Confidence: 0.786532095
- $00:34:25.480 \longrightarrow 00:34:26.100$ Maybe there.
- NOTE Confidence: 0.786532095
- $00:34:26.100 \rightarrow 00:34:28.270$ I think it combines two theories together.
- NOTE Confidence: 0.786532095
- $00{:}34{:}28{.}270 \dashrightarrow 00{:}34{:}30{.}547$ I tried to touch on that and that what
- NOTE Confidence: 0.786532095
- $00:34:30.547 \rightarrow 00:34:33.279$ we see is that the brain is trying to
- NOTE Confidence: 0.786532095
- $00:34:33.279 \rightarrow 00:34:35.679$ compensate the brains trying to compensate.
- NOTE Confidence: 0.786532095
- $00{:}34{:}35{.}680 \dashrightarrow 00{:}34{:}36{.}610$ As I mentioned.
- NOTE Confidence: 0.786532095
- $00:34:36.610 \longrightarrow 00:34:37.914$ And then, once the.
- NOTE Confidence: 0.786532095
- $00:34:37.914 \longrightarrow 00:34:39.624$ The normal processes of development
- NOTE Confidence: 0.786532095
- $00{:}34{:}39{.}624 \dashrightarrow 00{:}34{:}41{.}360$ that occur during adolescence,
- NOTE Confidence: 0.786532095
- $00:34:41.360 \longrightarrow 00:34:42.880$ which strips away these
- NOTE Confidence: 0.786532095
- $00:34:42.880 \rightarrow 00:34:44.400$ connections at reduced plasticity.
- NOTE Confidence: 0.786532095
- $00{:}34{:}44{.}400 \dashrightarrow 00{:}34{:}47{.}060$ With the closure of these neural Nets,
- NOTE Confidence: 0.786532095
- $00:34:47.060 \rightarrow 00:34:49.340$ you lose that compens atory mechanisms,
- NOTE Confidence: 0.786532095

- $00{:}34{:}49{.}340 \dashrightarrow 00{:}34{:}52{.}364$ and then that kind of breaks
- NOTE Confidence: 0.786532095
- $00:34:52.364 \rightarrow 00:34:55.819$ through and leads to the symptoms.
- NOTE Confidence: 0.786532095
- $00:34:55.820 \rightarrow 00:34:57.170$ Maybe that's something that needs
- NOTE Confidence: 0.786532095
- $00:34:57.170 \longrightarrow 00:34:58.522$ to be really studied, right?
- NOTE Confidence: 0.786532095
- $00{:}34{:}58{.}522 \dashrightarrow 00{:}35{:}00{.}698$ I mean, I think this is still something
- NOTE Confidence: 0.786532095
- $00:35:00.698 \dashrightarrow 00:35:02.838$ that we're looking at in a mouse model.
- NOTE Confidence: 0.786532095
- $00{:}35{:}02{.}840 \dashrightarrow 00{:}35{:}04{.}840$ I kind of pull on a little adult
- NOTE Confidence: 0.786532095
- $00:35:04.840 \longrightarrow 00:35:07.159$ data to try to give it some support.
- NOTE Confidence: 0.786532095
- $00{:}35{:}07{.}160 \dashrightarrow 00{:}35{:}07{.}700$ You're actually,
- NOTE Confidence: 0.786532095
- $00:35:07.700 \rightarrow 00:35:09.860$ I'm not familiar with the papers like ADHD,
- NOTE Confidence: 0.786532095
- $00:35:09.860 \longrightarrow 00:35:11.480$ so definitely to look those up,
- NOTE Confidence: 0.786532095
- $00:35:11.480 \longrightarrow 00:35:13.100$ 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
- $00:35:14.180 \longrightarrow 00:35:14.990$ The frontal cortex,
- NOTE Confidence: 0.786532095
- $00:35:14.990 \rightarrow 00:35:17.150$ 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
- $00:35:17.698 \rightarrow 00:35:19.616$ it's thought to be like a dopaminergic

- 00:35:19.616 -> 00:35:20.928 deficit that occurs in ADHD.
- NOTE Confidence: 0.786532095
- $00:35:20.930 \rightarrow 00:35:22.550$ That's why stimulant works so well.
- NOTE Confidence: 0.786532095
- $00{:}35{:}22{.}550 \dashrightarrow 00{:}35{:}23{.}888$ And so I wonder what would
- NOTE Confidence: 0.786532095
- $00:35:23.888 \longrightarrow 00:35:25.240$ be the secondary changes in
- NOTE Confidence: 0.786532095
- $00:35:25.240 \rightarrow 00:35:26.058$ dopaminergic innervation?
- NOTE Confidence: 0.786532095
- 00:35:26.060 00:35:27.236 We looked kinda early,
- NOTE Confidence: 0.786532095
- $00{:}35{:}27{.}236 \dashrightarrow 00{:}35{:}27{.}530$ but.
- NOTE Confidence: 0.786532095
- $00{:}35{:}27{.}530 \dashrightarrow 00{:}35{:}29{.}258$ Is there some subtle change and
- NOTE Confidence: 0.786532095
- $00:35:29.258 \rightarrow 00:35:30.854$ that's why antipsychotics work in
- NOTE Confidence: 0.786532095
- $00:35:30.854 \rightarrow 00:35:32.039$ schizophrenia despite focusing?
- NOTE Confidence: 0.786532095
- $00{:}35{:}32.040 \dashrightarrow 00{:}35{:}34.287$ I'm focusing on a non dopaminergic circuit,
- NOTE Confidence: 0.786532095
- $00:35:34.290 \longrightarrow 00:35:36.336$ so that's something that I probably
- NOTE Confidence: 0.786532095
- $00:35:36.336 \longrightarrow 00:35:38.479$ have to read into a lot more,
- NOTE Confidence: 0.786532095
- $00:35:38.480 \rightarrow 00:35:40.268$ but it's really interesting
- NOTE Confidence: 0.786532095

 $00:35:40.268 \rightarrow 00:35:42.503$ of like 80s ADHD symptoms.

NOTE Confidence: 0.786532095

 $00{:}35{:}42{.}510 \dashrightarrow 00{:}35{:}44{.}900$ 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

 $00:35:47.280 \longrightarrow 00:35:49.666$ that ADHD involves impaired development

NOTE Confidence: 0.8132778

 $00:35:49.666 \rightarrow 00:35:52.051$ of the right inferior frontal,

NOTE Confidence: 0.8132778

 $00{:}35{:}52.051 \dashrightarrow 00{:}35{:}54.916$ and one wonders if somehow that's

NOTE Confidence: 0.8132778

 $00{:}35{:}54{.}916 \dashrightarrow 00{:}35{:}56{.}820$ associated with reduced retinoic

NOTE Confidence: 0.8132778

 $00:35:56.820 \longrightarrow 00:36:00.158$ acid in a mosaic sort of way.

NOTE Confidence: 0.8132778

 $00{:}36{:}00{.}160 \dashrightarrow 00{:}36{:}03{.}498$ I also wonder if is there any

NOTE Confidence: 0.8132778

 $00{:}36{:}03{.}498 \dashrightarrow 00{:}36{:}05{.}402$ evidence that inflammation reduces

NOTE Confidence: 0.8132778

 $00:36:05.402 \longrightarrow 00:36:07.788$ 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

 $00:36:09.700 \dashrightarrow 00:36:12.630$ insults in utero and schizophrenia.

NOTE Confidence: 0.8132778

00:36:12.630 --> 00:36:13.302 Definitely. I mean,

NOTE Confidence: 0.8132778

 $00{:}36{:}13.302 \dashrightarrow 00{:}36{:}14.422$ I think the inflammation thing

NOTE Confidence: 0.8132778

 $00:36:14.422 \rightarrow 00:36:15.891$ is is quite interesting, right?

- NOTE Confidence: 0.8132778
- $00:36:15.891 \longrightarrow 00:36:17.146$ How can we coincide both?

 $00{:}36{:}17.150 \dashrightarrow 00{:}36{:}19.103$ 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

 $00:36:21.160 \longrightarrow 00:36:22.415$ so that's something that could

NOTE Confidence: 0.8132778

 $00:36:22.415 \longrightarrow 00:36:23.168$ be quite interesting.

NOTE Confidence: 0.8132778

 $00{:}36{:}23.170 \dashrightarrow 00{:}36{:}24.676$ And what I didn't touch it.

NOTE Confidence: 0.8132778

 $00{:}36{:}24.680 \dashrightarrow 00{:}36{:}26.186$ I think we talked a little

NOTE Confidence: 0.8132778

 $00:36:26.186 \longrightarrow 00:36:27.190$ bit before a while ago.

NOTE Confidence: 0.8132778

 $00{:}36{:}27.190 \dashrightarrow 00{:}36{:}28.912$ We were talking about the RA paper

NOTE Confidence: 0.8132778

 $00:36:28.912 \longrightarrow 00:36:30.697$ is what we show in the human,

NOTE Confidence: 0.8132778

 $00{:}36{:}30{.}700 \dashrightarrow 00{:}36{:}32{.}206$ at least compared to the mouse.

NOTE Confidence: 0.8132778

 $00{:}36{:}32{.}210 \dashrightarrow 00{:}36{:}33{.}911$ And there's a great expansion of retinoic

NOTE Confidence: 0.8132778

 $00:36:33.911 \longrightarrow 00:36:35.469$ acid signaling in the frontal cortex,

NOTE Confidence: 0.8132778

 $00{:}36{:}35{.}470 \dashrightarrow 00{:}36{:}36{.}996$ so you could see similar deficits may

NOTE Confidence: 0.8132778

 $00{:}36{:}36{.}996 \dashrightarrow 00{:}36{:}38{.}766$ be in the human that you don't see

 $00:36:38.766 \rightarrow 00:36:40.197$ 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

 $00:36:42.063 \dashrightarrow 00:36:45.508$ Association aspects of the frontal lobe.

