WEBVTT

NOTE duration:"01:07:11.7000000"

NOTE recognizability:0.802

NOTE language:en-us

NOTE Confidence: 0.773990660272727

00:00:17.190 --> 00:00:18.198 Welcome, everyone.

NOTE Confidence: 0.773990660272727

 $00{:}00{:}18.198 \dashrightarrow 00{:}00{:}20.718$  It's a pleasure today to

NOTE Confidence: 0.773990660272727

 $00{:}00{:}20.718 \dashrightarrow 00{:}00{:}22.710$  have Alan antiseptic here.

NOTE Confidence: 0.773990660272727

00:00:22.710 --> 00:00:24.026 Alan, I think many of you know,

NOTE Confidence: 0.773990660272727

 $00:00:24.030 \longrightarrow 00:00:26.030$  is an associate professor in

NOTE Confidence: 0.773990660272727

00:00:26.030 --> 00:00:29.170 the Department of Psychiatry.

NOTE Confidence: 0.773990660272727

 $00{:}00{:}29{.}170 \dashrightarrow 00{:}00{:}31{.}180$  As well as many other hats.

NOTE Confidence: 0.773990660272727

 $00{:}00{:}31.180 \dashrightarrow 00{:}00{:}34.069$  And his was a really a pioneer in our

NOTE Confidence: 0.773990660272727

00:00:34.069 --> 00:00:37.096 in our community and bringing high

NOTE Confidence: 0.773990660272727

00:00:37.096 --> 00:00:39.200 resolution human Connectome Project

NOTE Confidence: 0.773990660272727

 $00{:}00{:}39{.}200 \dashrightarrow 00{:}00{:}42{.}329$  style imaging to the community and

NOTE Confidence: 0.773990660272727

 $00{:}00{:}42.329 \dashrightarrow 00{:}00{:}44.646$  then applying innovative computational

NOTE Confidence: 0.773990660272727

 $00{:}00{:}44.646 \dashrightarrow 00{:}00{:}48.336$  strategies to analyzing these data.

00:00:48.340 --> 00:00:49.480 And then in more recent years,

NOTE Confidence: 0.773990660272727

 $00{:}00{:}49{.}480 \dashrightarrow 00{:}00{:}52{.}280$  it started to do some some really

NOTE Confidence: 0.773990660272727

 $00{:}00{:}52.280 \dashrightarrow 00{:}00{:}54.693$  exciting work in looking at the

NOTE Confidence: 0.773990660272727

 $00{:}00{:}54.693 \dashrightarrow 00{:}00{:}56.358$  brain effects first of ketamine

NOTE Confidence: 0.773990660272727

 $00{:}00{:}56.358 \dashrightarrow 00{:}00{:}58.504$  in his earlier work and then

NOTE Confidence: 0.773990660272727

 $00{:}00{:}58{.}504 \dashrightarrow 00{:}01{:}00{.}000$  more recently of psilocybin,

NOTE Confidence: 0.773990660272727

 $00{:}01{:}00{.}000 \dashrightarrow 00{:}01{:}01{.}572$  LSD and other psyched elics,

NOTE Confidence: 0.773990660272727

 $00:01:01.572 \longrightarrow 00:01:03.537$  which is the focus today.

NOTE Confidence: 0.773990660272727

00:01:03.540 --> 00:01:03.978 So Alan,

NOTE Confidence: 0.773990660272727

 $00:01:03.978 \longrightarrow 00:01:05.292$  thank you so much for being

NOTE Confidence: 0.773990660272727

 $00:01:05.292 \longrightarrow 00:01:06.659$  with us and we look forward

NOTE Confidence: 0.773990660272727

 $00:01:06.659 \rightarrow 00:01:07.780$  to to learning from you.

NOTE Confidence: 0.692835325

00:01:09.820 --> 00:01:13.288 Thanks, Chris. Mark Gustavo.

NOTE Confidence: 0.692835325

 $00:01:13.290 \longrightarrow 00:01:15.114$  Anytime at all.

NOTE Confidence: 0.692835325

 $00:01:15.114 \rightarrow 00:01:17.335$  It's really with this pandemic,

NOTE Confidence: 0.692835325

00:01:17.335 --> 00:01:19.680 I feel like I haven't seen you

- NOTE Confidence: 0.692835325
- $00{:}01{:}19.754 \dashrightarrow 00{:}01{:}21.930$  guys in forever and it's feeling
- NOTE Confidence: 0.692835325
- $00{:}01{:}21{.}930 \dashrightarrow 00{:}01{:}23{.}730$  more disconnected than ever,
- NOTE Confidence: 0.692835325
- $00:01:23.730 \longrightarrow 00:01:25.950$  but it's it's really.
- NOTE Confidence: 0.692835325
- $00:01:25.950 \longrightarrow 00:01:27.765$  I'm excited to tell you
- NOTE Confidence: 0.692835325
- $00{:}01{:}27.765 \dashrightarrow 00{:}01{:}29.910$  what we've been up to so.
- NOTE Confidence: 0.692835325
- $00:01:29.910 \dashrightarrow 00:01:35.246$  The the title is so let's see mapping
- NOTE Confidence: 0.692835325
- $00:01:35.246 \longrightarrow 00:01:36.694$  or behavioral heterogeneity of
- NOTE Confidence: 0.692835325
- $00:01:36.694 \rightarrow 00:01:38.180$  psychedelic neurology and humans.
- NOTE Confidence: 0.692835325
- 00:01:38.180 --> 00:01:40.916 So that's. An overly ambitious,
- NOTE Confidence: 0.692835325
- $00:01:40.916 \longrightarrow 00:01:42.364$  probably not true title.
- NOTE Confidence: 0.692835325
- $00:01:42.370 \longrightarrow 00:01:43.955$  So we're not quite there
- NOTE Confidence: 0.692835325
- $00{:}01{:}43.955 \dashrightarrow 00{:}01{:}45.223$  and this is a spirational.
- NOTE Confidence: 0.692835325
- $00:01:45.230 \longrightarrow 00:01:47.510$  And So what I'd like to kind of
- NOTE Confidence: 0.692835325
- 00:01:47.510 --> 00:01:49.630 talk about is as as Chris noted,
- NOTE Confidence: 0.692835325
- $00{:}01{:}49{.}630 \dashrightarrow 00{:}01{:}51{.}640$  what are the techniques and approaches
- NOTE Confidence: 0.692835325

 $00:01:51.702 \rightarrow 00:01:53.227$  we're bringing to bear towards

NOTE Confidence: 0.692835325

00:01:53.227 --> 00:01:55.382 this goal and some of the work

NOTE Confidence: 0.692835325

 $00:01:55.382 \dashrightarrow 00:01:57.349$  that's been coming out of the lab.

NOTE Confidence: 0.692835325

 $00:01:57.350 \longrightarrow 00:02:00.319$  So it will be a hybrid of sort of the, the,

NOTE Confidence: 0.692835325

 $00:02:00.319 \rightarrow 00:02:03.010$  the theme and the ethos of what we're doing,

NOTE Confidence: 0.692835325

 $00:02:03.010 \longrightarrow 00:02:08.006$  how some of the efforts in in mapping

NOTE Confidence: 0.692835325

 $00:02:08.006 \rightarrow 00:02:11.350$  variation in clinical populations.

NOTE Confidence: 0.692835325

 $00:02:11.350 \rightarrow 00:02:13.770$  Can be related to neuroimaging

NOTE Confidence: 0.692835325

00:02:13.770 --> 00:02:15.706 effects of pharmacological compounds

NOTE Confidence: 0.692835325

 $00:02:15.706 \longrightarrow 00:02:18.009$  with the focus on psychedelics.

NOTE Confidence: 0.692835325

 $00{:}02{:}18.010 \dashrightarrow 00{:}02{:}18.970$  So that's kind of the idea,

NOTE Confidence: 0.692835325

 $00:02:18.970 \longrightarrow 00:02:19.397$  right.

NOTE Confidence: 0.692835325

00:02:19.397 --> 00:02:22.813 And so I I want to just disclose

NOTE Confidence: 0.692835325

00:02:22.813 --> 00:02:26.435 that I'm a member of the TAB

NOTE Confidence: 0.692835325

 $00:02:26.435 \longrightarrow 00:02:29.600$  Technology Advisory Board for Nemora

NOTE Confidence: 0.692835325

 $00:02:29.600 \rightarrow 00:02:32.376$  Therapeutic Therapeutics I consult.

00:02:32.376 --> 00:02:35.057 For Gilgamesh and I just Co founded

NOTE Confidence: 0.692835325

 $00{:}02{:}35{.}057 \dashrightarrow 00{:}02{:}38{.}439$  a biotech with my colleague John

NOTE Confidence: 0.692835325

 $00:02:38.439 \longrightarrow 00:02:40.771$  Murray that's called Manifest

NOTE Confidence: 0.692835325

00:02:40.771 -> 00:02:43.471 Technologies and I I say this

NOTE Confidence: 0.692835325

 $00{:}02{:}43{.}471 \dashrightarrow 00{:}02{:}45{.}506$  really proudly because without the

NOTE Confidence: 0.692835325

 $00{:}02{:}45{.}510 \dashrightarrow 00{:}02{:}47{.}838$  support of Yale the spin out what it

NOTE Confidence: 0.692835325

 $00{:}02{:}47.838 \dashrightarrow 00{:}02{:}50.258$  would not be possible and so we're

NOTE Confidence: 0.692835325

 $00:02:50.258 \rightarrow 00:02:52.028$  we're really excited about this

NOTE Confidence: 0.692835325

 $00{:}02{:}52{.}099 \dashrightarrow 00{:}02{:}54{.}185$  work as it has this potential so.

NOTE Confidence: 0.692835325

 $00:02:54.190 \longrightarrow 00:02:56.290$  Basically the way I kind of

NOTE Confidence: 0.692835325

 $00:02:56.290 \longrightarrow 00:02:58.190$  think about the entire space.

NOTE Confidence: 0.879687514285714

 $00{:}03{:}00{.}630 \dashrightarrow 00{:}03{:}01{.}905$  Neuropsychiatric mapping is

NOTE Confidence: 0.879687514285714

 $00{:}03{:}01{.}905 \dashrightarrow 00{:}03{:}04{.}455$  really about the challenge and the

NOTE Confidence: 0.879687514285714

 $00{:}03{:}04.455 \dashrightarrow 00{:}03{:}06.102$  opportunity in front of us, right?

NOTE Confidence: 0.879687514285714

 $00:03:06.102 \dashrightarrow 00:03:08.438$  So there's two ways to think about it.

 $00:03:08.440 \longrightarrow 00:03:10.636$  And why has this opportunity not

NOTE Confidence: 0.879687514285714

 $00{:}03{:}10.636 \dashrightarrow 00{:}03{:}13.315$  been realized in the field of brain

NOTE Confidence: 0.879687514285714

00:03:13.315 --> 00:03:15.975 behavioral health and I'll use this term NOTE Confidence: 0.879687514285714

 $00:03:16.048 \rightarrow 00:03:18.806$  brain behavioral health because I I I

NOTE Confidence: 0.879687514285714

 $00{:}03{:}18.806 \dashrightarrow 00{:}03{:}22.210$  actually think it's important that we

NOTE Confidence: 0.879687514285714

 $00:03:22.210 \rightarrow 00:03:25.057$  destignatize this terminology, right.

NOTE Confidence: 0.879687514285714

 $00:03:25.057 \rightarrow 00:03:28.819$  So it's a difficulties in regulating

NOTE Confidence: 0.879687514285714

 $00:03:28.819 \rightarrow 00:03:31.603$  brain behavioral relationships that that

NOTE Confidence: 0.879687514285714

 $00{:}03{:}31{.}603 \dashrightarrow 00{:}03{:}34{.}859$  we're after and then I'll talk about a

NOTE Confidence: 0.879687514285714

 $00:03:34.944 \rightarrow 00:03:37.802$  framework for this quantitative and and.

NOTE Confidence: 0.879687514285714

00:03:37.802 --> 00:03:40.022 The neurobiological framework for mapping NOTE Confidence: 0.879687514285714

 $00:03:40.022 \rightarrow 00:03:42.236$  brain behavioral relationships with the

NOTE Confidence: 0.879687514285714

 $00{:}03{:}42.236 \dashrightarrow 00{:}03{:}44.346$  assistance obviously of pharmacological or

NOTE Confidence: 0.879687514285714

00:03:44.346 - > 00:03:46.968 imaging as a key tool in order to do this,

NOTE Confidence: 0.879687514285714

 $00:03:46.970 \longrightarrow 00:03:49.590$  right. So what's the challenge?

NOTE Confidence: 0.879687514285714

 $00:03:49.590 \rightarrow 00:03:51.670$  And so this is one of many challenges,

- NOTE Confidence: 0.879687514285714
- 00:03:51.670 00:03:53.526 but in my mind a very important one,
- NOTE Confidence: 0.879687514285714
- 00:03:53.530 -> 00:03:55.758 right, which is heterogeneity.
- NOTE Confidence: 0.879687514285714
- $00:03:55.758 \longrightarrow 00:03:57.429$  And by heterogeneity,
- NOTE Confidence: 0.879687514285714
- $00:03:57.430 \longrightarrow 00:04:00.238$  I mean both within a human being over
- NOTE Confidence: 0.879687514285714
- $00:04:00.238 \dashrightarrow 00:04:03.153$  time and across people in relation
- NOTE Confidence: 0.879687514285714
- $00:04:03.153 \rightarrow 00:04:05.732$  to brain behavioral variation, right.
- NOTE Confidence: 0.879687514285714
- $00:04:05.732 \longrightarrow 00:04:08.826$  And so this is an old problem.
- NOTE Confidence: 0.879687514285714
- $00:04:08.830 \longrightarrow 00:04:10.274$  We know this, right?
- NOTE Confidence: 0.879687514285714
- $00:04:10.274 \longrightarrow 00:04:12.392$  And so, but there are.
- NOTE Confidence: 0.879687514285714
- $00:04:12.392 \longrightarrow 00:04:15.640$  Questions that arise because of this problem
- NOTE Confidence: 0.879687514285714
- $00:04:15.719 \rightarrow 00:04:19.179$  and the opportunity in front of us is if we.
- NOTE Confidence: 0.879687514285714
- 00:04:19.180 --> 00:04:23.170 Have a drug like any compound.
- NOTE Confidence: 0.879687514285714
- $00:04:23.170 \dashrightarrow 00:04:25.720$  And psychedelics are a great example,
- NOTE Confidence: 0.879687514285714
- 00:04:25.720 --> 00:04:26.089 right?
- NOTE Confidence: 0.879687514285714
- $00{:}04{:}26.089 \dashrightarrow 00{:}04{:}28.672$  How do we select the optimal person
- NOTE Confidence: 0.879687514285714

 $00:04:28.672 \rightarrow 00:04:31.437$  who will benefit from that compound?

NOTE Confidence: 0.879687514285714

 $00:04:31.440 \rightarrow 00:04:33.480$  We don't have a principled quantitative,

NOTE Confidence: 0.879687514285714

 $00:04:33.480 \longrightarrow 00:04:35.600$  rationally guided framework for this,

NOTE Confidence: 0.879687514285714

 $00:04:35.600 \longrightarrow 00:04:38.120$  for anything in our field.

NOTE Confidence: 0.879687514285714

 $00:04:38.120 \longrightarrow 00:04:39.680$  And then in the future,

NOTE Confidence: 0.879687514285714

 $00:04:39.680 \longrightarrow 00:04:39.932$  right,

NOTE Confidence: 0.879687514285714

 $00:04:39.932 \longrightarrow 00:04:41.696$  if we do have a molecule right

NOTE Confidence: 0.879687514285714

00:04:41.696 --> 00:04:43.486 before we do not have a molecule,

NOTE Confidence: 0.879687514285714

 $00:04:43.490 \longrightarrow 00:04:45.268$  if we don't have a compound that

NOTE Confidence: 0.879687514285714

 $00{:}04{:}45.268 \dashrightarrow 00{:}04{:}46.763$  crosses the blood brain barrier

NOTE Confidence: 0.879687514285714

 $00:04:46.763 \longrightarrow 00:04:48.119$  safely or any the rapeutic,

NOTE Confidence: 0.879687514285714

 $00:04:48.120 \longrightarrow 00:04:50.376$  how do we develop one with

NOTE Confidence: 0.879687514285714

 $00:04:50.376 \longrightarrow 00:04:52.300$  individual precision as the goal,

NOTE Confidence: 0.879687514285714

 $00:04:52.300 \longrightarrow 00:04:55.052$  not patients versus controls,

NOTE Confidence: 0.879687514285714

 $00{:}04{:}55{.}052 \dashrightarrow 00{:}04{:}57{.}440$  but individual people, right.

NOTE Confidence: 0.879687514285714

 $00:04:57.440 \rightarrow 00:05:00.000$  So that's the opportunity as I see it,

 $00:05:00.000 \longrightarrow 00:05:01.143$  right and so.

NOTE Confidence: 0.879687514285714

 $00:05:01.143 \longrightarrow 00:05:03.429$  It's that how can we target

NOTE Confidence: 0.879687514285714

 $00:05:03.429 \rightarrow 00:05:04.800$  specific people with?

NOTE Confidence: 0.879687514285714

 $00:05:04.800 \longrightarrow 00:05:05.726$  Quantitative precision.

NOTE Confidence: 0.879687514285714

 $00:05:05.726 \rightarrow 00:05:09.430$  So this problem I see is mapping one

NOTE Confidence: 0.879687514285714

 $00:05:09.514 \rightarrow 00:05:11.833$  to many levels of analysis, right?

NOTE Confidence: 0.879687514285714

 $00:05:11.833 \rightarrow 00:05:13.930$  This is really what stands in front of us,

NOTE Confidence: 0.879687514285714

00:05:13.930 - 00:05:16.882 so I don't have to tell you guys that.

NOTE Confidence: 0.879687514285714

00:05:16.890 --> 00:05:22.398 Polygenic disturbances and variants.

NOTE Confidence: 0.879687514285714

 $00:05:22.400 \rightarrow 00:05:26.880$  Variations with rare mutations, right?

NOTE Confidence: 0.879687514285714

 $00:05:26.880 \dashrightarrow 00:05:29.250$  Basically those are the two lowest

NOTE Confidence: 0.879687514285714

 $00{:}05{:}29{.}250 \dashrightarrow 00{:}05{:}31{.}230$  level possibilities that our field

NOTE Confidence: 0.879687514285714

 $00:05:31.230 \rightarrow 00:05:33.533$  is studying and how they can affect.

NOTE Confidence: 0.879687514285714

 $00{:}05{:}33{.}540 \dashrightarrow 00{:}05{:}36{.}000$  Molecules, synapses and cells and the

NOTE Confidence: 0.879687514285714

 $00:05:36.000 \rightarrow 00:05:38.069$  balance between those cells, right?

 $00:05:38.069 \rightarrow 00:05:40.214$  That's that's at the very

NOTE Confidence: 0.879687514285714

 $00:05:40.214 \rightarrow 00:05:42.268$  baseline of the problem, right?

NOTE Confidence: 0.879687514285714

00:05:42.268 --> 00:05:42.944 In turn,

NOTE Confidence: 0.879687514285714

 $00{:}05{:}42{.}944 \dashrightarrow 00{:}05{:}45{.}310$  how do we take that information and

NOTE Confidence: 0.879687514285714

 $00:05:45.383 \rightarrow 00:05:47.837$  map it onto system level observation?

NOTE Confidence: 0.879687514285714

 $00{:}05{:}47{.}840 \dashrightarrow 00{:}05{:}49{.}472$  Some people would say this is an ill

NOTE Confidence: 0.879687514285714

 $00:05:49.472 \dashrightarrow 00:05:50.909$  posed problem because it's impossible.

NOTE Confidence: 0.879687514285714

00:05:50.910 --> 00:05:52.440 There's just too many mappings.

NOTE Confidence: 0.879687514285714

00:05:52.440 --> 00:05:53.313 But you know,

NOTE Confidence: 0.879687514285714

 $00{:}05{:}53{.}313 \dashrightarrow 00{:}05{:}55{.}059$  I'll leave that for debate later.

NOTE Confidence: 0.879687514285714

 $00:05:55.060 \longrightarrow 00:05:55.927$  And then finally,

NOTE Confidence: 0.879687514285714

 $00{:}05{:}55{.}927 \dashrightarrow 00{:}05{:}58{.}555$  how do we link this to Spectra of

NOTE Confidence: 0.879687514285714

 $00:05:58.555 \dashrightarrow 00:05:59.919$  behavioral disturbances, right.

NOTE Confidence: 0.879687514285714

 $00{:}05{:}59{.}919 \dashrightarrow 00{:}06{:}02{.}151$  And so I'd like to argue that this

NOTE Confidence: 0.879687514285714

00:06:02.151 --> 00:06:03.909 mapping is fundamentally unknown.

NOTE Confidence: 0.879687514285714

 $00:06:03.910 \longrightarrow 00:06:04.794$  We don't know it,

- NOTE Confidence: 0.879687514285714
- 00:06:04.794 --> 00:06:06.310 and if somebody argues that we do,
- NOTE Confidence: 0.879687514285714
- $00:06:06.310 \longrightarrow 00:06:08.980$  I think that they're flying.
- NOTE Confidence: 0.879687514285714
- $00{:}06{:}08{.}980 \dashrightarrow 00{:}06{:}11{.}032$  Even in circuits where we understand
- NOTE Confidence: 0.879687514285714
- 00:06:11.032 --> 00:06:13.090 our biology very well, like fear,
- NOTE Confidence: 0.879687514285714
- $00:06:13.090 \rightarrow 00:06:15.215$  we still can't treat PTSD, right?
- NOTE Confidence: 0.879687514285714
- $00{:}06{:}15{.}215 \dashrightarrow 00{:}06{:}17{.}980$  So just this mapping is not accomplished,
- NOTE Confidence: 0.879687514285714
- 00:06:17.980 --> 00:06:19.280 right?
- NOTE Confidence: 0.879687514285714
- 00:06:19.280 --> 00:06:21.074 And I actually think that system
- NOTE Confidence: 0.879687514285714
- $00:06:21.074 \longrightarrow 00:06:22.270$  level observations at the
- NOTE Confidence: 0.857824136521739
- $00:06:22.326 \rightarrow 00:06:24.132$  level of neural systems is where the
- NOTE Confidence: 0.857824136521739
- 00:06:24.132 --> 00:06:25.940 right link to behavior should be,
- NOTE Confidence: 0.857824136521739
- $00{:}06{:}25{.}940 \dashrightarrow 00{:}06{:}27{.}879$  not at the level of a synapse,
- NOTE Confidence: 0.857824136521739
- $00:06:27.880 \rightarrow 00:06:30.320$  because the heterogeneity just explodes,
- NOTE Confidence: 0.857824136521739
- $00{:}06{:}30{.}320 \dashrightarrow 00{:}06{:}32{.}455$  the combinatorics become impossible to
- NOTE Confidence: 0.857824136521739
- $00:06:32.455 \rightarrow 00:06:34.960$  intractable to quantify or deal with.
- NOTE Confidence: 0.857824136521739

 $00:06:34.960 \rightarrow 00:06:38.776$  So why have we not solved this problem right?

NOTE Confidence: 0.857824136521739

 $00:06:38.780 \longrightarrow 00:06:41.258$  Why is this opportunity not been realized?

NOTE Confidence: 0.857824136521739

 $00{:}06{:}41.260 \dashrightarrow 00{:}06{:}43.780$  And so I think that.

NOTE Confidence: 0.857824136521739

00:06:43.780 -> 00:06:46.408 I might argue my many reasons,

NOTE Confidence: 0.857824136521739

 $00:06:46.410 \longrightarrow 00:06:47.780$  but there's some legacy barriers,

NOTE Confidence: 0.857824136521739

 $00{:}06{:}47.780 \dashrightarrow 00{:}06{:}48.796$  right, that we're still

NOTE Confidence: 0.857824136521739

 $00:06:48.796 \longrightarrow 00:06:50.320$  trying to overcome as a field.

NOTE Confidence: 0.857824136521739

 $00{:}06{:}50{.}320 \dashrightarrow 00{:}06{:}54{.}080$  And I and the legacy approach are called

NOTE Confidence: 0.857824136521739

 $00{:}06{:}54.080 \dashrightarrow 00{:}06{:}56.848$  legacy because it's historically important

NOTE Confidence: 0.857824136521739

 $00:06:56.848 \longrightarrow 00:07:00.322$  to acknowledge that this is.

NOTE Confidence: 0.857824136521739

 $00{:}07{:}00{.}330 \dashrightarrow 00{:}07{:}02{.}004$  The framework that we have been

NOTE Confidence: 0.857824136521739

 $00:07:02.004 \rightarrow 00:07:03.455$  operating under is has tremendous

NOTE Confidence: 0.857824136521739

 $00{:}07{:}03.455 \dashrightarrow 00{:}07{:}05.129$  utility for what it was designed

NOTE Confidence: 0.857824136521739

00:07:05.129 --> 00:07:07.226 for and by that I mean DSM, right?

NOTE Confidence: 0.857824136521739

 $00:07:07.226 \longrightarrow 00:07:10.610$  It does what it was built for to do,

NOTE Confidence: 0.857824136521739

00:07:10.610 - 00:07:14.173 which is it reliably gets me and

 $00{:}07{:}14.173 \dashrightarrow 00{:}07{:}17.675$  every body else to agree that some person

NOTE Confidence: 0.857824136521739

 $00:07:17.675 \dashrightarrow 00:07:21.809$  has X out of P symptoms over T time.

NOTE Confidence: 0.857824136521739

 $00:07:21.810 \dashrightarrow 00:07:24.090$  That it does quantitatively accomplishes

NOTE Confidence: 0.857824136521739

 $00:07:24.090 \longrightarrow 00:07:26.640$  that, so we can reliably agree.

NOTE Confidence: 0.857824136521739

 $00{:}07{:}26.640 \dashrightarrow 00{:}07{:}29.340$  To categorize a human being as

NOTE Confidence: 0.857824136521739

00:07:29.340 --> 00:07:31.839 you showed X symptoms out of,

NOTE Confidence: 0.857824136521739

00:07:31.840 --> 00:07:34.500 you know, some rubric overtime.

NOTE Confidence: 0.857824136521739

 $00:07:34.500 \longrightarrow 00:07:36.285$  And then we give you a label.

NOTE Confidence: 0.857824136521739

 $00:07:36.290 \longrightarrow 00:07:37.898$  I'd like to argue that's ill

NOTE Confidence: 0.857824136521739

 $00:07:37.898 \longrightarrow 00:07:39.310$  fitting for what we need,

NOTE Confidence: 0.857824136521739

 $00:07:39.310 \rightarrow 00:07:41.914$  actually not wrong for what it was

NOTE Confidence: 0.857824136521739

 $00:07:41.914 \longrightarrow 00:07:44.640$  built to do, just not what we need.

NOTE Confidence: 0.857824136521739

 $00{:}07{:}44.640 \dashrightarrow 00{:}07{:}45.561$  And then further,

NOTE Confidence: 0.857824136521739

 $00{:}07{:}45{.}561 \dashrightarrow 00{:}07{:}47{.}403$  we lack data and methods to

NOTE Confidence: 0.857824136521739

 $00{:}07{:}47.403 \dashrightarrow 00{:}07{:}48.772$  quantitatively molecular benchmark

 $00:07:48.772 \rightarrow 00:07:50.550$  brain behavior relationships, right?

NOTE Confidence: 0.857824136521739

 $00:07:50.550 \longrightarrow 00:07:52.440$  So the legacy approach doesn't have it.

NOTE Confidence: 0.857824136521739

 $00{:}07{:}52{.}440 \dashrightarrow 00{:}07{:}54{.}378$  And then we don't have technological

NOTE Confidence: 0.857824136521739

 $00:07:54.378 \rightarrow 00:07:56.301$  solutions to actually scale this with

NOTE Confidence: 0.857824136521739

00:07:56.301 $\operatorname{-->}$ 00:07:58.317 the kinds of observations that are so

NOTE Confidence: 0.857824136521739

 $00{:}07{:}58.317 \dashrightarrow 00{:}08{:}00.421$  important in the area of psychedelic

NOTE Confidence: 0.857824136521739

 $00:08:00.421 \rightarrow 00:08:01.833$  medicine for precision therapeutics,

NOTE Confidence: 0.857824136521739

 $00:08:01.840 \longrightarrow 00:08:02.348$  right.

NOTE Confidence: 0.857824136521739

 $00{:}08{:}02{.}348 \dashrightarrow 00{:}08{:}06{.}920$  So this is a dystopian vision of the future,

NOTE Confidence: 0.857824136521739

00:08:06.920 --> 00:08:07.271 right,

NOTE Confidence: 0.857824136521739

 $00{:}08{:}07{.}271 \dashrightarrow 00{:}08{:}09{.}728$  that I'd like to show sometimes like

NOTE Confidence: 0.857824136521739

 $00:08:09.728 \rightarrow 00:08:12.165$  basically where we use computer assisted

NOTE Confidence: 0.857824136521739

00:08:12.165 --> 00:08:14.667 decision making or machine learning informed.

NOTE Confidence: 0.857824136521739

 $00{:}08{:}14.670 \dashrightarrow 00{:}08{:}16.240$  Decisions with multimodal data where

NOTE Confidence: 0.857824136521739

 $00:08:16.240 \rightarrow 00:08:18.481$  the brain is in the middle, right?

NOTE Confidence: 0.857824136521739

 $00:08:18.481 \dashrightarrow 00:08:20.249$  I'm not taking the person out of this.

00:08:20.250 --> 00:08:21.402 I'm not, you know,

NOTE Confidence: 0.857824136521739

 $00:08:21.402 \rightarrow 00:08:22.554$  reductionist to that point,

NOTE Confidence: 0.857824136521739

 $00:08:22.560 \longrightarrow 00:08:24.877$  but the organ has to be in

NOTE Confidence: 0.857824136521739

 $00:08:24.877 \rightarrow 00:08:26.619$  the middle in my mind.

NOTE Confidence: 0.857824136521739

 $00:08:26.620 \rightarrow 00:08:29.080$  And then we're hopefully optimizing these

NOTE Confidence: 0.857824136521739

 $00:08:29.080 \rightarrow 00:08:31.779$  two decisions through an iterative cycle,

NOTE Confidence: 0.857824136521739

 $00:08:31.780 \longrightarrow 00:08:32.110$  right?

NOTE Confidence: 0.857824136521739

 $00:08:32.110 \rightarrow 00:08:34.420$  But we're not there and and so,

NOTE Confidence: 0.857824136521739

 $00:08:34.420 \longrightarrow 00:08:36.254$  So what do we do about that?

NOTE Confidence: 0.857824136521739

00:08:36.260 --> 00:08:39.588 So my group here and our other collaborators

NOTE Confidence: 0.857824136521739

 $00:08:39.588 \rightarrow 00:08:43.380$  here at Yale are really approaching this in,

NOTE Confidence: 0.857824136521739

 $00{:}08{:}43{.}380 \dashrightarrow 00{:}08{:}44{.}748$  in the following way.

NOTE Confidence: 0.857824136521739

 $00:08:44.748 \rightarrow 00:08:47.880$  So let me walk you through the framework.

NOTE Confidence: 0.857824136521739

 $00{:}08{:}47{.}880 \dashrightarrow 00{:}08{:}51{.}864$  So we have to 1st agree that the

NOTE Confidence: 0.857824136521739

 $00{:}08{:}51{.}864 \dashrightarrow 00{:}08{:}53{.}911$  neurobehavioral mapping problem is

 $00:08:53.911 \dashrightarrow 00:08:56.559$  quantitatively A must, we have to do that.

NOTE Confidence: 0.857824136521739

00:08:56.560 --> 00:08:56.827 Correctly.

NOTE Confidence: 0.857824136521739

00:08:56.827 --> 00:08:59.290 And I'll explain what I mean by that, right?

NOTE Confidence: 0.857824136521739

 $00:08:59.290 \longrightarrow 00:09:01.530$  Because if if we are using an

NOTE Confidence: 0.857824136521739

 $00{:}09{:}01.530 \dashrightarrow 00{:}09{:}03.845$  ill fitting framework to map

NOTE Confidence: 0.857824136521739

 $00{:}09{:}03.845 \dashrightarrow 00{:}09{:}05.447$  onto neurobehavioral variation,

NOTE Confidence: 0.857824136521739

 $00:09:05.450 \longrightarrow 00:09:07.102$  then just won't work.

NOTE Confidence: 0.857824136521739

 $00:09:07.102 \rightarrow 00:09:10.050$  We won't even translate what we want.

NOTE Confidence: 0.857824136521739

00:09:10.050 --> 00:09:11.994 Gene expression alterations right

NOTE Confidence: 0.857824136521739

 $00:09:11.994 \rightarrow 00:09:14.424$  and disturbances in the way

NOTE Confidence: 0.857824136521739

 $00{:}09{:}14{.}424 \dashrightarrow 00{:}09{:}17{.}172$  that the circuits are formed are

NOTE Confidence: 0.857824136521739

 $00:09:17.172 \longrightarrow 00:09:18.618$  it's useful information.

