WEBVTT

NOTE duration:"01:02:02"

NOTE recognizability:0.840

NOTE language:en-us

NOTE Confidence: 0.76817679444445

 $00:00:00.000 \rightarrow 00:00:02.796$  Nelly, and for that really wonderful

NOTE Confidence: 0.76817679444445

 $00:00:02.796 \rightarrow 00:00:04.752$  introduction and for a persistence

NOTE Confidence: 0.76817679444445

 $00{:}00{:}04.752 \dashrightarrow 00{:}00{:}06.960$  in inviting me to to give this talk

NOTE Confidence: 0.76817679444445

00:00:07.019 --> 00:00:08.879 for the Department of Psychiatry.

NOTE Confidence: 0.76817679444445

 $00:00:08.880 \longrightarrow 00:00:11.102$  And this is a great honor, you know,

NOTE Confidence: 0.76817679444445

 $00{:}00{:}11.102 \dashrightarrow 00{:}00{:}13.290$  I've been at Yale for 11 years and I

NOTE Confidence: 0.76817679444445

 $00{:}00{:}13.290 \dashrightarrow 00{:}00{:}15.522$  over just the last year or two through

NOTE Confidence: 0.76817679444445

 $00:00:15.522 \rightarrow 00:00:16.931$  interactions with Chris Pittenger

NOTE Confidence: 0.76817679444445

 $00{:}00{:}16.931 \dashrightarrow 00{:}00{:}18.721$  and more interactions with other

NOTE Confidence: 0.76817679444445

00:00:18.721 --> 00:00:20.074 colleagues and psychiatry really,

NOTE Confidence: 0.76817679444445

 $00:00:20.074 \rightarrow 00:00:21.976$  really realized what a missed opportunity

NOTE Confidence: 0.76817679444445

 $00{:}00{:}21.976 \dashrightarrow 00{:}00{:}23.859$  that's being all this time for me to

NOTE Confidence: 0.76817679444445

 $00:00:23.859 \rightarrow 00:00:25.400$  not interact more with your department.

 $00:00:25.400 \longrightarrow 00:00:27.528$  So again, I hope this is just the

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 $00{:}00{:}27.528$  -->  $00{:}00{:}29.379$  beginning of a long standing set

NOTE Confidence: 0.76817679444445

 $00:00:29.379 \rightarrow 00:00:31.257$  of intersections that we can have,

NOTE Confidence: 0.76817679444445

 $00{:}00{:}31.260 \dashrightarrow 00{:}00{:}32.124$  and I think.

NOTE Confidence: 0.76817679444445

00:00:32.124 --> 00:00:32.700 In particular,

NOTE Confidence: 0.76817679444445

 $00{:}00{:}32.700 \dashrightarrow 00{:}00{:}35.352$  my research interests and my clinical

NOTE Confidence: 0.76817679444445

 $00:00:35.352 \rightarrow 00:00:37.120$  interests are really intersecting

NOTE Confidence: 0.76817679444445

 $00:00:37.183 \rightarrow 00:00:39.384$  with psychiatric disease, and again,

NOTE Confidence: 0.76817679444445

 $00:00:39.384 \longrightarrow 00:00:40.994$  the brain and the mind,

NOTE Confidence: 0.76817679444445

 $00{:}00{:}41.000 \dashrightarrow 00{:}00{:}42.904$  both in terms of cognition but also in

NOTE Confidence: 0.76817679444445

 $00{:}00{:}42.904 \dashrightarrow 00{:}00{:}44.699$  terms of mood disorders is something

NOTE Confidence: 0.76817679444445

 $00:00:44.699 \rightarrow 00:00:46.589$  that's really relevant to my work.

NOTE Confidence: 0.76817679444445

00:00:46.590 --> 00:00:49.677 So as you heard from Professor O'Malley,

NOTE Confidence: 0.76817679444445

 $00:00:49.680 \rightarrow 00:00:51.556$  I've been working for a long time

NOTE Confidence: 0.76817679444445

 $00:00:51.556 \rightarrow 00:00:53.410$  studying the effects of HIV in the brain.