NOTE Confidence: 0.8132778

 $00:36:45.510 \longrightarrow 00:36:46.668$ Arctic, this was real.

NOTE Confidence: 0.8132778

 $00:36:46.668 \rightarrow 00:36:47.244$ Thank you.

NOTE Confidence: 0.8132778

 $00{:}36{:}47.244 \dashrightarrow 00{:}36{:}48.980$ This was really great and one

NOTE Confidence: 0.8132778

 $00:36:48.980 \longrightarrow 00:36:51.006$ of the things I love when you

NOTE Confidence: 0.8132778

 $00:36:51.006 \rightarrow 00:36:53.026$ talk is that you always get us

NOTE Confidence: 0.8132778

 $00{:}36{:}53.026 \dashrightarrow 00{:}36{:}54.760$ 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

 $00{:}36{:}57{.}070 \dashrightarrow 00{:}36{:}58{.}510$ question about your idea about

NOTE Confidence: 0.82324153

 $00{:}36{:}58{.}510 \dashrightarrow 00{:}37{:}00{.}830$ stress and if you think of you know,

NOTE Confidence: 0.82324153

 $00:37:00.830 \longrightarrow 00:37:02.558$ as you suggested, that you know

NOTE Confidence: 0.82324153

 $00:37:02.560 \dashrightarrow 00:37:05.885$ later around the skits of the brain.

NOTE Confidence: 0.82324153

 $00{:}37{:}05{.}890 \dashrightarrow 00{:}37{:}06{.}988$ Of the schizophrenic,

NOTE Confidence: 0.82324153

00:37:06.988 --> 00:37:09.178 you know just can't manage all

 $00{:}37{:}09{.}178 \dashrightarrow 00{:}37{:}12{.}100$ the all the stress and all the the

NOTE Confidence: 0.82324153

 $00:37:12.100 \dashrightarrow 00:37:14.290$ the bombardment of demands on it.

NOTE Confidence: 0.82324153

 $00{:}37{:}14.290 \dashrightarrow 00{:}37{:}15.379$ 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

 $00{:}37{:}20{.}940 \dashrightarrow 00{:}37{:}23{.}236$ not being exposed to as much stress

NOTE Confidence: 0.81314194

 $00:37:23.236 \rightarrow 00:37:25.217$ and having much more early supports.

NOTE Confidence: 0.81314194

 $00{:}37{:}25{.}217 \dashrightarrow 00{:}37{:}28{.}160$ You know the the work of us in the

NOTE Confidence: 0.81314194

 $00{:}37{:}28{.}244 \dashrightarrow 00{:}37{:}30{.}152$ field of child psychiatry that would

NOTE Confidence: 0.81314194

 $00{:}37{:}30{.}152 \dashrightarrow 00{:}37{:}32{.}790$ somehow prepare them in a way to have

NOTE Confidence: 0.81314194

 $00{:}37{:}32.790 \dashrightarrow 00{:}37{:}35.030$ kind of a more resilient brain for

NOTE Confidence: 0.81314194

 $00{:}37{:}35{.}030 \dashrightarrow 00{:}37{:}37{.}390$ later on and hopes of doing better.

NOTE Confidence: 0.81314194

 $00:37:37.390 \longrightarrow 00:37:38.710$ Does that make any

NOTE Confidence: 0.81314194

00:37:38.710 --> 00:37:40.018 sense to you? I

NOTE Confidence: 0.81314194

 $00:37:40.020 \longrightarrow 00:37:41.340$ really like that approach.
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

 $00:37:45.950 \dashrightarrow 00:37:48.078$ 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

 $00:37:49.764 \dashrightarrow 00:37:51.851$ expression on this other thing, but.

NOTE Confidence: 0.81314194

 $00{:}37{:}51{.}851 \dashrightarrow 00{:}37{:}54{.}028$ I think we're quite far from that,

NOTE Confidence: 0.81314194

 $00{:}37{:}54.030 \dashrightarrow 00{:}37{:}55.405$ so building these skills very

NOTE Confidence: 0.81314194

 $00:37:55.405 \rightarrow 00:37:57.300$ early in these high risk children,

NOTE Confidence: 0.81314194

 $00:37:57.300 \dashrightarrow 00:37:58.780$ especially something like you know NOTE Confidence: 0.81314194

 $00:37:58.780 \rightarrow 00:38:00.240$ 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

 $00:38:02.342 \longrightarrow 00:38:04.148$ of interventions is that the risk

NOTE Confidence: 0.81314194

 $00:38:04.148 \longrightarrow 00:38:05.616$ profile is really low, right?

NOTE Confidence: 0.81314194

00:38:05.616 --> 00:38:07.096 If we're stimming a circuit,

NOTE Confidence: 0.81314194

 $00{:}38{:}07{.}100 \dashrightarrow 00{:}38{:}09{.}137$ or we're giving retinoic acid or work

NOTE Confidence: 0.81314194

 $00:38:09.137 \rightarrow 00:38:10.668$ virally infecting the brain, right?

00:38:10.668 --> 00:38:12.516 You have to be pretty confident

NOTE Confidence: 0.81314194

 $00:38:12.516 \rightarrow 00:38:14.615$ 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

 $00{:}38{:}17{.}790 \dashrightarrow 00{:}38{:}19{.}942$ And so I like building on these skills

NOTE Confidence: 0.81314194

 $00{:}38{:}19{.}942 \dashrightarrow 00{:}38{:}21{.}888$ because if this child doesn't convert

NOTE Confidence: 0.81314194

 $00:38:21.888 \rightarrow 00:38:24.290$ to psychosis even in the prodromal stage.

NOTE Confidence: 0.81314194

 $00{:}38{:}24{.}290 \dashrightarrow 00{:}38{:}26{.}586$ 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

 $00:38:28.360 \rightarrow 00:38:30.551$ and so building skills that I think

NOTE Confidence: 0.81314194

 $00:38:30.551 \dashrightarrow 00:38:32.605$ could help this child leaders and

NOTE Confidence: 0.81314194

 $00{:}38{:}32.605 \dashrightarrow 00{:}38{:}34.705$ 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

 $00:38:36.823 \rightarrow 00:38:38.187$ of severity of symptoms.

NOTE Confidence: 0.81314194

 $00:38:38.190 \rightarrow 00:38:42.168$ I think it just makes a ton of sense.

- $00:38:42.170 \longrightarrow 00:38:43.019$ It just fits
- NOTE Confidence: 0.8538997
- $00:38:43.020 \rightarrow 00:38:44.987$ so nicely with her model of lowering.
- NOTE Confidence: 0.8538997
- $00{:}38{:}44{.}990 \dashrightarrow 00{:}38{:}46{.}118$ You know inflammatory insult
- NOTE Confidence: 0.8538997
- $00:38:46.118 \longrightarrow 00:38:47.246$ from stress and things.
- NOTE Confidence: 0.8538997
- $00{:}38{:}47.250 \dashrightarrow 00{:}38{:}48.656$ So thank you very much.
- NOTE Confidence: 0.8538997
- $00{:}38{:}48.656 \dashrightarrow 00{:}38{:}52.050$ I really enjoyed this very much.
- NOTE Confidence: 0.8538997
- 00:38:52.050 --> 00:38:52.738 Hi Christine.
- NOTE Confidence: 0.8538997
- $00:38:52.738 \longrightarrow 00:38:54.458$ Hi, this is Flora vaccarino.
- NOTE Confidence: 0.8538997
- $00{:}38{:}54{.}460 \dashrightarrow 00{:}38{:}57{.}060$ I have a question very interesting so can
- NOTE Confidence: 0.8538997
- $00{:}38{:}57{.}060 \dashrightarrow 00{:}38{:}59{.}959$ 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
- $00{:}39{:}02{.}370 \dashrightarrow 00{:}39{:}05{.}706$ Do you think that there is a relative
- NOTE Confidence: 0.8538997
- $00:39:05.706 \longrightarrow 00:39:08.050$ 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
- $00:39:09.542 \rightarrow 00:39:11.780$ stunts the growth of this connection
- NOTE Confidence: 0.8538997
- $00:39:11.838 \longrightarrow 00:39:13.868$ downstream connection to that Alamos.

- NOTE Confidence: 0.8538997
- $00:39:13.870 \longrightarrow 00:39:16.600$ Do you think there is a chemoattractant

00:39:16.600 --> 00:39:19.685 role for 18 OIC acid in attracting

NOTE Confidence: 0.8538997

 $00:39:19.685 \longrightarrow 00:39:22.439$ those connections in that alamaze or?

NOTE Confidence: 0.8538997

 $00:39:22.440 \rightarrow 00:39:25.120$ Or what do you think is going on?

NOTE Confidence: 0.8538997

 $00{:}39{:}25{.}120 \dashrightarrow 00{:}39{:}27{.}160$ Because retinoic acid is thought to

NOTE Confidence: 0.8538997

 $00{:}39{:}27.160 \dashrightarrow 00{:}39{:}29.552$ be a very important more for John

NOTE Confidence: 0.8538997

 $00:39:29.552 \rightarrow 00:39:31.490$ earlier on to write much earlier,

NOTE Confidence: 0.8538997

 $00:39:31.490 \longrightarrow 00:39:33.765$ 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

 $00:39:35.510 \rightarrow 00:39:37.520$ where here you're talking about something

NOTE Confidence: 0.8538997

 $00:39:37.520 \dashrightarrow 00:39:38.860$ 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

 $00{:}39{:}43{.}020 \dashrightarrow 00{:}39{:}45{.}516$ Something that netted an in the lab is

NOTE Confidence: 0.78017604

 $00{:}39{:}45{.}516 \dashrightarrow 00{:}39{:}47{.}392$ talked about, kind of retinoic acid.