NOTE Confidence: 0.857824136521739

 $00{:}09{:}18.618 \dashrightarrow 00{:}09{:}21.546$  We harness that from say the island

NOTE Confidence: 0.857824136521739

 $00{:}09{:}21.546 \dashrightarrow 00{:}09{:}23.870$ human brain Atlas to inform our our

NOTE Confidence: 0.857824136521739

 $00{:}09{:}23{.}937 \dashrightarrow 00{:}09{:}26{.}643$  our models that then can simulate

NOTE Confidence: 0.857824136521739

 $00:09:26.643 \dashrightarrow 00:09:28.890$  pharmacological fMRI effects which in

 $00:09:28.890 \rightarrow 00:09:31.110$  turn can be fixed individual people.

NOTE Confidence: 0.857824136521739

 $00:09:31.110 \longrightarrow 00:09:33.168$  So this is just one way

NOTE Confidence: 0.857824136521739

 $00:09:33.168 \longrightarrow 00:09:34.540$  that we're approaching this

NOTE Confidence: 0.82290617

 $00:09:34.617 \rightarrow 00:09:36.927$  problem in the area of just mental

NOTE Confidence: 0.82290617

 $00:09:36.927 \rightarrow 00:09:39.143$  health and and psychedelic pharmacology.

NOTE Confidence: 0.82290617

 $00:09:39.143 \dashrightarrow 00:09:41.208$  Specifically, but there's there's many

NOTE Confidence: 0.82290617

 $00:09:41.208 \rightarrow 00:09:44.078$  other tools that we're leaving on the table,

NOTE Confidence: 0.82290617

 $00:09:44.080 \rightarrow 00:09:45.502$  but this is what I'm going to talk about,

NOTE Confidence: 0.82290617

 $00{:}09{:}45{.}510 \dashrightarrow 00{:}09{:}47{.}365$  right. So again I'd like to argue

NOTE Confidence: 0.82290617

 $00{:}09{:}47.365 \dashrightarrow 00{:}09{:}50.029$  that you know Chris asked me to talk

NOTE Confidence: 0.82290617

 $00:09:50.029 \rightarrow 00:09:51.473$  about neuroimaging today specifically

NOTE Confidence: 0.82290617

00:09:51.473 --> 00:09:53.370 and to really have that focus.

NOTE Confidence: 0.82290617

 $00{:}09{:}53{.}370 \dashrightarrow 00{:}09{:}56{.}066$  So I'd like to argue that new imaging

NOTE Confidence: 0.82290617

00:09:56.066 --> 00:09:59.130 is not an option anymore in our work.

NOTE Confidence: 0.82290617

 $00:09:59.130 \rightarrow 00:10:01.146$  And by that I mean normalizing broadly,

00:10:01.150 --> 00:10:03.958 right? But a necessity, because here,

NOTE Confidence: 0.82290617

 $00{:}10{:}03{.}960 \dashrightarrow 00{:}10{:}05{.}368$  here's a choice, right?

NOTE Confidence: 0.82290617

 $00:10:05.368 \rightarrow 00:10:08.408$  This is literally what we had on the table,

NOTE Confidence: 0.82290617

 $00:10:08.410 \longrightarrow 00:10:11.560$  right? But we need this.

NOTE Confidence: 0.82290617

 $00{:}10{:}11{.}560 \dashrightarrow 00{:}10{:}14{.}565$  And so I'd like to argue that if if you

NOTE Confidence: 0.82290617

00:10:14.565 --> 00:10:16.362 present the problem this way, right,

NOTE Confidence: 0.82290617

 $00{:}10{:}16{.}362 \dashrightarrow 00{:}10{:}18{.}938$  like how can we not leverage brain data

NOTE Confidence: 0.82290617

 $00:10:18.938 \rightarrow 00:10:22.014$  in the service of decision making as a must,

NOTE Confidence: 0.82290617

 $00{:}10{:}22.020 \dashrightarrow 00{:}10{:}24.190$  specifically for things as complicated

NOTE Confidence: 0.82290617

 $00{:}10{:}24.190 \dashrightarrow 00{:}10{:}25.926$  as psychedelic neurobiology at

NOTE Confidence: 0.82290617

 $00:10:25.926 \longrightarrow 00:10:27.773$  the individual level, right.

NOTE Confidence: 0.82290617

 $00{:}10{:}27.773 \dashrightarrow 00{:}10{:}28.116$  So.

NOTE Confidence: 0.82290617

 $00{:}10{:}28.116 \dashrightarrow 00{:}10{:}30.860$  So, OK, so how can we exploit imaging

NOTE Confidence: 0.82290617

 $00:10:30.936 \longrightarrow 00:10:32.940$  in the service of this goal?

NOTE Confidence: 0.82290617

 $00:10:32.940 \longrightarrow 00:10:34.760$  So that's the rest of the talk.

NOTE Confidence: 0.82290617

 $00:10:34.760 \longrightarrow 00:10:38.484$  So for those of you who haven't

- NOTE Confidence: 0.82290617
- $00:10:38.484 \longrightarrow 00:10:40.080$  really thought about.
- NOTE Confidence: 0.82290617
- $00:10:40.080 \longrightarrow 00:10:41.220$  Structural functional
- NOTE Confidence: 0.82290617
- 00:10:41.220 --> 00:10:42.930 multimodal imaging recently,
- NOTE Confidence: 0.82290617
- $00:10:42.930 \longrightarrow 00:10:44.882$  this is a very useful reminder of the
- NOTE Confidence: 0.82290617
- $00{:}10{:}44.882 \dashrightarrow 00{:}10{:}46.530$  resolution of what imaging straddles,
- NOTE Confidence: 0.82290617
- $00:10:46.530 \longrightarrow 00:10:46.906$  right.
- NOTE Confidence: 0.82290617
- $00:10:46.906 \longrightarrow 00:10:50.290$  So on the Y axis is the size of
- NOTE Confidence: 0.82290617
- $00{:}10{:}50{.}395 \dashrightarrow 00{:}10{:}53{.}510$  the observation and time is on the
- NOTE Confidence: 0.82290617
- $00{:}10{:}53{.}510 \dashrightarrow 00{:}10{:}56{.}300$  the X axis and and you'll notice
- NOTE Confidence: 0.82290617
- $00:10:56.300 \longrightarrow 00:10:58.050$  that human imaging across modality
- NOTE Confidence: 0.82290617
- $00:10:58.050 \rightarrow 00:11:00.006$  straddles a good bit of the space.
- NOTE Confidence: 0.82290617
- $00{:}11{:}00{.}010 \dashrightarrow 00{:}11{:}01{.}478$  We're not helpless right.
- NOTE Confidence: 0.82290617
- 00:11:01.478 --> 00:11:03.680 Like we can actually measure signals
- NOTE Confidence: 0.82290617
- 00:11:03.745 --> 00:11:06.286 in various ways in relation to various
- NOTE Confidence: 0.82290617
- 00:11:06.286 --> 00:11:07.790 phenomena, but we still are, you know,
- NOTE Confidence: 0.82290617

 $00:11:07.790 \longrightarrow 00:11:10.446$  out of reach of certain levels of analysis.

NOTE Confidence: 0.82290617

 $00{:}11{:}10{.}450 \dashrightarrow 00{:}11{:}12{.}154$  Like with human imaging with symptoms

NOTE Confidence: 0.82290617

00:11:12.154 --> 00:11:13.899 improving but still not quite there.

NOTE Confidence: 0.82290617

 $00:11:13.900 \longrightarrow 00:11:15.594$  And we also don't have just one

NOTE Confidence: 0.82290617

 $00:11:15.594 \rightarrow 00:11:16.640$  way to measure this,

NOTE Confidence: 0.82290617

00:11:16.640 --> 00:11:17.092 right.

NOTE Confidence: 0.82290617

 $00:11:17.092 \longrightarrow 00:11:20.256$  We have multiple modalities that now can

NOTE Confidence: 0.82290617

 $00:11:20.256 \rightarrow 00:11:23.045$  combine that give you different slices

NOTE Confidence: 0.82290617

 $00{:}11{:}23.045 \dashrightarrow 00{:}11{:}25.757$  of the signal that this incredibly

NOTE Confidence: 0.82290617

00:11:25.833 --> 00:11:28.318 complex piece of tissue produces,

NOTE Confidence: 0.82290617

00:11:28.320 --> 00:11:28.642 right.

NOTE Confidence: 0.82290617

00:11:28.642 --> 00:11:29.286 And so,

NOTE Confidence: 0.82290617

00:11:29.286 --> 00:11:31.540 so I'm going to talk about specifically

NOTE Confidence: 0.82290617

 $00:11:31.609 \rightarrow 00:11:34.300$  throughout the rest of talk about bold F MRI,

NOTE Confidence: 0.82290617

00:11:34.300 - 00:11:38.900 right, which is a measure that is is.

NOTE Confidence: 0.82290617

 $00:11:38.900 \rightarrow 00:11:41.060$  One of the expertise areas in my group,

- NOTE Confidence: 0.82290617
- $00:11:41.060 \longrightarrow 00:11:43.700$  right so.
- NOTE Confidence: 0.82290617
- 00:11:43.700 --> 00:11:44.095 Specifically,
- NOTE Confidence: 0.82290617
- $00:11:44.095 \longrightarrow 00:11:46.465$  the phenomena that for the rest
- NOTE Confidence: 0.82290617
- $00{:}11{:}46{.}465 \dashrightarrow 00{:}11{:}49{.}447$  of the the talk will focus on is
- NOTE Confidence: 0.82290617
- 00:11:49.447 --> 00:11:51.420 this idea of resting state, right?
- NOTE Confidence: 0.82290617
- $00{:}11{:}51{.}420 \dashrightarrow 00{:}11{:}53{.}340$  And so this is now a household name.
- NOTE Confidence: 0.82290617
- 00:11:53.340 --> 00:11:53.898 I, you know,
- NOTE Confidence: 0.82290617
- 00:11:53.898 --> 00:11:55.200 I don't have to go over this
- NOTE Confidence: 0.82290617
- $00{:}11{:}55{.}254 \dashrightarrow 00{:}11{:}56{.}119$  in a lot of detail,
- NOTE Confidence: 0.82290617
- $00:11:56.120 \longrightarrow 00:11:57.723$  but I'd like to kind of just
- NOTE Confidence: 0.82290617
- $00:11:57.723 \longrightarrow 00:11:58.759$  review the history of it.
- NOTE Confidence: 0.82290617
- 00:11:58.760 --> 00:12:00.672 I always like to do this because I
- NOTE Confidence: 0.82290617
- 00:12:00.672 --> 00:12:03.093 like to remind people that in 1995,
- NOTE Confidence: 0.82290617
- 00:12:03.093 --> 00:12:05.142 right, broad Biswal.
- NOTE Confidence: 0.82290617
- $00:12:05.142 \longrightarrow 00:12:07.874$  Actually observe this simply
- NOTE Confidence: 0.82290617

 $00:12:07.874 \longrightarrow 00:12:10.090$  by taking signal.

NOTE Confidence: 0.82290617

00:12:10.090 --> 00:12:12.918 Out of 1 hemisphere of the motor

NOTE Confidence: 0.82290617

 $00{:}12{:}12{.}918 \dashrightarrow 00{:}12{:}15{.}306$  cortex and asking where in the

NOTE Confidence: 0.82290617

 $00{:}12{:}15{.}306 \dashrightarrow 00{:}12{:}17{.}190$  brain is there time dependent

NOTE Confidence: 0.82290617

00:12:17.190 --> 00:12:19.470 covariation of signal within a person

NOTE Confidence: 0.82290617

 $00{:}12{:}19.537 \dashrightarrow 00{:}12{:}21.467$  and then average across people.

NOTE Confidence: 0.82290617

 $00:12:21.470 \longrightarrow 00:12:24.278$  And he saw this map right which is

NOTE Confidence: 0.82290617

 $00{:}12{:}24{.}278$  -->  $00{:}12{:}26{.}249$  bilateral motor cortex comes out.

NOTE Confidence: 0.82290617

 $00{:}12{:}26.250 \dashrightarrow 00{:}12{:}28.326$  And people thought this was junk.

NOTE Confidence: 0.82290617

00:12:28.330 --> 00:12:29.810 This was a compound, right?

NOTE Confidence: 0.82290617

 $00:12:29.810 \longrightarrow 00:12:31.194$  And they ignored it.

NOTE Confidence: 0.82290617

00:12:31.194 --> 00:12:33.330 In fact, he was attacked for it quite a lot,

NOTE Confidence: 0.883748563333333

 $00:12:33.330 \longrightarrow 00:12:35.610$  right? And then only a

NOTE Confidence: 0.883748563333333

 $00:12:35.610 \longrightarrow 00:12:37.434$  decade later with some.

NOTE Confidence: 0.544249814625

00:12:39.540 --> 00:12:41.060 Advances from Michael Greicius

NOTE Confidence: 0.544249814625

 $00:12:41.060 \rightarrow 00:12:42.580$  and then Marcus Raichle.

- NOTE Confidence: 0.544249814625
- $00:12:42.580 \rightarrow 00:12:44.500$  Did this phenomena really
- NOTE Confidence: 0.544249814625
- $00:12:44.500 \longrightarrow 00:12:45.940$  become a mainstream?
- NOTE Confidence: 0.544249814625
- 00:12:45.940 --> 00:12:47.613 And so now if you Fast forward
- NOTE Confidence: 0.544249814625
- $00:12:47.613 \rightarrow 00:12:49.130$  what is now a decade ago,
- NOTE Confidence: 0.544249814625
- $00:12:49.130 \longrightarrow 00:12:50.378$  which is hard to believe right,
- NOTE Confidence: 0.544249814625
- $00{:}12{:}50{.}380 \dashrightarrow 00{:}12{:}53{.}896$  that Thomas Yao and Randy Buckner
- NOTE Confidence: 0.544249814625
- 00:12:53.896 --> 00:12:56.240 actually mapped comprehensively right.
- NOTE Confidence: 0.544249814625
- $00:12:56.240 \longrightarrow 00:12:57.779$  Large scale networks
- NOTE Confidence: 0.544249814625
- $00:12:57.779 \longrightarrow 00:12:59.318$  across individuals right.
- NOTE Confidence: 0.544249814625
- $00:12:59.320 \longrightarrow 00:13:02.500$  And this is this is now a joke
- NOTE Confidence: 0.544249814625
- 00:13:02.500 -> 00:13:04.173 like we know we can do this now
- NOTE Confidence: 0.544249814625
- $00{:}13{:}04{.}173 \dashrightarrow 00{:}13{:}05{.}478$  and every single person right.
- NOTE Confidence: 0.544249814625
- 00:13:05.480 --> 00:13:06.944 But it was controversial
- NOTE Confidence: 0.544249814625
- $00{:}13{:}06{.}944 \dashrightarrow 00{:}13{:}09{.}140$  then and so then 2016 onward.
- NOTE Confidence: 0.544249814625
- $00:13:09.140 \rightarrow 00:13:10.832$  Human connectome produced sparse
- NOTE Confidence: 0.544249814625

 $00:13:10.832 \longrightarrow 00:13:13.830$  relation which gives you an index of

NOTE Confidence: 0.544249814625

 $00{:}13{:}13{.}830 \dashrightarrow 00{:}13{:}16{.}176$  the boundaries between the areas that

NOTE Confidence: 0.544249814625

 $00{:}13{:}16.176 \dashrightarrow 00{:}13{:}18.379$  is comprehensive but not definitive.

NOTE Confidence: 0.544249814625

 $00:13:18.380 \rightarrow 00:13:20.424$  This will probably improve it or actively,

NOTE Confidence: 0.544249814625

 $00:13:20.430 \longrightarrow 00:13:21.846$  but I'd like to tell you like we've

NOTE Confidence: 0.544249814625

00:13:21.846 --> 00:13:23.218 made some serious progress, right,

NOTE Confidence: 0.544249814625

 $00:13:23.218 \rightarrow 00:13:25.990$  with human or imaging and we can exploit it,

NOTE Confidence: 0.544249814625

00:13:25.990 --> 00:13:26.578 right?

NOTE Confidence: 0.544249814625

00:13:26.578 --> 00:13:27.754 And furthermore,

NOTE Confidence: 0.544249814625

 $00:13:27.754 \rightarrow 00:13:31.282$  this is something I will repeat

NOTE Confidence: 0.544249814625

 $00{:}13{:}31{.}282 \dashrightarrow 00{:}13{:}33{.}798$  in every talk I give.

NOTE Confidence: 0.544249814625

 $00{:}13{:}33{.}800 \dashrightarrow 00{:}13{:}36{.}068$  So the reason why the Human

NOTE Confidence: 0.544249814625

 $00{:}13{:}36.068 \dashrightarrow 00{:}13{:}37.964$  Connectome project pipelines and the

NOTE Confidence: 0.544249814625

 $00:13:37.964 \rightarrow 00:13:39.688$  entire effort towards so impactful,

NOTE Confidence: 0.544249814625

 $00:13:39.688 \rightarrow 00:13:42.236$  which is why I obviously drink the

NOTE Confidence: 0.544249814625

 $00:13:42.236 \rightarrow 00:13:46.410$  kool-aid because I trained there, but.

- NOTE Confidence: 0.544249814625
- $00{:}13{:}46{.}410 \dashrightarrow 00{:}13{:}48{.}912$  The human brain and the cortical
- NOTE Confidence: 0.544249814625
- $00{:}13{:}48{.}912 \dashrightarrow 00{:}13{:}51{.}117$  mantle is A2 dimensional surface
- NOTE Confidence: 0.544249814625
- $00:13:51.117 \rightarrow 00:13:53.883$  wrapped around white matter that is
- NOTE Confidence: 0.544249814625
- $00{:}13{:}53.883 \dashrightarrow 00{:}13{:}56.598$  about 4 millimeters thick and it's the
- NOTE Confidence: 0.544249814625
- $00{:}13{:}56{.}598 \dashrightarrow 00{:}13{:}59{.}254$  size of a pizza and that geometry matters.
- NOTE Confidence: 0.544249814625
- $00{:}13{:}59{.}254 \dashrightarrow 00{:}14{:}01{.}164$  It matters fundamentally when you're
- NOTE Confidence: 0.544249814625
- 00:14:01.164 --> 00:14:03.316 going to do precision medicine
- NOTE Confidence: 0.544249814625
- $00:14:03.316 \longrightarrow 00:14:05.196$  analytics with single subject
- NOTE Confidence: 0.544249814625
- 00:14:05.196 --> 00:14:06.824 human cortical surfaces, right?
- NOTE Confidence: 0.544249814625
- 00:14:06.824 --> 00:14:07.252 In fact,
- NOTE Confidence: 0.544249814625
- 00:14:07.252 --> 00:14:08.750 just before this talk I got off
- NOTE Confidence: 0.544249814625
- $00{:}14{:}08{.}803 \dashrightarrow 00{:}14{:}10{.}308$  the call with one of my students,
- NOTE Confidence: 0.544249814625
- $00:14:10.310 \longrightarrow 00:14:11.050$  Amber Howell,
- NOTE Confidence: 0.544249814625
- $00{:}14{:}11.050 \dashrightarrow 00{:}14{:}12.900$  deeply debating the importance of
- NOTE Confidence: 0.544249814625
- $00:14:12.900 \longrightarrow 00:14:14.383$  importance of social curvature
- NOTE Confidence: 0.544249814625

 $00:14:14.383 \longrightarrow 00:14:16.243$  and depth on a single subject

NOTE Confidence: 0.544249814625

 $00{:}14{:}16{.}243 \dashrightarrow 00{:}14{:}17{.}400$  level in relation to.

NOTE Confidence: 0.544249814625

00:14:17.400 --> 00:14:19.170 Diffusivity of white matter tracts,

NOTE Confidence: 0.544249814625

 $00:14:19.170 \longrightarrow 00:14:20.420$  and turns out it matters.

NOTE Confidence: 0.544249814625

 $00:14:20.420 \longrightarrow 00:14:22.990$  It matters a lot anyway.

NOTE Confidence: 0.544249814625

 $00{:}14{:}22{.}990 \dashrightarrow 00{:}14{:}25{.}168$  Analyzing your data on the surface,

NOTE Confidence: 0.544249814625

 $00{:}14{:}25{.}170 \dashrightarrow 00{:}14{:}28{.}878$  I think is is. I must like you.

NOTE Confidence: 0.544249814625

 $00:14:28.878 \longrightarrow 00:14:30.630$  You are blind without that to

NOTE Confidence: 0.544249814625

00:14:30.696 --> 00:14:33.240 individual variation, right?

NOTE Confidence: 0.544249814625

 $00:14:33.240 \longrightarrow 00:14:34.450$  So.

NOTE Confidence: 0.544249814625

 $00:14:34.450 \longrightarrow 00:14:35.930$  When you do this right,

NOTE Confidence: 0.544249814625

 $00:14:35.930 \longrightarrow 00:14:39.142$  then you can produce metrics in the

NOTE Confidence: 0.544249814625

 $00{:}14{:}39{.}142 \dashrightarrow 00{:}14{:}41{.}272$  geometry of the cortical surface

NOTE Confidence: 0.544249814625

00:14:41.272 --> 00:14:43.886 that can quantify some signal in

NOTE Confidence: 0.544249814625

 $00:14:43.886 \longrightarrow 00:14:45.986$  every cortical parcel or area.

NOTE Confidence: 0.544249814625

 $00:14:45.990 \longrightarrow 00:14:48.042$  I'll use the term parcel because

- NOTE Confidence: 0.544249814625
- $00{:}14{:}48.042 \dashrightarrow 00{:}14{:}49.410$  that's the formal definition.
- NOTE Confidence: 0.544249814625
- $00{:}14{:}49{.}410 \dashrightarrow 00{:}14{:}51{.}328$  And then you can operate with those
- NOTE Confidence: 0.544249814625
- $00:14:51.328 \longrightarrow 00:14:53.053$  metrics to analyze it within a
- NOTE Confidence: 0.544249814625
- $00:14:53.053 \rightarrow 00:14:54.745$  subject across people in various ways,
- NOTE Confidence: 0.544249814625
- $00{:}14{:}54{.}750 \dashrightarrow 00{:}14{:}55{.}118$  right.
- NOTE Confidence: 0.544249814625
- $00:14:55.118 \rightarrow 00:14:55.854$  So furthermore,
- NOTE Confidence: 0.544249814625
- $00:14:55.854 \rightarrow 00:14:59.389$  what we've done in my group out of necessity,
- NOTE Confidence: 0.544249814625
- 00:14:59.390 --> 00:14:59.723 right,
- NOTE Confidence: 0.544249814625
- $00{:}14{:}59{.}723 \dashrightarrow 00{:}15{:}02{.}054$  we started to use the cortical parcellation
- NOTE Confidence: 0.544249814625
- 00:15:02.054 --> 00:15:04.188 from the Human Connectome Project,
- NOTE Confidence: 0.544249814625
- $00:15:04.190 \longrightarrow 00:15:05.566$  which is shown here.
- NOTE Confidence: 0.544249814625
- 00:15:05.566 --> 00:15:06.598 These little borders,
- NOTE Confidence: 0.544249814625
- $00{:}15{:}06{.}600 \dashrightarrow 00{:}15{:}09{.}200$  but then we use the network partitions from
- NOTE Confidence: 0.544249814625
- $00{:}15{:}09{.}200 \dashrightarrow 00{:}15{:}11{.}538$  from other groups and they were great,
- NOTE Confidence: 0.544249814625
- $00:15:11.540 \longrightarrow 00:15:12.840$  they they worked really well.
- NOTE Confidence: 0.544249814625

 $00{:}15{:}12.840 \dashrightarrow 00{:}15{:}15.220$  But then we realized subcortical

NOTE Confidence: 0.544249814625

 $00:15:15.220 \rightarrow 00:15:17.124$  coverage is not there.

NOTE Confidence: 0.544249814625

00:15:17.130 --> 00:15:18.920 Like thalamus wasn't covered appropriately,

NOTE Confidence: 0.544249814625

 $00:15:18.920 \longrightarrow 00:15:20.366$  brainstem wasn't covered.

NOTE Confidence: 0.544249814625

 $00:15:20.366 \longrightarrow 00:15:23.268$  And you guys know that psychiatric

NOTE Confidence: 0.544249814625

 $00{:}15{:}23.268 \dashrightarrow 00{:}15{:}25.220$  medication works on subcortical

NOTE Confidence: 0.544249814625

00:15:25.220 --> 00:15:27.660 circuits and precision of isolating

NOTE Confidence: 0.544249814625

 $00{:}15{:}27.727 \dashrightarrow 00{:}15{:}29.612$  specific voxels in relation to

NOTE Confidence: 0.544249814625

 $00{:}15{:}29.612 \dashrightarrow 00{:}15{:}32.180$  networks and parcels is really important.

NOTE Confidence: 0.544249814625

 $00:15:32.180 \longrightarrow 00:15:34.112$  So what I'm showing you here is

NOTE Confidence: 0.544249814625

 $00{:}15{:}34{.}112 \dashrightarrow 00{:}15{:}35{.}920$  work produced by my student Lisa.

NOTE Confidence: 0.544249814625

 $00{:}15{:}35{.}920 \dashrightarrow 00{:}15{:}38{.}655$  Who's extended the cortical partition

NOTE Confidence: 0.544249814625

00:15:38.655 --> 00:15:40.843 into networks Cortically first,

NOTE Confidence: 0.544249814625

 $00{:}15{:}40.850 \dashrightarrow 00{:}15{:}43.855$  and then studied how subcortical

NOTE Confidence: 0.544249814625

 $00{:}15{:}43.855 \dashrightarrow 00{:}15{:}46.860$  voxels covary with those networks,

NOTE Confidence: 0.544249814625

 $00:15:46.860 \rightarrow 00:15:49.260$  assigning every single voxel in

- NOTE Confidence: 0.544249814625
- $00{:}15{:}49{.}260 \dashrightarrow 00{:}15{:}51{.}660$  subcortical brain matter to a
- NOTE Confidence: 0.544249814625
- $00:15:51.744 \rightarrow 00:15:54.576$  network until it reached split half?
- NOTE Confidence: 0.814083745
- $00:15:54.580 \rightarrow 00:15:57.598$  Stability across the entire HCP sample.
- NOTE Confidence: 0.814083745
- $00:15:57.600 \longrightarrow 00:15:58.937$  And so the reason why we did
- NOTE Confidence: 0.814083745
- $00{:}15{:}58{.}937 \dashrightarrow 00{:}16{:}00{.}777$  this out of necessity is we need
- NOTE Confidence: 0.814083745
- $00:16:00.777 \longrightarrow 00:16:01.993$  this for clinical application.
- NOTE Confidence: 0.814083745
- $00:16:02.000 \rightarrow 00:16:04.044$  We actually needed a whole brain partition
- NOTE Confidence: 0.814083745
- $00:16:04.044 \rightarrow 00:16:06.040$  to covers every piece of Gray matter.
- NOTE Confidence: 0.814083745
- $00{:}16{:}06{.}040 \dashrightarrow 00{:}16{:}07{.}979$  We can't leave things on the table.
- NOTE Confidence: 0.814083745
- $00{:}16{:}07{.}980 \dashrightarrow 00{:}16{:}09{.}771$  So now this is published and this is what
- NOTE Confidence: 0.814083745
- $00{:}16{:}09{.}771 \dashrightarrow 00{:}16{:}11{.}419$  we're going to be using for us to talk.
- NOTE Confidence: 0.814083745
- 00:16:11.420 --> 00:16:13.352 Now just to convince you that
- NOTE Confidence: 0.814083745
- $00:16:13.352 \longrightarrow 00:16:14.977$  this actually is better, right.
- NOTE Confidence: 0.814083745
- $00{:}16{:}14.977 \dashrightarrow 00{:}16{:}17.575$  So you can take a dense signal, right?
- NOTE Confidence: 0.814083745
- $00:16:17.575 \rightarrow 00:16:19.455$  In other words, at the level of vertex
- NOTE Confidence: 0.814083745

00:16:19.455 --> 00:16:21.586 on a cortical surface, you can parse,

NOTE Confidence: 0.814083745

 $00{:}16{:}21.586 \dashrightarrow 00{:}16{:}23.398$  relate it prior to computing some

NOTE Confidence: 0.814083745

00:16:23.398 --> 00:16:25.239 metric or you can parse relate it.

NOTE Confidence: 0.814083745

 $00:16:25.240 \longrightarrow 00:16:26.274$  Post right?

NOTE Confidence: 0.814083745

 $00:16:26.274 \longrightarrow 00:16:29.376$  So if the person relation is.

NOTE Confidence: 0.814083745

 $00{:}16{:}29{.}380 \dashrightarrow 00{:}16{:}31{.}820$  Valid and consistent across subjects,

NOTE Confidence: 0.814083745

 $00:16:31.820 \dashrightarrow 00:16:34.074$  then this should be better than that.

NOTE Confidence: 0.814083745

00:16:34.080 --> 00:16:35.348 And that's in fact true, right?

NOTE Confidence: 0.814083745

 $00:16:35.348 \longrightarrow 00:16:36.776$  And so this is not news,

NOTE Confidence: 0.814083745

 $00{:}16{:}36{.}780 \dashrightarrow 00{:}16{:}37{.}880$  not Glasser has shown this

NOTE Confidence: 0.814083745

 $00:16:37.880 \longrightarrow 00:16:39.180$  in his work and so on,

NOTE Confidence: 0.814083745

 $00{:}16{:}39{.}180 \dashrightarrow 00{:}16{:}41{.}988$  but it's just to convince you guys that

NOTE Confidence: 0.814083745

 $00:16:41.988 \rightarrow 00:16:43.840$  these parcellation are actually very,

NOTE Confidence: 0.814083745

 $00{:}16{:}43.840 \dashrightarrow 00{:}16{:}46.220$  very useful, not just quantitatively,

NOTE Confidence: 0.814083745

 $00:16:46.220 \rightarrow 00:16:48.536$  but as a feature space reduction,

NOTE Confidence: 0.814083745

 $00:16:48.540 \longrightarrow 00:16:50.448$  because now you are no longer

- NOTE Confidence: 0.814083745
- 00:16:50.448 --> 00:16:51.698 working with 95,000 voxels,
- NOTE Confidence: 0.814083745
- $00{:}16{:}51{.}698 \dashrightarrow 00{:}16{:}53{.}218$  you're working with 700 areas
- NOTE Confidence: 0.814083745
- $00:16:53.218 \rightarrow 00:16:55.358$  and now you can do some clever
- NOTE Confidence: 0.814083745
- $00:16:55.358 \rightarrow 00:16:57.116$  feature engineering on top of that.
- NOTE Confidence: 0.814083745
- $00:16:57.120 \longrightarrow 00:16:58.540$  So that matters, right?
- NOTE Confidence: 0.814083745
- $00:16:58.540 \longrightarrow 00:17:01.862$  So how do we now link this to
- NOTE Confidence: 0.814083745
- 00:17:01.862 --> 00:17:03.603 molecular mechanism, right,
- NOTE Confidence: 0.814083745
- $00:17:03.603 \rightarrow 00:17:06.768$  very broadly speaking and so.
- NOTE Confidence: 0.814083745
- 00:17:06.770 --> 00:17:07.244 So, so,
- NOTE Confidence: 0.814083745
- $00:17:07.244 \longrightarrow 00:17:09.140$  so the way we do this and the
- NOTE Confidence: 0.814083745
- $00{:}17{:}09{.}204 \dashrightarrow 00{:}17{:}11{.}124$  way we've approached this across
- NOTE Confidence: 0.814083745
- 00:17:11.124 --> 00:17:12.982 all compounds ketamine,
- NOTE Confidence: 0.814083745
- $00:17:12.982 \rightarrow 00:17:17.398$  single sideband as well as application
- NOTE Confidence: 0.814083745
- $00{:}17{:}17{.}398 \dashrightarrow 00{:}17{:}20{.}673$  to clinical questions is what
- NOTE Confidence: 0.814083745
- $00{:}17{:}20.673 \dashrightarrow 00{:}17{:}23.077$  are the principal organizational.
- NOTE Confidence: 0.875419238571428

00:17:26.120 --> 00:17:28.010 Features, if you will, of the human

NOTE Confidence: 0.875419238571428

 $00:17:28.010 \rightarrow 00:17:30.399$  brain or the mammalian brain in general,

NOTE Confidence: 0.875419238571428

00:17:30.400 --> 00:17:32.520 and I'd like to argue one that we know about,

NOTE Confidence: 0.875419238571428

 $00:17:32.520 \longrightarrow 00:17:34.266$  is functional specialization

NOTE Confidence: 0.875419238571428

 $00{:}17{:}34.266 \dashrightarrow 00{:}17{:}36.594$  across the cortical axis.