NOTE Confidence: 0.76817679444445

 $00:00:53.410 \longrightarrow 00:00:55.570$  And then of course, 2020,

 $00:00:55.570 \rightarrow 00:00:58.150$  because we had this massive onslaught

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 $00:00:58.150 \rightarrow 00:01:00.918$  of concerns about the brain and COVID,

NOTE Confidence: 0.76817679444445

 $00:01:00.920 \dashrightarrow 00:01:02.985$  this became an area that I've also.

NOTE Confidence: 0.76817679444445

00:01:02.990 --> 00:01:06.008 Started to investigate one thing.

NOTE Confidence: 0.76817679444445

 $00:01:06.008 \dashrightarrow 00:01:07.553$  That's a really important part

NOTE Confidence: 0.76817679444445

00:01:07.553 --> 00:01:10.024 of my sort of portfolio is I'm a

NOTE Confidence: 0.76817679444445

 $00:01:10.024 \dashrightarrow 00:01:12.342$  clinician and I see patients and so

NOTE Confidence: 0.76817679444445

 $00:01:12.342 \rightarrow 00:01:15.254$  I'm going to talk about the issues

NOTE Confidence: 0.76817679444445

00:01:15.254 --> 00:01:19.040 of CNS effects of COVID-19 really,

NOTE Confidence: 0.76817679444445

 $00:01:19.040 \rightarrow 00:01:20.970$  starting from a clinical perspective,

NOTE Confidence: 0.76817679444445

00:01:20.970 --> 00:01:22.824 and I think that I'm going to try to

NOTE Confidence: 0.76817679444445

 $00:01:22.824 \rightarrow 00:01:24.869$  kind of go through what we've understood

NOTE Confidence: 0.76817679444445

 $00:01:24.869 \rightarrow 00:01:27.068$  what we've learned over the last two years,

NOTE Confidence: 0.76817679444445

 $00:01:27.070 \longrightarrow 00:01:27.912$  and really,

NOTE Confidence: 0.76817679444445

 $00{:}01{:}27{.}912 \dashrightarrow 00{:}01{:}30{.}438$  all of that begins with clinical

00:01:30.438 --> 00:01:32.362 observations and and, you know,

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00:01:32.362 --> 00:01:33.460 people worldwide reports.

NOTE Confidence: 0.76817679444445

 $00{:}01{:}33{.}460 \dashrightarrow 00{:}01{:}34{.}996$  Worldwide and then some of our

NOTE Confidence: 0.76817679444445

 $00:01:34.996 \rightarrow 00:01:36.320$  own experience here at Yale.

NOTE Confidence: 0.76817679444445

 $00{:}01{:}36{.}320 \dashrightarrow 00{:}01{:}38{.}920$  So I'm gonna I'm gonna anchor the talk

NOTE Confidence: 0.76817679444445

00:01:38.920 --> 00:01:41.550 and talking about the CNS sorts of

NOTE Confidence: 0.768176794444445

00:01:41.550 --> 00:01:43.465 clinical reports and acute COVID-19.

NOTE Confidence: 0.76817679444445

 $00:01:43.470 \longrightarrow 00:01:45.129$  I'm going to then talk about what's

NOTE Confidence: 0.76817679444445

 $00{:}01{:}45{.}129 \dashrightarrow 00{:}01{:}46{.}626$  being learned over the last two

NOTE Confidence: 0.76817679444445

 $00:01:46.626 \rightarrow 00:01:47.856$  years about the neuropathic genesis

NOTE Confidence: 0.76817679444445

 $00{:}01{:}47.856 \dashrightarrow 00{:}01{:}49.359$  of that acute COVID infection.

NOTE Confidence: 0.76817679444445

 $00:01:49.360 \longrightarrow 00:01:50.142$  So really,

NOTE Confidence: 0.76817679444445

 $00{:}01{:}50{.}142 \dashrightarrow 00{:}01{:}52{.}488$  what's happening in the brain and

NOTE Confidence: 0.76817679444445

00:01:52.488 --> 00:01:54.360 people during acute COVID-19?