NOTE Confidence: 0.78017604

 $00:39{:}47.392 \dashrightarrow 00{:}39{:}48.957$ Historically we have been thought

 $00:39:48.957 \longrightarrow 00:39:50.816$ of as a post theorizing factor,

NOTE Confidence: 0.78017604

 $00:39:50.820 \longrightarrow 00:39:52.116$ especially in the hindbrain,

NOTE Confidence: 0.78017604

 $00{:}39{:}52{.}116 \dashrightarrow 00{:}39{:}54{.}706$ but I think then it has a more

NOTE Confidence: 0.78017604

 $00:39:54.706 \rightarrow 00:39:56.434$ 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

 $00:39:59.240 \longrightarrow 00:40:00.266$ that retinoic acid.

NOTE Confidence: 0.78017604

 $00:40:00.266 \longrightarrow 00:40:00.950$ Is pleiotropic.

NOTE Confidence: 0.78017604

00:40:00.950 --> 00:40:02.685 It's involved in almost every

NOTE Confidence: 0.78017604

 $00{:}40{:}02.685 \dashrightarrow 00{:}40{:}04.420$ process of brain development and

NOTE Confidence: 0.78017604

 $00{:}40{:}04{.}483 \dashrightarrow 00{:}40{:}06{.}331$ development overall and so I guess NOTE Confidence: 0.78017604

 $00:40:06.331 \rightarrow 00:40:08.171$ to answer the couple questions and NOTE Confidence: 0.78017604

 $00{:}40{:}08.171 \dashrightarrow 00{:}40{:}10.363$ remind me if I missed some of this. NOTE Confidence: 0.78017604

 $00{:}40{:}10.370 \dashrightarrow 00{:}40{:}12.466$ First, what we show in the paper is NOTE Confidence: 0.78017604

 $00{:}40{:}12.466 \dashrightarrow 00{:}40{:}14.368$ that retinoic acid during mid field

NOTE Confidence: 0.78017604

 $00:40:14.368 \rightarrow 00:40:15.692$ development is tightly regulated

NOTE Confidence: 0.78017604

 $00:40:15.692 \rightarrow 00:40:17.589$ to just the prefrontal cortex.

 $00:40:17.590 \longrightarrow 00:40:19.160$ So there's actually the sink,

NOTE Confidence: 0.78017604

 $00:40:19.160 \longrightarrow 00:40:21.393$ so there's 626B1 which is a retinoic

NOTE Confidence: 0.78017604

 $00:40:21.393 \longrightarrow 00:40:23.006$ acid degrading enzyme which is

NOTE Confidence: 0.78017604

 $00:40:23.006 \longrightarrow 00:40:24.788$ great enriched in the medial pre

NOTE Confidence: 0.78017604

 $00{:}40{:}24.788 \dashrightarrow 00{:}40{:}26.379$ installed in the motor cortex.

NOTE Confidence: 0.78017604

 $00:40:26.380 \longrightarrow 00:40:28.088$ So that kind of restricts it to

NOTE Confidence: 0.78017604

 $00{:}40{:}28.088 \dashrightarrow 00{:}40{:}30.195$ and then we also showed various

NOTE Confidence: 0.78017604

 $00:40:30.195 \longrightarrow 00:40:31.947$ 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

 $00{:}40{:}33{.}984 \dashrightarrow 00{:}40{:}35{.}988$ to the parenchyma itself as well

NOTE Confidence: 0.78017604

 $00{:}40{:}35{.}988 \dashrightarrow 00{:}40{:}38{.}018$ 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

 $00{:}40{:}39{.}912 \dashrightarrow 00{:}40{:}41{.}795$ seem to be expressing a retinoic

NOTE Confidence: 0.78017604

 $00{:}40{:}41.795 \dashrightarrow 00{:}40{:}42.800$ acid synthesizing enzyme.

NOTE Confidence: 0.78017604

 $00:40:42.800 \longrightarrow 00:40:44.810$ So it seems to tightly restrict

 $00:40:44.866 \longrightarrow 00:40:46.391$ it that mechanism that first

NOTE Confidence: 0.78017604

 $00:40:46.391 \longrightarrow 00:40:47.916$ question you asked is something

NOTE Confidence: 0.78017604

 $00:40:47.967 \longrightarrow 00:40:49.387$ that I'm very interested in.

NOTE Confidence: 0.78017604

 $00:40:49.390 \rightarrow 00:40:51.178$ So what is retinoic acid actually

NOTE Confidence: 0.78017604

 $00:40:51.178 \rightarrow 00:40:52.870$ doing in making this circuit?

NOTE Confidence: 0.78017604

 $00{:}40{:}52.870 \dashrightarrow 00{:}40{:}55.200$ And So what we looked at is so we have

NOTE Confidence: 0.78017604

 $00{:}40{:}55{.}263 \dashrightarrow 00{:}40{:}57{.}630$ we did RNA seek in our mouse model where

NOTE Confidence: 0.78017604

 $00{:}40{:}57.630 \dashrightarrow 00{:}41{:}00.167$ 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

 $00:41:03.772 \longrightarrow 00:41:04.816$ medial prefrontal cortex.

NOTE Confidence: 0.78017604

 $00{:}41{:}04{.}820 \dashrightarrow 00{:}41{:}06{.}512$ Orbital frontal cortex in the motor

NOTE Confidence: 0.78017604

 $00{:}41{:}06{.}512 \dashrightarrow 00{:}41{:}08{.}304$ cortex and looked at what's different

NOTE Confidence: 0.78017604

 $00{:}41{:}08{.}304 \dashrightarrow 00{:}41{:}10{.}453$ between the control and the wild type.

NOTE Confidence: 0.78017604

 $00:41:10.460 \longrightarrow 00:41:12.836$ And we found a lot of target genes,

NOTE Confidence: 0.78017604

 $00:41:12.840 \rightarrow 00:41:13.869$ specifically adhesion molecules

- NOTE Confidence: 0.78017604
- $00{:}41{:}13.869 \dashrightarrow 00{:}41{:}15.584$ instead of chemo attractants that
- NOTE Confidence: 0.78017604
- $00{:}41{:}15{.}584 \dashrightarrow 00{:}41{:}17{.}287$ 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
- $00:41:19.450 \longrightarrow 00:41:21.447$ general interest is in cortical connectivity,
- NOTE Confidence: 0.78017604
- $00:41:21.450 \rightarrow 00:41:22.822$ especially long range connectivity,
- NOTE Confidence: 0.78017604
- $00:41:22.822 \rightarrow 00:41:25.228$ and so we're I'm thinking is that
- NOTE Confidence: 0.78017604
- $00{:}41{:}25{.}228 \dashrightarrow 00{:}41{:}27{.}251$ these axons are able to navigate the
- NOTE Confidence: 0.78017604
- $00{:}41{:}27{.}251 \dashrightarrow 00{:}41{:}29{.}121$ striatum and all these cues there to
- NOTE Confidence: 0.78017604
- $00:41:29.121 \longrightarrow 00:41:30.908$ get to the doorstep of the cortex,
- NOTE Confidence: 0.78017604
- $00:41:30.908 \rightarrow 00:41:32.552$ but they're not getting that final
- NOTE Confidence: 0.78017604
- $00:41:32.552 \rightarrow 00:41:33.477$ chemoattractant that retinoic
- NOTE Confidence: 0.78017604
- $00{:}41{:}33{.}477 \dashrightarrow 00{:}41{:}34{.}817$ acid is specifically regulating,
- NOTE Confidence: 0.78017604
- $00:41:34.820 \rightarrow 00:41:37.298$ 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
- $00{:}41{:}39{.}478 \dashrightarrow 00{:}41{:}42{.}298$ actually kind of loses it and I forgot
- NOTE Confidence: 0.78017604

 $00:41:42.298 \rightarrow 00:41:44.780$ 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

 $00:41:46.140 \longrightarrow 00:41:47.160$ 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

 $00:41:50.560 \longrightarrow 00:41:52.260$ Yeah doctrina, that's a vacuum.

NOTE Confidence: 0.78017604

 $00:41:52.260 \longrightarrow 00:41:53.808$ That's a great question,

NOTE Confidence: 0.78017604

 $00{:}41{:}53{.}808 \dashrightarrow 00{:}41{:}55{.}743$ and that's something that we're

NOTE Confidence: 0.78017604

 $00:41:55.743 \rightarrow 00:41:58.107$ really careful to show in the paper

NOTE Confidence: 0.78017604

 $00{:}41{:}58{.}107 \dashrightarrow 00{:}42{:}00{.}051$ that we're not altering cell number

NOTE Confidence: 0.78017604

 $00{:}42{:}00{.}051 \dashrightarrow 00{:}42{:}02{.}158$ or brain size or all these other

NOTE Confidence: 0.78017604

 $00{:}42{:}02{.}158 \dashrightarrow 00{:}42{:}04{.}065$ kind of factors that retinoic acid

NOTE Confidence: 0.78017604

 $00:42:04.065 \rightarrow 00:42:06.458$ is involved in seems to be very

NOTE Confidence: 0.78017604

 $00{:}42{:}06{.}458 \dashrightarrow 00{:}42{:}08{.}636$ selectively involved in kind of circuit.