NOTE Confidence: 0.875419238571428

 $00{:}17{:}36{.}600 \dashrightarrow 00{:}17{:}38{.}864$  So we know that lower order and higher

NOTE Confidence: 0.875419238571428

 $00{:}17{:}38{.}864 \dashrightarrow 00{:}17{:}41{.}333$  order areas have very distinct patterns of

NOTE Confidence: 0.875419238571428

 $00:17:41.333 \rightarrow 00:17:43.500$  feed forward and back connections, right?

NOTE Confidence: 0.875419238571428

 $00{:}17{:}43.500 \dashrightarrow 00{:}17{:}45.100$  So that's an organizational principle.

NOTE Confidence: 0.875419238571428

 $00{:}17{:}45{.}100 \dashrightarrow 00{:}17{:}47{.}340$  This is a classic picture from the

NOTE Confidence: 0.875419238571428

 $00:17:47.340 \longrightarrow 00:17:48.961$  Fellman and Vanessa and publication,

NOTE Confidence: 0.875419238571428

 $00{:}17{:}48.961 \dashrightarrow 00{:}17{:}51.908$  which also highlights that there is a

NOTE Confidence: 0.875419238571428

 $00{:}17{:}51{.}908 \dashrightarrow 00{:}17{:}54{.}669$  hierarchy and information processing from.

NOTE Confidence: 0.875419238571428

00:17:54.670 --> 00:17:56.880 Answer to association agents, right?

NOTE Confidence: 0.875419238571428

 $00{:}17{:}56.880 \dashrightarrow 00{:}18{:}00.648$  We also know from work such as this

NOTE Confidence: 0.875419238571428

00:18:00.648 --> 00:18:04.159 paper from John Murray while he was

00:18:04.160 --> 00:18:06.428 starting here at Yale that there

NOTE Confidence: 0.875419238571428

 $00:18:06.428 \rightarrow 00:18:09.130$  is a difference in the spontaneous

NOTE Confidence: 0.875419238571428

 $00:18:09.130 \longrightarrow 00:18:11.354$  autocorrelated activity across areas

NOTE Confidence: 0.875419238571428

00:18:11.354 --> 00:18:15.103 from non human primate data and this

NOTE Confidence: 0.875419238571428

 $00:18:15.103 \rightarrow 00:18:17.031$  intrinsic activity scales suggesting

NOTE Confidence: 0.875419238571428

00:18:17.031 --> 00:18:19.458 a hierarchy of functional hierarchy.

NOTE Confidence: 0.875419238571428

00:18:19.458 --> 00:18:19.947 Furthermore,

NOTE Confidence: 0.875419238571428

 $00:18:19.947 \rightarrow 00:18:22.881$  we know that during cognitive operations

NOTE Confidence: 0.875419238571428

00:18:22.881 --> 00:18:24.950 such as working memory primary.

NOTE Confidence: 0.875419238571428

 $00{:}18{:}24{.}950 \dashrightarrow 00{:}18{:}28{.}710$  Visual areas such as Mt do not sustain

NOTE Confidence: 0.875419238571428

 $00:18:28.710 \rightarrow 00:18:31.527$  signal during the mnemonic phase,

NOTE Confidence: 0.875419238571428

00:18:31.530 --> 00:18:35.352 whereas areas such as LP FC sustain

NOTE Confidence: 0.875419238571428

00:18:35.352 --> 00:18:37.890 a recurrent reverberatory activity,

NOTE Confidence: 0.875419238571428

00:18:37.890 --> 00:18:39.902 right again highlighting distinct

NOTE Confidence: 0.875419238571428

 $00{:}18{:}39{.}902 \dashrightarrow 00{:}18{:}41{.}914$  functional specialization in this

 $00:18:41.914 \longrightarrow 00:18:43.240$  very coarse way.

NOTE Confidence: 0.875419238571428

 $00:18:43.240 \rightarrow 00:18:47.244$  Furthermore, we know that we can leverage.

NOTE Confidence: 0.875419238571428

 $00{:}18{:}47.250 \dashrightarrow 00{:}18{:}51.044$  Microstructure values from the T1 and T2

NOTE Confidence: 0.875419238571428

 $00:18:51.044 \rightarrow 00:18:55.626$  maps to derive a proxy of myelin cortically,

NOTE Confidence: 0.875419238571428

 $00:18:55.630 \longrightarrow 00:18:57.818$  which shows a hierarchy.

NOTE Confidence: 0.875419238571428

00:18:57.818 --> 00:19:00.006 It smoothly varies from

NOTE Confidence: 0.875419238571428

 $00{:}19{:}00{.}006 \dashrightarrow 00{:}19{:}02{.}409$  association to sensory areas.

NOTE Confidence: 0.875419238571428

 $00:19:02.410 \rightarrow 00:19:05.050$  And this is also true in the macaque,

NOTE Confidence: 0.875419238571428

00:19:05.050 --> 00:19:05.305 right?

NOTE Confidence: 0.875419238571428

 $00{:}19{:}05{.}305 \dashrightarrow 00{:}19{:}07{.}345$  So now we have some clues that the

NOTE Confidence: 0.875419238571428

 $00{:}19{:}07{.}345 \dashrightarrow 00{:}19{:}09{.}458$  brain varies hierarchically and this

NOTE Confidence: 0.875419238571428

00:19:09.458 --> 00:19:11.352 shouldn't be controversial, right?

NOTE Confidence: 0.875419238571428

 $00{:}19{:}11{.}352 \dashrightarrow 00{:}19{:}14{.}604$  Can we leverage this information to

NOTE Confidence: 0.875419238571428

 $00:19:14.604 \rightarrow 00:19:17.502$  understand how the effects of pharmacology?

NOTE Confidence: 0.875419238571428

 $00:19:17.502 \longrightarrow 00:19:20.220$  Which we'll get to and so.

NOTE Confidence: 0.875419238571428

 $00:19:20.220 \rightarrow 00:19:22.642$  The the motivation for this work was

00:19:22.642 --> 00:19:25.710 driven by a grad student in John's lab,

NOTE Confidence: 0.875419238571428

00:19:25.710 --> 00:19:28.002 Josh Burt, who did some really

NOTE Confidence: 0.875419238571428

00:19:28.002 --> 00:19:29.530 elegant gene expression mapping.

NOTE Confidence: 0.875419238571428

 $00:19:29.530 \rightarrow 00:19:31.066$  And I'll walk you through why this matters,

NOTE Confidence: 0.875419238571428

00:19:31.070 --> 00:19:31.362 right.

NOTE Confidence: 0.875419238571428

 $00{:}19{:}31{.}362 \dashrightarrow 00{:}19{:}33{.}774$  So we have this human myelin map, right?

NOTE Confidence: 0.875419238571428

 $00{:}19{:}33{.}774 \dashrightarrow 00{:}19{:}35{.}958$  We've established that it has a

NOTE Confidence: 0.875419238571428

00:19:35.958 --> 00:19:36.988 hierarchical organization, right.

NOTE Confidence: 0.875419238571428

00:19:36.988 --> 00:19:39.074 And what he's just shown that when

NOTE Confidence: 0.875419238571428

00:19:39.074 --> 00:19:41.189 you use Lisas network partition,

NOTE Confidence: 0.875419238571428

 $00:19:41.190 \longrightarrow 00:19:43.367$  but in fact there is a difference

NOTE Confidence: 0.875419238571428

 $00:19:43.367 \longrightarrow 00:19:43.989$  across networks,

NOTE Confidence: 0.875419238571428

00:19:43.990 --> 00:19:44.350 right,

NOTE Confidence: 0.875419238571428

 $00{:}19{:}44.350 \dashrightarrow 00{:}19{:}46.510$  that the association networks have less

NOTE Confidence: 0.875419238571428

 $00:19:46.510 \rightarrow 00:19:48.789$  myelin than sensory somatomotor networks.

00:19:48.790 --> 00:19:50.720 OK, just the validity check.

NOTE Confidence: 0.875419238571428

00:19:50.720 --> 00:19:51.213 Furthermore,

NOTE Confidence: 0.875419238571428

00:19:51.213 --> 00:19:53.678 he's taken mcac myelin values,

NOTE Confidence: 0.875419238571428

 $00:19:53.680 \longrightarrow 00:19:56.080$  and he's taken tracer data,

NOTE Confidence: 0.875419238571428

 $00:19:56.080 \longrightarrow 00:19:57.795$  defining the hierarchy as feed

NOTE Confidence: 0.875419238571428

 $00{:}19{:}57.795 \dashrightarrow 00{:}19{:}59.510$  forward and feedback connections in

NOTE Confidence: 0.875419238571428

 $00:19:59.566 \rightarrow 00:20:01.696$  collaboration with David Vanessa's group.

NOTE Confidence: 0.875419238571428

 $00:20:01.700 \longrightarrow 00:20:03.035$  And he's correlated.

NOTE Confidence: 0.875419238571428

 $00{:}20{:}03.035 \dashrightarrow 00{:}20{:}04.815$  This again establishing that

NOTE Confidence: 0.875419238571428

00:20:04.815 --> 00:20:06.610 there is hierarchy right.

NOTE Confidence: 0.875419238571428

 $00:20:06.610 \longrightarrow 00:20:07.382$  So far,

NOTE Confidence: 0.875419238571428

 $00:20:07.382 \longrightarrow 00:20:08.154$  so good.

NOTE Confidence: 0.875419238571428

 $00{:}20{:}08.154 \dashrightarrow 00{:}20{:}11.192$  Then he went into the alien human

NOTE Confidence: 0.875419238571428

00:20:11.192 --> 00:20:14.337 Brain Atlas gene expression database.

NOTE Confidence: 0.875419238571428

 $00{:}20{:}14.340 \dashrightarrow 00{:}20{:}17.538$  And he's taken from every cortical

NOTE Confidence: 0.875419238571428

 $00:20:17.538 \rightarrow 00:20:20.437$  microarray a probe across something
- NOTE Confidence: 0.875419238571428
- $00:20:20.437 \longrightarrow 00:20:23.137$  like 20,000 different genes.
- NOTE Confidence: 0.875419238571428
- $00{:}20{:}23.140 \dashrightarrow 00{:}20{:}25.420$  And because the amount of human
- NOTE Confidence: 0.875419238571428
- 00:20:25.420 --> 00:20:26.940 brain Atlas has serendipitously,
- NOTE Confidence: 0.875419238571428
- $00:20:26.940 \longrightarrow 00:20:27.854$  thank goodness,
- NOTE Confidence: 0.875419238571428
- $00:20:27.854 \rightarrow 00:20:30.139$  scanned every single person of
- NOTE Confidence: 0.875419238571428
- $00:20:30.139 \longrightarrow 00:20:32.940$  the six people that they studied.
- NOTE Confidence: 0.875419238571428
- $00:20:32.940 \longrightarrow 00:20:33.454$  Postmortem.
- NOTE Confidence: 0.875419238571428
- $00{:}20{:}33{.}454 \dashrightarrow 00{:}20{:}36{.}538$  We could then reconstruct the cortical
- NOTE Confidence: 0.875419238571428
- $00{:}20{:}36{.}538 \dashrightarrow 00{:}20{:}39{.}176$  surface right anatomy postmortem and
- NOTE Confidence: 0.875419238571428
- $00{:}20{:}39{.}176 \dashrightarrow 00{:}20{:}43.012$  map it onto the human Connectome Atlas.
- NOTE Confidence: 0.875419238571428
- $00:20:43.020 \rightarrow 00:20:45.015$  Particulate it right using the
- NOTE Confidence: 0.875419238571428
- $00{:}20{:}45.015 \dashrightarrow 00{:}20{:}47.010$  parcellation that I just introduced.
- NOTE Confidence: 0.875419238571428
- $00{:}20{:}47.010 \dashrightarrow 00{:}20{:}49.677$  Do this for every person from the
- NOTE Confidence: 0.875419238571428
- $00{:}20{:}49.677 \dashrightarrow 00{:}20{:}52.039$  island human brain Atlas and then
- NOTE Confidence: 0.875419238571428
- $00{:}20{:}52{.}039 \dashrightarrow 00{:}20{:}54{.}325$  average it to get the aggregate
- NOTE Confidence: 0.875419238571428

00:20:54.325 --> 00:20:56.537 group map across every gene

NOTE Confidence: 0.875419238571428

 $00{:}20{:}56{.}537 \dashrightarrow 00{:}20{:}58{.}293$  for every cortical parcel.

NOTE Confidence: 0.875419238571428

 $00:20:58.300 \rightarrow 00:20:59.996$  Now you can imagine why this is powerful.

NOTE Confidence: 0.859097170434783

 $00:21:00.000 \rightarrow 00:21:02.149$  Now we have an actual gene expression

NOTE Confidence: 0.859097170434783

 $00:21:02.149 \rightarrow 00:21:03.613$  topography for every gene across

NOTE Confidence: 0.859097170434783

 $00{:}21{:}03.613 \dashrightarrow 00{:}21{:}05.314$  all the areas that we have our

NOTE Confidence: 0.859097170434783

00:21:05.314 --> 00:21:06.800 new imaging maps for, right?

NOTE Confidence: 0.859097170434783

 $00:21:06.800 \longrightarrow 00:21:08.760$  So what can we do with this?

NOTE Confidence: 0.859097170434783

 $00:21:08.760 \longrightarrow 00:21:10.000$  So the first question is,

NOTE Confidence: 0.859097170434783

 $00:21:10.000 \rightarrow 00:21:12.080$  what is the principal gradient,

NOTE Confidence: 0.859097170434783

 $00{:}21{:}12.080 \dashrightarrow 00{:}21{:}14.630$  the first principal component of

NOTE Confidence: 0.859097170434783

 $00:21:14.630 \rightarrow 00:21:16.446$  gene expression topography, right.

NOTE Confidence: 0.859097170434783

 $00:21:16.446 \longrightarrow 00:21:17.876$  And this is the picture.

NOTE Confidence: 0.859097170434783

 $00:21:17.880 \longrightarrow 00:21:19.453$  This is how it varies, right?

NOTE Confidence: 0.859097170434783

 $00:21:19.453 \longrightarrow 00:21:21.518$  And it varies this way,

NOTE Confidence: 0.859097170434783

 $00:21:21.520 \longrightarrow 00:21:22.650$  so much so that it

 $00:21:23.290 \longrightarrow 00:21:25.663$  did you say that this this expression

NOTE Confidence: 0.783418904545454

 $00:21:25.663 \rightarrow 00:21:28.910$  is from 6 brains, six people. OK.

NOTE Confidence: 0.783418904545454

 $00:21:28.910 \rightarrow 00:21:30.910$  So I'm wondering how that limits the power

NOTE Confidence: 0.783418904545454

 $00:21:30.910 \rightarrow 00:21:32.949$  of this kind of correlation analysis.

NOTE Confidence: 0.783418904545454

00:21:32.950 --> 00:21:34.777 If you only have you have a huge number

NOTE Confidence: 0.783418904545454

00:21:34.777 --> 00:21:37.580 of genes but you only have 6 replicates

NOTE Confidence: 0.783418904545454

 $00:21:37.580 \rightarrow 00:21:40.188$  at each for each gene in each parcel,

NOTE Confidence: 0.829708503333333

 $00:21:40.500 \longrightarrow 00:21:41.404$  that's a great question.

NOTE Confidence: 0.829708503333333

 $00:21:41.404 \longrightarrow 00:21:42.534$  So let me go back.

NOTE Confidence: 0.829708503333333

 $00:21:42.540 \longrightarrow 00:21:45.372$  So, So what Chris is really

NOTE Confidence: 0.829708503333333

 $00:21:45.372 \rightarrow 00:21:47.590$  highlighting is something that is.

NOTE Confidence: 0.829708503333333

 $00:21:47.590 \rightarrow 00:21:51.550$  Rental, which is you when you're running any

NOTE Confidence: 0.829708503333333

 $00:21:51.550 \rightarrow 00:21:55.378$  analysis on the matrix of genes by parcels,

NOTE Confidence: 0.829708503333333

 $00{:}21{:}55{.}380 \dashrightarrow 00{:}21{:}57{.}866$  notice that their group averaged, right?

NOTE Confidence: 0.829708503333333

00:21:57.866 - 00:22:01.918 So what we do is we first ask, what is the?

 $00:22:01.918 \rightarrow 00:22:04.048$  Coverage of that microarray probe

NOTE Confidence: 0.829708503333333

 $00{:}22{:}04.048 \dashrightarrow 00{:}22{:}06.630$  in that cortical location, right.

NOTE Confidence: 0.829708503333333

 $00:22:06.630 \longrightarrow 00:22:07.730$  Is there a good signal?

NOTE Confidence: 0.829708503333333

 $00:22:07.730 \longrightarrow 00:22:10.250$  And then we evaluate the differential

NOTE Confidence: 0.829708503333333

 $00{:}22{:}10.250 \dashrightarrow 00{:}22{:}11.776$  stability across individuals, right.

NOTE Confidence: 0.829708503333333

 $00{:}22{:}11.776 \dashrightarrow 00{:}22{:}13.904$  So we want to be confident that it's

NOTE Confidence: 0.829708503333333

 $00:22:13.904 \rightarrow 00:22:15.409$  consistent across these six people,

NOTE Confidence: 0.829708503333333

 $00:22:15.410 \rightarrow 00:22:17.450$  right, and that there's good coverage.

NOTE Confidence: 0.829708503333333

 $00:22:17.450 \rightarrow 00:22:19.610$  Then we produce a single value single number,

NOTE Confidence: 0.829708503333333

 $00:22:19.610 \longrightarrow 00:22:21.350$  which is the average right

NOTE Confidence: 0.829708503333333

 $00:22:21.350 \longrightarrow 00:22:22.742$  across these six people.

NOTE Confidence: 0.829708503333333

 $00{:}22{:}22{.}750 \dashrightarrow 00{:}22{:}25{.}190$  All the analysis are done on the data

NOTE Confidence: 0.829708503333333

00:22:25.190 --> 00:22:27.000 object that's you're seeing here,

NOTE Confidence: 0.829708503333333

 $00:22:27.000 \rightarrow 00:22:29.247$  which is at the group parcel level.

NOTE Confidence: 0.829708503333333

 $00:22:29.250 \longrightarrow 00:22:30.300$  In other words,

NOTE Confidence: 0.829708503333333

 $00:22:30.300 \rightarrow 00:22:32.400$  the principal component does not consider.

- NOTE Confidence: 0.829708503333333
- 00:22:32.400 -> 00:22:33.798 Variation across people,
- NOTE Confidence: 0.829708503333333
- 00:22:33.798 --> 00:22:36.128 it considers variation across areas,
- NOTE Confidence: 0.829708503333333
- 00:22:36.130 --> 00:22:36.529 right,
- NOTE Confidence: 0.829708503333333
- $00:22:36.529 \rightarrow 00:22:38.524$  with the assumption obviously that
- NOTE Confidence: 0.829708503333333
- $00:22:38.524 \rightarrow 00:22:40.120$  people are consistently expressing
- NOTE Confidence: 0.829708503333333
- $00{:}22{:}40.177 \dashrightarrow 00{:}22{:}42.067$  these genes in these areas and
- NOTE Confidence: 0.829708503333333
- $00:22:42.067 \longrightarrow 00:22:43.327$  that's an empirical question,
- NOTE Confidence: 0.829708503333333
- 00:22:43.330 --> 00:22:43.594 right?
- NOTE Confidence: 0.829708503333333
- $00:22:43.594 \rightarrow 00:22:45.442$  One that we keep talking to NIH
- NOTE Confidence: 0.829708503333333
- $00{:}22{:}45{.}442 \dashrightarrow 00{:}22{:}47{.}437$  and the on human brain that was
- NOTE Confidence: 0.829708503333333
- $00:22:47.437 \rightarrow 00:22:49.310$  folks that they need more brains.
- NOTE Confidence: 0.829708503333333
- 00:22:49.310 --> 00:22:51.830 They need to produce this kind of
- NOTE Confidence: 0.829708503333333
- $00{:}22{:}51{.}830 \dashrightarrow 00{:}22{:}54{.}262$  mapping a sample of sufficient size
- NOTE Confidence: 0.829708503333333
- $00{:}22{:}54{.}262 \dashrightarrow 00{:}22{:}56{.}387$  that we can interrogate whether
- NOTE Confidence: 0.829708503333333
- 00:22:56.387 --> 00:22:58.968 there is true human variability.
- NOTE Confidence: 0.829708503333333

- $00:22:58.970 \longrightarrow 00:22:59.722$  And furthermore,
- NOTE Confidence: 0.829708503333333
- $00{:}22{:}59{.}722 \dashrightarrow 00{:}23{:}01{.}978$  you could imagine this matters for
- NOTE Confidence: 0.829708503333333
- $00:23:01.978 \rightarrow 00:23:03.906$  psychedelic cardiology which is if your 5 HD.
- NOTE Confidence: 0.829708503333333
- $00:23:03.910 \longrightarrow 00:23:04.133$  Receptors,
- NOTE Confidence: 0.829708503333333
- $00:23:04.133 \rightarrow 00:23:05.694$  which I'll talk about in a second,
- NOTE Confidence: 0.829708503333333
- $00{:}23{:}05{.}700 \dashrightarrow 00{:}23{:}06{.}880$  very differentiated across people.
- NOTE Confidence: 0.829708503333333
- $00{:}23{:}06{.}880 \dashrightarrow 00{:}23{:}09{.}008$  One could argue that some of the
- NOTE Confidence: 0.829708503333333
- $00:23:09.008 \rightarrow 00:23:10.820$  conclusions that will draw are incorrect,
- NOTE Confidence: 0.829708503333333
- 00:23:10.820 --> 00:23:12.372 but I think you're,
- NOTE Confidence: 0.829708503333333
- 00:23:12.372 --> 00:23:14.700 you're you're as always always go
- NOTE Confidence: 0.829708503333333
- $00:23:14.776 \longrightarrow 00:23:17.116$  to the key intuition right away,
- NOTE Confidence: 0.829708503333333
- $00:23:17.120 \longrightarrow 00:23:19.376$  which is that these maps are
- NOTE Confidence: 0.829708503333333
- $00:23:19.376 \rightarrow 00:23:21.535$  average across people and therefore
- NOTE Confidence: 0.829708503333333
- $00:23:21.535 \rightarrow 00:23:23.284$  limits generalizability across
- NOTE Confidence: 0.829708503333333
- $00:23:23.284 \rightarrow 00:23:25.905$  the the entire population, right.
- NOTE Confidence: 0.829708503333333
- $00:23:25.905 \rightarrow 00:23:26.760$  We don't know

- NOTE Confidence: 0.70763251
- $00:23:26.940 \rightarrow 00:23:28.746$  and also implies that your principal

 $00{:}23{:}28{.}746 \dashrightarrow 00{:}23{:}30{.}709$  components are dependent on multiple genes.

NOTE Confidence: 0.70763251

00:23:30.710 --> 00:23:31.826 They're looking for patterns

NOTE Confidence: 0.70763251

 $00{:}23{:}31.826 \dashrightarrow 00{:}23{:}33.221$  of multiple genes across areas

NOTE Confidence: 0.70763251

00:23:33.221 --> 00:23:34.898 they're not going to give. Exactly.

NOTE Confidence: 0.70763251

 $00{:}23{:}34{.}900 \dashrightarrow 00{:}23{:}37{.}294$  Whereas if you had a much larger data set,

NOTE Confidence: 0.70763251

 $00{:}23{:}37{.}300 \dashrightarrow 00{:}23{:}38{.}956$  you could look for components that

NOTE Confidence: 0.70763251

 $00:23:38.956 \rightarrow 00:23:40.749$  are for grades within single genes,

NOTE Confidence: 0.70763251

 $00{:}23{:}40.750 \dashrightarrow 00{:}23{:}42.800$  but you can't do that in this data set, so.

NOTE Confidence: 0.897958445555556

 $00:23:44.220 \longrightarrow 00:23:45.014$  Exactly, exactly.

NOTE Confidence: 0.897958445555556

 $00{:}23{:}45.014 \dashrightarrow 00{:}23{:}48.160$  So you could ask the question of is

NOTE Confidence: 0.897958445555556

 $00{:}23{:}48.160 \dashrightarrow 00{:}23{:}51.040$  there a gradient of a single gene across

NOTE Confidence: 0.897958445555556

 $00{:}23{:}51{.}040 \dashrightarrow 00{:}23{:}53{.}767$  people in an area or across areas, right.

NOTE Confidence: 0.897958445555556

00:23:53.767 --> 00:23:55.452 That's another level of variance

NOTE Confidence: 0.897958445555556

 $00:23:55.452 \longrightarrow 00:23:57.480$  that is left on the table.

 $00:23:57.480 \longrightarrow 00:23:58.748$  But the first question,

NOTE Confidence: 0.897958445555556

 $00:23:58.748 \rightarrow 00:24:01.396$  the only question really that we could ask

NOTE Confidence: 0.897958445555556

 $00:24:01.396 \rightarrow 00:24:03.419$  was what's the spatial gradient, right?

NOTE Confidence: 0.897958445555556

 $00:24:03.419 \rightarrow 00:24:05.971$  What is the spatial topography of the way

NOTE Confidence: 0.897958445555556

 $00:24:05.971 \rightarrow 00:24:08.300$  these genes vary across cortical areas,

NOTE Confidence: 0.897958445555556

 $00:24:08.300 \rightarrow 00:24:11.380$  right. And this is how they vary.

NOTE Confidence: 0.897958445555556

 $00{:}24{:}11{.}380 \dashrightarrow 00{:}24{:}13{.}908$  And so it turns out that that explains

NOTE Confidence: 0.897958445555556

 $00:24:13.908 \rightarrow 00:24:15.700$  almost 30% of all the variants, right?

NOTE Confidence: 0.897958445555556

00:24:15.700 --> 00:24:18.131 Not, not everything, but a lot, right?

NOTE Confidence: 0.897958445555556

00:24:18.131 --> 00:24:19.757 And so now you could say,

NOTE Confidence: 0.897958445555556

 $00:24:19.760 \longrightarrow 00:24:21.098$  oh, what does this look like?

NOTE Confidence: 0.897958445555556

00:24:21.100 --> 00:24:22.643 What kind of looks like Milan, right?

NOTE Confidence: 0.897958445555556

00:24:22.643 --> 00:24:24.418 So you could quantify that, right?

NOTE Confidence: 0.897958445555556

 $00{:}24{:}24{.}418 \dashrightarrow 00{:}24{:}27{.}220$  And it turns out it looks a lot like my own.

NOTE Confidence: 0.897958445555556

 $00:24:27.220 \longrightarrow 00:24:28.531$  In other words,

NOTE Confidence: 0.897958445555556

00:24:28.531 --> 00:24:31.086 it varies along a hierarchy, right?

 $00:24:31.086 \rightarrow 00:24:33.648$  Almost 1/3 of all the variants in

NOTE Confidence: 0.897958445555556

 $00{:}24{:}33.648 \dashrightarrow 00{:}24{:}36.088$  human gene expression in the adult

NOTE Confidence: 0.897958445555556

 $00:24:36.088 \rightarrow 00:24:38.542$  brains with this these six people

NOTE Confidence: 0.897958445555556

 $00:24:38.614 \rightarrow 00:24:40.909$  varies along the principal axis,

NOTE Confidence: 0.897958445555556

 $00:24:40.910 \longrightarrow 00:24:44.320$  where it's high in sensory

NOTE Confidence: 0.897958445555556

 $00:24:44.320 \longrightarrow 00:24:46.366$  somatomotor or low.

NOTE Confidence: 0.897958445555556

 $00{:}24{:}46{.}370 \dashrightarrow 00{:}24{:}50{.}304$  And low or high in association cortices,

NOTE Confidence: 0.897958445555556

 $00:24:50.310 \longrightarrow 00:24:50.641$  right?

NOTE Confidence: 0.897958445555556

 $00:24:50.641 \rightarrow 00:24:53.289$  This is this gradient can go both ways,

NOTE Confidence: 0.897958445555556

00:24:53.290 --> 00:24:53.628 right?

NOTE Confidence: 0.897958445555556

 $00:24:53.628 \longrightarrow 00:24:54.980$  And this is cool,

NOTE Confidence: 0.897958445555556

 $00{:}24{:}54{.}980 \dashrightarrow 00{:}24{:}56{.}702$  because now you can imagine this is

NOTE Confidence: 0.897958445555556

 $00:24:56.702 \longrightarrow 00:24:58.649$  the key way that the brain breaks,

NOTE Confidence: 0.897958445555556

 $00{:}24{:}58.650 \dashrightarrow 00{:}25{:}00{.}384$  which is across this cortical hierarchy

NOTE Confidence: 0.897958445555556

 $00{:}25{:}00{.}384 \dashrightarrow 00{:}25{:}02{.}390$  and its pattern of gene expression.

 $00{:}25{:}04.030 \dashrightarrow 00{:}25{:}07.124$  Can you then look at what genes

NOTE Confidence: 0.865513212666667

 $00{:}25{:}07{.}124 \dashrightarrow 00{:}25{:}09{.}016$  are contributing substantially to

NOTE Confidence: 0.865513212666667

 $00:25:09.016 \rightarrow 00:25:10.956$  that first principal component?

NOTE Confidence: 0.865513212666667

00:25:10.960 --> 00:25:13.090 Because you would predict that,

NOTE Confidence: 0.865513212666667

 $00:25:13.090 \rightarrow 00:25:15.534$  for example, oligodendrocyte genes

NOTE Confidence: 0.865513212666667

 $00:25:15.534 \rightarrow 00:25:17.367$  might contribute significantly.

NOTE Confidence: 0.8655132126666667

 $00:25:17.370 \rightarrow 00:25:19.220$  So if oligodendrocyte genes covary

NOTE Confidence: 0.865513212666667

 $00:25:19.220 \longrightarrow 00:25:21.429$  with the myelin density map, that's.

NOTE Confidence: 0.865513212666667

00:25:21.429 --> 00:25:23.224 A different way of measuring

NOTE Confidence: 0.865513212666667

 $00:25:23.224 \rightarrow 00:25:24.660$  exactly the same thing.

NOTE Confidence: 0.865513212666667

 $00{:}25{:}24.660 \dashrightarrow 00{:}25{:}26.011$  It's not telling you something new as

NOTE Confidence: 0.8655132126666667

 $00:25:26.011 \rightarrow 00:25:27.501$  opposed to if there are other neural

NOTE Confidence: 0.8655132126666667

 $00:25:27.501 \rightarrow 00:25:28.797$  genes that might be less intuitive

NOTE Confidence: 0.8655132126666667

00:25:28.841 --> 00:25:29.999 that they should vary and that

NOTE Confidence: 0.8655132126666667

 $00:25:29.999 \rightarrow 00:25:31.266$  might be telling you something new.

NOTE Confidence: 0.8655132126666667

 $00:25:31.266 \rightarrow 00:25:32.967$  So can you dig into the contributors

- NOTE Confidence: 0.865513212666667
- $00{:}25{:}32{.}967 \dashrightarrow 00{:}25{:}34{.}522$  to this component and start to
- NOTE Confidence: 0.865513212666667
- $00:25:34.522 \longrightarrow 00:25:35.782$  make that kind of inference.
- NOTE Confidence: 0.829545776190476
- 00:25:36.020 --> 00:25:37.952 Yeah of course you can check what's
- NOTE Confidence: 0.829545776190476
- $00:25:37.952 \rightarrow 00:25:40.016$  the loading of each gene onto this
- NOTE Confidence: 0.829545776190476
- $00:25:40.016 \rightarrow 00:25:42.000$  component and so on so definitely so.
- NOTE Confidence: 0.829545776190476
- $00{:}25{:}42.000 \dashrightarrow 00{:}25{:}43.536$  So I don't know if Josh has that
- NOTE Confidence: 0.829545776190476
- $00:25:43.536 \longrightarrow 00:25:44.988$  in one of the tables are not
- NOTE Confidence: 0.829545776190476
- $00:25:44.988 \longrightarrow 00:25:46.549$  in the paper but we can check.
- NOTE Confidence: 0.829545776190476
- $00{:}25{:}46{.}550 \dashrightarrow 00{:}25{:}48{.}926$  It's a really good question right and and
- NOTE Confidence: 0.829545776190476
- $00{:}25{:}48{.}926 \dashrightarrow 00{:}25{:}51{.}049$  allows for another access to exploration
- NOTE Confidence: 0.829545776190476
- $00:25:51.049 \rightarrow 00:25:53.245$  but the point that you're already.
- NOTE Confidence: 0.829545776190476
- $00{:}25{:}53{.}250 \dashrightarrow 00{:}25{:}55{.}371$  You know, your your questions and and
- NOTE Confidence: 0.829545776190476
- $00:25:55.371 \rightarrow 00:25:56.670$  suggestions are already highlighting
- NOTE Confidence: 0.829545776190476
- $00{:}25{:}56{.}670 \dashrightarrow 00{:}25{:}58{.}698$  this which is the cortical gene
- NOTE Confidence: 0.829545776190476
- $00:25:58.698 \rightarrow 00:26:00.260$  expression variation is dominated,
- NOTE Confidence: 0.829545776190476

00:26:00.260 - 00:26:02.390 right, by a single principle axis

NOTE Confidence: 0.829545776190476

 $00{:}26{:}02{.}390 \dashrightarrow 00{:}26{:}04{.}661$  which is highly correlated with these

NOTE Confidence: 0.829545776190476

 $00:26:04.661 \rightarrow 00:26:07.013$  expressions of hierarchy and that's great.