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 $00:01:54.360 \rightarrow 00:01:56.000$  Primarily people who were pretty

NOTE Confidence: 0.76817679444445

 $00:01:56.000 \rightarrow 00:01:58.008$  severely ill is where most of

- NOTE Confidence: 0.76817679444445
- 00:01:58.008 --> 00:01:59.538 our information has come from,
- NOTE Confidence: 0.76817679444445
- $00:01:59.540 \longrightarrow 00:02:01.511$  and this is going to be sort of the
- NOTE Confidence: 0.76817679444445
- $00:02:01.511 \rightarrow 00:02:03.513$  jumping off point for the rest of my talk,
- NOTE Confidence: 0.76817679444445
- $00:02:03.520 \longrightarrow 00:02:05.040$  which is talking about.
- NOTE Confidence: 0.76817679444445
- 00:02:05.040 --> 00:02:05.800 Nervous system,
- NOTE Confidence: 0.76817679444445
- $00{:}02{:}05{.}800 \dashrightarrow 00{:}02{:}09{.}118$  long COVID or post acute sequelae
- NOTE Confidence: 0.76817679444445
- $00:02:09.118 \longrightarrow 00:02:10.224$  of COVID-19.
- NOTE Confidence: 0.76817679444445
- $00:02:10.230 \longrightarrow 00:02:11.742$  So the first thing I'm going
- NOTE Confidence: 0.76817679444445
- $00:02:11.742 \longrightarrow 00:02:13.108$  to describe is neurologic and
- NOTE Confidence: 0.76817679444445
- $00:02:13.108 \rightarrow 00:02:14.628$  psychiatric reports in acute COVID,
- NOTE Confidence: 0.76817679444445
- $00:02:14.630 \longrightarrow 00:02:17.006$  and I think that we as a globe
- NOTE Confidence: 0.76817679444445
- $00{:}02{:}17.006 \dashrightarrow 00{:}02{:}19.623$  first heard about the concern that
- NOTE Confidence: 0.76817679444445
- $00{:}02{:}19.623 \dashrightarrow 00{:}02{:}22.063$  there might be quote neurologic
- NOTE Confidence: 0.76817679444445
- $00{:}02{:}22.063 \dashrightarrow 00{:}02{:}23.870$  manifestations and people with
- NOTE Confidence: 0.76817679444445
- 00:02:23.870 --> 00:02:26.366 COVID-19 from this report from Wuhan,
- NOTE Confidence: 0.76817679444445

00:02:26.370 --> 00:02:26.603 China,

NOTE Confidence: 0.76817679444445

 $00{:}02{:}26.603 \dashrightarrow 00{:}02{:}28.234$  and this was from one of the

NOTE Confidence: 0.76817679444445

00:02:28.234 --> 00:02:29.160 major hospitals that had,

NOTE Confidence: 0.76817679444445

 $00{:}02{:}29{.}160 \dashrightarrow 00{:}02{:}29{.}952$  you know,

NOTE Confidence: 0.76817679444445

 $00:02:29.952 \longrightarrow 00:02:32.724$  thousands and thousands of patients in the

NOTE Confidence: 0.76817679444445

 $00:02:32.724 \rightarrow 00:02:35.152$  first wave and what emerged from this.

NOTE Confidence: 0.76817679444445

 $00{:}02{:}35{.}152 \dashrightarrow 00{:}02{:}37{.}270$  This hospital experience and actually was

NOTE Confidence: 0.76817679444445

 $00:02:37.329 \rightarrow 00:02:39.450$  originally a preprint in March of 2020,

NOTE Confidence: 0.76817679444445

 $00{:}02{:}39{.}450 \dashrightarrow 00{:}02{:}40{.}750$  was this.