NOTE Confidence: 0.78017604

 $00{:}42{:}08.640 \dashrightarrow 00{:}42{:}11.056$ 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
- $00:42:13.083 \rightarrow 00:42:15.120$ there asking the obvious question.

00:42:15.120 --> 00:42:16.600 Organize stuff.

NOTE Confidence: 0.79421383

 $00:42:16.600 \longrightarrow 00:42:18.301$ 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

 $00:42:20.226 \longrightarrow 00:42:21.616$ So this is something that

NOTE Confidence: 0.78806835

 $00:42:21.620 \longrightarrow 00:42:22.748$ we're really interested in.

NOTE Confidence: 0.78806835

 $00{:}42{:}22.748 \dashrightarrow 00{:}42{:}25.283$ I I know that you're so far ahead in

NOTE Confidence: 0.78806835

 $00{:}42{:}25{.}283 \dashrightarrow 00{:}42{:}27{.}103$ the field and we've been reading a

NOTE Confidence: 0.78806835

 $00{:}42{:}27.164 \dashrightarrow 00{:}42{:}29.159$ lot of assembly papers in the paper.

NOTE Confidence: 0.78806835

 $00:42:29.160 \longrightarrow 00:42:30.833$ I was really like the Pasco paper

NOTE Confidence: 0.78806835

 $00{:}42{:}30{.}833 \dashrightarrow 00{:}42{:}32{.}611$ 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

 $00:42:33.620 \longrightarrow 00:42:34.700$ It's really interesting that

NOTE Confidence: 0.78806835

 $00:42:34.700 \longrightarrow 00:42:36.050$ that connectivity can then maybe

- $00:42:36.050 \rightarrow 00:42:36.969$ alter the properties,
- NOTE Confidence: 0.78806835
- $00{:}42{:}36{.}970 \dashrightarrow 00{:}42{:}39{.}077$ so I think that's a great mechanism
- NOTE Confidence: 0.78806835
- $00{:}42{:}39{.}077 \dashrightarrow 00{:}42{:}40{.}523$ to study specifically human if
- NOTE Confidence: 0.78806835
- $00{:}42{:}40{.}523 \dashrightarrow 00{:}42{:}41{.}987$ 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
- $00{:}42{:}43.106 \dashrightarrow 00{:}42{:}45.060$ 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
- $00:42:49.617 \rightarrow 00:42:52.749$ developing a system where you can develop,
- NOTE Confidence: 0.8024582
- $00:42:52.750 \longrightarrow 00:42:54.940$ organize from different brain regions
- NOTE Confidence: 0.8024582
- $00:42:54.940 \rightarrow 00:42:56.692$ using gradients of morphogens,
- NOTE Confidence: 0.8024582
- $00:42:56.700 \longrightarrow 00:43:00.092$ 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
- $00:43:02.362 \rightarrow 00:43:05.032$ particles system that you could use.
- NOTE Confidence: 0.8024582
- $00:43:05.040 \longrightarrow 00:43:06.351$ That sounds great.
- NOTE Confidence: 0.8024582
- 00:43:06.351 --> 00:43:08.550 Yeah, 'cause it is. Great
- NOTE Confidence: 0.8024582
- $00:43:08.550 \longrightarrow 00:43:09.870$ idea. Yeah thank

00:43:09.870 --> 00:43:14.385 can I can I? I'm delighted to see how

NOTE Confidence: 0.8024582

 $00{:}43{:}14.385 \dashrightarrow 00{:}43{:}16.697$ much interest your talk has taken and

NOTE Confidence: 0.8024582

 $00{:}43{:}16.697 \dashrightarrow 00{:}43{:}18.846$ 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

 $00{:}43{:}21{.}413 \dashrightarrow 00{:}43{:}23{.}660$ because one of the things then Karthik.

NOTE Confidence: 0.8024582

 $00{:}43{:}23.660 \dashrightarrow 00{:}43{:}25.646$ We've had the pleasure of working

NOTE Confidence: 0.8024582

 $00:43:25.646 \longrightarrow 00:43:27.942$ together and I've seen you as a

NOTE Confidence: 0.8024582

 $00:43:27.942 \rightarrow 00:43:29.754$ clinician and your clinician as well.

NOTE Confidence: 0.8024582

 $00{:}43{:}29.760 \dashrightarrow 00{:}43{:}32.007$ 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

 $00:43:32.970 \longrightarrow 00:43:34.896$ which is something that we see

NOTE Confidence: 0.8024582

 $00{:}43{:}34{.}896 \dashrightarrow 00{:}43{:}37{.}470$ 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

 $00{:}43{:}39{.}391 \dashrightarrow 00{:}43{:}41{.}317$ thank you for mentioning gating systems.

NOTE Confidence: 0.8024582

 $00:43:41.320 \rightarrow 00:43:43.735$ You know there's a question about gating.

00:43:43.740 --> 00:43:46.372 I want to call your attention and to

NOTE Confidence: 0.8024582

 $00{:}43{:}46{.}372 \dashrightarrow 00{:}43{:}48{.}333$ every one 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

 $00:43:50.793 \rightarrow 00:43:53.198$ 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

 $00{:}43{:}55{.}402 \dashrightarrow 00{:}43{:}57{.}117$ and what's interesting is both

NOTE Confidence: 0.8024582

 $00{:}43{:}57{.}117 \dashrightarrow 00{:}43{:}58{.}492$ the experience of schizophrenia.

NOTE Confidence: 0.8024582

 $00:43:58.492 \rightarrow 00:44:01.574$ But this is a family that was followed very,

NOTE Confidence: 0.8024582

 $00{:}44{:}01{.}580 \dashrightarrow 00{:}44{:}03{.}290$ very closely by Robert Friedman.

NOTE Confidence: 0.8024582

00:44:03.290 --> 00:44:03.922 You know,

NOTE Confidence: 0.8024582

 $00{:}44{:}03{.}922 \dashrightarrow 00{:}44{:}05{.}502$ the great psychiatrist in Colorado

NOTE Confidence: 0.8024582

 $00:44:05.502 \longrightarrow 00:44:07.647$ who was the pioneer of gating

NOTE Confidence: 0.8024582

 $00:44:07.647 \longrightarrow 00:44:08.778$ 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

 $00{:}44{:}10.834 \dashrightarrow 00{:}44{:}12.554$ about gating and then moving

NOTE Confidence: 0.8024582

 $00:44:12.554 \rightarrow 00:44:14.208$ in the humanoid direction.

- NOTE Confidence: 0.8024582
- 00:44:14.210 $\operatorname{-->}$ 00:44:16.091 I wanna after you answer that I want to

00:44:16.091 --> 00:44:18.158 call our attention to Doctor Yankee Yazgan,

NOTE Confidence: 0.8024582

 $00:44:18.160 \longrightarrow 00:44:19.684$ who is our colleague from Turkey

NOTE Confidence: 0.8024582

 $00:44:19.684 \longrightarrow 00:44:21.459$ who is joining us here and he

NOTE Confidence: 0.8024582

 $00{:}44{:}21{.}459 \dashrightarrow 00{:}44{:}23{.}097$ will have a comment after you met.

NOTE Confidence: 0.8024582

 $00{:}44{:}23.100 \dashrightarrow 00{:}44{:}24.285$ 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: 0.839699199999999

 $00{:}44{:}26.810 \dashrightarrow 00{:}44{:}28.448$ it first before I actually reflect on

NOTE Confidence: 0.839699199999999

 $00:44:28.448 \longrightarrow 00:44:30.747$ some of my time back on when he wanted

NOTE Confidence: 0.839699199999999

 $00{:}44{:}30{.}747 \dashrightarrow 00{:}44{:}32{.}545$ something that did strike me when I

NOTE Confidence: 0.83969919999999

 $00{:}44{:}32{.}545 \dashrightarrow 00{:}44{:}34{.}211$ was there 'cause we were actually doing

NOTE Confidence: 0.839699199999999

 $00{:}44{:}34{.}220 \dashrightarrow 00{:}44{:}36{.}434$ the work while I was on when he won.

NOTE Confidence: 0.839699199999999

00:44:36.440 --> 00:44:38.501 My last run. Was that some of the kids

 $00:44:38.501 \rightarrow 00:44:40.357$ that come in with early onset psychosis

NOTE Confidence: 0.839699199999999

 $00:44:40.357 \rightarrow 00:44:42.370$ or a couple of stick in my head.

NOTE Confidence: 0.83969919999999

00:44:42.370 -> 00:44:44.236 I won't give the names obviously.

NOTE Confidence: 0.839699199999999

 $00:44:44.240 \rightarrow 00:44:45.950$ But they showed distinct low IQ's.

NOTE Confidence: 0.839699199999999

00:44:45.950 --> 00:44:47.882 I think they were running in the

NOTE Confidence: 0.839699199999999

 $00{:}44{:}47.882 \dashrightarrow 00{:}44{:}50.549$ 60s and 70s and so that kind of was

NOTE Confidence: 0.839699199999999

 $00:44:50.549 \rightarrow 00:44:52.607$ something that I always kind of brewing

NOTE Confidence: 0.839699199999999

00:44:52.607 - 00:44:54.785 that idea as as I was going there.

NOTE Confidence: 0.839699199999999

 $00{:}44{:}54{.}785 \dashrightarrow 00{:}44{:}56{.}495$ Yet gaining is a really interesting

NOTE Confidence: 0.83969919999999

 $00:44:56.495 \rightarrow 00:44:57.065$ question right?

NOTE Confidence: 0.839699199999999

 $00:44:57.070 \rightarrow 00:44:58.490$ Especially for positive symptoms, right?