NOTE Confidence: 0.829545776190476

00:26:07.020 --> 00:26:08.980 OK, that's an observation, right.

NOTE Confidence: 0.829545776190476

 $00{:}26{:}08{.}980 \dashrightarrow 00{:}26{:}11{.}062$  And these gradients of micro scale

NOTE Confidence: 0.829545776190476

 $00:26:11.062 \rightarrow 00:26:12.995$  properties then can contribute perhaps

NOTE Confidence: 0.829545776190476

00:26:12.995 --> 00:26:14.959 to sensory association specialization,

NOTE Confidence: 0.829545776190476

00:26:14.960 - 00:26:16.516 but furthermore may contribute

NOTE Confidence: 0.829545776190476

 $00:26:16.516 \longrightarrow 00:26:18.461$  to the effects of pharmacology

NOTE Confidence: 0.829545776190476

 $00:26:18.461 \rightarrow 00:26:20.525$  across these cortical areas, right.

NOTE Confidence: 0.829545776190476

 $00{:}26{:}20{.}525 \dashrightarrow 00{:}26{:}23{.}360$  And so this is this is work.

NOTE Confidence: 0.829545776190476

 $00:26:23.360 \rightarrow 00:26:25.106$  That we've published on and actually

NOTE Confidence: 0.829545776190476

 $00{:}26{:}25{.}106 \dashrightarrow 00{:}26{:}26{.}997$  I'm I'm also really proud of this

NOTE Confidence: 0.829545776190476

 $00{:}26{:}26{.}997 \dashrightarrow 00{:}26{:}28{.}874$  John and I Co wrote a patient with

NOTE Confidence: 0.829545776190476

 $00:26:28.874 \rightarrow 00:26:30.404$  our colleague Bill Martin who is

NOTE Confidence: 0.829545776190476

00:26:30.404 --> 00:26:33.066 now head of Global Neuro at J&J

 $00:26:33.066 \rightarrow 00:26:34.860$  and this was just recently awarded.

NOTE Confidence: 0.829545776190476

 $00:26:34.860 \rightarrow 00:26:36.124$  So now we have a patent on this,

NOTE Confidence: 0.829545776190476

 $00:26:36.130 \longrightarrow 00:26:38.374$  not with that useful for anything

NOTE Confidence: 0.829545776190476

 $00{:}26{:}38{.}374 \dashrightarrow 00{:}26{:}40{.}640$  but was it was something that we

NOTE Confidence: 0.829545776190476

 $00{:}26{:}40.640 \dashrightarrow 00{:}26{:}42.555$  wanted to develop and really kind

NOTE Confidence: 0.829545776190476

 $00:26:42.555 \longrightarrow 00:26:46.210$  of drive forward anyway so.

NOTE Confidence: 0.829545776190476

00:26:46.210 --> 00:26:47.476 Sharp left turn.

NOTE Confidence: 0.829545776190476

 $00{:}26{:}47{.}476 \dashrightarrow 00{:}26{:}50{.}008$  How does this relate to pharmacological

NOTE Confidence: 0.829545776190476

 $00{:}26{:}50{.}008 \dashrightarrow 00{:}26{:}52{.}310$  effects of any kind and psychedelic

NOTE Confidence: 0.829545776190476

00:26:52.310 --> 00:26:53.930 psychedelics in particular?

NOTE Confidence: 0.829545776190476

 $00:26:53.930 \rightarrow 00:26:55.266$  You guys are probably thinking when is he

NOTE Confidence: 0.829545776190476

00:26:55.266 --> 00:26:56.847 going to get to anything psychedelic related?

NOTE Confidence: 0.829545776190476

 $00:26:56.850 \rightarrow 00:26:58.194$  Like why am I listening to this?

NOTE Confidence: 0.829545776190476

 $00{:}26{:}58.200 \dashrightarrow 00{:}27{:}02.990$  So, so we're we're getting there, so.

NOTE Confidence: 0.829545776190476

 $00{:}27{:}02{.}990 \dashrightarrow 00{:}27{:}06{.}732$  OK, this map and and I had some

- $00:27:06.732 \longrightarrow 00:27:07.824$  set up slides, but,
- NOTE Confidence: 0.829545776190476
- 00:27:07.824 --> 00:27:09.390 but I actually want to go a little faster,
- NOTE Confidence: 0.829545776190476
- $00:27:09.390 \longrightarrow 00:27:09.736$  right.
- NOTE Confidence: 0.829545776190476
- $00:27:09.736 \longrightarrow 00:27:12.158$  So this is a paper published by
- NOTE Confidence: 0.829545776190476
- 00:27:12.158 --> 00:27:14.688 Katrine in elife a couple years ago,
- NOTE Confidence: 0.829545776190476
- $00{:}27{:}14.690 \dashrightarrow 00{:}27{:}15.070$  right.
- NOTE Confidence: 0.829545776190476
- $00{:}27{:}15{.}070 \dashrightarrow 00{:}27{:}17{.}350$  And So what she's done is
- NOTE Confidence: 0.829545776190476
- $00:27:17.350 \longrightarrow 00:27:21.498$  basically giving people a.
- NOTE Confidence: 0.829545776190476
- 00:27:21.500 --> 00:27:25.343 A pill of LSD which targets the
- NOTE Confidence: 0.829545776190476
- $00:27:25.343 \rightarrow 00:27:27.860$  serotonin receptor versus placebo.
- NOTE Confidence: 0.829545776190476
- $00{:}27{:}27{.}860 \dashrightarrow 00{:}27{:}30{.}114$  And what we've done is we've computed
- NOTE Confidence: 0.829545776190476
- $00:27:30.114 \longrightarrow 00:27:32.973$  a map of unresting state of the effect
- NOTE Confidence: 0.829545776190476
- $00{:}27{:}32{.}973 \dashrightarrow 00{:}27{:}35{.}980$  of LSD on every single person and this
- NOTE Confidence: 0.829545776190476
- $00{:}27{:}35{.}980 \dashrightarrow 00{:}27{:}38{.}577$  is the average across all the people,
- NOTE Confidence: 0.829545776190476
- 00:27:38.580 --> 00:27:40.710 right?
- NOTE Confidence: 0.829545776190476
- $00{:}27{:}40{.}710 \dashrightarrow 00{:}27{:}43{.}464$  In the effects of LSD on a metric that

 $00:27:43.464 \rightarrow 00:27:46.167$  we call global brain connectivity.

NOTE Confidence: 0.829545776190476

 $00:27:46.170 \longrightarrow 00:27:47.818$  So let me unpack this a little bit

NOTE Confidence: 0.829545776190476

 $00:27:47.818 \rightarrow 00:27:49.698$  so you so you develop an intuition.

NOTE Confidence: 0.829545776190476

00:27:49.700 -> 00:27:52.395 Every warm area that you see here

NOTE Confidence: 0.829545776190476

 $00{:}27{:}52{.}395 \dashrightarrow 00{:}27{:}55{.}667$  is an area that has an elevation

NOTE Confidence: 0.829545776190476

00:27:55.667 -> 00:27:58.197 in its brain wide covariation.

NOTE Confidence: 0.829545776190476

 $00:27:58.200 \rightarrow 00:28:00.318$  When people are given LSD relative

NOTE Confidence: 0.829545776190476

 $00:28:00.318 \rightarrow 00:28:02.512$  to cell cycle, so in other words,

NOTE Confidence: 0.829545776190476

 $00{:}28{:}02{.}512 \dashrightarrow 00{:}28{:}04{.}210$  you could you could say it's

NOTE Confidence: 0.829545776190476

00:28:04.274 --> 00:28:05.738 a hyperconnectivity, right?

NOTE Confidence: 0.829545776190476

 $00{:}28{:}05{.}738 \dashrightarrow 00{:}28{:}07{.}802$  But I don't like to use that term

NOTE Confidence: 0.829545776190476

00:28:07.802 --> 00:28:09.517 before impacting it first, right?

NOTE Confidence: 0.829545776190476

00:28:09.517 --> 00:28:10.558 So for instance,

NOTE Confidence: 0.829545776190476

 $00{:}28{:}10.558 \dashrightarrow 00{:}28{:}14.090$  the visual cortex here would.

NOTE Confidence: 0.829545776190476

 $00{:}28{:}14.090 \dashrightarrow 00{:}28{:}16.500$  This the interpretation is that

 $00:28:16.500 \rightarrow 00:28:18.823$  LSD elevates the connectivity with

NOTE Confidence: 0.829545776190476

 $00{:}28{:}18{.}823 \dashrightarrow 00{:}28{:}21{.}980$  the rest of the brain for visual

NOTE Confidence: 0.829545776190476

 $00:28:22.068 \rightarrow 00:28:24.908$  cortex bilaterally and for sensory

NOTE Confidence: 0.829545776190476

 $00:28:24.910 \longrightarrow 00:28:27.618$  somatomotor cortex and MTV.

NOTE Confidence: 0.829545776190476

 $00{:}28{:}27.618 \dashrightarrow 00{:}28{:}30.976$  But it reduces connectivity in

NOTE Confidence: 0.829545776190476

 $00{:}28{:}30{.}976 \dashrightarrow 00{:}28{:}33{.}560$  these association areas, right?

NOTE Confidence: 0.829545776190476

 $00:28:33.560 \longrightarrow 00:28:34.820$  So this is important, right?

NOTE Confidence: 0.829545776190476

 $00:28:34.820 \longrightarrow 00:28:35.975$  In other words,

NOTE Confidence: 0.829545776190476

 $00{:}28{:}35{.}975 \dashrightarrow 00{:}28{:}37{.}900$  there is a bidirectional effect

NOTE Confidence: 0.829545776190476

00:28:37.900 --> 00:28:40.874 of LSD versus placebo on sensory

NOTE Confidence: 0.829545776190476

 $00:28:40.874 \longrightarrow 00:28:42.871$  versus association regions, right?

NOTE Confidence: 0.829545776190476

 $00{:}28{:}42{.}871 \dashrightarrow 00{:}28{:}44{.}737$  At least it appears that way,

NOTE Confidence: 0.918407525

 $00{:}28{:}44.740 \dashrightarrow 00{:}28{:}48.753$  right? And so we can now isolate the Type

NOTE Confidence: 0.918407525

00:28:48.753 --> 00:28:51.560 1 error protected effect right by doing

NOTE Confidence: 0.918407525

 $00:28:51.633 \rightarrow 00:28:54.566$  TFCC protection at the whole brain level.

NOTE Confidence: 0.918407525

00:28:54.570 --> 00:28:56.845 And now you can see this values,

 $00:28:56.850 \rightarrow 00:28:59.132$  this is what's pulling out the values

NOTE Confidence: 0.918407525

 $00:28:59.132 \longrightarrow 00:29:02.198$  out of this area now what Katrina has

NOTE Confidence: 0.918407525

 $00:29:02.198 \rightarrow 00:29:04.990$  also done which is. Pretty clever.

NOTE Confidence: 0.918407525

 $00{:}29{:}04{.}990 \dashrightarrow 00{:}29{:}08{.}246$  She's given people ketanser in prior to the

NOTE Confidence: 0.918407525

 $00{:}29{:}08{.}246$  -->  $00{:}29{:}10{.}598$  administration of LSD right and contains.

NOTE Confidence: 0.918407525

 $00{:}29{:}10.600 \dashrightarrow 00{:}29{:}14.040$  Azrin is thought to be a very selective

NOTE Confidence: 0.918407525

 $00{:}29{:}14.040 \dashrightarrow 00{:}29{:}16.927$  ant agonist of the five HT 2A receptor.

NOTE Confidence: 0.918407525

00:29:16.930 --> 00:29:18.994 And you'll notice that when people

NOTE Confidence: 0.918407525

 $00{:}29{:}18{.}994 \dashrightarrow 00{:}29{:}20{.}370$  are pretreated with ketan serin,

NOTE Confidence: 0.918407525

 $00:29:20.370 \longrightarrow 00:29:23.458$  they look just like.

NOTE Confidence: 0.918407525

00:29:23.460 --> 00:29:24.012 Placebo right.

NOTE Confidence: 0.918407525

 $00{:}29{:}24.012 \dashrightarrow 00{:}29{:}24.840$  In other words,

NOTE Confidence: 0.918407525

 $00{:}29{:}24.840 \dashrightarrow 00{:}29{:}26.694$  there is no effect of LSD in those areas.

NOTE Confidence: 0.918407525

 $00{:}29{:}26.700 \dashrightarrow 00{:}29{:}28.884$  And this is true for the areas that

NOTE Confidence: 0.918407525

 $00{:}29{:}28{.}884 \dashrightarrow 00{:}29{:}30{.}631$  show a reduction in connectivity

 $00:29:30.631 \rightarrow 00:29:33.270$  by LSD and the regions that show

NOTE Confidence: 0.918407525

 $00:29:33.341 \rightarrow 00:29:35.615$  an increase in connectivity by LSD.

NOTE Confidence: 0.918407525

 $00{:}29{:}35{.}620 \dashrightarrow 00{:}29{:}38{.}374$  So there is a full blockade of the effect

NOTE Confidence: 0.918407525

00:29:38.374 --> 00:29:41.444 of LSD by Captain Strand on average, right?

NOTE Confidence: 0.918407525

 $00:29:41.444 \longrightarrow 00:29:43.434$  So that's pretty cool, right.

NOTE Confidence: 0.918407525

 $00{:}29{:}43{.}434 \dashrightarrow 00{:}29{:}46{.}620$  And and I remember showing this to to John NOTE Confidence: 0.918407525

 $00:29:46.694 \rightarrow 00:29:49.638$  Crystal years ago when we first saw this

NOTE Confidence: 0.918407525

 $00:29:49.638 \rightarrow 00:29:52.618$  effect and saying like look the two maps,

NOTE Confidence: 0.918407525

00:29:52.620 --> 00:29:54.690 the LSD versus place<br/>bo and the

NOTE Confidence: 0.918407525

 $00{:}29{:}54.690 \dashrightarrow 00{:}29{:}56.544$  LSD plus captain string versus

NOTE Confidence: 0.918407525

 $00{:}29{:}56{.}544 \dashrightarrow 00{:}29{:}58{.}180$  LSD are super correlated.

NOTE Confidence: 0.918407525

 $00:29:58.180 \longrightarrow 00:29:59.860$  Look, they're almost the same.

NOTE Confidence: 0.918407525

 $00:29:59.860 \longrightarrow 00:30:01.939$  And and I'll show you what they

NOTE Confidence: 0.918407525

 $00:30:01.939 \longrightarrow 00:30:03.808$  look like side by side, right.

NOTE Confidence: 0.918407525

 $00:30:03.808 \dashrightarrow 00:30:06.506$  This is same people, two different days.

NOTE Confidence: 0.918407525

 $00:30:06.506 \rightarrow 00:30:08.416$  One day they're given LSD

- NOTE Confidence: 0.918407525
- 00:30:08.416 --> 00:30:09.780 alone versus placebo,
- NOTE Confidence: 0.918407525
- $00:30:09.780 \longrightarrow 00:30:11.240$  the other day they're given
- NOTE Confidence: 0.918407525
- $00:30:11.240 \longrightarrow 00:30:12.408$  contains trend prior to.
- NOTE Confidence: 0.918407525
- $00:30:12.410 \longrightarrow 00:30:16.057$  Was the and then contrasted to placebo.
- NOTE Confidence: 0.918407525
- 00:30:16.060 --> 00:30:17.398 And I'm like, this is incredible.
- NOTE Confidence: 0.918407525
- $00:30:17.400 \longrightarrow 00:30:18.020$  They look the same.
- NOTE Confidence: 0.918407525
- $00:30:18.020 \longrightarrow 00:30:18.950$  And he just laughed at me.
- NOTE Confidence: 0.918407525
- 00:30:18.950 --> 00:30:19.758 He was like, ohh,
- NOTE Confidence: 0.918407525
- 00:30:19.758 --> 00:30:20.566 of course it's pharmacology.
- NOTE Confidence: 0.918407525
- $00{:}30{:}20{.}570 \dashrightarrow 00{:}30{:}21{.}694$  It has to be.
- NOTE Confidence: 0.918407525
- 00:30:21.694 --> 00:30:22.256 Was like,
- NOTE Confidence: 0.918407525
- $00:30:22.260 \longrightarrow 00:30:22.500$  well,
- NOTE Confidence: 0.918407525
- $00{:}30{:}22{.}500 \dashrightarrow 00{:}30{:}24{.}420$  I'm so glad it's so obvious to you
- NOTE Confidence: 0.918407525
- $00:30:24.420 \longrightarrow 00:30:26.700$  that that you're going to get such a
- NOTE Confidence: 0.918407525
- $00{:}30{:}26.700 \dashrightarrow 00{:}30{:}28.331$  correspondence in the within subject
- NOTE Confidence: 0.918407525

 $00:30:28.331 \rightarrow 00:30:30.146$  effect of pharmacological effects on

NOTE Confidence: 0.918407525

 $00{:}30{:}30{.}146 \dashrightarrow 00{:}30{:}32{.}143$  brain imaging at the surface level.

NOTE Confidence: 0.918407525

 $00:30:32.143 \longrightarrow 00:30:33.949$  Like I wouldn't have guessed that,

NOTE Confidence: 0.918407525

00:30:33.950 --> 00:30:36.110 right, but this is important,

NOTE Confidence: 0.918407525

00:30:36.110 --> 00:30:36.489 right,

NOTE Confidence: 0.918407525

 $00{:}30{:}36{.}489 \dashrightarrow 00{:}30{:}38{.}763$  because it highlights that we can

NOTE Confidence: 0.918407525

 $00:30:38.763 \rightarrow 00:30:40.300$  leverage surface based topography

NOTE Confidence: 0.918407525

 $00:30:40.300 \longrightarrow 00:30:42.617$  as an index of the effect of

NOTE Confidence: 0.918407525

 $00{:}30{:}42.617 \dashrightarrow 00{:}30{:}44.696$  pharmacology on the human brain, right.

NOTE Confidence: 0.918407525

 $00:30:44.696 \rightarrow 00:30:47.784$  And so now, now we get this map,

NOTE Confidence: 0.918407525

00:30:47.790 --> 00:30:50.390 this delta map, delta GBC,

NOTE Confidence: 0.918407525

 $00:30:50.390 \longrightarrow 00:30:52.050$  right and now we ask.

NOTE Confidence: 0.918407525

 $00:30:52.050 \rightarrow 00:30:54.120$  OK, what about gene expression patterns,

NOTE Confidence: 0.918407525

 $00:30:54.120 \longrightarrow 00:30:54.408$  right?

NOTE Confidence: 0.918407525

 $00{:}30{:}54{.}408 \dashrightarrow 00{:}30{:}56{.}424$  If this is truly related to the

NOTE Confidence: 0.918407525

 $00:30:56.424 \rightarrow 00:30:58.360$  seroton in 5H2 receptor which we

- NOTE Confidence: 0.918407525
- $00:30:58.360 \rightarrow 00:31:00.410$  believe contains from this blocking?
- NOTE Confidence: 0.918407525
- $00{:}31{:}00{.}410 \dashrightarrow 00{:}31{:}02{.}816$  Then presumably the 5H2 receptor map
- NOTE Confidence: 0.918407525
- $00:31:02.816 \longrightarrow 00:31:05.420$  ought to look like this map, right?
- NOTE Confidence: 0.918407525
- $00:31:05.420 \longrightarrow 00:31:06.770$  So that's what we tried.
- NOTE Confidence: 0.918407525
- $00:31:06.770 \dashrightarrow 00:31:08.330$  We took the gene expression map,
- NOTE Confidence: 0.918407525
- 00:31:08.330 --> 00:31:08.730 right,
- NOTE Confidence: 0.918407525
- $00:31:08.730 \longrightarrow 00:31:10.730$  and we computed the correlation
- NOTE Confidence: 0.918407525
- $00:31:10.730 \longrightarrow 00:31:12.707$  right across these two, right.
- NOTE Confidence: 0.918407525
- $00:31:12.707 \rightarrow 00:31:15.723$  And we also took some other target genes,
- NOTE Confidence: 0.918407525
- 00:31:15.730 --> 00:31:16.246 right,
- NOTE Confidence: 0.918407525
- $00{:}31{:}16.246 \dashrightarrow 00{:}31{:}19.342$  that are thought in the literature
- NOTE Confidence: 0.918407525
- $00:31:19.342 \longrightarrow 00:31:21.629$  to be targeted by LSD.
- NOTE Confidence: 0.918407525
- $00{:}31{:}21.630 \dashrightarrow 00{:}31{:}24.206$  And then we computed a similarity of
- NOTE Confidence: 0.918407525
- $00{:}31{:}24.206 \dashrightarrow 00{:}31{:}26.257$  correlation between this and this is
- NOTE Confidence: 0.918407525
- $00:31:26.257 \rightarrow 00:31:28.033$  serotonin is right up here, right.
- NOTE Confidence: 0.918407525

 $00:31:28.033 \rightarrow 00:31:30.876$  So it's the of these, it's the most.

NOTE Confidence: 0.918407525

 $00{:}31{:}30.876 \dashrightarrow 00{:}31{:}31.760$  Positively correlated.

NOTE Confidence: 0.918407525

 $00:31:31.760 \longrightarrow 00:31:34.147$  And then we repeated this for the

NOTE Confidence: 0.918407525

 $00:31:34.147 \longrightarrow 00:31:35.891$  entire distribution of all genes

NOTE Confidence: 0.918407525

00:31:35.891 - > 00:31:37.853 from the alien human brain Atlas.

NOTE Confidence: 0.918407525

00:31:37.860 --> 00:31:38.732 And again,

NOTE Confidence: 0.918407525

 $00:31:38.732 \longrightarrow 00:31:41.350$  seroton in comes out here in the

NOTE Confidence: 0.918407525

00:31:41.350 --> 00:31:43.704 95th at almost 96 percentile, right?

NOTE Confidence: 0.918407525

 $00{:}31{:}43.704 \dashrightarrow 00{:}31{:}44.748$  So there are some things that

NOTE Confidence: 0.918407525

 $00:31:44.748 \longrightarrow 00:31:45.270$  by chance could

NOTE Confidence: 0.8335458966666667

00:31:45.305 - 00:31:46.796 be higher, but this is pretty.

NOTE Confidence: 0.8335458966666667

00:31:46.796 --> 00:31:48.530 Encouraging as a initial proof of

NOTE Confidence: 0.8335458966666667

 $00{:}31{:}48.587 \dashrightarrow 00{:}31{:}50.519$  principle that we can actually map

NOTE Confidence: 0.8335458966666667

00:31:50.519 --> 00:31:52.193 human gene expression in relation

NOTE Confidence: 0.8335458966666667

 $00:31:52.193 \dashrightarrow 00:31:53.853$  to the pharmacological effects on

NOTE Confidence: 0.8335458966666667

 $00:31:53.853 \rightarrow 00:31:56.982$  the human brain in vivo of a given

- NOTE Confidence: 0.8335458966666667
- $00:31:56.982 \dashrightarrow 00:31:59.670$  pharmacological agent that was blocked by
- NOTE Confidence: 0.8335458966666667
- 00:31:59.757 --> 00:32:03.132 the hypothesized receptor antagonist, right?
- NOTE Confidence: 0.8335458966666667
- 00:32:03.132 --> 00:32:05.904 That's in my mind pretty cool.
- NOTE Confidence: 0.8335458966666667
- $00:32:05.910 \dashrightarrow 00:32:08.790$  And so, so you also see the opposite,
- NOTE Confidence: 0.8335458966666667
- $00{:}32{:}08{.}790 \dashrightarrow 00{:}32{:}10.966$  which is HR7, which in my mind has
- NOTE Confidence: 0.8335458966666667
- $00:32:10.966 \rightarrow 00:32:13.130$  some very interesting pharmacology,
- NOTE Confidence: 0.8335458966666667
- $00:32:13.130 \longrightarrow 00:32:14.813$  but we won't get into that today, right?
- NOTE Confidence: 0.8335458966666667
- 00:32:14.813 --> 00:32:16.794 It's just you also see the opposite
- NOTE Confidence: 0.8335458966666667
- $00{:}32{:}16.794 \dashrightarrow 00{:}32{:}19.306$  effects in this, this kind of analysis.
- NOTE Confidence: 0.8335458966666667
- $00:32:19.306 \longrightarrow 00:32:22.968$  OK. So. How do we take
- NOTE Confidence: 0.860314308571429
- $00:32:22.980 \longrightarrow 00:32:24.120$  this quick question?
- NOTE Confidence: 0.860314308571429
- 00:32:24.120 --> 00:32:26.696 If you go back, I'm thinking about
- NOTE Confidence: 0.860314308571429
- $00:32:26.696 \rightarrow 00:32:28.808$  the 1A receptor which is usually
- NOTE Confidence: 0.860314308571429
- 00:32:28.808 --> 00:32:30.957 pre synaptic on Axon terminals,
- NOTE Confidence: 0.860314308571429
- $00:32:30.960 \longrightarrow 00:32:33.534$  which means that the receptor is
- NOTE Confidence: 0.860314308571429

 $00:32:33.534 \rightarrow 00:32:37.036$  not in the same place as the M RNA.

NOTE Confidence: 0.860314308571429

 $00:32:37.040 \longrightarrow 00:32:39.484$  That's what you're doing here.

NOTE Confidence: 0.860314308571429

 $00{:}32{:}39{.}484 \dashrightarrow 00{:}32{:}41{.}393$  When you're when you're looking at the

NOTE Confidence: 0.860314308571429

 $00:32:41.393 \rightarrow 00:32:42.883$  distribution of gene expression across

NOTE Confidence: 0.860314308571429

00:32:42.883 --> 00:32:45.320 the brain, you're looking at M RNA,

NOTE Confidence: 0.860314308571429

 $00:32:45.320 \longrightarrow 00:32:48.736$  which is basically where the cell bodies. NOTE Confidence: 0.860314308571429

 $00{:}32{:}48.740 \dashrightarrow 00{:}32{:}52.075$  Right and. That should be pretty good

NOTE Confidence: 0.860314308571429

 $00{:}32{:}52.075 \dashrightarrow 00{:}32{:}53.220$  because it's amended and Reddick.

NOTE Confidence: 0.860314308571429

 $00:32:53.220 \longrightarrow 00:32:54.648$  But for the 1A receptor there,

NOTE Confidence: 0.860314308571429

 $00:32:54.650 \dashrightarrow 00:32:56.750$  there's going to be a substantial

NOTE Confidence: 0.860314308571429

 $00{:}32{:}56.750 \dashrightarrow 00{:}32{:}58.451$  dissociation between where the M

NOTE Confidence: 0.860314308571429

 $00{:}32{:}58.451 \dashrightarrow 00{:}33{:}00{.}124$  RNA is and where the receptor is,

NOTE Confidence: 0.860314308571429

00:33:00.130 --> 00:33:01.124 which I don't think you can get

NOTE Confidence: 0.860314308571429

 $00:33:01.124 \rightarrow 00:33:01.930$  it at this technique.

NOTE Confidence: 0.860314308571429

 $00:33:01.930 \longrightarrow 00:33:04.098$  So just for some receptors that may be

NOTE Confidence: 0.5617697675

 $00:33:04.200 \rightarrow 00:33:06.188$  applicant, you're absolutely right.

 $00{:}33{:}06{.}190 \dashrightarrow 00{:}33{:}08{.}058$  So you're absolutely right.

NOTE Confidence: 0.5617697675

 $00:33:08.058 \rightarrow 00:33:10.690$  So what you're highlighting is the nuance,

NOTE Confidence: 0.5617697675

 $00:33:10.690 \rightarrow 00:33:12.560$  the Super important nuance between

NOTE Confidence: 0.5617697675

 $00:33:12.560 \rightarrow 00:33:14.634$  the ligand and the receptor, right.

NOTE Confidence: 0.5617697675

 $00{:}33{:}14.634 \dashrightarrow 00{:}33{:}16.266$  And basically the fact that the M RNA

NOTE Confidence: 0.5617697675

 $00{:}33{:}16.266 \dashrightarrow 00{:}33{:}17.907$  may be coding for the ligand or the

NOTE Confidence: 0.5617697675

 $00{:}33{:}17{.}907 \dashrightarrow 00{:}33{:}19{.}512$  receptor and in the cases where it's

NOTE Confidence: 0.5617697675

 $00:33:19.512 \rightarrow 00:33:21.560$  coding for the receptor, this analysis.

NOTE Confidence: 0.5617697675

00:33:21.560 --> 00:33:23.986 Approach may be very informative,

NOTE Confidence: 0.5617697675

 $00:33:23.986 \longrightarrow 00:33:25.462$  but in the cases where it's

NOTE Confidence: 0.5617697675

 $00:33:25.462 \longrightarrow 00:33:26.560$  coding for the ligand,

NOTE Confidence: 0.5617697675

 $00{:}33{:}26{.}560 \dashrightarrow 00{:}33{:}27{.}750$  it may or may not be informative.

NOTE Confidence: 0.780933518571429

 $00:33:27.760 \longrightarrow 00:33:29.097$  It's not about whether it's the ligand,

NOTE Confidence: 0.780933518571429

 $00{:}33{:}29{.}100 \dashrightarrow 00{:}33{:}33{.}484$  it's where the receptor is on the neuron.

NOTE Confidence: 0.780933518571429

 $00{:}33{:}33{.}490 \dashrightarrow 00{:}33{:}36{.}170$  So for pre, for pre synaptic receptors,

 $00:33:36.170 \longrightarrow 00:33:37.214$  for receptors that are

NOTE Confidence: 0.780933518571429

 $00{:}33{:}37{.}214 \dashrightarrow 00{:}33{:}38{.}795$  targeted to Axon terminals,

NOTE Confidence: 0.780933518571429

 $00{:}33{:}38{.}795 \dashrightarrow 00{:}33{:}40{.}784$  we see this in the animal literature

NOTE Confidence: 0.780933518571429

 $00:33:40.784 \longrightarrow 00:33:41.996$  all the time where the receptor

NOTE Confidence: 0.780933518571429

 $00{:}33{:}41.996 \dashrightarrow 00{:}33{:}43.305$  in the M RNA are in different

NOTE Confidence: 0.780933518571429

 $00{:}33{:}43.305 \dashrightarrow 00{:}33{:}44.367$  places because the receptor is

NOTE Confidence: 0.780933518571429

00:33:44.367 - > 00:33:45.609 way out on the Axon terminals,

NOTE Confidence: 0.780933518571429

 $00{:}33{:}45{.}610 \dashrightarrow 00{:}33{:}47{.}563$  which is in a different part of

NOTE Confidence: 0.780933518571429

 $00{:}33{:}47{.}563 \dashrightarrow 00{:}33{:}49{.}310$  the brain from the cell body.

NOTE Confidence: 0.780933518571429

 $00:33:49.310 \longrightarrow 00:33:50.330$  It's not about the ligand,

NOTE Confidence: 0.780933518571429

 $00{:}33{:}50{.}330 \dashrightarrow 00{:}33{:}51{.}825$  it's about where the receptor

NOTE Confidence: 0.780933518571429

 $00:33:51.825 \longrightarrow 00:33:53.320$  is localized in the neuron.

NOTE Confidence: 0.714856385

 $00:33:53.450 \rightarrow 00:33:54.770$  So you're highlighting something

NOTE Confidence: 0.714856385

 $00:33:54.770 \longrightarrow 00:33:56.374$  even different, right, which is which

NOTE Confidence: 0.714856385

 $00:33:56.374 \rightarrow 00:33:57.790$  is now beginning to appreciate it.

NOTE Confidence: 0.714856385

 $00:33:57.790 \rightarrow 00:34:00.748$  So you're saying that the postsynaptic

 $00{:}34{:}00{.}748 \dashrightarrow 00{:}34{:}03{.}410$  receptor expression of the five HD.

NOTE Confidence: 0.714856385

 $00{:}34{:}03{.}410 \dashrightarrow 00{:}34{:}06{.}566$  Way. Is potentially captured very well

NOTE Confidence: 0.714856385

 $00{:}34{:}06{.}566$  -->  $00{:}34{:}11{.}745$  by the M RNA and the the probes

NOTE Confidence: 0.714856385

 $00{:}34{:}11.745 \dashrightarrow 00{:}34{:}15.285$  whereas the presynaptic 1A may may be a NOTE Confidence: 0.714856385

00:34:15.285 --> 00:34:17.040 very different phenomenon because it's

NOTE Confidence: 0.714856385

 $00:34:17.111 \dashrightarrow 00:34:19.386$  on the presynaptic terminals right.