NOTE Confidence: 0.76817679444445

 $00:02:40.750 \longrightarrow 00:02:42.050$  Fairly generalized,

NOTE Confidence: 0.76817679444445

 $00:02:42.050 \rightarrow 00:02:45.300$  very clinically based report suggesting

NOTE Confidence: 0.76817679444445

 $00:02:45.300 \rightarrow 00:02:48.338$  that 36% of people who were hospitalized

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 $00{:}02{:}48.338 \dashrightarrow 00{:}02{:}49.930$  with laboratory confirmed COVID-19

NOTE Confidence: 0.76817679444445

 $00{:}02{:}49{.}995 \dashrightarrow 00{:}02{:}51{.}475$  had neurologic manifestations of

NOTE Confidence: 0.76817679444445

 $00{:}02{:}51{.}475 \dashrightarrow 00{:}02{:}53{.}695$  disease and what you'll see here

NOTE Confidence: 0.919579350416667

 $00:02:53.756 \rightarrow 00:02:55.180$  under the nervous system.

 $00:02:55.180 \longrightarrow 00:02:57.100$  Symptoms in this table is that

NOTE Confidence: 0.919579350416667

00:02:57.100 --> 00:02:58.380 it's pretty broad definitions,

NOTE Confidence: 0.919579350416667

 $00:02:58.380 \longrightarrow 00:03:00.075$  so CNS conditions,

NOTE Confidence: 0.919579350416667

00:03:00.075 --> 00:03:02.335 including things like dizziness,

NOTE Confidence: 0.919579350416667

 $00:03:02.340 \dashrightarrow 00:03:04.232$  headache, and her consciousness,

NOTE Confidence: 0.919579350416667

 $00:03:04.232 \rightarrow 00:03:07.070$  acute with vascular disease or stroke,

NOTE Confidence: 0.919579350416667

 $00:03:07.070 \rightarrow 00:03:09.518$  and then there were also changes in smell,

NOTE Confidence: 0.919579350416667

 $00:03:09.520 \longrightarrow 00:03:10.990$  taste, and vision which were

NOTE Confidence: 0.919579350416667

 $00{:}03{:}10{.}990 \dashrightarrow 00{:}03{:}11{.}872$  considered peripheral nervous

NOTE Confidence: 0.919579350416667

 $00:03:11.872 \dashrightarrow 00:03:13.399$  system and also skeletal muscle.

NOTE Confidence: 0.919579350416667

 $00:03:13.400 \rightarrow 00:03:15.992$  Injury now this is the type of report that

NOTE Confidence: 0.919579350416667

 $00:03:15.992 \dashrightarrow 00:03:18.536$  was available early on in the pandemic,

NOTE Confidence: 0.919579350416667

 $00:03:18.540 \rightarrow 00:03:20.120$  primarily because research investigation

NOTE Confidence: 0.919579350416667

 $00{:}03{:}20{.}120 \dashrightarrow 00{:}03{:}22{.}095$  of these patients wasn't possible.

NOTE Confidence: 0.919579350416667

 $00{:}03{:}22{.}100 \dashrightarrow 00{:}03{:}23{.}815$  These hospitals were overwhelmed as

 $00:03:23.815 \longrightarrow 00:03:26.719$  we also were at Yale with just an

NOTE Confidence: 0.919579350416667

 $00{:}03{:}26.719$  -->  $00{:}03{:}28.589$  on slaught of patients and research

NOTE Confidence: 0.919579350416667

 $00{:}03{:}28{.}589 \dashrightarrow 00{:}03{:}31{.}017$  collection of samples or data or

NOTE Confidence: 0.919579350416667

 $00:03:31.017 \rightarrow 00:03:32.633$  even neuroimaging was essentially

NOTE Confidence: 0.919579350416667

 $00{:}03{:}32{.}633 \dashrightarrow 00{:}03{:}34{.}761$  not available in most patients

NOTE Confidence: 0.919579350416667

 $00{:}03{:}34{.}761 \dashrightarrow 00{:}03{:}36{.}509$  because of infection concerns.