NOTE Confidence: 0.839699199999999

00:44:58.490 --> 00:44:59.920 Can you gate sensory information?

NOTE Confidence: 0.839699199999999

 $00:44:59.920 \longrightarrow 00:45:01.630$ That's going into the cortex right?

NOTE Confidence: 0.83969919999999

 $00{:}45{:}01{.}630 \dashrightarrow 00{:}45{:}03{.}910$ And and there's great work by Al Powers.

NOTE Confidence: 0.839699199999999

 $00:45:03.910 \longrightarrow 00:45:05.330$ Who's in the adult Department?

NOTE Confidence: 0.83969919999999

 $00:45:05.330 \rightarrow 00:45:07.325$ He's a young faculty of the question.

- NOTE Confidence: 0.83969919999999
- $00:45:07.330 \rightarrow 00:45:09.171$ It is actually the information that's going
- NOTE Confidence: 0.839699199999999
- $00:45:09.171 \longrightarrow 00:45:11.597$ in from the founders of the cortex incorrect?
- NOTE Confidence: 0.839699199999999
- $00:45:11.600 \rightarrow 00:45:13.025$ Or is the cortex processing
- NOTE Confidence: 0.839699199999999
- $00:45:13.025 \rightarrow 00:45:13.880$ that information incorrectly?
- NOTE Confidence: 0.839699199999999
- $00:45:13.880 \longrightarrow 00:45:15.806$ And I think that kind of.
- NOTE Confidence: 0.839699199999999
- 00:45:15.810 --> 00:45:18.082 Really eludes to kind of what I was
- NOTE Confidence: 0.839699199999999
- $00:45:18.082 \rightarrow 00:45:19.996$ saying without trying to put my foot
- NOTE Confidence: 0.839699199999999
- $00:45:19.996 \rightarrow 00:45:22.157$ down that as the you're getting abnormal
- NOTE Confidence: 0.83969919999999
- $00:45:22.157 \rightarrow 00:45:24.207$ extra connectivity with these sensory
- NOTE Confidence: 0.83969919999999
- $00:45:24.207 \rightarrow 00:45:26.724$ areas between the thalamus in the cortex,
- NOTE Confidence: 0.839699199999999
- $00:45:26.724 \rightarrow 00:45:28.650$ so maybe you're getting too much
- NOTE Confidence: 0.839699199999999
- $00{:}45{:}28.707 \dashrightarrow 00{:}45{:}30.954$ information going in and you're not able
- NOTE Confidence: 0.83969919999999
- $00:45:30.954 \rightarrow 00:45:32.902$ to really parse what's truly occurring
- NOTE Confidence: 0.83969919999999
- 00:45:32.902 --> 00:45:35.391 as well as a kind of background noise,
- NOTE Confidence: 0.839699199999999
- $00:45:35.391 \rightarrow 00:45:38.280$ and that could be a nice kind of circuit.
- NOTE Confidence: 0.839699199999999

 $00:45:38.280 \longrightarrow 00:45:40.122$ Kind of psychobiology kind of thought

NOTE Confidence: 0.83969919999999

 $00:45:40.122 \rightarrow 00:45:42.726$ about how you create a hallucination or a

NOTE Confidence: 0.839699199999999

 $00:45:42.726 \longrightarrow 00:45:44.700$ delusion or disorganized thought as well.

NOTE Confidence: 0.839699199999999

00:45:44.700 - 00:45:46.390 Any of the positive symptoms.

NOTE Confidence: 0.839699199999999

 $00{:}45{:}46{.}390 \dashrightarrow 00{:}45{:}47{.}368$ To be honest,

NOTE Confidence: 0.7796665

 $00:45:47.370 \longrightarrow 00:45:48.990$ 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

 $00:45:50.940 \rightarrow 00:45:52.895$ then to France. So Yankee asking,

NOTE Confidence: 0.7796665

 $00{:}45{:}52.895 \dashrightarrow 00{:}45{:}54.840$ and then Lilia Benoit Yankee, please.

NOTE Confidence: 0.86525387

 $00:45:57.210 \longrightarrow 00:45:58.760$ Just hi there everybody.

NOTE Confidence: 0.86525387

 $00{:}45{:}58{.}760 \dashrightarrow 00{:}46{:}01{.}478$ So glad to be back in New

NOTE Confidence: 0.86525387

 $00{:}46{:}01{.}480 \dashrightarrow 00{:}46{:}03{.}808$ Haven, at least for a couple

NOTE Confidence: 0.86525387

 $00:46:03.810 \longrightarrow 00:46:05.750$ of weeks after 25 years.

NOTE Confidence: 0.86525387

 $00:46:05.750 \longrightarrow 00:46:07.686$ So I've been following what's

NOTE Confidence: 0.86525387

 $00{:}46{:}07.686 \dashrightarrow 00{:}46{:}10.012$ going on at child study closely,

NOTE Confidence: 0.86525387

 $00{:}46{:}10.012 \dashrightarrow 00{:}46{:}13.120$ but haven't had the chance to be in

00:46:13.120 --> 00:46:16.848 grand rounds for awhile. Thanks for.

NOTE Confidence: 0.86525387

 $00{:}46{:}16.850 \dashrightarrow 00{:}46{:}19.703$ Including me and great to see

NOTE Confidence: 0.86525387

 $00:46:19.703 \rightarrow 00:46:22.075$ friend friendly faces and friends.

NOTE Confidence: 0.86525387

 $00:46:22.075 \longrightarrow 00:46:24.450$ I'm really impressed by the

NOTE Confidence: 0.86525387

 $00{:}46{:}24.450 \dashrightarrow 00{:}46{:}27.775$ quality of the work that says that

NOTE Confidence: 0.86525387

 $00:46:27.775 \longrightarrow 00:46:30.626$ seemed to that will be changing

NOTE Confidence: 0.86525387

 $00:46:30.626 \rightarrow 00:46:33.950$ the way we deal with these cases,

NOTE Confidence: 0.86525387

 $00{:}46{:}33{.}950 \dashrightarrow 00{:}46{:}36{.}802$ but so if you questions or

NOTE Confidence: 0.86525387

 $00:46:36.802 \longrightarrow 00:46:38.230$ minor questions probably.

NOTE Confidence: 0.86525387

 $00{:}46{:}38{.}230 \dashrightarrow 00{:}46{:}41{.}080$ I'm also I have been interested

NOTE Confidence: 0.86525387

 $00{:}46{:}41.080 \dashrightarrow 00{:}46{:}43.930$ in the neuromotor signs as an

NOTE Confidence: 0.86525387

 $00:46:43.930 \longrightarrow 00:46:45.830$ indicator of future psychopathology

NOTE Confidence: 0.86525387

 $00:46:45.830 \longrightarrow 00:46:49.448$ an my my question would be.

NOTE Confidence: 0.86525387

 $00{:}46{:}49{.}450 \dashrightarrow 00{:}46{:}53{.}272$ How would how is the the diagnostic

NOTE Confidence: 0.86525387

 $00{:}46{:}53.272 \dashrightarrow 00{:}46{:}54.910$ specifity established either

 $00:46:54.997 \longrightarrow 00:46:57.589$ schizophrenia or as pergers or

NOTE Confidence: 0.86525387

 $00:46:57.589 \longrightarrow 00:47:00.580$ 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

 $00{:}47{:}04.044 \dashrightarrow 00{:}47{:}06.884$ with ASD or with another

NOTE Confidence: 0.86525387

 $00{:}47{:}06{.}884 \dashrightarrow 00{:}47{:}08{.}790$ new developmental disorder

NOTE Confidence: 0.8256377

 $00{:}47{:}08.790 \dashrightarrow 00{:}47{:}12.890$ on neurological terms? Thank you party, nice

NOTE Confidence: 0.8256377

 $00:47:12.890 \longrightarrow 00:47:17.786$ nice meeting you by the way.

NOTE Confidence: 0.8256377

 $00:47:17.790 \longrightarrow 00:47:19.050$ 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

 $00:47:20.999 \rightarrow 00:47:22.407$ Walker specifically said that

NOTE Confidence: 0.8256377

 $00:47:22.407 \longrightarrow 00:47:24.165$ this is not specific, right?

NOTE Confidence: 0.8256377

 $00{:}47{:}24.165 \dashrightarrow 00{:}47{:}26.235$ Like there, other disorders ASD that

NOTE Confidence: 0.8256377

 $00{:}47{:}26.235 \dashrightarrow 00{:}47{:}28.180$ showed these same type of things.

NOTE Confidence: 0.8256377

 $00{:}47{:}28.180 \dashrightarrow 00{:}47{:}31.350$ So I think the diagnostic.