NOTE Confidence: 0.714856385

 $00{:}34{:}19{.}390 \dashrightarrow 00{:}34{:}21{.}308$  And therefore you're not binding to it.

NOTE Confidence: 0.714856385

 $00{:}34{:}21{.}310 \dashrightarrow 00{:}34{:}23{.}415$  And then furthermore furthermore it's

NOTE Confidence: 0.714856385

 $00{:}34{:}23{.}415 \dashrightarrow 00{:}34{:}26{.}330$  this is where my thinking was going

NOTE Confidence: 0.714856385

 $00{:}34{:}26{.}330 \dashrightarrow 00{:}34{:}28{.}927$  which is the ligand versus the receptor,

NOTE Confidence: 0.714856385

 $00:34:28.930 \longrightarrow 00:34:30.953$  right because now you have that third

NOTE Confidence: 0.714856385

 $00{:}34{:}30{.}953 \dashrightarrow 00{:}34{:}33{.}454$  axis of variation and so and and to your

NOTE Confidence: 0.714856385

 $00{:}34{:}33{.}454 \dashrightarrow 00{:}34{:}34{.}980$  point this gets complicated because.

NOTE Confidence: 0.714856385

 $00{:}34{:}34{.}980 \dashrightarrow 00{:}34{:}37{.}636$  When you give a substance like a psyched elic,

NOTE Confidence: 0.714856385

 $00:34:37.640 \longrightarrow 00:34:39.446$  you have post,

 $00{:}34{:}39{.}446 \dashrightarrow 00{:}34{:}42{.}898$  you have polysynaptic distal effects, right?

NOTE Confidence: 0.714856385

00:34:42.898 --> 00:34:46.402 Which is it's going to travel right through NOTE Confidence: 0.714856385

 $00{:}34{:}46{.}402 \dashrightarrow 00{:}34{:}50{.}009$  the Axon and potentially shuttle onto the. NOTE Confidence: 0.714856385

 $00{:}34{:}50{.}010$  -->  $00{:}34{:}51{.}990$  Receptors and activate those terminals

NOTE Confidence: 0.714856385

00:34:51.990 --> 00:34:54.971 on distal neurons that are not in the

NOTE Confidence: 0.714856385

00:34:54.971 --> 00:34:57.148 local tissue bed of the high expression,

NOTE Confidence: 0.714856385

 $00{:}34{:}57{.}150 \dashrightarrow 00{:}34{:}59{.}460$  which is why and this is actually

NOTE Confidence: 0.714856385

 $00{:}34{:}59{.}460 \dashrightarrow 00{:}35{:}01{.}396$  gets really nuanced why looking at

NOTE Confidence: 0.714856385

 $00{:}35{:}01{.}396 \dashrightarrow 00{:}35{:}03{.}883$  the dense GBC at the voxel level and

NOTE Confidence: 0.714856385

 $00{:}35{:}03{.}883 \dashrightarrow 00{:}35{:}05{.}753$  partially the GBC doesn't necessarily

NOTE Confidence: 0.714856385

 $00{:}35{:}05{.}753 \dashrightarrow 00{:}35{:}08{.}970$  fully map onto one another because that

NOTE Confidence: 0.714856385

 $00{:}35{:}08{.}970 \dashrightarrow 00{:}35{:}11{.}226$  level of granularity begins to matter,

NOTE Confidence: 0.714856385

 $00:35:11.230 \longrightarrow 00:35:11.496$  right.

NOTE Confidence: 0.714856385

00:35:11.496 --> 00:35:13.092 And you can now appreciate right

NOTE Confidence: 0.714856385

 $00{:}35{:}13.092 \dashrightarrow 00{:}35{:}14.823$  that if you are averaging signal

NOTE Confidence: 0.714856385

 $00:35:14.823 \longrightarrow 00:35:16.867$  within an area or if you're looking

- NOTE Confidence: 0.714856385
- $00:35:16.925 \longrightarrow 00:35:18.437$  at boxing level pharmacology,
- NOTE Confidence: 0.714856385
- $00:35:18.440 \rightarrow 00:35:20.408$  right and furthermore if you can.
- NOTE Confidence: 0.714856385
- $00:35:20.410 \longrightarrow 00:35:21.810$  Some even deeper into
- NOTE Confidence: 0.714856385
- 00:35:21.810 --> 00:35:22.860 columnar level pharmacology,
- NOTE Confidence: 0.714856385
- $00:35:22.860 \rightarrow 00:35:25.342$  but they're an important ones here, right?
- NOTE Confidence: 0.714856385
- $00:35:25.342 \longrightarrow 00:35:27.994$  But at the very coarse level,
- NOTE Confidence: 0.714856385
- 00:35:28.000 -> 00:35:29.740 you can at least begin to
- NOTE Confidence: 0.714856385
- $00:35:29.740 \dashrightarrow 00:35:30.900$  identify these first principles,
- NOTE Confidence: 0.714856385
- $00{:}35{:}30{.}900 \dashrightarrow 00{:}35{:}32{.}760$  which is pharmacological
- NOTE Confidence: 0.714856385
- $00:35:32.760 \rightarrow 00:35:35.240$  neuroimaging topographies with GBC,
- NOTE Confidence: 0.714856385
- $00:35:35.240 \rightarrow 00:35:37.019$  which is this random freaking measure, right?
- NOTE Confidence: 0.714856385
- $00{:}35{:}37{.}019 \dashrightarrow 00{:}35{:}39{.}164$  That that seemingly has these
- NOTE Confidence: 0.714856385
- $00:35:39.164 \rightarrow 00:35:41.904$  properties that we really like maps
- NOTE Confidence: 0.714856385
- $00{:}35{:}41{.}904 \dashrightarrow 00{:}35{:}44{.}045$  onto gene expression gradients, right?
- NOTE Confidence: 0.714856385
- $00:35:44.045 \rightarrow 00:35:45.515$  Like who would have thunk it?
- NOTE Confidence: 0.714856385

- $00:35:45.520 \rightarrow 00:35:46.357$  And it's not.
- NOTE Confidence: 0.714856385
- $00{:}35{:}46{.}357 \dashrightarrow 00{:}35{:}48{.}310$  And and the important thing about this
- NOTE Confidence: 0.714856385
- $00:35:48.368 \rightarrow 00:35:50.511$  is that if you use some graph, theoretical.
- NOTE Confidence: 0.714856385
- $00:35:50.511 \longrightarrow 00:35:51.042$  Distraction.
- NOTE Confidence: 0.714856385
- $00:35:51.042 \rightarrow 00:35:53.166$  Without a surface map,
- NOTE Confidence: 0.714856385
- $00{:}35{:}53{.}170 \dashrightarrow 00{:}35{:}54{.}742$  there's no freaking way you can
- NOTE Confidence: 0.714856385
- $00:35:54.742 \longrightarrow 00:35:55.528$  get this right.
- NOTE Confidence: 0.714856385
- $00:35:55.530 \dashrightarrow 00:35:57.546$  And that's actually kind of the take
- NOTE Confidence: 0.714856385
- $00{:}35{:}57{.}546 \dashrightarrow 00{:}36{:}00{.}061$  away that I was trying to get at right
- NOTE Confidence: 0.714856385
- $00{:}36{:}00{.}061 \dashrightarrow 00{:}36{:}02{.}264$  is that that this is obscured if you
- NOTE Confidence: 0.714856385
- $00:36:02.264 \rightarrow 00:36:04.244$  do not have a surface map, right?
- NOTE Confidence: 0.714856385
- 00:36:04.244 --> 00:36:06.927 You just can never see it, Umm,
- NOTE Confidence: 0.714856385
- $00{:}36{:}06{.}927 \dashrightarrow 00{:}36{:}09{.}712$  because that's what drives the
- NOTE Confidence: 0.714856385
- $00:36:09.712 \rightarrow 00:36:12.070$  correspondence, right, and the location.
- NOTE Confidence: 0.714856385
- 00:36:12.070 --> 00:36:13.430 So anyway, so, so,
- NOTE Confidence: 0.714856385
- 00:36:13.430 --> 00:36:15.809 so now I I want to be sensitive to time,

- NOTE Confidence: 0.714856385
- $00:36:15.810 \longrightarrow 00:36:16.834$  so I may have to kind of speed
- NOTE Confidence: 0.714856385
- $00:36:16.834 \longrightarrow 00:36:17.807$  up to some of this stuff.
- NOTE Confidence: 0.714856385
- $00:36:17.810 \longrightarrow 00:36:20.010$  So, so basically the point of this is
- NOTE Confidence: 0.714856385
- $00:36:20.010 \rightarrow 00:36:22.690$  how do we map this onto neurobehavioral,
- NOTE Confidence: 0.714856385
- $00{:}36{:}22.690 \dashrightarrow 00{:}36{:}25.575$  geometric models in in clinical
- NOTE Confidence: 0.714856385
- 00:36:25.575 -> 00:36:27.306 population level analysis,
- NOTE Confidence: 0.714856385
- $00:36:27.310 \longrightarrow 00:36:27.616$  right.
- NOTE Confidence: 0.714856385
- $00:36:27.616 \longrightarrow 00:36:29.452$  And so this cartoon is just
- NOTE Confidence: 0.714856385
- $00{:}36{:}29{.}452 \dashrightarrow 00{:}36{:}30{.}743$  highlighting that there's some
- NOTE Confidence: 0.714856385
- $00:36:30.743 \longrightarrow 00:36:32.348$  brain to behavioral relationship and
- NOTE Confidence: 0.714856385
- $00:36:32.348 \rightarrow 00:36:34.349$  that it's probably or some oblique,
- NOTE Confidence: 0.714856385
- 00:36:34.350 --> 00:36:35.378 maybe even not linear.
- NOTE Confidence: 0.714856385
- $00{:}36{:}35{.}378 \dashrightarrow 00{:}36{:}37{.}140$  And we don't know what it is.
- NOTE Confidence: 0.714856385
- $00{:}36{:}37{.}140 \dashrightarrow 00{:}36{:}41{.}048$  And so this is work really purely done
- NOTE Confidence: 0.714856385
- $00:36:41.048 \rightarrow 00:36:43.452$  by my former student now research
- NOTE Confidence: 0.714856385

 $00:36:43.452 \rightarrow 00:36:45.017$  scientist here in our department,

NOTE Confidence: 0.714856385

 $00{:}36{:}45{.}020 \dashrightarrow 00{:}36{:}47{.}805$  Lisa and and she's published

NOTE Confidence: 0.714856385

 $00:36:47.805 \longrightarrow 00:36:51.210$  this in life earlier last year.

NOTE Confidence: 0.714856385

 $00:36:51.210 \longrightarrow 00:36:53.370$  After a whole saga.

NOTE Confidence: 0.714856385

 $00{:}36{:}53{.}370 \dashrightarrow 00{:}36{:}53{.}910$  So,

NOTE Confidence: 0.714856385

 $00:36:53.910 \longrightarrow 00:36:55.820$  so I I I want to this gets a little

NOTE Confidence: 0.767347726363636

00:36:55.882 --> 00:36:58.278 technical, so I'll try to kind of keep

NOTE Confidence: 0.767347726363636

 $00:36:58.278 \dashrightarrow 00:37:00.925$  it clear and then get to the key points.

NOTE Confidence: 0.767347726363636

 $00{:}37{:}00{.}930 \dashrightarrow 00{:}37{:}03{.}354$  So if we're going to leverage

NOTE Confidence: 0.767347726363636

 $00{:}37{:}03{.}354 \dashrightarrow 00{:}37{:}04{.}970$  pharmacological new imaging that's

NOTE Confidence: 0.767347726363636

 $00{:}37{:}05{.}041 \dashrightarrow 00{:}37{:}07{.}237$  even benchmark with gene expression or

NOTE Confidence: 0.767347726363636

 $00:37:07.237 \longrightarrow 00:37:09.880$  what have you right to achieve brain

NOTE Confidence: 0.767347726363636

 $00{:}37{:}09{.}880 \dashrightarrow 00{:}37{:}12{.}220$  behavioral models that can actually be

NOTE Confidence: 0.767347726363636

 $00:37:12.220 \rightarrow 00:37:14.388$  deployed for any therapeutic purpose.

NOTE Confidence: 0.767347726363636

 $00{:}37{:}14.390 \dashrightarrow 00{:}37{:}16.398$  There are some criteria that I'd like to

NOTE Confidence: 0.767347726363636

 $00:37:16.398 \rightarrow 00:37:18.744$  argue we need to really hold in mind, right.

- NOTE Confidence: 0.767347726363636
- $00{:}37{:}18.744 \dashrightarrow 00{:}37{:}21.496$  And these criteria are not exhaustive and
- NOTE Confidence: 0.767347726363636
- $00:37:21.496 \rightarrow 00:37:24.006$  things that I've learned the hard way that,
- NOTE Confidence: 0.767347726363636
- 00:37:24.010 --> 00:37:26.040 you know, if you don't do this,
- NOTE Confidence: 0.767347726363636
- $00:37:26.040 \longrightarrow 00:37:27.060$  things are just brittle.
- NOTE Confidence: 0.767347726363636
- $00{:}37{:}27.060 \dashrightarrow 00{:}37{:}28.590$  So the first one is more
- NOTE Confidence: 0.767347726363636
- $00:37:28.649 \rightarrow 00:37:30.107$  kind of for the whole field,
- NOTE Confidence: 0.767347726363636
- $00:37:30.110 \longrightarrow 00:37:32.270$  which is that anything that we
- NOTE Confidence: 0.767347726363636
- $00{:}37{:}32{.}270 \dashrightarrow 00{:}37{:}35{.}482$  produce as a field has to scale and
- NOTE Confidence: 0.767347726363636
- $00:37:35.482 \longrightarrow 00:37:37.602$  interoperate in an informatics way.
- NOTE Confidence: 0.767347726363636
- $00:37:37.610 \longrightarrow 00:37:38.537$  So for instance,
- NOTE Confidence: 0.767347726363636
- $00{:}37{:}38{.}537 \dashrightarrow 00{:}37{:}40{.}700$  what Pronet is doing and what Professor
- NOTE Confidence: 0.767347726363636
- $00:37:40.764 \longrightarrow 00:37:42.913$  Woods is doing in our department with
- NOTE Confidence: 0.767347726363636
- $00{:}37{:}42.913 \dashrightarrow 00{:}37{:}44.520$  this massive worldwide consortium.
- NOTE Confidence: 0.767347726363636
- 00:37:44.520 --> 00:37:45.015 Right.
- NOTE Confidence: 0.767347726363636
- $00{:}37{:}45.015 \dashrightarrow 00{:}37{:}48.670$  So, so the days of me working on my PC
- NOTE Confidence: 0.767347726363636

00:37:48.670 --> 00:37:50.603 and producing imaging are gone, right?

NOTE Confidence: 0.767347726363636

 $00{:}37{:}50{.}603 \dashrightarrow 00{:}37{:}52{.}418$  Like it's no longer that.

NOTE Confidence: 0.767347726363636

 $00:37:52.420 \longrightarrow 00:37:55.470$  So then the measure selection,

NOTE Confidence: 0.767347726363636

 $00{:}37{:}55{.}470 \dashrightarrow 00{:}37{:}57{.}626$  and I mean the behavioral measure selection

NOTE Confidence: 0.767347726363636

 $00{:}37{:}57.626 \dashrightarrow 00{:}37{:}59.478$  matters here and it matters a lot.

NOTE Confidence: 0.767347726363636

 $00:37:59.480 \longrightarrow 00:38:01.588$  And I'll show you why. Then.

NOTE Confidence: 0.767347726363636

 $00{:}38{:}01{.}588 \dashrightarrow 00{:}38{:}04{.}456$  How do we cross validate those

NOTE Confidence: 0.767347726363636

 $00:38:04.456 \rightarrow 00:38:05.412$  behavioral models,

NOTE Confidence: 0.767347726363636

 $00:38:05.420 \longrightarrow 00:38:05.708$  right.

NOTE Confidence: 0.767347726363636

 $00{:}38{:}05{.}708 \dashrightarrow 00{:}38{:}08{.}300$  And this is stuff that has to do with

NOTE Confidence: 0.767347726363636

 $00{:}38{:}08{.}367 \dashrightarrow 00{:}38{:}10{.}251$  trustworthiness of the reproducibility

NOTE Confidence: 0.767347726363636

 $00:38:10.251 \dashrightarrow 00:38:13.540$  of those models at the behavioral level.

NOTE Confidence: 0.767347726363636

 $00:38:13.540 \longrightarrow 00:38:14.605$  No imaging yet.

NOTE Confidence: 0.767347726363636

 $00{:}38{:}14.605 \dashrightarrow 00{:}38{:}17.090$  This is this is something that that

NOTE Confidence: 0.767347726363636

 $00:38:17.168 \rightarrow 00:38:19.674$  we also found out is very important.

NOTE Confidence: 0.767347726363636

 $00:38:19.680 \longrightarrow 00:38:22.304$  Then Criterion 4 is how do we then

- NOTE Confidence: 0.767347726363636
- $00:38:22.304 \rightarrow 00:38:25.109$  produce a robust and interpretable
- NOTE Confidence: 0.767347726363636
- $00{:}38{:}25{.}109 \dashrightarrow 00{:}38{:}27{.}548$  neuroimaging maps that are linkable
- NOTE Confidence: 0.767347726363636
- $00:38:27.548 \longrightarrow 00:38:29.296$  to that behavioral variation?
- NOTE Confidence: 0.767347726363636
- $00:38:29.300 \longrightarrow 00:38:30.155$  And then finally,
- NOTE Confidence: 0.767347726363636
- $00{:}38{:}30{.}155 \dashrightarrow 00{:}38{:}31{.}865$  how do we cross validate that
- NOTE Confidence: 0.767347726363636
- 00:38:31.865 --> 00:38:32.800 brain behavioral?
- NOTE Confidence: 0.767347726363636
- $00:38:32.800 \longrightarrow 00:38:33.046$  Right.
- NOTE Confidence: 0.767347726363636
- $00:38:33.046 \longrightarrow 00:38:35.260$  So this is a lot of stuff to cover
- NOTE Confidence: 0.767347726363636
- $00:38:35.320 \longrightarrow 00:38:36.460$  in like 15 minutes.
- NOTE Confidence: 0.767347726363636
- $00:38:36.460 \longrightarrow 00:38:38.660$  So some of the hit on some of the highlights
- NOTE Confidence: 0.767347726363636
- $00:38:38.710 \longrightarrow 00:38:40.510$  and then we'll pause your questions.
- NOTE Confidence: 0.767347726363636
- $00{:}38{:}40{.}510 \dashrightarrow 00{:}38{:}41{.}866$  So this is.
- NOTE Confidence: 0.767347726363636
- 00:38:41.866 --> 00:38:42.770 You know,
- NOTE Confidence: 0.767347726363636
- $00{:}38{:}42.770 \dashrightarrow 00{:}38{:}44.074$  a trivial point, right,
- NOTE Confidence: 0.767347726363636
- 00:38:44.074 --> 00:38:45.704 it's just hard to do,
- NOTE Confidence: 0.767347726363636

 $00:38:45.710 \longrightarrow 00:38:47.290$  which is we need informatics

NOTE Confidence: 0.767347726363636

 $00:38:47.290 \longrightarrow 00:38:48.238$  solutions that scale.

NOTE Confidence: 0.767347726363636

 $00{:}38{:}48{.}240 \dashrightarrow 00{:}38{:}50{.}288$  And Yale is at the forefront of this.

NOTE Confidence: 0.767347726363636

 $00:38:50.290 \longrightarrow 00:38:52.138$  I think that what we're doing

NOTE Confidence: 0.767347726363636

 $00{:}38{:}52{.}138 \dashrightarrow 00{:}38{:}53{.}062$  in our department,

NOTE Confidence: 0.767347726363636

 $00{:}38{:}53{.}070 \dashrightarrow 00{:}38{:}54{.}456$  I'm tremendously proud of and I

NOTE Confidence: 0.767347726363636

 $00{:}38{:}54{.}456 \dashrightarrow 00{:}38{:}56{.}133$  think some of the work of faculty

NOTE Confidence: 0.767347726363636

 $00{:}38{:}56{.}133 \dashrightarrow 00{:}38{:}57{.}778$  on this call and others like we're

NOTE Confidence: 0.767347726363636

 $00:38:57.832 \dashrightarrow 00:38:59.530$  really pushing the boundary of this.

NOTE Confidence: 0.767347726363636

 $00:38:59.530 \rightarrow 00:39:01.196$  This is the point is really things

NOTE Confidence: 0.767347726363636

 $00{:}39{:}01{.}196 \dashrightarrow 00{:}39{:}03{.}115$  have to scale and drop rate if

NOTE Confidence: 0.767347726363636

 $00:39:03.115 \rightarrow 00:39:04.555$  we're going to develop precision

NOTE Confidence: 0.767347726363636

00:39:04.555 -> 00:39:05.702 medicine solutions, right.

NOTE Confidence: 0.767347726363636

 $00:39:05.702 \longrightarrow 00:39:07.574$  So I'll just forward and just

NOTE Confidence: 0.767347726363636

 $00:39:07.574 \longrightarrow 00:39:10.182$  say a key thing inside this

NOTE Confidence: 0.767347726363636

 $00:39:10.182 \rightarrow 00:39:12.314$  architecture is analytic discovering.
- NOTE Confidence: 0.767347726363636
- $00{:}39{:}12{.}320 \dashrightarrow 00{:}39{:}12{.}629$  Years.
- NOTE Confidence: 0.767347726363636
- $00:39{:}12.629 \dashrightarrow 00{:}39{:}14.792$  And so this is the workflow from
- NOTE Confidence: 0.767347726363636
- 00:39:14.792 --> 00:39:15.410 Lisa's paper,
- NOTE Confidence: 0.767347726363636
- $00:39:15.410 \longrightarrow 00:39:17.330$  just as a shameless plug.
- NOTE Confidence: 0.767347726363636
- $00:39:17.330 \longrightarrow 00:39:20.120$  But the point is that analytics have to be
- NOTE Confidence: 0.767347726363636
- $00:39:20.120 \longrightarrow 00:39:22.428$  organically built into this for the Discovery
- NOTE Confidence: 0.767347726363636
- $00:39:22.428 \rightarrow 00:39:24.868$  science engine to work where it cannot be.
- NOTE Confidence: 0.767347726363636
- $00:39:24.870 \longrightarrow 00:39:27.410$  Data collection devoid of analytics.
- NOTE Confidence: 0.767347726363636
- 00:39:27.410 --> 00:39:28.550 It's it's it's all,
- NOTE Confidence: 0.767347726363636
- $00:39:28.550 \rightarrow 00:39:29.700$  it's all combined, right?
- NOTE Confidence: 0.767347726363636
- $00:39:29.700 \rightarrow 00:39:32.020$  So talk through how we do this with
- NOTE Confidence: 0.767347726363636
- $00:39:32.020 \rightarrow 00:39:34.119$  a particular analytic framework using
- NOTE Confidence: 0.767347726363636
- $00{:}39{:}34{.}119 \dashrightarrow 00{:}39{:}37{.}130$  a data set that's called Beast Snip.
- NOTE Confidence: 0.767347726363636
- 00:39:37.130 --> 00:39:37.994 Our colleague,
- NOTE Confidence: 0.767347726363636
- $00{:}39{:}37{.}994 \dashrightarrow 00{:}39{:}40{.}586$ Godfrey Pearlson was one of the
- NOTE Confidence: 0.767347726363636

 $00:39:40.586 \rightarrow 00:39:42.508$  principal investigators on the original.

NOTE Confidence: 0.767347726363636

 $00:39:42.510 \rightarrow 00:39:44.350$  Snip that made it into the public domain,

NOTE Confidence: 0.767347726363636

 $00{:}39{:}44{.}350 \dashrightarrow 00{:}39{:}46{.}206$  and now they're on to be snipped too.

NOTE Confidence: 0.827432568

 $00:39:46.210 \longrightarrow 00:39:47.310$  I don't even know three,

NOTE Confidence: 0.827432568

 $00:39:47.310 \longrightarrow 00:39:49.080$  but this is a public domain

NOTE Confidence: 0.827432568

 $00:39:49.080 \longrightarrow 00:39:50.809$  datasets that made it into NH.

NOTE Confidence: 0.827432568

 $00{:}39{:}50{.}810 \dashrightarrow 00{:}39{:}53{.}120$  We downloaded it out of the National

NOTE Confidence: 0.827432568

 $00:39:53.120 \rightarrow 00:39:56.068$  Debt archive and processed it using the

NOTE Confidence: 0.827432568

 $00{:}39{:}56.068 \dashrightarrow 00{:}39{:}57.964$  human connectome processing pipelines.

NOTE Confidence: 0.827432568

00:39:57.970 --> 00:39:59.602 Like that's as much as I'll

NOTE Confidence: 0.827432568

 $00:39:59.602 \rightarrow 00:40:01.125$  say to speed ahead, OK?

NOTE Confidence: 0.827432568

 $00{:}40{:}01.125 \dashrightarrow 00{:}40{:}03.735$  So I've shown this several times.

NOTE Confidence: 0.827432568

 $00{:}40{:}03.740 \dashrightarrow 00{:}40{:}05.636$  Maybe some of you have seen these data,

NOTE Confidence: 0.827432568

 $00{:}40{:}05{.}640 \dashrightarrow 00{:}40{:}07{.}488$  but now it's published and I can kind

NOTE Confidence: 0.827432568

 $00:40:07.488 \rightarrow 00:40:09.395$  of show you the full gamut of this.

NOTE Confidence: 0.827432568

 $00:40:09.400 \longrightarrow 00:40:12.767$  So the first question that we asked

- NOTE Confidence: 0.827432568
- $00:40:12.767 \longrightarrow 00:40:16.041$  ourselves was what is the covariance
- NOTE Confidence: 0.827432568
- 00:40:16.041 --> 00:40:19.515 structure across people in the symptom
- NOTE Confidence: 0.827432568
- $00:40:19.515 \rightarrow 00:40:22.480$  geometry of the psychosis spectrum
- NOTE Confidence: 0.827432568
- $00:40:22.480 \longrightarrow 00:40:24.890$  population of these 436 people?
- NOTE Confidence: 0.827432568
- 00:40:24.890 --> 00:40:26.615 And you're looking at pans,
- NOTE Confidence: 0.827432568
- $00:40:26.620 \longrightarrow 00:40:28.480$  these are pans items, right?
- NOTE Confidence: 0.827432568
- $00:40:28.480 \longrightarrow 00:40:31.036$  The backs is on top backs,
- NOTE Confidence: 0.827432568
- $00:40:31.040 \longrightarrow 00:40:32.444$  which is the brief.
- NOTE Confidence: 0.827432568
- $00:40:32.444 \longrightarrow 00:40:33.848$  Assessment of cognition and
- NOTE Confidence: 0.827432568
- $00:40:33.848 \longrightarrow 00:40:35.299$  then pans items here.
- NOTE Confidence: 0.827432568
- $00:40:35.300 \longrightarrow 00:40:37.922$  So this is the covariance matrix
- NOTE Confidence: 0.827432568
- $00{:}40{:}37{.}922 \dashrightarrow 00{:}40{:}40{.}212$  and there's some correlation between
- NOTE Confidence: 0.827432568
- $00:40:40.212 \longrightarrow 00:40:41.960$  these right across 436 people.
- NOTE Confidence: 0.827432568
- $00:40:41.960 \longrightarrow 00:40:42.660$  So in other words,
- NOTE Confidence: 0.827432568
- $00:40:42.660 \rightarrow 00:40:45.030$  they're structure between these symptoms,
- NOTE Confidence: 0.827432568

- $00:40:45.030 \longrightarrow 00:40:46.101$  which is expected.
- NOTE Confidence: 0.827432568
- $00{:}40{:}46{.}101 \dashrightarrow 00{:}40{:}49{.}270$  This is not new, this is, this makes sense.
- NOTE Confidence: 0.827432568
- $00{:}40{:}49{.}270 \dashrightarrow 00{:}40{:}50{.}745$  But when you plotted across
- NOTE Confidence: 0.827432568
- $00:40:50.745 \rightarrow 00:40:51.981$  the DSM categories, right,
- NOTE Confidence: 0.827432568
- $00:40:51.981 \rightarrow 00:40:54.087$  where bipolar is shown in yellow,
- NOTE Confidence: 0.827432568
- $00{:}40{:}54.090 \dashrightarrow 00{:}40{:}55.563$  schizoaffective in this
- NOTE Confidence: 0.827432568
- 00:40:55.563 --> 00:40:57.527 kind of orangish color,
- NOTE Confidence: 0.827432568
- $00:40:57.530 \rightarrow 00:41:00.026$  dark red is schizophrenia and all pro bands,
- NOTE Confidence: 0.827432568
- $00{:}41{:}00{.}030 \dashrightarrow 00{:}41{:}01{.}848$  all patients are shown in black,
- NOTE Confidence: 0.827432568
- $00:41:01.850 \longrightarrow 00:41:05.710$  you know, I like to argue that.
- NOTE Confidence: 0.827432568
- $00{:}41{:}05{.}710 \dashrightarrow 00{:}41{:}08{.}868$  There's a lot of variation in each one of
- NOTE Confidence: 0.827432568
- $00:41:08.868 \rightarrow 00:41:11.900$  these sub scores on the pans and cognition,
- NOTE Confidence: 0.827432568
- 00:41:11.900 --> 00:41:13.468 but not really clear,
- NOTE Confidence: 0.827432568
- $00:41:13.468 \longrightarrow 00:41:15.036$  very clear distinctions between
- NOTE Confidence: 0.827432568
- 00:41:15.036 --> 00:41:16.202 diagnostic categories, right?
- NOTE Confidence: 0.827432568
- $00:41:16.202 \rightarrow 00:41:18.494$  And so this is not news.

- NOTE Confidence: 0.827432568
- 00:41:18.500 --> 00:41:20.420 Psychosis spectrum disorder is heterogeneous,
- NOTE Confidence: 0.827432568
- $00:41:20.420 \longrightarrow 00:41:21.599$  exhibits covariation symptoms
- NOTE Confidence: 0.827432568
- 00:41:21.599 --> 00:41:23.608 across clinical scales. OK, great.
- NOTE Confidence: 0.827432568
- $00:41:23.608 \rightarrow 00:41:25.678$  You know, cool story Allen.
- NOTE Confidence: 0.827432568
- $00:41:25.680 \longrightarrow 00:41:26.418$  So now what?
- NOTE Confidence: 0.827432568
- $00:41:26.418 \longrightarrow 00:41:28.140$  So the question is what is the
- NOTE Confidence: 0.827432568
- 00:41:28.204 --> 00:41:30.040 dimensionality of this solution,
- NOTE Confidence: 0.827432568
- 00:41:30.040 --> 00:41:30.305 right.
- NOTE Confidence: 0.827432568
- $00{:}41{:}30{.}305 \dashrightarrow 00{:}41{:}32{.}160$  Is there a low dimensional solution that
- NOTE Confidence: 0.827432568
- $00:41:32.160 \longrightarrow 00:41:34.420$  we can reduce the map to the brain right.
- NOTE Confidence: 0.827432568
- $00{:}41{:}34{.}420 \dashrightarrow 00{:}41{:}37{.}220$  Can we do that and simply right.
- NOTE Confidence: 0.827432568
- 00:41:37.220 --> 00:41:40.006 You could ask is there say principal
- NOTE Confidence: 0.827432568
- $00{:}41{:}40.006 \dashrightarrow 00{:}41{:}41.620$  component analytic solution that
- NOTE Confidence: 0.827432568
- $00{:}41{:}41{.}620 \dashrightarrow 00{:}41{:}44{.}098$  explains these data or a factor analytic
- NOTE Confidence: 0.827432568
- $00{:}41{:}44.098 \dashrightarrow 00{:}41{:}46.617$  solution or K means clustering solution,
- NOTE Confidence: 0.827432568

- $00:41:46.620 \rightarrow 00:41:48.960$  just something that is looking at
- NOTE Confidence: 0.827432568
- 00:41:48.960 --> 00:41:50.935 the covariance structure of the
- NOTE Confidence: 0.827432568
- $00{:}41{:}50{.}935 \dashrightarrow 00{:}41{:}53{.}017$  data in a lower dimensional space.
- NOTE Confidence: 0.827432568
- $00:41:53.020 \rightarrow 00:41:54.556$  And so it turns out yes.
- NOTE Confidence: 0.827432568
- $00:41:54.560 \longrightarrow 00:41:54.815$  Right.
- NOTE Confidence: 0.827432568
- $00{:}41{:}54.815 \dashrightarrow 00{:}41{:}56.855$  So these are the components that come out,
- NOTE Confidence: 0.827432568
- 00:41:56.860 00:41:59.216 which brings me to criterion too, right?
- NOTE Confidence: 0.827432568
- $00:41:59.216 \longrightarrow 00:42:00.872$  Can we select the right measures
- NOTE Confidence: 0.827432568
- $00{:}42{:}00{.}872 \dashrightarrow 00{:}42{:}02{.}706$  to map onto the brain? Right.
- NOTE Confidence: 0.827432568
- $00:42:02.706 \rightarrow 00:42:05.142$  And can we obtain an interpretable
- NOTE Confidence: 0.827432568
- $00:42:05.142 \longrightarrow 00:42:05.954$  solution here?
- NOTE Confidence: 0.827432568
- $00{:}42{:}05{.}960 \dashrightarrow 00{:}42{:}06{.}181$  Right.
- NOTE Confidence: 0.827432568
- 00:42:06.181 --> 00:42:07.949 So, I mean, I'm not going to walk
- NOTE Confidence: 0.827432568
- $00{:}42{:}07{.}949 \dashrightarrow 00{:}42{:}09{.}459$  through these principal components.
- NOTE Confidence: 0.827432568
- $00:42:09.460 \longrightarrow 00:42:09.976$  More importantly,
- NOTE Confidence: 0.827432568
- $00:42:09.976 \rightarrow 00:42:12.341$  when I want to highlight is what the geometry

- NOTE Confidence: 0.827432568
- $00:42:12.341 \rightarrow 00:42:14.618$  looks like just so you can get an intuition.