NOTE Confidence: 0.919579350416667

 $00{:}03{:}36{.}510 \dashrightarrow 00{:}03{:}38{.}344$  But this was the first hint that

NOTE Confidence: 0.919579350416667

 $00:03:38.344 \rightarrow 00:03:40.358$  there might be a neurologic concern,

NOTE Confidence: 0.919579350416667

 $00{:}03{:}40{.}360 \dashrightarrow 00{:}03{:}41{.}893$  and I think one of the most

NOTE Confidence: 0.919579350416667

 $00:03:41.893 \rightarrow 00:03:43.142$  important findings of this initial

NOTE Confidence: 0.919579350416667

 $00:03:43.142 \longrightarrow 00:03:44.218$  report was the finding.

NOTE Confidence: 0.919579350416667

 $00:03:44.220 \longrightarrow 00:03:46.008$  Some of the patients came to

NOTE Confidence: 0.919579350416667

00:03:46.010 --> 00:03:48.110 the hospital with an primarily

NOTE Confidence: 0.919579350416667

00:03:48.110 --> 00:03:49.370 in neurologic manifestation,

NOTE Confidence: 0.919579350416667

 $00:03:49.370 \rightarrow 00:03:51.380$  as they're preventing presenting syndrome,

NOTE Confidence: 0.919579350416667

 $00:03:51.380 \longrightarrow 00:03:53.258$  so that was probably the first

 $00:03:53.258 \rightarrow 00:03:55.495$  clue that COVID is not necessarily

NOTE Confidence: 0.919579350416667

 $00:03:55.495 \rightarrow 00:03:57.327$  only a respiratory disease,

NOTE Confidence: 0.919579350416667

 $00:03:57.330 \longrightarrow 00:04:00.494$  but in fact also has an impact

NOTE Confidence: 0.919579350416667

 $00:04:00.494 \rightarrow 00:04:03.568$  in other organ systems as well.

NOTE Confidence: 0.919579350416667

 $00{:}04{:}03.570 \dashrightarrow 00{:}04{:}05.271$  And So what we were able to do here

NOTE Confidence: 0.919579350416667

 $00{:}04{:}05{.}271 \dashrightarrow 00{:}04{:}07{.}220$  at Yale because we had this sort of

NOTE Confidence: 0.919579350416667

 $00:04:07.220 \longrightarrow 00:04:09.073$  warning ahead of time that there were

NOTE Confidence: 0.919579350416667

 $00:04:09.073 \rightarrow 00:04:11.230$  concerns coming out of both China and Europe.

NOTE Confidence: 0.919579350416667

 $00{:}04{:}11.230 \dashrightarrow 00{:}04{:}13.754$  And also when we sort of knew that the

NOTE Confidence: 0.919579350416667

 $00:04:13.754 \rightarrow 00:04:16.154$  wave was coming in the beginning of March,

NOTE Confidence: 0.919579350416667

 $00:04:16.160 \longrightarrow 00:04:17.816$  we sort of scrambled to put

NOTE Confidence: 0.919579350416667

 $00:04:17.816 \longrightarrow 00:04:19.702$  together what we called a neuro

NOTE Confidence: 0.919579350416667

 $00:04:19.702 \dashrightarrow 00:04:21.146$  COVID inpatient console service.

NOTE Confidence: 0.919579350416667

 $00{:}04{:}21{.}150 \dashrightarrow 00{:}04{:}22{.}692$  And this was essentially me working

NOTE Confidence: 0.919579350416667

 $00{:}04{:}22.692 \dashrightarrow 00{:}04{:}24.770$  with a couple of neurology residents,

00:04:24.770 --> 00:04:25.742 primarily Lindsey McAlpine

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 $00{:}04{:}25.742 \dashrightarrow 00{:}04{:}27.686$  shown up here on the right,

NOTE Confidence: 0.919579350416667

 $00:04:27.690 \longrightarrow 00:04:29.594$  but also to have a garden is

NOTE Confidence: 0.919579350416667

00:04:29.594 --> 00:04:31.259 also coming into your program,

NOTE Confidence: 0.919579350416667

 $00:04:31.260 \dashrightarrow 00:04:34.606$  and we essentially were whenever there was.