NOTE Confidence: 0.8256377

 $00{:}47{:}31{.}350 \dashrightarrow 00{:}47{:}32{.}558$ Capacity of these things

NOTE Confidence: 0.8256377

 $00:47:32.558 \rightarrow 00:47:33.766$ is probably quite for,

- NOTE Confidence: 0.8256377
- $00:47:33.770 \longrightarrow 00:47:35.290$ I think, over all right.
- NOTE Confidence: 0.8256377
- $00{:}47{:}35{.}290 \dashrightarrow 00{:}47{:}36{.}805$ 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
- $00:47:38.020 \rightarrow 00:47:41.350$ and so if you look at the kind of the listed,
- NOTE Confidence: 0.8256377
- $00{:}47{:}41.350 \dashrightarrow 00{:}47{:}42.865$ all the criteria they looked
- NOTE Confidence: 0.8256377
- $00:47:42.865 \longrightarrow 00:47:44.077$ at through motor right?
- NOTE Confidence: 0.8256377
- $00:47:44.080 \longrightarrow 00:47:45.898$ So it was like increased tone
- NOTE Confidence: 0.8256377
- $00{:}47{:}45.898 \dashrightarrow 00{:}47{:}47.110$ like abnormal hand movements.
- NOTE Confidence: 0.8256377
- $00{:}47{:}47{.}110 \dashrightarrow 00{:}47{:}49{.}808$ All these things that we could see in a
- NOTE Confidence: 0.8256377
- $00:47:49.808 \longrightarrow 00:47:51.253$ lot of developmental disorders because
- NOTE Confidence: 0.8256377
- $00:47:51.253 \rightarrow 00:47:53.470$ they if we think of cerebral palsy,
- NOTE Confidence: 0.8256377
- $00{:}47{:}53.470 \dashrightarrow 00{:}47{:}55.288$ 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
- $00{:}47{:}56{.}800 \dashrightarrow 00{:}47{:}57{.}706$ circuit formation early.
- NOTE Confidence: 0.8256377
- $00{:}47{:}57{.}710 \dashrightarrow 00{:}47{:}59{.}528$ They show these signs very distinctly,
- NOTE Confidence: 0.8256377

- $00:47:59.530 \longrightarrow 00:48:00.898$ so I think the.
- NOTE Confidence: 0.8256377
- 00:48:00.898 --> 00:48:02.266 Specificity is probably extremely
- NOTE Confidence: 0.8256377
- $00:48:02.266 \rightarrow 00:48:04.337$ low for these types of things,
- NOTE Confidence: 0.8256377
- $00{:}48{:}04{.}340 \dashrightarrow 00{:}48{:}06{.}876$ but I think that as we start turning
- NOTE Confidence: 0.8256377
- $00{:}48{:}06{.}876 \dashrightarrow 00{:}48{:}09{.}439$ 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
- $00:48:13.180 \longrightarrow 00:48:15.343$ I think maybe we can narrow it
- NOTE Confidence: 0.8256377
- $00{:}48{:}15{.}343 \dashrightarrow 00{:}48{:}16{.}920$ down to something specific.
- NOTE Confidence: 0.8256377
- $00:48:16.920 \longrightarrow 00:48:18.775$ One thing I didn't know in these NOTE Confidence: 0.8256377
- $00{:}48{:}18{.}775 \dashrightarrow 00{:}48{:}20{.}725$ 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
- $00{:}48{:}22.185 \dashrightarrow 00{:}48{:}24.520$ 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
- $00:48:26.100 \longrightarrow 00:48:27.800$ those time control don't show
- NOTE Confidence: 0.8256377
- $00:48:27.800 \longrightarrow 00:48:28.820$ these motor signs,

- NOTE Confidence: 0.8256377
- $00:48:28.820 \rightarrow 00:48:31.347$ 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
- $00:48:33.234 \rightarrow 00:48:34.176$ Palsy and schizophrenic.
- NOTE Confidence: 0.8256377
- $00:48:34.180 \longrightarrow 00:48:36.064$ 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
- $00:48:37.958 \rightarrow 00:48:40.191$ both in the time period that specifically
- NOTE Confidence: 0.8256377
- $00:48:40.191 \rightarrow 00:48:42.030$ sensitive the cells that are affected,
- NOTE Confidence: 0.8256377
- $00:48:42.030 \longrightarrow 00:48:43.600$ the jeans that are effective.
- NOTE Confidence: 0.8256377
- $00{:}48{:}43.600 \dashrightarrow 00{:}48{:}45.322$ There seems to be similar processes
- NOTE Confidence: 0.8256377
- $00{:}48{:}45{.}322 \dashrightarrow 00{:}48{:}47{.}548$ that are affected or altered and why
- NOTE Confidence: 0.8256377
- $00{:}48{:}47{.}548 \dashrightarrow 00{:}48{:}49{.}248$ 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
- $00{:}48{:}51{.}760 \dashrightarrow 00{:}48{:}54{.}268$ and it needs a lot of research to
- NOTE Confidence: 0.8256377
- $00{:}48{:}54{.}268 \dashrightarrow 00{:}48{:}57{.}709$ make sense that thanks very much.
- NOTE Confidence: 0.8256377

- $00:48:57.710 \longrightarrow 00:48:59.000$ Paid Lilia and
- NOTE Confidence: 0.8062014
- $00{:}48{:}59{.}000 \dashrightarrow 00{:}49{:}01{.}150$ 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
- $00:49:03.300 \longrightarrow 00:49:04.660$ So just a comment.
- NOTE Confidence: 0.8062014
- $00{:}49{:}04{.}660 \dashrightarrow 00{:}49{:}07{.}630$ We had just seeing that the 30 years
- NOTE Confidence: 0.8062014
- $00{:}49{:}07{.}630 \dashrightarrow 00{:}49{:}09{.}770$ of research carried on clinical
- NOTE Confidence: 0.8062014
- $00:49:09.770 \rightarrow 00:49:12.760$ 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
- $00{:}49{:}15.610 \dashrightarrow 00{:}49{:}18.878$ to build clinical tools like the cars
- NOTE Confidence: 0.8062014
- $00{:}49{:}18.878 \dashrightarrow 00{:}49{:}21.028$ and following clinical subjects like
- NOTE Confidence: 0.8062014
- $00{:}49{:}21.028 \dashrightarrow 00{:}49{:}24.178$ we see with the drama that it's not
- NOTE Confidence: 0.8062014
- $00:49:24.178 \rightarrow 00:49:27.890$ really working as as we would have reached 2.
- NOTE Confidence: 0.8062014
- $00:49:27.890 \longrightarrow 00:49:30.011$ Because it was a great hope to
- NOTE Confidence: 0.8062014
- $00{:}49{:}30{.}011 \dashrightarrow 00{:}49{:}32{.}491$ to have those clinical tools and
- NOTE Confidence: 0.8062014
- $00:49:32.491 \longrightarrow 00:49:34.495$ 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
- $00:49:37.108 \rightarrow 00:49:40.337$ that we still need the fundamental research,

 $00{:}49{:}40{.}340 \dashrightarrow 00{:}49{:}42.668$ so that's still very much needed,

NOTE Confidence: 0.8062014

 $00:49:42.670 \longrightarrow 00:49:46.045$ so it's interesting.

NOTE Confidence: 0.8062014

 $00{:}49{:}46.045 \dashrightarrow 00{:}49{:}49.504$ But I think that's something that was

NOTE Confidence: 0.8062014

 $00{:}49{:}49{.}504 \dashrightarrow 00{:}49{:}51{.}555$ also interesting in this clinical

NOTE Confidence: 0.8062014

 $00{:}49{:}51{.}555 \dashrightarrow 00{:}49{:}54{.}544$ assessment was to build strong cohorts an,

NOTE Confidence: 0.8062014

 $00:49:54.550 \longrightarrow 00:49:56.600$ so that's something that they

NOTE Confidence: 0.8062014

 $00:49:56.600 \longrightarrow 00:49:58.650$ they really managed to do,

NOTE Confidence: 0.8062014

 $00{:}49{:}58.650 \dashrightarrow 00{:}50{:}00{.}470$ and I'm wondering because.

NOTE Confidence: 0.8062014

 $00{:}50{:}00{.}470 \dashrightarrow 00{:}50{:}02{.}745$ Cohorts that you cited include

NOTE Confidence: 0.8062014

 $00:50:02.745 \longrightarrow 00:50:04.230$ 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

 $00:50:07.692 \longrightarrow 00:50:10.000$ cohort that would maybe?

NOTE Confidence: 0.8062014

 $00{:}50{:}10.000 \dashrightarrow 00{:}50{:}12.280$ Gather better data on neuromuscular skills,

NOTE Confidence: 0.8062014

 $00{:}50{:}12.280 \dashrightarrow 00{:}50{:}12.660$ etc.

- $00:50:12.660 \rightarrow 00:50:13.420$ 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
- $00{:}50{:}15{.}320 \dashrightarrow 00{:}50{:}18{.}050$ them or the clinical world as I
- NOTE Confidence: 0.81124085
- $00:50:18.050 \rightarrow 00:50:20.012$ actually recently talked to one
- NOTE Confidence: 0.81124085
- $00{:}50{:}20.012 \dashrightarrow 00{:}50{:}22.154$ 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
- $00:50:23.300 \rightarrow 00:50:25.200$ who's now faculty at Penn,
- NOTE Confidence: 0.81124085
- $00{:}50{:}25{.}200 \dashrightarrow 00{:}50{:}27{.}874$ and he's working as part of the
- NOTE Confidence: 0.81124085
- $00:50:27.874 \rightarrow 00:50:30.140$ lifespan lifespan group with the girls,
- NOTE Confidence: 0.81124085
- $00{:}50{:}30{.}140 \dashrightarrow 00{:}50{:}32{.}800$ and so they have this larger study.
- NOTE Confidence: 0.81124085
- $00{:}50{:}32{.}800 \dashrightarrow 00{:}50{:}35{.}080$ 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
- $00:50:36.220 \rightarrow 00:50:37.740$ something where they're really
- NOTE Confidence: 0.81124085
- $00:50:37.740 \longrightarrow 00:50:38.880$ deeply profiling children,
- NOTE Confidence: 0.81124085
- $00:50:38.880 \longrightarrow 00:50:40.648$ just agnostically kids that.

 $00:50:40.648 \longrightarrow 00:50:42.440$ Initially, like a lot of the

NOTE Confidence: 0.81124085

 $00:50:42.440 \longrightarrow 00:50:44.173$ work was focused on stress and

NOTE Confidence: 0.81124085

 $00:50:44.173 \dashrightarrow 00:50:46.069$ like kind of exposure to trauma.