 $00:42:14.620 \longrightarrow 00:42:16.120$  Every dot is a patient.

NOTE Confidence: 0.827432568

 $00:42:16.120 \longrightarrow 00:42:18.480$  They're color-coded as noted here,

NOTE Confidence: 0.827432568

00:42:18.480 --> 00:42:19.040 right?

NOTE Confidence: 0.827432568

 $00{:}42{:}19{.}040 \dashrightarrow 00{:}42{:}22{.}400$  These arrows in this space are

NOTE Confidence: 0.827432568

 $00:42:22.400 \longrightarrow 00:42:25.810$  vectors of the pans and backs.

NOTE Confidence: 0.801581658571428

00:42:28.300 --> 00:42:31.877 Average scores. The green arrow is backs,

NOTE Confidence: 0.801581658571428

 $00:42:31.880 \longrightarrow 00:42:33.348$  which is almost perfectly

NOTE Confidence: 0.801581658571428

 $00{:}42{:}33{.}348 \dashrightarrow 00{:}42{:}35{.}140$  collinear with the cognition axis.

NOTE Confidence: 0.801581658571428

 $00:42:35.140 \rightarrow 00:42:37.060$  That's one of the principal components,

NOTE Confidence: 0.801581658571428

 $00:42:37.060 \longrightarrow 00:42:39.713$  the black dots that you may see

NOTE Confidence: 0.801581658571428

 $00:42:39.713 \longrightarrow 00:42:41.360$  here healthy controls right?

NOTE Confidence: 0.801581658571428

 $00{:}42{:}41{.}360 \dashrightarrow 00{:}42{:}44{.}853$  And then the two the the the

NOTE Confidence: 0.801581658571428

 $00{:}42{:}44.853 \dashrightarrow 00{:}42{:}48.026$  arrows that are coming up the

NOTE Confidence: 0.801581658571428

 $00{:}42{:}48.026 \dashrightarrow 00{:}42{:}51.673$  the blue and the purple are the.

00:42:51.680 --> 00:42:53.952 Negative and positive symptoms,

NOTE Confidence: 0.801581658571428

 $00:42:53.952 \longrightarrow 00:42:55.090$  respectively, right?

NOTE Confidence: 0.801581658571428

 $00:42:55.090 \longrightarrow 00:42:57.940$  Notice that they project onto

NOTE Confidence: 0.801581658571428

 $00:42:57.940 \longrightarrow 00:43:00.920$  this access under an angle.

NOTE Confidence: 0.801581658571428

00:43:00.920 --> 00:43:03.400 It's not. They're not collinear,

NOTE Confidence: 0.801581658571428

 $00:43:03.400 \rightarrow 00:43:06.390$  and they're obliquely rotated, right?

NOTE Confidence: 0.801581658571428

 $00{:}43{:}06{.}390 \dashrightarrow 00{:}43{:}08{.}514$  And then there's a global dysfunction

NOTE Confidence: 0.801581658571428

 $00:43:08.514 \longrightarrow 00:43:11.153$  which is all the patients are not

NOTE Confidence: 0.801581658571428

 $00{:}43{:}11.153 \dashrightarrow 00{:}43{:}12.968$  functioning as well as controls.

NOTE Confidence: 0.801581658571428

 $00:43:12.970 \longrightarrow 00:43:15.070$  So it's this PC three that we're

NOTE Confidence: 0.801581658571428

 $00:43:15.070 \longrightarrow 00:43:16.792$  going to talk about, right.

NOTE Confidence: 0.801581658571428

 $00:43:16.792 \rightarrow 00:43:20.050$  So this is a static picture of that solution,

NOTE Confidence: 0.801581658571428

00:43:20.050 --> 00:43:20.513 right.

NOTE Confidence: 0.801581658571428

00:43:20.513 --> 00:43:24.217 And if if you can see after correct

NOTE Confidence: 0.801581658571428

 $00:43:24.217 \rightarrow 00:43:25.880$  schizoaffective is misspelled,

NOTE Confidence: 0.801581658571428

 $00:43:25.880 \longrightarrow 00:43:27.721$  but if you can see the positive

- NOTE Confidence: 0.801581658571428
- $00:43:27.721 \longrightarrow 00:43:29.010$  and the negative vectors,
- NOTE Confidence: 0.801581658571428
- $00:43:29.010 \rightarrow 00:43:32.270$  they form a 45 degree angle onto PC-3.
- NOTE Confidence: 0.801581658571428
- $00:43:32.270 \longrightarrow 00:43:32.550$  OK.
- NOTE Confidence: 0.801581658571428
- $00:43:32.550 \longrightarrow 00:43:34.510$  So now what is this action you
- NOTE Confidence: 0.801581658571428
- $00:43:34.510 \longrightarrow 00:43:36.289$  look like numerically, right?
- NOTE Confidence: 0.801581658571428
- $00:43:36.289 \rightarrow 00:43:39.321$  Zoom in and these are the linear combinations
- NOTE Confidence: 0.801581658571428
- $00:43:39.321 \rightarrow 00:43:42.140$  and this solution right in this sample.
- NOTE Confidence: 0.801581658571428
- 00:43:42.140 --> 00:43:44.177 So if I plot the DSM categories,
- NOTE Confidence: 0.801581658571428
- $00:43:44.180 \longrightarrow 00:43:46.620$  you'd say there's an effect.
- NOTE Confidence: 0.801581658571428
- 00:43:46.620 --> 00:43:48.500 Right. They don't differ,
- NOTE Confidence: 0.801581658571428
- $00:43:48.500 \rightarrow 00:43:50.850$  but that's actually the point.
- NOTE Confidence: 0.801581658571428
- $00:43:50.850 \longrightarrow 00:43:53.853$  The point is that when you cut
- NOTE Confidence: 0.801581658571428
- $00:43:53.853 \rightarrow 00:43:55.969$  through this geometry with the.
- NOTE Confidence: 0.801581658571428
- $00{:}43{:}55{.}970 \dashrightarrow 00{:}43{:}56{.}616$  Data-driven solution.
- NOTE Confidence: 0.801581658571428
- $00{:}43{:}56.616 \dashrightarrow 00{:}43{:}59.200$  You ought not to see differences in DSM
- NOTE Confidence: 0.801581658571428

 $00:43:59.255 \rightarrow 00:44:01.541$  categories because they don't seem to

NOTE Confidence: 0.801581658571428

00:44:01.541 --> 00:44:03.318 actually follow natural variation, right?

NOTE Confidence: 0.801581658571428

00:44:03.318 --> 00:44:05.967 And so how can I convince you of that, right?

NOTE Confidence: 0.801581658571428

 $00{:}44{:}05{.}967 \dashrightarrow 00{:}44{:}06{.}384$  So.

NOTE Confidence: 0.801581658571428

 $00{:}44{:}06{.}384 \dashrightarrow 00{:}44{:}09{.}303$  So let's take a look at the

NOTE Confidence: 0.801581658571428

00:44:09.303 --> 00:44:11.508 configuration of the PC-3 items, right.

NOTE Confidence: 0.801581658571428

 $00:44:11.508 \rightarrow 00:44:13.944$  So typical person would be somewhat

NOTE Confidence: 0.801581658571428

 $00:44:13.950 \rightarrow 00:44:15.660$  delusional, conceptual, disorganized.

NOTE Confidence: 0.801581658571428

 $00{:}44{:}15.660 \dashrightarrow 00{:}44{:}17.370$  They are hall ucinating,

NOTE Confidence: 0.801581658571428

 $00:44:17.370 \longrightarrow 00:44:18.882$  they have some excitement,

NOTE Confidence: 0.801581658571428

00:44:18.882 --> 00:44:19.711 grandiosity, right?

NOTE Confidence: 0.801581658571428

00:44:19.711 --> 00:44:21.966 But they're not, you know,

NOTE Confidence: 0.801581658571428

 $00:44:21.970 \rightarrow 00:44:23.848$  purely collinear with the negative symptoms.

NOTE Confidence: 0.801581658571428

00:44:23.850 - 00:44:25.548 They have something, some they don't.

NOTE Confidence: 0.801581658571428

 $00:44:25.550 \rightarrow 00:44:27.158$  They're a little bit cognitively impaired,

NOTE Confidence: 0.801581658571428

 $00:44:27.160 \longrightarrow 00:44:27.633$  right?

- NOTE Confidence: 0.801581658571428
- 00:44:27.633 --> 00:44:30.668 But again not a clean, you know,
- NOTE Confidence: 0.801581658571428
- $00{:}44{:}30{.}668 \dashrightarrow 00{:}44{:}33{.}340$  one to one mapping between these these axes,
- NOTE Confidence: 0.801581658571428
- $00:44:33.340 \rightarrow 00:44:35.700$  right, between the the subscores of the pans.
- NOTE Confidence: 0.801581658571428
- 00:44:35.700 --> 00:44:36.540 So again, you know,
- NOTE Confidence: 0.801581658571428
- $00:44:36.540 \longrightarrow 00:44:37.800$  let's put this to the test
- NOTE Confidence: 0.801581658571428
- 00:44:37.847 --> 00:44:39.077 I I'm a competitive person,
- NOTE Confidence: 0.801581658571428
- 00:44:39.080 --> 00:44:40.448 I like competition, right.
- NOTE Confidence: 0.801581658571428
- 00:44:40.448 --> 00:44:43.060 And and I like to, you know,
- NOTE Confidence: 0.801581658571428
- $00:44:43.060 \longrightarrow 00:44:43.960$  create competitions,
- NOTE Confidence: 0.801581658571428
- $00:44:43.960 \rightarrow 00:44:45.155$  incentive questions, right.
- NOTE Confidence: 0.801581658571428
- 00:44:45.155 --> 00:44:47.515 So let's see is the SM going to
- NOTE Confidence: 0.801581658571428
- $00{:}44{:}47{.}515 \dashrightarrow 00{:}44{:}49{.}643$  outperform a data-driven solution, right.
- NOTE Confidence: 0.801581658571428
- $00{:}44{:}49{.}643 \dashrightarrow 00{:}44{:}52{.}324$  Because we need it to map it
- NOTE Confidence: 0.801581658571428
- $00:44:52.324 \rightarrow 00:44:53.417$  onto pharmacology, right?
- NOTE Confidence: 0.801581658571428
- $00{:}44{:}53{.}417 \dashrightarrow 00{:}44{:}57{.}790$  Like we need something that is robust, so.
- NOTE Confidence: 0.801581658571428

- $00:44:57.790 \longrightarrow 00:44:58.534$  Criterion 3.
- NOTE Confidence: 0.801581658571428
- $00:44:58.534 \rightarrow 00:45:00.766$  Before we even get there right,
- NOTE Confidence: 0.801581658571428
- $00{:}45{:}00{.}770 \dashrightarrow 00{:}45{:}02{.}642$  we have to check that the
- NOTE Confidence: 0.801581658571428
- $00{:}45{:}02.642 \dashrightarrow 00{:}45{:}04.609$  solution of this model is stable.
- NOTE Confidence: 0.801581658571428
- $00{:}45{:}04{.}610 \dashrightarrow 00{:}45{:}07{.}202$  So this is a summary of the leave
- NOTE Confidence: 0.801581658571428
- $00{:}45{:}07{.}202 \dashrightarrow 00{:}45{:}09{.}508$  each site out cross validation,
- NOTE Confidence: 0.801581658571428
- $00:45:09.510 \longrightarrow 00:45:11.160$  a summary of the predicted
- NOTE Confidence: 0.801581658571428
- $00:45:11.160 \rightarrow 00:45:12.150$  versus observed scores,
- NOTE Confidence: 0.801581658571428
- $00:45:12.150 \rightarrow 00:45:14.550$  a summary of the predicted versus
- NOTE Confidence: 0.801581658571428
- $00:45:14.550 \rightarrow 00:45:16.150$  observed single subject scores
- NOTE Confidence: 0.801581658571428
- 00:45:16.221 --> 00:45:17.849 from K fold bootstrapping,
- NOTE Confidence: 0.801581658571428
- $00{:}45{:}17.850 \dashrightarrow 00{:}45{:}19.908$  and similarity of the actual loadings
- NOTE Confidence: 0.801581658571428
- $00{:}45{:}19{.}908 \dashrightarrow 00{:}45{:}22{.}927$  on the PCA for leave site out five
- NOTE Confidence: 0.801581658571428
- 00:45:22.927 --> 00:45:24.902 fold bootstrapping and split half.
- NOTE Confidence: 0.801581658571428
- $00:45:24.910 \rightarrow 00:45:26.512$  And hopefully this shows you that
- NOTE Confidence: 0.801581658571428
- $00:45:26.512 \rightarrow 00:45:27.970$  the solution is really stable.

 $00{:}45{:}27{.}970 \dashrightarrow 00{:}45{:}29{.}770$  Which means that the basement consortium

NOTE Confidence: 0.801581658571428

00:45:29.770 --> 00:45:31.699 did a really good job actually,

NOTE Confidence: 0.801581658571428

00:45:31.700 --> 00:45:32.088 right.

NOTE Confidence: 0.801581658571428

 $00:45:32.088 \rightarrow 00:45:34.416$  They collected and asset clinically

NOTE Confidence: 0.801581658571428

 $00{:}45{:}34{.}416 \dashrightarrow 00{:}45{:}36{.}854$  the data in a very consistent way

NOTE Confidence: 0.801581658571428

 $00{:}45{:}36{.}854 \dashrightarrow 00{:}45{:}39{.}212$  and we're able to get a pretty

NOTE Confidence: 0.801581658571428

00:45:39.212 --> 00:45:41.140 good stable behavioral model,

NOTE Confidence: 0.715133701428571

 $00:45:41.140 \rightarrow 00:45:44.654$  right. So the PCA variance is generalizes,

NOTE Confidence: 0.715133701428571

 $00{:}45{:}44.660 \dashrightarrow 00{:}45{:}46.496$  the score is generalized and the

NOTE Confidence: 0.715133701428571

00:45:46.496 --> 00:45:47.683 PC weights generalized, right.

NOTE Confidence: 0.715133701428571

 $00:45:47.683 \rightarrow 00:45:49.524$  Otherwise why are we mapping it onto

NOTE Confidence: 0.715133701428571

 $00:45:49.524 \longrightarrow 00:45:51.596$  the brain if it doesn't, right? Cool.

NOTE Confidence: 0.715133701428571

 $00{:}45{:}51{.}596 \dashrightarrow 00{:}45{:}54{.}382$  So now let's actually go even further

NOTE Confidence: 0.715133701428571

 $00{:}45{:}54{.}382 \dashrightarrow 00{:}45{:}57{.}470$  from DSM and take pans positive symptoms.

NOTE Confidence: 0.715133701428571

 $00{:}45{:}57{.}470 \dashrightarrow 00{:}45{:}59{.}304$  Let's give pans a fair shot because

 $00:45:59.304 \rightarrow 00:46:01.464$  this is what the industry uses, right?

NOTE Confidence: 0.715133701428571

 $00{:}46{:}01{.}464 \dashrightarrow 00{:}46{:}03{.}468$  If you're going to test if

NOTE Confidence: 0.715133701428571

00:46:03.468 --> 00:46:04.470 a antipsychotic works,

NOTE Confidence: 0.715133701428571

 $00:46:04.470 \rightarrow 00:46:06.227$  you're going to use pans positive symptoms.

NOTE Confidence: 0.715133701428571

 $00:46:06.230 \longrightarrow 00:46:07.208$  That's your benchmark.

NOTE Confidence: 0.715133701428571

 $00:46:07.208 \rightarrow 00:46:09.490$  That's the gold standard for the industry,

NOTE Confidence: 0.715133701428571

 $00:46:09.490 \longrightarrow 00:46:12.754$  right. And and this is the

NOTE Confidence: 0.715133701428571

 $00:46:12.754 \rightarrow 00:46:14.930$  psychosis configuration PCA effect,

NOTE Confidence: 0.715133701428571

 $00:46:14.930 \longrightarrow 00:46:18.002$  which required only only one level

NOTE Confidence: 0.715133701428571

 $00:46:18.002 \rightarrow 00:46:20.550$  of supervision, which is to pick PCA.

NOTE Confidence: 0.715133701428571

 $00:46:20.550 \longrightarrow 00:46:21.750$  That's it. We just said.

NOTE Confidence: 0.715133701428571

 $00:46:21.750 \longrightarrow 00:46:23.102$  Let's run a PCA.

NOTE Confidence: 0.715133701428571

00:46:23.102 --> 00:46:24.800 So now, which one will give you

NOTE Confidence: 0.715133701428571

 $00:46:24.800 \rightarrow 00:46:25.933$  a better brain map, right?

NOTE Confidence: 0.715133701428571

 $00:46:25.933 \longrightarrow 00:46:27.498$  That's what we care about.

NOTE Confidence: 0.715133701428571

 $00{:}46{:}27{.}500 \dashrightarrow 00{:}46{:}30{.}559$  We care which Brain Mac is better.

 $00:46:30.560 \longrightarrow 00:46:31.355$  And so again,

NOTE Confidence: 0.715133701428571

00:46:31.355 --> 00:46:33.210 we're going to use GBC as the

NOTE Confidence: 0.715133701428571

 $00:46:33.271 \rightarrow 00:46:35.521$  brain measure and we're going to

NOTE Confidence: 0.715133701428571

 $00{:}46{:}35{.}521 \dashrightarrow 00{:}46{:}37{.}400$  calculate the variation from each.

NOTE Confidence: 0.715133701428571

 $00:46:37.400 \longrightarrow 00:46:39.647$  Parcel to every other parcel using this

NOTE Confidence: 0.715133701428571

 $00{:}46{:}39{.}647 \dashrightarrow 00{:}46{:}41{.}240$  quantitative technique that I explained,

NOTE Confidence: 0.715133701428571

 $00:46:41.240 \longrightarrow 00:46:41.597$  right.

NOTE Confidence: 0.715133701428571

 $00:46:41.597 \rightarrow 00:46:44.453$  And so the intuition again is that we're

NOTE Confidence: 0.715133701428571

 $00{:}46{:}44{.}453 \dashrightarrow 00{:}46{:}47{.}246$  going to get this value for every parcel.

NOTE Confidence: 0.715133701428571

 $00:46:47.250 \longrightarrow 00:46:49.395$  We're going to then correlate

NOTE Confidence: 0.715133701428571

 $00:46:49.395 \longrightarrow 00:46:52.080$  the area level signal with the

NOTE Confidence: 0.715133701428571

 $00{:}46{:}52.080 \dashrightarrow 00{:}46{:}53.920$  symptom for every patient.

NOTE Confidence: 0.715133701428571

 $00{:}46{:}53{.}920 \dashrightarrow 00{:}46{:}56{.}192$  And then we're going to get in a

NOTE Confidence: 0.715133701428571

 $00{:}46{:}56.192 \dashrightarrow 00{:}46{:}58.079$  cross subject map that tells us

NOTE Confidence: 0.715133701428571

 $00{:}46{:}58.079 \dashrightarrow 00{:}46{:}59.963$  how people vary across the sample

 $00:47:00.034 \rightarrow 00:47:01.962$  with respect to their GBC, right.

NOTE Confidence: 0.715133701428571

 $00{:}47{:}01{.}962 \dashrightarrow 00{:}47{:}03{.}894$  So it's an individual difference analysis.

NOTE Confidence: 0.715133701428571

 $00{:}47{:}03{.}900 \dashrightarrow 00{:}47{:}07{.}020$  And so this is the map you get with pans

NOTE Confidence: 0.715133701428571

 $00:47:07.107 \longrightarrow 00:47:08.659$  with 436 people and this is the map.

NOTE Confidence: 0.715133701428571

 $00:47:08.660 \rightarrow 00:47:12.001$  You get when you use the PC-3.

NOTE Confidence: 0.715133701428571

 $00:47:12.001 \longrightarrow 00:47:12.402$  Now.

NOTE Confidence: 0.715133701428571

 $00:47:12.402 \longrightarrow 00:47:15.209$  I want to just pause here because

NOTE Confidence: 0.715133701428571

 $00:47:15.209 \longrightarrow 00:47:16.965$  hopefully it's self-evident to

NOTE Confidence: 0.715133701428571

 $00{:}47{:}16.965 \dashrightarrow 00{:}47{:}19.085$  every body which one is better

NOTE Confidence: 0.715133701428571

 $00{:}47{:}19.085 \dashrightarrow 00{:}47{:}21.200$  and if some body says a.

NOTE Confidence: 0.715133701428571

00:47:21.200 --> 00:47:23.510 I I hope they're joking.

NOTE Confidence: 0.715133701428571

 $00{:}47{:}23.510 \dashrightarrow 00{:}47{:}23.971$  So.

NOTE Confidence: 0.715133701428571

 $00{:}47{:}23.971 \dashrightarrow 00{:}47{:}27.198$  This is not nothing done except simply

NOTE Confidence: 0.715133701428571

 $00:47:27.198 \longrightarrow 00:47:29.507$  taking a data-driven behavioral

NOTE Confidence: 0.715133701428571

 $00{:}47{:}29.507 \dashrightarrow 00{:}47{:}32.737$  analysis of pens and backs,

NOTE Confidence: 0.715133701428571

 $00{:}47{:}32.740 \dashrightarrow 00{:}47{:}34.950$  a data-driven neural measure with

 $00:47:34.950 \dashrightarrow 00:47:37.660$  the only piece of supervision being.

NOTE Confidence: 0.715133701428571

00:47:37.660 --> 00:47:41.307 Reduction of the FC matrix using GBC.

NOTE Confidence: 0.715133701428571

 $00:47:41.310 \longrightarrow 00:47:43.417$  And then you get this slice through

NOTE Confidence: 0.715133701428571

 $00:47:43.417 \longrightarrow 00:47:45.064$  the geometry that hopefully one

NOTE Confidence: 0.715133701428571

 $00{:}47{:}45.064 \dashrightarrow 00{:}47{:}47.110$  could argue is is better and

NOTE Confidence: 0.715133701428571

00:47:47.110 --> 00:47:48.792 quantitatively it is better, right?

NOTE Confidence: 0.715133701428571

 $00{:}47{:}48.792 \dashrightarrow 00{:}47{:}51.024$  You can actually check that statistically

NOTE Confidence: 0.715133701428571

 $00{:}47{:}51.024 \dashrightarrow 00{:}47{:}52.965$  that the variance covered is higher

NOTE Confidence: 0.715133701428571

 $00{:}47{:}52.965 \dashrightarrow 00{:}47{:}55.760$  and that the range of the Z values is better.

NOTE Confidence: 0.715133701428571

00:47:55.760 --> 00:47:57.064 You can do all sorts of other things,

NOTE Confidence: 0.715133701428571

 $00:47:57.070 \longrightarrow 00:47:59.150$  but it's just better.

NOTE Confidence: 0.715133701428571

00:47:59.150 --> 00:48:03.042 So, OK, now we have something right

NOTE Confidence: 0.715133701428571

 $00{:}48{:}03.042 \dashrightarrow 00{:}48{:}05.290$  now criterion 5 is,

NOTE Confidence: 0.715133701428571

 $00:48:05.290 \longrightarrow 00:48:07.014$  is this thing generalizable?

NOTE Confidence: 0.715133701428571

 $00{:}48{:}07{.}014 \dashrightarrow 00{:}48{:}11{.}009$  And what I mean by that is if I were to.

00:48:11.010 --> 00:48:12.650 Say Mark or Chris,

NOTE Confidence: 0.715133701428571

 $00{:}48{:}12.650 \dashrightarrow 00{:}48{:}15.110$  can you guys use the weights,

NOTE Confidence: 0.715133701428571

 $00:48:15.110 \longrightarrow 00:48:17.528$  the actual thing that I found

NOTE Confidence: 0.715133701428571

 $00:48:17.530 \longrightarrow 00:48:21.418$  here and reproduce the exact map?

NOTE Confidence: 0.715133701428571

 $00{:}48{:}21{.}420 \dashrightarrow 00{:}48{:}23{.}844$  Using a split half cross validation

NOTE Confidence: 0.715133701428571

 $00:48:23.844 \longrightarrow 00:48:25.056$  of the model,

NOTE Confidence: 0.715133701428571

00:48:25.060 - 00:48:27.937 can you get the same picture again?

NOTE Confidence: 0.715133701428571

 $00{:}48{:}27{.}940 \dashrightarrow 00{:}48{:}29{.}398$  That's that's what we care about.

NOTE Confidence: 0.715133701428571

00:48:29.400 --> 00:48:31.016 Not just that you can point to five,

NOTE Confidence: 0.715133701428571

 $00:48:31.020 \rightarrow 00:48:32.940$  reject the null and publish,

NOTE Confidence: 0.715133701428571

 $00{:}48{:}32{.}940 \dashrightarrow 00{:}48{:}35{.}964$  but that the picture of the neural

NOTE Confidence: 0.715133701428571

 $00:48:35.964 \rightarrow 00:48:37.260$  topography is reproducible.

NOTE Confidence: 0.715133701428571

 $00:48:37.260 \longrightarrow 00:48:39.258$  And this is what we get in this case,

NOTE Confidence: 0.715133701428571

 $00:48:39.260 \rightarrow 00:48:39.683$  right?

NOTE Confidence: 0.715133701428571

 $00:48:39.683 \rightarrow 00:48:42.652$  So and we did this 10,000 times,

NOTE Confidence: 0.715133701428571

 $00{:}48{:}42.652 \dashrightarrow 00{:}48{:}46.060$  but half and various ways and tried to

00:48:46.143 --> 00:48:48.448 break it. You know, pretty robust.

NOTE Confidence: 0.854820509166667

00:48:48.448 --> 00:48:51.588 Both dense level and the parcel level, right?

NOTE Confidence: 0.854820509166667

00:48:51.588 --> 00:48:53.901 And this is only 219 people, right?

NOTE Confidence: 0.854820509166667

 $00:48:53.901 \rightarrow 00:48:56.223$  We're not talking gargantuan samples here,

NOTE Confidence: 0.854820509166667

 $00:48:56.230 \rightarrow 00:48:59.472$  right? It's just that you have the

NOTE Confidence: 0.854820509166667

 $00{:}48{:}59{.}472 \dashrightarrow 00{:}49{:}01{.}220$  right slice through the geometry and

NOTE Confidence: 0.854820509166667

 $00:49:01.220 \rightarrow 00:49:03.236$  then all of a sudden you're getting

NOTE Confidence: 0.854820509166667

 $00:49:03.236 \rightarrow 00:49:05.326$  maps that reproduce even in patients.

NOTE Confidence: 0.854820509166667

 $00:49:05.330 \longrightarrow 00:49:08.130$  So now this is the engine that we

NOTE Confidence: 0.854820509166667

 $00{:}49{:}08{.}130 \dashrightarrow 00{:}49{:}10{.}941$  submit this to in order to select

NOTE Confidence: 0.854820509166667

 $00:49:10.941 \rightarrow 00:49:12.823$  the most stable features, right.

NOTE Confidence: 0.854820509166667

 $00{:}49{:}12.823 \dashrightarrow 00{:}49{:}14.594$  And I'm not going to walk through

NOTE Confidence: 0.854820509166667

 $00{:}49{:}14.594 \dashrightarrow 00{:}49{:}16.150$  this because it's certainly dense,

NOTE Confidence: 0.854820509166667

00:49:16.150 --> 00:49:18.706 but it's, it's simply, you know,

NOTE Confidence: 0.854820509166667

 $00{:}49{:}18.710 \dashrightarrow 00{:}49{:}21.170$  under the hood it's some basic

 $00:49:21.170 \rightarrow 00:49:23.292$  linear algebra of optimizing each

NOTE Confidence: 0.854820509166667

 $00{:}49{:}23.292 \dashrightarrow 00{:}49{:}25.342$  feature in relation to stability

NOTE Confidence: 0.854820509166667

 $00:49:25.342 \longrightarrow 00:49:27.749$  criteria from the out of sample.

NOTE Confidence: 0.854820509166667

 $00:49:27.750 \longrightarrow 00:49:28.114$  Generalization.

NOTE Confidence: 0.854820509166667

 $00:49:28.114 \longrightarrow 00:49:31.795$  And so then you can ask the question of which

NOTE Confidence: 0.854820509166667

 $00:49:31.795 \rightarrow 00:49:34.774$  parcels of the map should we trust the most?

NOTE Confidence: 0.854820509166667

 $00:49:34.780 \longrightarrow 00:49:36.220$  And those are the parcels that

NOTE Confidence: 0.854820509166667

 $00:49:36.220 \rightarrow 00:49:38.326$  then we can use as a, you know,

NOTE Confidence: 0.854820509166667

 $00{:}49{:}38{.}326 \dashrightarrow 00{:}49{:}39{.}978$  for further feature engineering.

NOTE Confidence: 0.854820509166667

 $00:49:39.980 \rightarrow 00:49:40.546$  Interestingly though,

NOTE Confidence: 0.854820509166667

 $00:49:40.546 \rightarrow 00:49:42.810$  what you can also do is then once

NOTE Confidence: 0.854820509166667

 $00{:}49{:}42{.}871 \dashrightarrow 00{:}49{:}44{.}755$  you've done this and you find

NOTE Confidence: 0.854820509166667

 $00{:}49{:}44.755 \dashrightarrow 00{:}49{:}46.011$  your trustworthy parcels right,

NOTE Confidence: 0.854820509166667

 $00:49:46.020 \longrightarrow 00:49:48.220$  the ones that truly generalize,

NOTE Confidence: 0.854820509166667

 $00{:}49{:}48.220 \dashrightarrow 00{:}49{:}50.938$  you can then ask how do they covary in

NOTE Confidence: 0.854820509166667

 $00:49:50.938 \rightarrow 00:49:53.626$  relation to the behavioral feature selection?

- NOTE Confidence: 0.854820509166667
- $00:49:53.630 \rightarrow 00:49:55.610$  Turns out there's a nonlinear relationship,
- NOTE Confidence: 0.854820509166667
- $00:49:55.610 \rightarrow 00:49:55.933$  right?
- NOTE Confidence: 0.854820509166667
- $00{:}49{:}55{.}933 \dashrightarrow 00{:}49{:}58{.}194$  Which means that the more extreme the
- NOTE Confidence: 0.854820509166667
- $00:49:58.194 \rightarrow 00:50:00.579$  person is on their behavioral loading,
- NOTE Confidence: 0.854820509166667
- $00:50:00.580 \rightarrow 00:50:03.247$  the more you trust their neural net.
- NOTE Confidence: 0.854820509166667
- $00:50:03.250 \rightarrow 00:50:05.022$  That makes sense, right?
- NOTE Confidence: 0.854820509166667
- $00:50:05.022 \longrightarrow 00:50:05.908$  That's intuitive.
- NOTE Confidence: 0.854820509166667
- $00:50:05.910 \rightarrow 00:50:08.952$  And so when you then do this and purely
- NOTE Confidence: 0.854820509166667
- 00:50:08.952 --> 00:50:11.210 filter people based on behavior,
- NOTE Confidence: 0.854820509166667
- $00:50:11.210 \longrightarrow 00:50:12.938$  just take the 10th.
- NOTE Confidence: 0.854820509166667
- $00:50:12.938 \longrightarrow 00:50:15.530$  And the 90th percentiles of the
- NOTE Confidence: 0.854820509166667
- $00{:}50{:}15{.}616 \dashrightarrow 00{:}50{:}18{.}916$  behavioral scores and segment that way.
- NOTE Confidence: 0.854820509166667
- $00{:}50{:}18{.}920 \dashrightarrow 00{:}50{:}22{.}280$  Then you can begin to segment
- NOTE Confidence: 0.854820509166667
- $00{:}50{:}22.280 \dashrightarrow 00{:}50{:}24.520$  based on neurobehavioral similarity
- NOTE Confidence: 0.854820509166667
- $00:50:24.606 \rightarrow 00:50:26.760$  of the map until you get.
- NOTE Confidence: 0.854820509166667

 $00:50:26.760 \longrightarrow 00:50:28.874$  To the very peak of this patient

NOTE Confidence: 0.854820509166667

 $00{:}50{:}28.874 \dashrightarrow 00{:}50{:}30.958$  selection and then you ask how accurate

NOTE Confidence: 0.854820509166667

 $00{:}50{:}30{.}958 \dashrightarrow 00{:}50{:}33{.}600$  is this model and then you can see that

NOTE Confidence: 0.854820509166667

 $00:50:33.600 \rightarrow 00:50:35.714$  it's pretty damn accurate at a sample,

NOTE Confidence: 0.854820509166667

00:50:35.720 --> 00:50:36.007 right.