NOTE Confidence: 0.919579350416667

 $00{:}04{:}34{.}610 \dashrightarrow 00{:}04{:}35{.}642$  Inpatient neurology konsult

NOTE Confidence: 0.919579350416667

 $00{:}04{:}35{.}642 \dashrightarrow 00{:}04{:}38{.}050$  on on some one who was known to

NOTE Confidence: 0.919579350416667

 $00:04:38.110 \longrightarrow 00:04:39.890$  have COVID-19 in the hospital.

NOTE Confidence: 0.919579350416667

 $00{:}04{:}39{.}890 \dashrightarrow 00{:}04{:}41{.}792$  We essentially got involved in the

NOTE Confidence: 0.919579350416667

 $00{:}04{:}41.792 \dashrightarrow 00{:}04{:}43.730$  consultation so we mostly did this

NOTE Confidence: 0.919579350416667

00:04:43.730 --> 00:04:45.260 through virtual chart reviews and

NOTE Confidence: 0.919579350416667

00:04:45.260 --> 00:04:47.113 looking up data that was available

NOTE Confidence: 0.919579350416667

 $00{:}04{:}47.113 \dashrightarrow 00{:}04{:}48.859$  in the patients and then advising

NOTE Confidence: 0.919579350416667

 $00{:}04{:}48.859 \dashrightarrow 00{:}04{:}50.350$  on clinical care of these patients

NOTE Confidence: 0.919579350416667

 $00:04:50.350 \longrightarrow 00:04:52.341$  and a lot of this was running by

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 $00:04:52.341 \longrightarrow 00:04:53.811$  the seat of our pants because

 $00:04:53.811 \longrightarrow 00:04:55.461$  there wasn't a lot of data about

NOTE Confidence: 0.919579350416667

 $00:04:55.461 \rightarrow 00:04:56.706$  how to manage these patients,

NOTE Confidence: 0.919579350416667

 $00{:}04{:}56.706 \dashrightarrow 00{:}04{:}59.233$  but we were trying to sort of sift

NOTE Confidence: 0.919579350416667

 $00{:}04{:}59{.}233 \dashrightarrow 00{:}05{:}00{.}638$  through the emerging case reports

NOTE Confidence: 0.919579350416667

 $00{:}05{:}00{.}638 \dashrightarrow 00{:}05{:}02{.}664$  that were coming out while we were

NOTE Confidence: 0.919579350416667

 $00:05:02.664 \dashrightarrow 00:05:04.480$  running this console service to try to.

NOTE Confidence: 0.919579350416667

 $00:05:04.480 \rightarrow 00:05:05.872$  Harmonize what we were trying to

NOTE Confidence: 0.919579350416667

 $00:05:05.872 \longrightarrow 00:05:07.350$  do for these patients with what

NOTE Confidence: 0.919579350416667

00:05:07.350 -> 00:05:08.610 was happening around the world,

NOTE Confidence: 0.919579350416667

 $00:05:08.610 \longrightarrow 00:05:10.296$  and what other people have learned.

NOTE Confidence: 0.919579350416667

 $00:05:10.300 \longrightarrow 00:05:12.228$  And this is a snapshot of our sort

NOTE Confidence: 0.919579350416667

 $00:05:12.228 \longrightarrow 00:05:14.524$  of first 100 consoles that we saw on NOTE Confidence: 0.919579350416667

00:05:14.524 --> 00:05:16.200 this neuro COVID console service,

NOTE Confidence: 0.919579350416667

 $00:05:16.200 \longrightarrow 00:05:18.020$  showing you the sort of panoply of NOTE Confidence: 0.919579350416667

00:05:18.020 --> 00:05:19.716 different kinds of conditions of the

 $00{:}05{:}19.716 \dashrightarrow 00{:}05{:}21.542$  consoles were forced so there was a

NOTE Confidence: 0.919579350416667

00:05:21.542 --> 00:05:23.110 large chunk of people who had had

NOTE Confidence: 0.919579350416667

 $00:05:23.165 \rightarrow 00:05:25.104$  seizures in the setting of acute COVID.