NOTE Confidence: 0.81124085

 $00:50:46.070 \rightarrow 00:50:48.184$ We heard like a presentation from we

NOTE Confidence: 0.81124085

 $00:50:48.184 \rightarrow 00:50:50.759$ went there for a treat a couple years ago,

NOTE Confidence: 0.81124085

 $00{:}50{:}50{.}760 \dashrightarrow 00{:}50{:}52{.}220$ but they are actually interested

NOTE Confidence: 0.81124085

 $00:50:52.220 \longrightarrow 00:50:54.024$ in psychosis and so they are

NOTE Confidence: 0.81124085

 $00:50:54.024 \rightarrow 00:50:55.740$ looking more closely at that group.

NOTE Confidence: 0.81124085

 $00{:}50{:}55{.}740 \dashrightarrow 00{:}50{:}57{.}320$ That same group actually does

NOTE Confidence: 0.81124085

 $00:50:57.320 \longrightarrow 00:50:59.260$ looks at patients of 22 Q 11,

NOTE Confidence: 0.81124085

 $00{:}50{:}59{.}260 \dashrightarrow 00{:}51{:}01{.}018$ 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

 $00{:}51{:}02.716 \dashrightarrow 00{:}51{:}03.804$ developing schizophrenia is way

NOTE Confidence: 0.81124085

 $00{:}51{:}03{.}804 \dashrightarrow 00{:}51{:}05{.}409$ higher than the normal population.

NOTE Confidence: 0.81124085

 $00{:}51{:}05{.}410 \dashrightarrow 00{:}51{:}07{.}258$ So there are also carefully built a

- $00:51:07.258 \rightarrow 00:51:09.090$ large cohort of these patients because
- NOTE Confidence: 0.81124085
- $00{:}51{:}09{.}090 \dashrightarrow 00{:}51{:}11{.}379$ 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
- $00{:}51{:}21{.}829 \dashrightarrow 00{:}51{:}23{.}461$ are some of these genetic disorders
- NOTE Confidence: 0.81124085
- $00:51:23.527 \rightarrow 00:51:25.459$ that you can pick out immediately.
- NOTE Confidence: 0.81124085
- $00:51:25.460 \rightarrow 00:51:28.205$ 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
- $00:51:29.450 \dashrightarrow 00:51:31.880$ 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
- $00:51:35.250 \longrightarrow 00:51:36.830$ But I think the Philadelphia
- NOTE Confidence: 0.81124085
- $00:51:36.830 \longrightarrow 00:51:38.750$ size actually is really cool work
- NOTE Confidence: 0.81124085
- $00:51:38.750 \longrightarrow 00:51:40.135$ in the garage slab there.
- NOTE Confidence: 0.8354016
- $00:51:41.170 \longrightarrow 00:51:43.218$ Can I just say before LL and will
- NOTE Confidence: 0.8354016
- $00{:}51{:}43.218 \dashrightarrow 00{:}51{:}44.970$ have one last question and then
- NOTE Confidence: 0.8354016
- 00:51:44.970 --> 00:51:47.220 we can hang out with Wartik?
- NOTE Confidence: 0.8354016
- $00{:}51{:}47{.}220 \dashrightarrow 00{:}51{:}49{.}356$ 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
- $00{:}51{:}51{.}707 \dashrightarrow 00{:}51{:}53{.}523$ call your attention to next week's
- NOTE Confidence: 0.8354016
- $00:51:53.523 \rightarrow 00:51:55.567$ grand rounds which is going to be
- NOTE Confidence: 0.8354016
- $00{:}51{:}55{.}567 \dashrightarrow 00{:}51{:}57{.}300$ 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
- $00:51:58.740 \rightarrow 00:52:00.924$ one of our newest faculty members is going
- NOTE Confidence: 0.8354016
- $00:52:00.924 \dashrightarrow 00:52:03.347$ to be talking to us about early early,
- NOTE Confidence: 0.8354016
- $00{:}52{:}03{.}350 \dashrightarrow 00{:}52{:}05{.}036$ early, early early years and the
- NOTE Confidence: 0.8354016

 $00:52:05.036 \rightarrow 00:52:06.510$ 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

 $00:52:08.590 \longrightarrow 00:52:10.260$ in keeping with today's talk.

NOTE Confidence: 0.8354016

 $00:52:10.260 \dashrightarrow 00:52:13.008$ So Ellen last question for Karthik.

NOTE Confidence: 0.8354016

 $00:52:13.010 \longrightarrow 00:52:13.390$ Carter

NOTE Confidence: 0.78803855

 $00{:}52{:}13.390 \dashrightarrow 00{:}52{:}16.029$ great great talk, I really enjoyed it.

NOTE Confidence: 0.78803855

 $00{:}52{:}16.030 \dashrightarrow 00{:}52{:}19.180$ You know, I guess as we think about a lot

NOTE Confidence: 0.78803855

 $00:52:19.262 \longrightarrow 00:52:21.890$ of different questions that one question

NOTE Confidence: 0.78803855

 $00{:}52{:}21.890 \dashrightarrow 00{:}52{:}25.109$ which I wrote in the chat with you.

NOTE Confidence: 0.78803855

 $00:52:25.110 \longrightarrow 00:52:26.995$ Sorry you arrived at the

NOTE Confidence: 0.78803855

 $00:52:26.995 \longrightarrow 00:52:28.126$ retinoic acid pathway.

NOTE Confidence: 0.78803855

 $00{:}52{:}28{.}130 \dashrightarrow 00{:}52{:}30{.}344$ Sort of thinking about risk genes

NOTE Confidence: 0.78803855

 $00:52:30.344 \longrightarrow 00:52:32.290$ or following the genes there.

NOTE Confidence: 0.78803855

 $00{:}52{:}32{.}290 \dashrightarrow 00{:}52{:}34{.}906$ So to what extent do you think that

NOTE Confidence: 0.78803855

 $00{:}52{:}34{.}906 \dashrightarrow 00{:}52{:}37{.}431$ this pathway and the thalamus to

NOTE Confidence: 0.78803855

 $00:52:37.431 \rightarrow 00:52:39.231$ prefrontal cortex connection might

- NOTE Confidence: 0.78803855
- $00:52:39.231 \rightarrow 00:52:41.700$ represent a common pathway across?

00:52:41.700 --> 00:52:43.700 Schizophrenia risk genes versus one

NOTE Confidence: 0.78803855

 $00{:}52{:}43.700 \dashrightarrow 00{:}52{:}46.429$ of several routes there and the sort

NOTE Confidence: 0.78803855

 $00:52:46.429 \longrightarrow 00:52:48.427$ of related to the other question.

NOTE Confidence: 0.78803855

00:52:48.430 --> 00:52:49.050 Previous question,

NOTE Confidence: 0.78803855

 $00{:}52{:}49{.}050 \dashrightarrow 00{:}52{:}50{.}910$ to what extent might this represent

NOTE Confidence: 0.78803855

 $00:52:50.910 \longrightarrow 00:52:53.055$ a common pathway across other

NOTE Confidence: 0.78803855

 $00:52:53.055 \rightarrow 00:52:54.039$ neurodevelopmental disorders?

NOTE Confidence: 0.78803855

 $00{:}52{:}54{.}040 \dashrightarrow 00{:}52{:}55{.}910$ And that's such an important

NOTE Confidence: 0.78803855

 $00:52:55.910 \longrightarrow 00:52:57.406$ question for us to

NOTE Confidence: 0.81150025

 $00:52:57.410 \longrightarrow 00:52:59.275$ really be able to transition

NOTE Confidence: 0.81150025

 $00:52:59.275 \longrightarrow 00:53:00.394$ this intervention right?

NOTE Confidence: 0.81150025

 $00:53:00.400 \rightarrow 00:53:03.393$ Because as this was a mouse model, right?

NOTE Confidence: 0.81150025

 $00{:}53{:}03{.}393 \dashrightarrow 00{:}53{:}04{.}885$ And we actually we ren't

NOTE Confidence: 0.81150025

 $00:53:04.885 \rightarrow 00:53:06.004$ looking at schizophrenia,

 $00:53:06.010 \rightarrow 00:53:07.726$ we were really interesting.

NOTE Confidence: 0.81150025

00:53:07.726 --> 00:53:09.442 Just prefrontal cortex evolution

NOTE Confidence: 0.81150025

 $00{:}53{:}09{.}442 \dashrightarrow 00{:}53{:}11{.}329$ 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

 $00:53:13.261 \rightarrow 00:53:15.449$ acid actually agnostically popped up.

NOTE Confidence: 0.81150025

 $00{:}53{:}15{.}450 \dashrightarrow 00{:}53{:}16{.}854$ There was some data before from NOTE Confidence: 0.81150025

 $00:53:16.854 \rightarrow 00:53:18.380$ an earlier study in this testing

NOTE Confidence: 0.81150025

 $00:53:18.380 \rightarrow 00:53:20.000$ lab that pointed at retinoic acid,

NOTE Confidence: 0.81150025

 $00{:}53{:}20.000 \dashrightarrow 00{:}53{:}22.586$ and then we kind of reconfirmed

NOTE Confidence: 0.81150025

 $00:53:22.586 \longrightarrow 00:53:24.650$ it and then analyzed it.

NOTE Confidence: 0.81150025

 $00{:}53{:}24.650 \dashrightarrow 00{:}53{:}25.649$ Retinoic acid specific.