NOTE Confidence: 0.854820509166667

 $00{:}50{:}36{.}007 \dashrightarrow 00{:}50{:}38{.}303$  So in other words it's classifying people as

NOTE Confidence: 0.854820509166667

 $00{:}50{:}38{.}303 \dashrightarrow 00{:}50{:}40{.}539$  plus or minus and in terms of their range.

NOTE Confidence: 0.854820509166667

 $00:50:40.540 \longrightarrow 00:50:42.990$  And then you can repeat this on

NOTE Confidence: 0.854820509166667

 $00:50:42.990 \rightarrow 00:50:44.428$  a completely independent sample

NOTE Confidence: 0.854820509166667

 $00:50:44.428 \longrightarrow 00:50:46.354$  and again show that it works.

NOTE Confidence: 0.854820509166667

 $00:50:46.360 \rightarrow 00:50:48.278$  In terms of segmentation by the way,

NOTE Confidence: 0.854820509166667

00:50:48.280 --> 00:50:48.848 Chris,

NOTE Confidence: 0.854820509166667

 $00{:}50{:}48.848 \dashrightarrow 00{:}50{:}53.392$  this is the OCD and and skids data

NOTE Confidence: 0.854820509166667

 $00{:}50{:}53{.}392 \dashrightarrow 00{:}50{:}55{.}485$  set which is cross diagnostic that

NOTE Confidence: 0.854820509166667

 $00:50:55.485 \longrightarrow 00:50:57.234$  we tried this with, right so.

NOTE Confidence: 0.854820509166667

 $00:50:57.234 \rightarrow 00:50:58.544$  This isn't even patients schizophrenia

- NOTE Confidence: 0.854820509166667
- 00:50:58.544 --> 00:50:59.068 anymore right.
- NOTE Confidence: 0.854820509166667
- 00:50:59.070 --> 00:51:01.338 It's just saying does your brain
- NOTE Confidence: 0.854820509166667
- 00:51:01.338 --> 00:51:04.266 map look like some norm that we
- NOTE Confidence: 0.854820509166667
- $00:51:04.266 \rightarrow 00:51:06.046$  can behaviorally incur right.
- NOTE Confidence: 0.854820509166667
- $00{:}51{:}06{.}050 \dashrightarrow 00{:}51{:}08{.}135$  So it's really about symptom
- NOTE Confidence: 0.854820509166667
- 00:51:08.135 --> 00:51:08.969 configurations right.
- NOTE Confidence: 0.854820509166667
- 00:51:08.970 --> 00:51:11.226 No longer about our you know,
- NOTE Confidence: 0.854820509166667
- 00:51:11.230 --> 00:51:12.982 do you have a diagnostic category
- NOTE Confidence: 0.854820509166667
- $00:51:12.982 \longrightarrow 00:51:13.904$  in it anyway,
- NOTE Confidence: 0.854820509166667
- $00:51:13.904 \rightarrow 00:51:15.908$  how can we leverage gene expression
- NOTE Confidence: 0.854820509166667
- $00:51:15.908 \rightarrow 00:51:17.610$  out to molecularly benchmark this
- NOTE Confidence: 0.854820509166667
- $00{:}51{:}17.610 \dashrightarrow 00{:}51{:}19.548$  and link it back to pharmacology.
- NOTE Confidence: 0.854820509166667
- 00:51:19.550 --> 00:51:21.374 So again I'm going to just remind you
- NOTE Confidence: 0.854820509166667
- 00:51:21.374 --> 00:51:23.304 of this framework Gemini dot, right.
- NOTE Confidence: 0.854820509166667
- $00{:}51{:}23{.}304 \dashrightarrow 00{:}51{:}26{.}136$  So now we can take this PC three
- NOTE Confidence: 0.854820509166667

 $00:51:26.136 \longrightarrow 00:51:28.220$  map that is trustworthy.

NOTE Confidence: 0.854820509166667

00:51:28.220 --> 00:51:28.920 And again,

NOTE Confidence: 0.854820509166667

 $00:51:28.920 \rightarrow 00:51:30.670$  correlated with gene expression patterns

NOTE Confidence: 0.854820509166667

 $00:51:30.670 \rightarrow 00:51:33.399$  in the same way that we've done with MSD.

NOTE Confidence: 0.854820509166667

00:51:33.400 --> 00:51:35.017 And this is just proof of principle,

NOTE Confidence: 0.854820509166667

 $00:51:35.020 \rightarrow 00:51:35.342$  right?

NOTE Confidence: 0.854820509166667

 $00{:}51{:}35{.}342 \dashrightarrow 00{:}51{:}37{.}274$  Again, we can show some relationships,

NOTE Confidence: 0.854820509166667

00:51:37.280 --> 00:51:39.179 I'm not going to get into this too much,

NOTE Confidence: 0.854820509166667

 $00{:}51{:}39{.}180 \dashrightarrow 00{:}51{:}40{.}329$  but for instance,

NOTE Confidence: 0.854820509166667

 $00{:}51{:}40{.}329 \dashrightarrow 00{:}51{:}43{.}010$  you can show that the interneuron markers

NOTE Confidence: 0.768201470772727

00:51:43.076 --> 00:51:45.411 or GABA subunits or seroton<br/>in

NOTE Confidence: 0.768201470772727

00:51:45.411 --> 00:51:46.812 receptor subunits have

NOTE Confidence: 0.768201470772727

 $00:51:46.812 \dashrightarrow 00:51:48.400$  correspondence with this map.

NOTE Confidence: 0.768201470772727

 $00{:}51{:}48{.}400 \dashrightarrow 00{:}51{:}51{.}515$  It's I'm not claiming mechanism or anything,

NOTE Confidence: 0.768201470772727

 $00{:}51{:}51{.}520 \dashrightarrow 00{:}51{:}52{.}780$  I'm just saying you could do this,

NOTE Confidence: 0.768201470772727

 $00:51:52.780 \longrightarrow 00:51:54.920$  right. This is doable.

 $00:51:54.920 \longrightarrow 00:51:58.866$  But finally to conclude, you can then.

NOTE Confidence: 0.768201470772727

00:51:58.866 --> 00:52:01.274 Benchmark this against our

NOTE Confidence: 0.768201470772727

 $00:52:01.274 \longrightarrow 00:52:02.478$  pharmacological targets.

NOTE Confidence: 0.768201470772727

 $00:52:02.480 \rightarrow 00:52:05.630$  So this is actually an in vivo ketamine map,

NOTE Confidence: 0.768201470772727

 $00{:}52{:}05{.}630 \dashrightarrow 00{:}52{:}07{.}262$  same GBC measure,

NOTE Confidence: 0.768201470772727

 $00:52:07.262 \rightarrow 00:52:09.438$  healthies versus healthy people,

NOTE Confidence: 0.768201470772727

 $00{:}52{:}09{.}440 \dashrightarrow 00{:}52{:}10{.}530$  place bo versus.

NOTE Confidence: 0.822075590526316

00:52:13.210 --> 00:52:14.048 Infusion, right?

NOTE Confidence: 0.822075590526316

 $00{:}52{:}14.048 \dashrightarrow 00{:}52{:}17.400$  And then we can select people along the

NOTE Confidence: 0.822075590526316

 $00:52:17.482 \rightarrow 00:52:20.080$  axis that presumably varies in relation

NOTE Confidence: 0.822075590526316

 $00:52:20.080 \longrightarrow 00:52:22.560$  to that work without ever optimizing it.

NOTE Confidence: 0.822075590526316

 $00:52:22.560 \longrightarrow 00:52:24.035$  We're not optimizing it yet.

NOTE Confidence: 0.822075590526316

 $00{:}52{:}24.040 \dashrightarrow 00{:}52{:}25.456$  And then you take two people

NOTE Confidence: 0.822075590526316

 $00{:}52{:}25{.}456 \dashrightarrow 00{:}52{:}26{.}670$  on the extreme ends, right,

NOTE Confidence: 0.822075590526316

 $00{:}52{:}26.670 \dashrightarrow 00{:}52{:}28.560$  and these are their actual brain maps.

 $00:52:28.560 \rightarrow 00:52:29.985$  These are two people diagnosed

NOTE Confidence: 0.822075590526316

 $00:52:29.985 \longrightarrow 00:52:30.831$  with schizophrenia, right?

NOTE Confidence: 0.822075590526316

 $00:52:30.831 \rightarrow 00:52:32.457$  They both have the same diagnosis.

NOTE Confidence: 0.822075590526316

 $00:52:32.460 \longrightarrow 00:52:34.652$  Yet I'd like to argue that their symptom

NOTE Confidence: 0.822075590526316

 $00:52:34.652 \rightarrow 00:52:35.844$  configurations are completely different

NOTE Confidence: 0.822075590526316

 $00{:}52{:}35{.}844 \dashrightarrow 00{:}52{:}37{.}937$  and their brains don't look the same.

NOTE Confidence: 0.822075590526316

 $00:52:37.940 \dashrightarrow 00:52:39.550$  Right. Yet we're treating them the same.

NOTE Confidence: 0.822075590526316

 $00:52:39.550 \rightarrow 00:52:42.030$  We're giving D2 blockers to both of these

NOTE Confidence: 0.822075590526316

 $00:52:42.030 \rightarrow 00:52:44.430$  people as the initial line of defense,

NOTE Confidence: 0.822075590526316

 $00:52:44.430 \longrightarrow 00:52:45.870$  when in fact, who knows,

NOTE Confidence: 0.822075590526316

00:52:45.870 --> 00:52:46.845 maybe one person would respond

NOTE Confidence: 0.822075590526316

 $00:52:46.845 \rightarrow 00:52:48.070$  way better to close the people.

NOTE Confidence: 0.822075590526316

 $00{:}52{:}48.070 \dashrightarrow 00{:}52{:}49.799$  And we have no idea that that

NOTE Confidence: 0.822075590526316

 $00:52:49.799 \rightarrow 00:52:51.766$  is true or not true, right?

NOTE Confidence: 0.822075590526316

 $00:52:51.766 \rightarrow 00:52:56.008$  But you can then quantify that using.

NOTE Confidence: 0.822075590526316

 $00:52:56.010 \longrightarrow 00:52:56.377$  This.

 $00{:}52{:}56{.}377 \dashrightarrow 00{:}52{:}58{.}579$  Framework that Lisa has advanced in

NOTE Confidence: 0.822075590526316

 $00{:}52{:}58{.}579 \dashrightarrow 00{:}53{:}01{.}383$  relation to a given target and you can

NOTE Confidence: 0.822075590526316

 $00:53:01.383 \rightarrow 00:53:03.991$  say which person is more similar, right?

NOTE Confidence: 0.822075590526316

 $00:53:03.991 \rightarrow 00:53:06.182$  So this person looks like PC-3,

NOTE Confidence: 0.822075590526316

 $00:53:06.182 \longrightarrow 00:53:07.510$  which looks like ketamine.

NOTE Confidence: 0.822075590526316

 $00{:}53{:}07{.}510 \dashrightarrow 00{:}53{:}09{.}076$  So presumably this person will get

NOTE Confidence: 0.822075590526316

 $00:53:09.076 \rightarrow 00:53:11.338$  worse if you give them ketamine and this

NOTE Confidence: 0.822075590526316

 $00:53:11.338 \rightarrow 00:53:13.398$  person would maybe even get better, right?

NOTE Confidence: 0.822075590526316

 $00:53:13.398 \longrightarrow 00:53:14.322$  I don't know.

NOTE Confidence: 0.822075590526316

 $00:53:14.322 \rightarrow 00:53:16.952$  But you could do the same thing with

NOTE Confidence: 0.822075590526316

 $00{:}53{:}16{.}952 \dashrightarrow 00{:}53{:}19{.}437$  LSD now and repeat this for another

NOTE Confidence: 0.822075590526316

 $00{:}53{:}19{.}437 \dashrightarrow 00{:}53{:}22{.}008$  access and recapitulate this principle.

NOTE Confidence: 0.822075590526316

 $00:53:22.010 \rightarrow 00:53:26.574$  Now these maps can be iteratively optimized.

NOTE Confidence: 0.822075590526316

 $00{:}53{:}26{.}580 \dashrightarrow 00{:}53{:}27{.}879$  This is a.

NOTE Confidence: 0.822075590526316

 $00{:}53{:}27.879 \dashrightarrow 00{:}53{:}29.178$  Feature selection problem.

 $00:53:29.180 \longrightarrow 00:53:31.136$  Now we can use the LSD,

NOTE Confidence: 0.822075590526316

00:53:31.140 --> 00:53:32.636 psychedelic or ketamine target

NOTE Confidence: 0.822075590526316

 $00:53:32.636 \rightarrow 00:53:34.880$  maps to find people who may

NOTE Confidence: 0.822075590526316

 $00:53:34.952 \rightarrow 00:53:37.020$  benefit the most quantitatively,

NOTE Confidence: 0.822075590526316

 $00{:}53{:}37{.}020 \dashrightarrow 00{:}53{:}37{.}517$  rationally,

NOTE Confidence: 0.822075590526316

 $00{:}53{:}37{.}517 \dashrightarrow 00{:}53{:}40{.}996$  iteratively in a fast fail algorithm that

NOTE Confidence: 0.822075590526316

 $00:53:40.996 \rightarrow 00:53:43.555$  says these two patient populations ought

NOTE Confidence: 0.822075590526316

 $00:53:43.555 \rightarrow 00:53:46.520$  to show the opposite effects of this drug.

NOTE Confidence: 0.822075590526316

 $00:53:46.520 \longrightarrow 00:53:48.155$  And that's a strong inference

NOTE Confidence: 0.822075590526316

00:53:48.155 --> 00:53:49.335 rational framework, right?

NOTE Confidence: 0.822075590526316

00:53:49.335 --> 00:53:51.960 And so just to summarize,

NOTE Confidence: 0.822075590526316

00:53:51.960 --> 00:53:53.958 like I do think we need

NOTE Confidence: 0.822075590526316

00:53:53.958 --> 00:53:54.957 informatics and scalability.

NOTE Confidence: 0.822075590526316

 $00:53:54.960 \dashrightarrow 00:53:57.678$  I do think we need to first and foremost.

NOTE Confidence: 0.822075590526316

 $00:53:57.680 \longrightarrow 00:53:58.492$  Their behavior,

NOTE Confidence: 0.822075590526316

 $00:53:58.492 \rightarrow 00:53:58.898$  right?

 $00:53:58.898 \rightarrow 00:54:01.740$  Select the right combination we need to

NOTE Confidence: 0.822075590526316

 $00{:}54{:}01{.}812 \dashrightarrow 00{:}54{:}03{.}908$  achieve criteria for trustworthiness

NOTE Confidence: 0.822075590526316

 $00:54:03.908 \rightarrow 00:54:06.642$  of those behavioral models, right?

NOTE Confidence: 0.822075590526316

 $00{:}54{:}06{.}642 \dashrightarrow 00{:}54{:}09{.}170$  That's that's a must.

NOTE Confidence: 0.822075590526316

 $00:54:09.170 \rightarrow 00:54:11.990$  Then and only then do we go to brain imaging,

NOTE Confidence: 0.822075590526316

 $00{:}54{:}11{.}990 \dashrightarrow 00{:}54{:}14{.}288$  and then we need an interpretable.

NOTE Confidence: 0.822075590526316

 $00{:}54{:}14{.}290 \dashrightarrow 00{:}54{:}16{.}595$  Robust and generalizable solution of

NOTE Confidence: 0.822075590526316

 $00{:}54{:}16{.}595 \dashrightarrow 00{:}54{:}20{.}391$  the brain back which in turn then we

NOTE Confidence: 0.822075590526316

 $00{:}54{:}20{.}391 \dashrightarrow 00{:}54{:}22{.}736$  can cross validate with pharmacological

NOTE Confidence: 0.822075590526316

 $00:54:22.736 \longrightarrow 00:54:25.907$  and gene expression and other metrics

NOTE Confidence: 0.822075590526316

 $00:54:25.910 \longrightarrow 00:54:28.350$  that that the field is bringing to bear.

NOTE Confidence: 0.822075590526316

 $00:54:28.350 \longrightarrow 00:54:29.150$  So, so in summary,

NOTE Confidence: 0.822075590526316

00:54:29.150 --> 00:54:31.047 I I do think that we have an

NOTE Confidence: 0.822075590526316

 $00{:}54{:}31{.}047 \dashrightarrow 00{:}54{:}31{.}921$  opportunity here, right.

NOTE Confidence: 0.822075590526316

 $00{:}54{:}31{.}921 \dashrightarrow 00{:}54{:}33{.}769$  I think that what we're doing in our

 $00:54:33.769 \rightarrow 00:54:35.069$  department is truly transformative.

NOTE Confidence: 0.822075590526316

00:54:35.070 -> 00:54:37.310 I'm just one out of many people who

NOTE Confidence: 0.822075590526316

 $00{:}54{:}37{.}310 \dashrightarrow 00{:}54{:}39{.}881$  are doing this work and we have I

NOTE Confidence: 0.822075590526316

 $00:54:39.881 \rightarrow 00:54:42.217$  think an iterative framework right for

NOTE Confidence: 0.822075590526316

 $00:54:42.217 \rightarrow 00:54:44.169$  really dissecting heterogeneity with.

NOTE Confidence: 0.822075590526316

00:54:44.170 - 00:54:45.250 Imaging and behavior.

NOTE Confidence: 0.822075590526316

 $00:54:45.250 \rightarrow 00:54:47.410$  And this can be optimized actually

NOTE Confidence: 0.822075590526316

 $00{:}54{:}47{.}410 \dashrightarrow 00{:}54{:}49{.}456$  again for patient selection and

NOTE Confidence: 0.822075590526316

 $00:54:49.456 \rightarrow 00:54:51.486$  precise delivery of of psychedelic

NOTE Confidence: 0.822075590526316

 $00:54:51.486 \longrightarrow 00:54:53.179$  compounds to the right patient.

NOTE Confidence: 0.822075590526316

 $00{:}54{:}53{.}180 \dashrightarrow 00{:}54{:}54{.}638$  So I'll stop there and think

NOTE Confidence: 0.822075590526316

 $00{:}54{:}54{.}638 \dashrightarrow 00{:}54{:}55{.}610$  I'm actually in time.

NOTE Confidence: 0.822075590526316

00:54:55.610 --> 00:54:56.120 Remarkable.

NOTE Confidence: 0.51398486

00:54:58.180 --> 00:55:01.669 Impressive. Thank you, Alan.

NOTE Confidence: 0.51398486

 $00:55:01.669 \rightarrow 00:55:03.727$  That was a remarkably lucid presentation

NOTE Confidence: 0.51398486

 $00:55:03.727 \rightarrow 00:55:05.900$  of some very complicated material.

 $00{:}55{:}09{.}470 \dashrightarrow 00{:}55{:}11{.}720$  Questions. Comments. We have just a

NOTE Confidence: 0.76870465

 $00:55:11.720 \longrightarrow 00:55:13.810$  couple minutes before official end time.

NOTE Confidence: 0.865789598

00:55:25.040 --> 00:55:27.248 Ellen, I wonder if you could

NOTE Confidence: 0.865789598

 $00:55:27.248 \longrightarrow 00:55:28.720$  swing back to speculate.

NOTE Confidence: 0.865789598

 $00:55:28.720 \rightarrow 00:55:31.553$  Since sort of the motivating you,

NOTE Confidence: 0.865789598

 $00{:}55{:}31{.}553 \dashrightarrow 00{:}55{:}32{.}764$  you've spent a lot of time talking

NOTE Confidence: 0.865789598

 $00:55:32.764 \rightarrow 00:55:34.170$  about the framework, the technology,

NOTE Confidence: 0.865789598

 $00{:}55{:}34{.}170 \dashrightarrow 00{:}55{:}36{.}515$  the analytics and the potential and and

NOTE Confidence: 0.865789598

 $00{:}55{:}36{.}515 \dashrightarrow 00{:}55{:}38{.}925$  just a couple slides on the psyched elics.

NOTE Confidence: 0.865789598

 $00:55:38.930 \longrightarrow 00:55:40.028$  In the middle,

NOTE Confidence: 0.865789598

 $00{:}55{:}40{.}028 \dashrightarrow 00{:}55{:}43{.}058$  which I think is fine because, you know,

NOTE Confidence: 0.865789598

 $00{:}55{:}43.058 \dashrightarrow 00{:}55{:}45.956$  it's important for us to recognize this.

NOTE Confidence: 0.865789598

00:55:45.960 - 00:55:47.118 What what what you're working on,

NOTE Confidence: 0.865789598

 $00{:}55{:}47{.}120 \dashrightarrow 00{:}55{:}49{.}960$  but I wonder if you could project OK.

NOTE Confidence: 0.865789598

 $00{:}55{:}49{.}960 \dashrightarrow 00{:}55{:}52{.}011$  This group is motivated primarily by an

 $00:55:52.011 \rightarrow 00:55:54.279$  interest in how do the psychedelics work?

NOTE Confidence: 0.865789598

 $00:55:54.280 \longrightarrow 00:55:56.416$  Who can they help? You know,

NOTE Confidence: 0.865789598

 $00:55:56.420 \rightarrow 00:55:58.420$  how would you imagine over the coming years?

NOTE Confidence: 0.865789598

 $00:55:58.420 \dashrightarrow 00:55:59.764$  And I know you've thought about

NOTE Confidence: 0.865789598

 $00{:}55{:}59{.}764 \dashrightarrow 00{:}56{:}01{.}155$  this a lot because you're doing

NOTE Confidence: 0.865789598

 $00:56:01.155 \longrightarrow 00:56:02.560$  it and planning on doing it.

NOTE Confidence: 0.865789598

 $00{:}56{:}02{.}560 \dashrightarrow 00{:}56{:}04{.}966$  So how, how would you envision

NOTE Confidence: 0.865789598

 $00:56:04.966 \rightarrow 00:56:07.139$  applying this framework to a deep,

NOTE Confidence: 0.865789598

 $00{:}56{:}07{.}140 \dashrightarrow 00{:}56{:}09{.}304$  to developing a deeper

NOTE Confidence: 0.865789598

 $00:56:09.304 \rightarrow 00:56:11.468$  understanding of how psychedelics?

NOTE Confidence: 0.865789598

 $00{:}56{:}11.470 \dashrightarrow 00{:}56{:}13.042$  Affect the brain both in terms

NOTE Confidence: 0.865789598

 $00:56:13.042 \rightarrow 00:56:14.766$  of their acute, you know,

NOTE Confidence: 0.865789598

00:56:14.766 --> 00:56:15.702 psychotomimetic, dissociative,

NOTE Confidence: 0.865789598

 $00{:}56{:}15.702 \dashrightarrow 00{:}56{:}18.510$  whatever effects and in terms of

NOTE Confidence: 0.865789598

 $00:56:18.574 \dashrightarrow 00:56:21.009$  their longer term the rapeutic effects.

NOTE Confidence: 0.865789598

 $00:56:21.010 \rightarrow 00:56:24.260$  Yeah, so.

 $00:56:24.260 \longrightarrow 00:56:24.770$  So there

NOTE Confidence: 0.861475407222222

 $00:56:24.780 \longrightarrow 00:56:25.875$  there's two pieces of work

NOTE Confidence: 0.861475407222222

00:56:25.875 --> 00:56:27.497 that I didn't have the time to

NOTE Confidence: 0.861475407222222

 $00{:}56{:}27.497 \dashrightarrow 00{:}56{:}28.937$  highlight and I was wrestling with.

NOTE Confidence: 0.861475407222222

 $00:56:28.940 \longrightarrow 00:56:30.452$  Do I want to go into them or not?

NOTE Confidence: 0.861475407222222

 $00{:}56{:}30{.}460 \dashrightarrow 00{:}56{:}33{.}274$  And so, so one paper that Katrin

NOTE Confidence: 0.861475407222222

 $00:56:33.274 \longrightarrow 00:56:35.000$  published is looking at time

NOTE Confidence: 0.861475407222222

 $00:56:35.000 \dashrightarrow 00:56:36.980$  dependent effects on the brain of

NOTE Confidence: 0.861475407222222

 $00{:}56{:}37.048 \dashrightarrow 00{:}56{:}39.400$  silybin and the same imaging session.

NOTE Confidence: 0.861475407222222

 $00{:}56{:}39{.}400 \dashrightarrow 00{:}56{:}41{.}792$  So one thing that she's done that I

NOTE Confidence: 0.861475407222222

 $00:56:41.792 \longrightarrow 00:56:44.175$  think is really impressive as shown

NOTE Confidence: 0.861475407222222

 $00{:}56{:}44.175 \dashrightarrow 00{:}56{:}46.315$  the evolving neural neural effect

NOTE Confidence: 0.861475407222222

 $00{:}56{:}46{.}315 \dashrightarrow 00{:}56{:}48{.}724$  of these compounds in the same

NOTE Confidence: 0.861475407222222

 $00{:}56{:}48.724 \dashrightarrow 00{:}56{:}51.175$  person and showing how these maps,

NOTE Confidence: 0.861475407222222

 $00{:}56{:}51{.}175 \dashrightarrow 00{:}56{:}53{.}900$  these topographies evolve as we.

 $00:56:53.900 \rightarrow 00:56:56.235$  Selecting data overtime and that

NOTE Confidence: 0.861475407222222

 $00:56:56.235 \rightarrow 00:57:01.020$  gives us confidence of the, the, the.

NOTE Confidence: 0.861475407222222

00:57:01.020 --> 00:57:02.256 Basically neural targeting engagement.

NOTE Confidence: 0.861475407222222

 $00{:}57{:}02.256 \dashrightarrow 00{:}57{:}04.455$  So that's one thing that I think

NOTE Confidence: 0.861475407222222

 $00{:}57{:}04{.}455 \dashrightarrow 00{:}57{:}06{.}520$  we really need more of these neural

NOTE Confidence: 0.861475407222222

 $00{:}57{:}06{.}520$  -->  $00{:}57{:}08{.}166$  targeting management and so then then NOTE Confidence: 0.861475407222222

 $00:57:08.166 \rightarrow 00:57:09.678$  what Josh has actually done cleverly

NOTE Confidence: 0.861475407222222

 $00:57:09.680 \rightarrow 00:57:12.480$  in in a in a sister paper to Lisa's paper,

NOTE Confidence: 0.861475407222222

 $00:57:12.480 \longrightarrow 00:57:13.884$  which is a whole nother beast

NOTE Confidence: 0.861475407222222

 $00:57:13.884 \longrightarrow 00:57:15.459$  that I didn't want to get into.

NOTE Confidence: 0.861475407222222

 $00:57:15.460 \longrightarrow 00:57:16.900$  John senior author on that,

NOTE Confidence: 0.861475407222222

 $00:57:16.900 \longrightarrow 00:57:19.168$  he's actually taken the the observation

NOTE Confidence: 0.861475407222222

00:57:19.168 --> 00:57:21.177 from Katrina was the observation

NOTE Confidence: 0.861475407222222

 $00{:}57{:}21.177 \dashrightarrow 00{:}57{:}24.180$  and then fit gene expression to the

NOTE Confidence: 0.861475407222222

 $00{:}57{:}24.180 \dashrightarrow 00{:}57{:}26.297$  computational models out of John's labs.

NOTE Confidence: 0.861475407222222

 $00:57:26.300 \longrightarrow 00:57:26.734$  And I,

 $00:57:26.734 \dashrightarrow 00:57:28.844$  I I really didn't want to get into that

NOTE Confidence: 0.861475407222222

 $00{:}57{:}28.844 \dashrightarrow 00{:}57{:}31.070$  because the the technical detail behind it.

NOTE Confidence: 0.861475407222222

 $00:57:31.070 \rightarrow 00:57:34.206$  This is maybe beyond our time scope today,

NOTE Confidence: 0.861475407222222

 $00:57:34.210 \longrightarrow 00:57:35.400$  but you guys should invite

NOTE Confidence: 0.861475407222222

 $00{:}57{:}35{.}400 \dashrightarrow 00{:}57{:}36{.}590$  him to talk about that.

NOTE Confidence: 0.861475407222222

 $00:57:36.590 \longrightarrow 00:57:40.078$  And So what he's done is put in

NOTE Confidence: 0.861475407222222

00:57:40.078 --> 00:57:42.254 gradients of 5H2A pharmacology

NOTE Confidence: 0.861475407222222

 $00:57:42.254 \rightarrow 00:57:44.430$  into the biophysical models,

NOTE Confidence: 0.861475407222222

00:57:44.430 --> 00:57:44.846 right,

NOTE Confidence: 0.861475407222222

 $00{:}57{:}44.846 \dashrightarrow 00{:}57{:}46.926$  simulated surrogate models and then

NOTE Confidence: 0.861475407222222

 $00{:}57{:}46{.}926 \dashrightarrow 00{:}57{:}49{.}407$  fit them to individual people given

NOTE Confidence: 0.861475407222222

00:57:49.407 --> 00:57:51.639 LSD and found that actually explains

NOTE Confidence: 0.861475407222222

 $00{:}57{:}51{.}639 \dashrightarrow 00{:}57{:}54{.}177$  the data way better in relation to

NOTE Confidence: 0.861475407222222

 $00{:}57{:}54{.}177 \dashrightarrow 00{:}57{:}56{.}290$  their symptoms that they get a cutely.

NOTE Confidence: 0.861475407222222

 $00:57:56.290 \longrightarrow 00:57:58.190$  So that's that's another paper.

00:57:58.190 -> 00:57:59.870 So these two pieces of work are all

NOTE Confidence: 0.861475407222222

 $00{:}57{:}59{.}870 \dashrightarrow 00{:}58{:}01{.}130$  about neural target engagement.

NOTE Confidence: 0.861475407222222

 $00:58:01.130 \longrightarrow 00:58:01.395$  Confidence.

NOTE Confidence: 0.861475407222222

00:58:01.395 --> 00:58:02.190 And then Chris,

NOTE Confidence: 0.861475407222222

 $00:58:02.190 \rightarrow 00:58:04.380$  your question is how do we apply this?

NOTE Confidence: 0.861475407222222

 $00{:}58{:}04{.}380 \dashrightarrow 00{:}58{:}06{.}716$  What do we do with this in relation

NOTE Confidence: 0.861475407222222

00:58:06.716 --> 00:58:08.870 to helping people who may benefit

NOTE Confidence: 0.861475407222222

 $00{:}58{:}08{.}870 \dashrightarrow 00{:}58{:}10.745$  from the the administration of

NOTE Confidence: 0.861475407222222

 $00{:}58{:}10.745 \dashrightarrow 00{:}58{:}12.687$  these psyched elics and that has

NOTE Confidence: 0.861475407222222

 $00{:}58{:}12.687 \dashrightarrow 00{:}58{:}14.937$  to do with finding individuals in

NOTE Confidence: 0.861475407222222

 $00:58:14.940 \longrightarrow 00:58:17.960$  the general population whose?

NOTE Confidence: 0.861475407222222

00:58:17.960 --> 00:58:21.136 Purported or potential neural

NOTE Confidence: 0.861475407222222

 $00:58:21.136 \rightarrow 00:58:23.518$  system disturbance alteration,

NOTE Confidence: 0.861475407222222

 $00:58:23.520 \rightarrow 00:58:25.278$  whatever term you want to use

NOTE Confidence: 0.861475407222222

 $00{:}58{:}25{.}278 \dashrightarrow 00{:}58{:}27{.}040$  in relation to their behavior.

NOTE Confidence: 0.861475407222222

 $00:58:27.040 \longrightarrow 00:58:30.862$  In this case mood maps onto that
$00:58:30.862 \rightarrow 00:58:33.940$  neural target engagement profile right.

NOTE Confidence: 0.861475407222222

 $00{:}58{:}33{.}940 \dashrightarrow 00{:}58{:}36{.}472$  And so the question becomes there

NOTE Confidence: 0.861475407222222

 $00{:}58{:}36{.}472 \dashrightarrow 00{:}58{:}39{.}412$  are two questions right that we're

NOTE Confidence: 0.861475407222222

 $00{:}58{:}39{.}412 \dashrightarrow 00{:}58{:}42{.}224$  after is the effect of LSD and or

NOTE Confidence: 0.861475407222222

 $00:58:42.224 \rightarrow 00:58:44.119$  silicide been uniform across people.

NOTE Confidence: 0.861475407222222

 $00:58:44.120 \longrightarrow 00:58:46.115$  In other words if you give it

NOTE Confidence: 0.861475407222222

 $00:58:46.115 \longrightarrow 00:58:48.290$  to me and you and mark and.

NOTE Confidence: 0.861475407222222

 $00{:}58{:}48{.}290 \dashrightarrow 00{:}58{:}49{.}412$  Anita across.

NOTE Confidence: 0.861475407222222

 $00{:}58{:}49{.}412 \dashrightarrow 00{:}58{:}49{.}973$  Doses.

NOTE Confidence: 0.861475407222222

 $00:58:49.973 \rightarrow 00:58:54.480$  Is our brain topography gonna look the same?

NOTE Confidence: 0.861475407222222

 $00{:}58{:}54{.}480 \dashrightarrow 00{:}58{:}55{.}884$  Turns out not,

NOTE Confidence: 0.861475407222222

 $00{:}58{:}55{.}884 \dashrightarrow 00{:}58{:}58{.}692$  that's not true and that matters.

NOTE Confidence: 0.861475407222222

 $00{:}58{:}58{.}700 \dashrightarrow 00{:}59{:}00{.}548$  So for patient precision

NOTE Confidence: 0.861475407222222

 $00{:}59{:}00{.}548 \dashrightarrow 00{:}59{:}02{.}364$  delivery that matters, right,

NOTE Confidence: 0.861475407222222

 $00{:}59{:}02{.}364 \dashrightarrow 00{:}59{:}04{.}908$  because if say you are particularly

 $00:59:04.908 \rightarrow 00:59:07.419$  amenable to respond to that compound,

NOTE Confidence: 0.861475407222222

00:59:07.420 --> 00:59:08.248 but I'm not right,

NOTE Confidence: 0.861475407222222

 $00:59:08.248 \rightarrow 00:59:09.670$  then you wouldn't give it to me.

NOTE Confidence: 0.861475407222222

 $00:59:09.670 \longrightarrow 00:59:12.393$  And that has nothing to do with

NOTE Confidence: 0.861475407222222

 $00:59:12.393 \rightarrow 00:59:14.119$  my behavioral alteration per se,

NOTE Confidence: 0.861475407222222

 $00:59:14.120 \longrightarrow 00:59:16.500$  but it may have a lot to do with the

NOTE Confidence: 0.861475407222222

 $00{:}59{:}16{.}575 \dashrightarrow 00{:}59{:}19{.}559$  receptor occupancy and the the nature of the,

NOTE Confidence: 0.861475407222222

 $00:59:19.560 \longrightarrow 00:59:20.625$  you know, individual.

NOTE Confidence: 0.861475407222222

 $00{:}59{:}20.625 \dashrightarrow 00{:}59{:}20.980$  Creation.

NOTE Confidence: 0.861475407222222

00:59:20.980 --> 00:59:23.110 Turns out this is unpublished work,

NOTE Confidence: 0.861475407222222

 $00{:}59{:}23.110 \dashrightarrow 00{:}59{:}25.406$  but ketamine is even more high than.

NOTE Confidence: 0.861475407222222

00:59:25.410 --> 00:59:25.692 Functional,

NOTE Confidence: 0.861475407222222

 $00{:}59{:}25.692 \dashrightarrow 00{:}59{:}25.974$  right?

NOTE Confidence: 0.861475407222222

 $00{:}59{:}25{.}974 \dashrightarrow 00{:}59{:}28{.}230$  Turns out that there is no one axis

NOTE Confidence: 0.760663160526316

 $00{:}59{:}28{.}287 \dashrightarrow 00{:}59{:}29{.}423$  of the average effect

NOTE Confidence: 0.760663160526316

 $00:59:29.423 \longrightarrow 00:59:30.843$  Academy on the human brain.

- NOTE Confidence: 0.760663160526316
- 00:59:30.850 --> 00:59:33.202 It's actually highly dimensional,
- NOTE Confidence: 0.760663160526316
- $00:59:33.202 \rightarrow 00:59:34.966$  which obscures paradoxically
- NOTE Confidence: 0.760663160526316
- $00:59:34.966 \longrightarrow 00:59:36.963$  the average effect, right,
- NOTE Confidence: 0.760663160526316
- $00:59:36.963 \rightarrow 00:59:38.128$  if you have multiple dimensions.
- NOTE Confidence: 0.760663160526316
- $00{:}59{:}38{.}130 \dashrightarrow 00{:}59{:}39{.}327$  And so this is what we're after.
- NOTE Confidence: 0.760663160526316
- $00{:}59{:}39{.}330 \dashrightarrow 00{:}59{:}41{.}540$  We're after mapping variation of
- NOTE Confidence: 0.760663160526316
- $00:59:41.540 \rightarrow 00:59:42.866$  psychopharmacology within and
- NOTE Confidence: 0.760663160526316
- $00:59:42.866 \longrightarrow 00:59:45.047$  across people in order to then
- NOTE Confidence: 0.760663160526316
- $00:59:45.047 \longrightarrow 00:59:46.587$  informed precision of how it
- NOTE Confidence: 0.760663160526316
- $00:59:46.587 \dashrightarrow 00:59:48.298$  relates to circuit disturbance.
- NOTE Confidence: 0.85620485375
- $00:59:52.840 \dashrightarrow 00:59:54.412$  I don't thank you very much for your call.
- NOTE Confidence: 0.85620485375
- $00{:}59{:}54{.}412 \dashrightarrow 00{:}59{:}57{.}480$  I have a question about the study
- NOTE Confidence: 0.85620485375
- $00:59:57.480 \longrightarrow 01:00:01.026$  that you show about the functional
- NOTE Confidence: 0.85620485375
- $01{:}00{:}01{.}026 \dashrightarrow 01{:}00{:}05{.}020$  connectivity after LSD and was it in the
- NOTE Confidence: 0.85620485375
- $01{:}00{:}05{.}020 \dashrightarrow 01{:}00{:}07{.}519$  acute phase or like post acute or like,
- NOTE Confidence: 0.85620485375

 $01:00:07.520 \rightarrow 01:00:10.080$  I just want to know how long after

NOTE Confidence: 0.85620485375

 $01{:}00{:}10.080 \dashrightarrow 01{:}00{:}12.130$  those of like any psychedelic,

NOTE Confidence: 0.54301478

 $01:00:12.200 \longrightarrow 01:00:15.922$  we have a question. And two scans,

NOTE Confidence: 0.54301478

 $01:00:15.922 \rightarrow 01:00:18.400$  one at 75 minutes, one at 300 minutes.

NOTE Confidence: 0.54301478

 $01{:}00{:}18{.}400 \dashrightarrow 01{:}00{:}20{.}826$  So you could argue because the ketan serin

NOTE Confidence: 0.54301478

 $01{:}00{:}20.826 \dashrightarrow 01{:}00{:}23.689$  and the LSD half lives have slightly

NOTE Confidence: 0.54301478

 $01:00:23.689 \dashrightarrow 01:00:25.619$  overlapping and distinct curves.

NOTE Confidence: 0.54301478

 $01:00:25.620 \rightarrow 01:00:27.780$  So we wanted one early and one late,

NOTE Confidence: 0.54301478

 $01{:}00{:}27.780 \dashrightarrow 01{:}00{:}29.089$  and it turns out that that matters.

NOTE Confidence: 0.900398085714286

 $01:00:30.890 \rightarrow 01:00:32.570$  So like do you know of any?

NOTE Confidence: 0.900398085714286

01:00:32.570 --> 01:00:35.080 Like is the Hyperconnectivity continues

NOTE Confidence: 0.900398085714286

 $01:00:35.080 \rightarrow 01:00:38.040$  after for example after one week?

NOTE Confidence: 0.817742935

01:00:39.430 --> 01:00:40.618 I don't know. We don't know.

NOTE Confidence: 0.817742935

 $01:00:40.620 \rightarrow 01:00:42.077$  That's a wide open question, right.

NOTE Confidence: 0.817742935

01:00:42.077 --> 01:00:44.363 So. So I don't know that anybody's

NOTE Confidence: 0.817742935

 $01{:}00{:}44.363 \dashrightarrow 01{:}00{:}45.678$  looked at these sustained effects.

- NOTE Confidence: 0.817742935
- $01{:}00{:}45.680 \dashrightarrow 01{:}00{:}47.857$  What we have some stuff from Arena

01:00:47.860 --> 01:00:49.212 Australia's data set, right.

NOTE Confidence: 0.817742935

01:00:49.212 --> 01:00:51.560 Which again I it's it's really her

NOTE Confidence: 0.817742935

 $01:00:51.560 \longrightarrow 01:00:53.366$  story to report but but it turns

NOTE Confidence: 0.817742935

 $01:00:53.366 \rightarrow 01:00:54.993$  out also when we give ketamine

NOTE Confidence: 0.817742935

 $01:00:54.993 \rightarrow 01:00:56.937$  and look at people a day later,

NOTE Confidence: 0.817742935

01:00:56.937 --> 01:00:59.079 right, with F MRI and behavior,

NOTE Confidence: 0.817742935

 $01{:}00{:}59{.}080 \dashrightarrow 01{:}01{:}00{.}720$  there's this and you guys know this, right.

NOTE Confidence: 0.817742935

01:01:00.720 --> 01:01:02.940 There's this crazy inverted V relationship.

NOTE Confidence: 0.817742935

 $01{:}01{:}02{.}940 \dashrightarrow 01{:}01{:}05{.}691$  Some people have a sustained effect of

NOTE Confidence: 0.817742935

 $01{:}01{:}05{.}691 \dashrightarrow 01{:}01{:}07{.}513$  the antidepressant phenomenon and other

NOTE Confidence: 0.817742935

 $01{:}01{:}07{.}513 \dashrightarrow 01{:}01{:}09{.}825$  people go right back to where they were.

NOTE Confidence: 0.817742935

 $01:01:09.830 \longrightarrow 01:01:11.545$  And we don't know why this is.

NOTE Confidence: 0.817742935

 $01:01:11.550 \rightarrow 01:01:14.160$  This is unexplored neurobehavioral effects.

NOTE Confidence: 0.817742935

01:01:14.160 --> 01:01:15.330 We don't know,

 $01:01:15.330 \longrightarrow 01:01:17.280$  but we know that everybody

NOTE Confidence: 0.817742935

 $01:01:17.280 \longrightarrow 01:01:19.058$  acutely shows some kind of.

NOTE Confidence: 0.817742935

01:01:19.060 --> 01:01:19.722 Clinical efficacy,

NOTE Confidence: 0.817742935

 $01:01:19.722 \rightarrow 01:01:22.742$  but then a day later you have this rebound

NOTE Confidence: 0.817742935

 $01:01:22.742 \rightarrow 01:01:25.496$  and who is rebounding and who is not why?

NOTE Confidence: 0.817742935

01:01:25.500 --> 01:01:27.762 You know there's ideas about synaptic

NOTE Confidence: 0.817742935

 $01{:}01{:}27.762 \dashrightarrow 01{:}01{:}29.700$  plasticity and LTP like phenomena

NOTE Confidence: 0.817742935

 $01:01:29.700 \longrightarrow 01:01:32.255$  and and you know which people have

NOTE Confidence: 0.817742935

 $01{:}01{:}32.255 \dashrightarrow 01{:}01{:}33.801$  that dendritic proliferation would

NOTE Confidence: 0.817742935

 $01{:}01{:}33{.}801 \dashrightarrow 01{:}01{:}36{.}063$  then stabilizes and who is most

NOTE Confidence: 0.817742935

 $01{:}01{:}36.063 \dashrightarrow 01{:}01{:}38.692$  likely to be nefit from that kind

NOTE Confidence: 0.817742935

 $01:01:38.692 \rightarrow 01:01:40.440$  of and you know psychedelics and

NOTE Confidence: 0.817742935

01:01:40.440 --> 01:01:41.720 ketamine very different from ecology,

NOTE Confidence: 0.817742935

 $01:01:41.720 \longrightarrow 01:01:42.049$  very,

NOTE Confidence: 0.817742935

 $01:01:42.049 \rightarrow 01:01:44.023$  very different but maybe converging on

NOTE Confidence: 0.817742935

 $01:01:44.023 \rightarrow 01:01:46.054$  some endpoint of exciting and driving

- NOTE Confidence: 0.817742935
- 01:01:46.054 --> 01:01:48.357 the circuits into an LTP like phenomena,

 $01:01:48.360 \longrightarrow 01:01:49.491$  we don't know.

NOTE Confidence: 0.817742935

01:01:49.491 --> 01:01:49.868 And

NOTE Confidence: 0.873927528888889

 $01:01:49.880 \longrightarrow 01:01:51.576$  is there any relationship,

NOTE Confidence: 0.873927528888889

 $01:01:51.576 \longrightarrow 01:01:53.272$  any association between the

NOTE Confidence: 0.873927528888889

01:01:53.272 --> 01:01:55.560 degree of this hyperconnectivity

NOTE Confidence: 0.873927528888889

 $01:01:55.560 \rightarrow 01:01:57.008$  and response to treatment?

NOTE Confidence: 0.744778377058824

 $01:01:57.880 \longrightarrow 01:02:00.466$  We don't know that's nobody has

NOTE Confidence: 0.744778377058824

 $01{:}02{:}00.466 \dashrightarrow 01{:}02{:}02{.}751$  that data set again nobody's

NOTE Confidence: 0.744778377058824

01:02:02.751 --> 01:02:05.577 done MD either you know major,

NOTE Confidence: 0.744778377058824

 $01:02:05.580 \rightarrow 01:02:08.044$  major depression or you know severe mood

NOTE Confidence: 0.744778377058824

 $01{:}02{:}08.044 \dashrightarrow 01{:}02{:}10.156$  disturbance data set or experiment in

NOTE Confidence: 0.744778377058824

 $01:02:10.156 \rightarrow 01:02:12.498$  which people were given either ketamine,

NOTE Confidence: 0.744778377058824

 $01{:}02{:}12.498 \dashrightarrow 01{:}02{:}16.061$  indoor sily bin or randomized to one of

NOTE Confidence: 0.744778377058824

 $01{:}02{:}16.061 \dashrightarrow 01{:}02{:}19.238$  these arms scanned prior at baseline.

 $01:02:19.240 \longrightarrow 01:02:20.580$  Scanned acutely scanned post

NOTE Confidence: 0.744778377058824

 $01:02:20.580 \longrightarrow 01:02:22.590$  and then scanned later when they

NOTE Confidence: 0.744778377058824

 $01{:}02{:}22.648 \dashrightarrow 01{:}02{:}24.543$  either sustain their recovered and

NOTE Confidence: 0.744778377058824

 $01:02:24.543 \rightarrow 01:02:26.438$  understood what predicts it right.

NOTE Confidence: 0.744778377058824

 $01:02:26.440 \longrightarrow 01:02:27.488$  Like wide open question.

NOTE Confidence: 0.744778377058824

 $01{:}02{:}27{.}488 \dashrightarrow 01{:}02{:}29{.}384$  And I think our department is unique

NOTE Confidence: 0.744778377058824

 $01:02:29.384 \longrightarrow 01:02:31.004$  position to go after this right.

NOTE Confidence: 0.744778377058824

01:02:31.010 --> 01:02:32.620 I think there's plenty of

NOTE Confidence: 0.744778377058824

 $01:02:32.620 \longrightarrow 01:02:34.700$  people who have the means,

NOTE Confidence: 0.744778377058824

 $01{:}02{:}34.700 \dashrightarrow 01{:}02{:}36.368$  expertise and talent to go after

NOTE Confidence: 0.744778377058824

 $01{:}02{:}36{.}368 \dashrightarrow 01{:}02{:}38{.}177$  this and it's a fascinating question

NOTE Confidence: 0.744778377058824

 $01:02:38.177 \rightarrow 01:02:40.721$  like this is what we need to know.

NOTE Confidence: 0.744778377058824

 $01{:}02{:}40.730 \dashrightarrow 01{:}02{:}42.649$  Thank you. No, my pleasure.

NOTE Confidence: 0.69949868

 $01:02:44.520 \longrightarrow 01:02:46.220$  Anahita stole my question.

NOTE Confidence: 0.69949868

 $01:02:46.220 \longrightarrow 01:02:48.459$  I I also had the question about can

NOTE Confidence: 0.69949868

 $01:02:48.460 \rightarrow 01:02:50.259$  we predict who was going to respond

- NOTE Confidence: 0.69949868
- $01:02:50.260 \longrightarrow 01:02:52.120$  if they have a certain a certain
- NOTE Confidence: 0.69949868
- $01{:}02{:}52{.}120 \dashrightarrow 01{:}02{:}55{.}298$  pattern that that that shows up.
- NOTE Confidence: 0.69949868
- 01:02:55.300 --> 01:02:57.332 But I also wonder whether there have
- NOTE Confidence: 0.69949868
- $01:02:57.332 \rightarrow 01:02:58.486$  been other neuroimaging studies,
- NOTE Confidence: 0.69949868
- $01:02:58.486 \longrightarrow 01:03:00.199$  not with psychedelics but with
- NOTE Confidence: 0.69949868
- $01{:}03{:}00.200 \dashrightarrow 01{:}03{:}02.384$  other treatments that showed
- NOTE Confidence: 0.69949868
- $01{:}03{:}02{.}384 \dashrightarrow 01{:}03{:}04{.}644$  changes in the connectivity such
- NOTE Confidence: 0.52348149
- 01:03:04.660 --> 01:03:08.544 as T or presence. Totally, totally.
- NOTE Confidence: 0.52348149
- 01:03:08.544 --> 01:03:09.760 So actually I forgot.
- NOTE Confidence: 0.52348149
- 01:03:09.760 --> 01:03:12.160 So charity of Donna did a nice study
- NOTE Confidence: 0.52348149
- $01:03:12.160 \longrightarrow 01:03:14.827$  where he looked at meta analysis of of.
- NOTE Confidence: 0.52348149
- 01:03:14.830 --> 01:03:16.944 Uh, effects of ketamine. I don't wanna,
- NOTE Confidence: 0.52348149
- 01:03:16.950 --> 01:03:18.924 I actually don't wanna forget that I
- NOTE Confidence: 0.52348149
- $01{:}03{:}18{.}924 \dashrightarrow 01{:}03{:}20{.}836$  think John's on the paper, John Christow.
- NOTE Confidence: 0.52348149
- $01{:}03{:}20.836 \dashrightarrow 01{:}03{:}22.700$  So there is some evidence of this in
- NOTE Confidence: 0.52348149

 $01:03:22.754 \rightarrow 01:03:24.446$  the literature that people have done,

NOTE Confidence: 0.52348149

 $01:03:24.450 \longrightarrow 01:03:26.124$  but just not the experiments that

NOTE Confidence: 0.52348149

 $01:03:26.124 \rightarrow 01:03:27.870$  you guys were asking about that.

NOTE Confidence: 0.52348149

01:03:27.870 --> 01:03:29.290 But to your point, yes.

NOTE Confidence: 0.52348149

 $01{:}03{:}29{.}290 \dashrightarrow 01{:}03{:}31{.}834$  In fact, we worked with Anil Malhotra and

NOTE Confidence: 0.52348149

 $01{:}03{:}31{.}834 \dashrightarrow 01{:}03{:}34{.}529$  to look at the effect of clozapine, right.

NOTE Confidence: 0.52348149

 $01:03:34.529 \dashrightarrow 01:03:35.724$  We're actually writing this up

NOTE Confidence: 0.52348149

 $01:03:35.724 \longrightarrow 01:03:36.970$  for publication as we speak.

NOTE Confidence: 0.52348149

 $01:03:36.970 \longrightarrow 01:03:37.672$  And so, yes,

NOTE Confidence: 0.52348149

01:03:37.672 --> 01:03:39.310 in fact you can predict and and

NOTE Confidence: 0.52348149

 $01:03:39.363 \rightarrow 01:03:41.519$  turns out that these are very strong

NOTE Confidence: 0.52348149

 $01:03:41.519 \rightarrow 01:03:43.104$  effects actually when you get

NOTE Confidence: 0.52348149

 $01:03:43.104 \rightarrow 01:03:44.872$  people who are responding, right.

NOTE Confidence: 0.52348149

 $01:03:44.872 \rightarrow 01:03:48.158$  The neural maps of predicting who responds

NOTE Confidence: 0.52348149

 $01:03:48.158 \rightarrow 01:03:50.234$  are actually quite nice and clean.

NOTE Confidence: 0.52348149

 $01:03:50.240 \rightarrow 01:03:52.718$  It's just that these are small samples

- NOTE Confidence: 0.52348149
- 01:03:52.718 --> 01:03:54.497 like we're talking 141520 people, right.

01:03:54.497 --> 01:03:56.170 So it's just the first wave of

NOTE Confidence: 0.52348149

01:03:56.221 --> 01:03:57.574 work that's coming out, right?

NOTE Confidence: 0.52348149

 $01:03:57.574 \rightarrow 01:03:59.338$  Like this is the next generation,

NOTE Confidence: 0.52348149

 $01:03:59.340 \longrightarrow 01:03:59.763$  right.

NOTE Confidence: 0.52348149

01:03:59.763 --> 01:04:01.878 They don't like precision pharmacology

NOTE Confidence: 0.52348149

 $01{:}04{:}01{.}878 \dashrightarrow 01{:}04{:}04{.}062$  to dissect individual variation in

NOTE Confidence: 0.52348149

 $01{:}04{:}04{.}062 \dashrightarrow 01{:}04{:}05{.}778$  relation to neurobehavioral effects.

NOTE Confidence: 0.52348149

01:04:05.780 --> 01:04:07.790 Like, I I'm just super excited,

NOTE Confidence: 0.52348149

01:04:07.790 --> 01:04:08.051 right,

NOTE Confidence: 0.52348149

 $01:04:08.051 \rightarrow 01:04:09.878$  because I think this is actually happening.

NOTE Confidence: 0.52348149

 $01{:}04{:}09{.}880 \dashrightarrow 01{:}04{:}11{.}364$  Like we actually see this now like

NOTE Confidence: 0.52348149

 $01:04:11.364 \longrightarrow 01:04:13.179$  the next 5 to 10 years as possible.

NOTE Confidence: 0.8752906

 $01{:}04{:}16.220 \dashrightarrow 01{:}04{:}16.890$  Great. Thanks.

NOTE Confidence: 0.781236963333333

 $01{:}04{:}20{.}000 \dashrightarrow 01{:}04{:}23{.}618$  Very excited. I'm sorry, go ahead.

01:04:23.620 --> 01:04:25.321 I was just going to say we're

NOTE Confidence: 0.781236963333333

01:04:25.321 --> 01:04:26.612 overtime and I wonder if

NOTE Confidence: 0.781236963333333

 $01:04:26.612 \longrightarrow 01:04:28.106$  we should wrap up that if.

NOTE Confidence: 0.781236963333333

01:04:28.110 --> 01:04:29.846 Well, I was just going to say,

NOTE Confidence: 0.781236963333333

 $01{:}04{:}29.850 \dashrightarrow 01{:}04{:}31.190$  I'll make it quick then.

NOTE Confidence: 0.781236963333333

 $01:04:31.190 \longrightarrow 01:04:32.219$  So very exciting

NOTE Confidence: 0.789216434

 $01{:}04{:}32{.}230 \dashrightarrow 01{:}04{:}37{.}230$  work, great presentation and the

NOTE Confidence: 0.789216434

 $01:04:37.230 \longrightarrow 01:04:39.960$  several questions that were just

NOTE Confidence: 0.789216434

 $01{:}04{:}39{.}960 \dashrightarrow 01{:}04{:}42{.}921$  asked made me think about some of our NOTE Confidence: 0.789216434

01:04:42.921 --> 01:04:44.612 work in the psychotherapy Development

NOTE Confidence: 0.789216434

01:04:44.612 $\operatorname{-->}$ 01:04:47.489 Center and the data that we've been

NOTE Confidence: 0.789216434

 $01:04:47.489 \longrightarrow 01:04:49.450$  collecting over the past 15 years

NOTE Confidence: 0.789216434

 $01:04:49.450 \rightarrow 01:04:51.440$  by integrating F MRI measures into

NOTE Confidence: 0.789216434

 $01{:}04{:}51{.}440 \dashrightarrow 01{:}04{:}53{.}462$  randomized clinical trials and the

NOTE Confidence: 0.789216434

 $01:04:53.462 \longrightarrow 01:04:55.326$  potential for these approaches we've

NOTE Confidence: 0.789216434

 $01{:}04{:}55{.}326 \dashrightarrow 01{:}04{:}57{.}600$  been using things like connectome based.

01:04:57.600 --> 01:04:59.000 Predictive modeling, but there

NOTE Confidence: 0.8450367575

01:04:59.010 --> 01:05:02.800 are many different approaches to understand

NOTE Confidence: 0.950403578571429

 $01:05:03.270 \rightarrow 01:05:07.988$  better how people may respond to treatment.

NOTE Confidence: 0.950403578571429

01:05:07.990 --> 01:05:11.665 So I think again very exciting work

NOTE Confidence: 0.950403578571429

 $01{:}05{:}11{.}670 \dashrightarrow 01{:}05{:}15{.}478$  would be great to to speak further.

NOTE Confidence: 0.950403578571429

 $01{:}05{:}15{.}480 \dashrightarrow 01{:}05{:}17{.}470$  Because I think that we are at a

NOTE Confidence: 0.950403578571429

 $01{:}05{:}17{.}470 \dashrightarrow 01{:}05{:}19{.}635$  stage and as you mentioned uniquely

NOTE Confidence: 0.950403578571429

 $01:05:19.635 \longrightarrow 01:05:22.365$  positioned within our department to

NOTE Confidence: 0.950403578571429

 $01{:}05{:}22.365 \dashrightarrow 01{:}05{:}24.860$  make significant contributions to the

NOTE Confidence: 0.950403578571429

 $01:05:24.860 \longrightarrow 01:05:27.212$  understanding of how we might best

NOTE Confidence: 0.950403578571429

 $01:05:27.212 \rightarrow 01:05:29.056$  advance psychiatric care for people.

NOTE Confidence: 0.950403578571429

01:05:29.056 --> 01:05:30.816 I couldn't agree more mark.

NOTE Confidence: 0.950403578571429

 $01{:}05{:}30{.}820 \dashrightarrow 01{:}05{:}33{.}948$  And I think that your point there's many

NOTE Confidence: 0.950403578571429

 $01{:}05{:}33{.}948 \dashrightarrow 01{:}05{:}36{.}419$  different ways that we'll all be in some

NOTE Confidence: 0.950403578571429

 $01{:}05{:}36{.}419 \dashrightarrow 01{:}05{:}38{.}557$  family of general linear models, right.

 $01{:}05{:}38{.}557 \dashrightarrow 01{:}05{:}40{.}459$  So and and people can approach

NOTE Confidence: 0.950403578571429

 $01:05:40.459 \rightarrow 01:05:41.880$  this from various angles.

NOTE Confidence: 0.950403578571429

01:05:41.880 --> 01:05:43.714 I think that you know to your

NOTE Confidence: 0.950403578571429

 $01:05:43.714 \rightarrow 01:05:45.420$  point it's going to be the data.

NOTE Confidence: 0.950403578571429

 $01{:}05{:}45{.}420 \dashrightarrow 01{:}05{:}47{.}380$  That you guys have and we're going to

NOTE Confidence: 0.950403578571429

 $01{:}05{:}47{.}380 \dashrightarrow 01{:}05{:}49{.}298$  continue to collect and it's going to

NOTE Confidence: 0.950403578571429

 $01:05:49.298 \longrightarrow 01:05:51.005$  be about the right behavioral response

NOTE Confidence: 0.950403578571429

 $01:05:51.005 \rightarrow 01:05:53.229$  mapping which all of you are alluding to.

NOTE Confidence: 0.950403578571429

 $01{:}05{:}53{.}230 \dashrightarrow 01{:}05{:}56{.}119$  So I I couldn't agree more and I think

NOTE Confidence: 0.950403578571429

01:05:56.119 --> 01:05:59.290 it's just it's just kind of you know.

NOTE Confidence: 0.950403578571429

 $01:05:59.290 \rightarrow 01:06:00.420$  Maybe it's the sunny day,

NOTE Confidence: 0.950403578571429

 $01:06:00.420 \longrightarrow 01:06:01.948$  so I feel optimistic,

NOTE Confidence: 0.950403578571429

 $01:06:01.948 \rightarrow 01:06:05.632$  but but I I I genuinely think that this

NOTE Confidence: 0.950403578571429

 $01:06:05.632 \rightarrow 01:06:08.466$  was not possible 15 years ago, right?

NOTE Confidence: 0.950403578571429

01:06:08.466 --> 01:06:10.500 Like we didn't have the tech to do this

NOTE Confidence: 0.950403578571429

 $01:06:10.559 \rightarrow 01:06:12.674$  and we actually now not only have the tech,

- NOTE Confidence: 0.950403578571429
- $01:06:12.680 \longrightarrow 01:06:14.420$  but the information to do it.
- NOTE Confidence: 0.950403578571429
- $01:06:14.420 \longrightarrow 01:06:15.848$  And so I want to just leave
- NOTE Confidence: 0.950403578571429
- $01:06:15.848 \rightarrow 01:06:16.740$  people with that idea,
- NOTE Confidence: 0.950403578571429
- $01:06:16.740 \longrightarrow 01:06:20.730$  right, that that you know.
- NOTE Confidence: 0.950403578571429
- $01:06:20.730 \longrightarrow 01:06:22.613$  And the fact that Yale is really
- NOTE Confidence: 0.950403578571429
- $01:06:22.613 \longrightarrow 01:06:23.793$  stepping up into psychedelic
- NOTE Confidence: 0.950403578571429
- $01{:}06{:}23.793 \dashrightarrow 01{:}06{:}25.984$  medicine and that you guys are
- NOTE Confidence: 0.950403578571429
- $01:06:25.984 \rightarrow 01:06:27.938$  doing this work and I couldn't
- NOTE Confidence: 0.950403578571429
- $01{:}06{:}27{.}938 \dashrightarrow 01{:}06{:}29{.}523$  be more supportive and whatever,
- NOTE Confidence: 0.950403578571429
- $01:06:29.530 \rightarrow 01:06:31.350$  whatever you need on on,
- NOTE Confidence: 0.950403578571429
- $01:06:31.350 \longrightarrow 01:06:32.040$  happy to help.
- NOTE Confidence: 0.891830826
- 01:06:36.300 --> 01:06:37.692 So with that, I think we
- NOTE Confidence: 0.891830826
- 01:06:37.692 --> 01:06:39.190 should close for today. Alan.
- NOTE Confidence: 0.891830826
- $01{:}06{:}39{.}190 \dashrightarrow 01{:}06{:}42{.}830$  Thank you again for being here with us
- NOTE Confidence: 0.891830826
- $01{:}06{:}42.830 \dashrightarrow 01{:}06{:}45.540$  today and for covering this material.
- NOTE Confidence: 0.891830826

- 01:06:45.540 --> 01:06:48.120 I believe next month, tentatively,
- NOTE Confidence: 0.891830826
- $01{:}06{:}48.120 \dashrightarrow 01{:}06{:}50.164$  Cyril has agreed to present either he
- NOTE Confidence: 0.891830826
- $01{:}06{:}50{.}164 \dashrightarrow 01{:}06{:}52{.}429$  or some one from his group or about some
- NOTE Confidence: 0.891830826
- $01:06:52.429 \longrightarrow 01:06:54.420$  of the work that they've been doing,
- NOTE Confidence: 0.891830826
- $01:06:54.420 \longrightarrow 01:06:55.398$  perhaps about DMT,
- NOTE Confidence: 0.891830826
- $01:06:55.398 \rightarrow 01:06:58.040$  where they've done some of the first work,
- NOTE Confidence: 0.891830826
- $01{:}06{:}58.040 \dashrightarrow 01{:}06{:}59.846$  both in health and in individuals
- NOTE Confidence: 0.891830826
- $01:06:59.846 \rightarrow 01:07:01.293$  with depressions. That'd be exciting.
- NOTE Confidence: 0.891830826
- 01:07:01.293 --> 01:07:02.417 That's not confirmed yet,
- NOTE Confidence: 0.891830826
- $01{:}07{:}02.420 \dashrightarrow 01{:}07{:}05.521$  but we'll send out emails once we
- NOTE Confidence: 0.891830826
- $01{:}07{:}05{.}521 \dashrightarrow 01{:}07{:}07{.}968$  have a confirmation and a title
- NOTE Confidence: 0.891830826
- $01:07:07.968 \longrightarrow 01:07:10.369$  and hope to see you all then.
- NOTE Confidence: 0.891830826
- $01:07:10.370 \longrightarrow 01:07:11.699$  Take care, everybody.