NOTE Confidence: 0.81150025

 $00{:}53{:}25{.}649 \dashrightarrow 00{:}53{:}27{.}647$ There's a couple of papers that

NOTE Confidence: 0.81150025

 $00{:}53{:}27{.}647 \dashrightarrow 00{:}53{:}29{.}542$ have really kind of focused on

NOTE Confidence: 0.81150025

 $00:53:29.542 \longrightarrow 00:53:31.456$ retinoic acid as as possible as

NOTE Confidence: 0.81150025

 $00{:}53{:}31{.}456 \dashrightarrow 00{:}53{:}32{.}876$ a possible signaling pathway.

NOTE Confidence: 0.81150025

00:53:32.880 --> 00:53:35.183 I still I'm kind of wary about

 $00:53:35.183 \rightarrow 00:53:36.170$ specifically retinoic acid.

NOTE Confidence: 0.81150025

 $00{:}53{:}36{.}170 \dashrightarrow 00{:}53{:}38{.}246$ I think as Doctor Vaccarino mentioned

NOTE Confidence: 0.81150025

 $00{:}53{:}38{.}246 \dashrightarrow 00{:}53{:}40{.}063$ is I think something downstream

NOTE Confidence: 0.81150025

 $00:53:40.063 \rightarrow 00:53:42.247$ and also kind of putting together

NOTE Confidence: 0.81150025

 $00{:}53{:}42.247 \dashrightarrow 00{:}53{:}43.934$ with our current knowledge that

NOTE Confidence: 0.81150025

 $00{:}53{:}43{.}934 \dashrightarrow 00{:}53{:}46{.}038$ 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

 $00:53:47.027 \rightarrow 00:53:49.330$ autism will soon be at the synapse.

NOTE Confidence: 0.81150025

 $00{:}53{:}49{.}330 \dashrightarrow 00{:}53{:}50{.}798$ Maybe it's something specifically

NOTE Confidence: 0.81150025

 $00{:}53{:}50{.}798 \dashrightarrow 00{:}53{:}52{.}633$ about Synapse connectivity and we

NOTE Confidence: 0.81150025

 $00{:}53{:}52{.}633 \dashrightarrow 00{:}53{:}54{.}635$ just happened to stumble upon it by.

NOTE Confidence: 0.81150025

 $00{:}53{:}54{.}640 \dashrightarrow 00{:}53{:}56{.}330$ Going the retinoic acid path,

NOTE Confidence: 0.81150025

 $00{:}53{:}56{.}330 \dashrightarrow 00{:}53{:}58{.}696$ I do though to you later point.

NOTE Confidence: 0.81150025

00:53:58.700 --> 00:54:00.905 I do think plama cortical dysfunction may

NOTE Confidence: 0.81150025

 $00{:}54{:}00{.}905 \dashrightarrow 00{:}54{:}03{.}428$ be some core pathology in the disorder,

 $00{:}54{:}03{.}430 \dashrightarrow 00{:}54{:}05{.}614$ and that I like that circuit based

NOTE Confidence: 0.81150025

 $00:54:05.614 \rightarrow 00:54:07.820$ 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

 $00:54:09.172 \longrightarrow 00:54:10.524$ as I mentioned before,

NOTE Confidence: 0.81150025

 $00{:}54{:}10{.}530 \dashrightarrow 00{:}54{:}12{.}546$ like retinoic acid involved in everything.

NOTE Confidence: 0.81150025

 $00:54:12.550 \rightarrow 00:54:15.592$ 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

 $00{:}54{:}17{.}958 \dashrightarrow 00{:}54{:}19{.}940$ coming together that Flamel cortical

NOTE Confidence: 0.81150025

 $00{:}54{:}19{.}940 \dashrightarrow 00{:}54{:}22{.}015$ dys function is specifically an issue,

NOTE Confidence: 0.81150025

 $00:54:22.020 \rightarrow 00:54:23.031$ whether it's specifically

NOTE Confidence: 0.81150025

 $00{:}54{:}23.031 \dashrightarrow 00{:}54{:}24.379$ thalamic to prefrontal cortex.

NOTE Confidence: 0.81150025

 $00{:}54{:}24{.}380 \dashrightarrow 00{:}54{:}26{.}516$ I think that might be at

NOTE Confidence: 0.81150025

 $00{:}54{:}26{.}516 \dashrightarrow 00{:}54{:}27{.}584$ least a subpopulation.

NOTE Confidence: 0.81150025

 $00:54:27.590 \longrightarrow 00:54:29.050$ Of it will be interesting,

NOTE Confidence: 0.81150025

 $00{:}54{:}29{.}050 \dashrightarrow 00{:}54{:}30{.}500$ 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
- $00:54:31.684 \rightarrow 00:54:32.868$ Lima cortical connectivity deficits

 $00:54:32.868 \longrightarrow 00:54:33.990$ 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

 $00:54:36.240 \longrightarrow 00:54:38.647$ a lot of time before this talk,

NOTE Confidence: 0.81150025

 $00{:}54{:}38{.}650 \dashrightarrow 00{:}54{:}40{.}660$ like kind of reading through all

NOTE Confidence: 0.81150025

 $00{:}54{:}40.660 \dashrightarrow 00{:}54{:}41.665$ this schizophrenia literature

NOTE Confidence: 0.81150025

 $00{:}54{:}41.665 \dashrightarrow 00{:}54{:}43.393$ because I spend more time reading

NOTE Confidence: 0.81150025

 $00{:}54{:}43{.}393 \dashrightarrow 00{:}54{:}45{.}031$ like gene regulation stuff and one

NOTE Confidence: 0.81150025

 $00{:}54{:}45{.}031 \dashrightarrow 00{:}54{:}46{.}507$ of the theories has put forward.

NOTE Confidence: 0.81150025

 $00{:}54{:}46{.}510 \dashrightarrow 00{:}54{:}48{.}250$ There's almost two types of schizophrenia.

NOTE Confidence: 0.81150025

 $00{:}54{:}48{.}250 \dashrightarrow 00{:}54{:}49{.}705$ 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

 $00{:}54{:}50{.}870 \dashrightarrow 00{:}54{:}51{.}671$ word, psychotic symptoms,

NOTE Confidence: 0.81150025

 $00{:}54{:}51{.}671 \dashrightarrow 00{:}54{:}53{.}540$ 1st and then you kind of progressives

NOTE Confidence: 0.81150025

 $00{:}54{:}53{.}585 \dashrightarrow 00{:}54{:}55{.}240$ are very responsive to antipsychotic's.

 $00{:}54{:}55{.}240 \dashrightarrow 00{:}54{:}56{.}770$ But there's also the second

NOTE Confidence: 0.81150025

 $00{:}54{:}56{.}770 \dashrightarrow 00{:}54{:}58{.}300$ type which is very driven.

NOTE Confidence: 0.81150025

 $00:54:58.300 \rightarrow 00:54:59.672$ 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

 $00{:}55{:}01{.}995 \dashrightarrow 00{:}55{:}03{.}570$ one population is specifically shows

NOTE Confidence: 0.81150025

 $00{:}55{:}03.570 \dashrightarrow 00{:}55{:}05.518$ this Pfc Flamel cortical deficit,

NOTE Confidence: 0.81150025

 $00:55:05.520 \rightarrow 00:55:07.590$ 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

 $00:55:09.998 \dashrightarrow 00:55:11.030$ thalamic cortical connectivity.

NOTE Confidence: 0.81150025

 $00{:}55{:}11.030 \dashrightarrow 00{:}55{:}12.745$ Maybe something that spans across

NOTE Confidence: 0.81150025

 $00{:}55{:}12.745 \dashrightarrow 00{:}55{:}14.117$ 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

 $00{:}55{:}16.880 \dashrightarrow 00{:}55{:}17.568$ thoughtful thinking.

NOTE Confidence: 0.81150025

00:55:17.568 --> 00:55:18.600 Like I guess,

NOTE Confidence: 0.81150025

 $00:55:18.600 \rightarrow 00:55:20.116$ characterization of these patients

- NOTE Confidence: 0.81150025
- $00:55:20.116 \longrightarrow 00:55:21.632$ of patients schizophrenia to

00:55:21.632 --> 00:55:23.408 really kind of link a disorder.

NOTE Confidence: 0.81150025

 $00{:}55{:}23{.}410 \dashrightarrow 00{:}55{:}23{.}986$ But yeah,

NOTE Confidence: 0.81150025

 $00:55:23.986 \dashrightarrow 00:55:25.714$ 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

 $00{:}55{:}27{.}540 \dashrightarrow 00{:}55{:}28{.}580$ It's always in some.

NOTE Confidence: 0.81150025

 $00:55:28.580 \rightarrow 00:55:30.140$ I've been interested in that may

NOTE Confidence: 0.81150025

 $00:55:30.194 \rightarrow 00:55:32.159$ underlie schizophrenia across the board.

NOTE Confidence: 0.8470596

 $00{:}55{:}34{.}470 \dashrightarrow 00{:}55{:}36{.}138$ Well Kartik, thank you for a

NOTE Confidence: 0.8470596

 $00:55:36.138 \rightarrow 00:55:37.250$ really magnificent grand rounds.

NOTE Confidence: 0.8470596

 $00:55:37.250 \longrightarrow 00:55:38.948$ 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

 $00{:}55{:}40{.}590 \dashrightarrow 00{:}55{:}42{.}246$ but I want to thank you.

NOTE Confidence: 0.8470596

 $00:55:42.250 \longrightarrow 00:55:44.231$ And you've taught us a lot of

NOTE Confidence: 0.8470596

 $00{:}55{:}44{.}231 \dashrightarrow 00{:}55{:}45{.}589$ science science with a heart,
$00{:}55{:}45{.}590 \dashrightarrow 00{:}55{:}47{.}455$ so that's that's really good.