NOTE Confidence: 0.919579350416667

 $00:05:25.110 \rightarrow 00:05:26.874$  Most of these people were people who

NOTE Confidence: 0.919579350416667

00:05:26.874 --> 00:05:28.110 had underlying seizure disorders,

NOTE Confidence: 0.919579350416667

 $00{:}05{:}28.110$  -->  $00{:}05{:}29.974$  and then they were coming in and in

NOTE Confidence: 0.919579350416667

 $00{:}05{:}29{.}974 \dashrightarrow 00{:}05{:}31{.}488$  the setting of a febrile illness

NOTE Confidence: 0.790354097142857

00:05:31.490 --> 00:05:33.300 had a probably an unmasking

NOTE Confidence: 0.790354097142857

00:05:33.300 --> 00:05:34.882 of seizures, which is common.

NOTE Confidence: 0.790354097142857

 $00:05:34.882 \rightarrow 00:05:36.586$  In anyone who has a seizure

NOTE Confidence: 0.790354097142857

 $00:05:36.586 \longrightarrow 00:05:38.137$  disorder when they have some

NOTE Confidence: 0.790354097142857

 $00:05:38.137 \dashrightarrow 00:05:39.652$  other kind of systemic illness.

NOTE Confidence: 0.790354097142857

 $00:05:39.660 \longrightarrow 00:05:42.240$  But interestingly, 26% of these people

NOTE Confidence: 0.790354097142857

00:05:42.240 --> 00:05:44.660 had acute stroke during COVID-19,

NOTE Confidence: 0.790354097142857

00:05:44.660 - 00:05:46.160 and then we had another large

NOTE Confidence: 0.790354097142857

00:05:46.160 --> 00:05:47.861 swath of people who would have

- NOTE Confidence: 0.790354097142857
- $00:05:47.861 \rightarrow 00:05:49.466$  what we called himself allopathy.
- NOTE Confidence: 0.790354097142857
- $00{:}05{:}49{.}470 \dashrightarrow 00{:}05{:}51{.}808$  And most of these people were either
- NOTE Confidence: 0.790354097142857
- $00:05:51.808 \rightarrow 00:05:53.341$  people who presented initially
- NOTE Confidence: 0.790354097142857
- 00:05:53.341 00:05:55.740 with confusion as as a primary
- NOTE Confidence: 0.790354097142857
- 00:05:55.740 --> 00:05:57.200 presenting symptom of COVID,
- NOTE Confidence: 0.790354097142857
- $00:05:57.200 \rightarrow 00:05:58.992$  or there were people who had what
- NOTE Confidence: 0.790354097142857
- $00:05:58.992 \longrightarrow 00:06:01.239$  we sort of thought in the end
- NOTE Confidence: 0.790354097142857
- $00:06:01.239 \longrightarrow 00:06:02.659$  was encephalopathy or difficulty
- NOTE Confidence: 0.790354097142857
- $00{:}06{:}02.659 \dashrightarrow 00{:}06{:}04.648$  waking up out of proportion to,
- NOTE Confidence: 0.790354097142857
- $00:06:04.650 \longrightarrow 00:06:05.508$  for example,
- NOTE Confidence: 0.790354097142857
- $00:06:05.508 \longrightarrow 00:06:07.653$  situation or other aspects of
- NOTE Confidence: 0.790354097142857
- $00:06:07.653 \longrightarrow 00:06:08.940$  their systemic illness.
- NOTE Confidence: 0.790354097142857
- 00:06:08.940 --> 00:06:10.326 That's a difficult thing to term,
- NOTE Confidence: 0.790354097142857
- 00:06:10.330 --> 00:06:12.045 because of course a lot of people
- NOTE Confidence: 0.790354097142857
- $00:06:12.045 \longrightarrow 00:06:13.385$  have just hospital delirium in
- NOTE Confidence: 0.790354097142857

 $00:06:13.385 \rightarrow 00:06:14.765$  the setting of acute illness,

NOTE Confidence: 0.790354097142857

 $00{:}06{:}14.770 \dashrightarrow 00{:}06{:}16.198$  but these were people that seem

NOTE Confidence: 0.790354097142857

 $00:06:16.198 \longrightarrow 00:06:17.703$  to really have more of this

NOTE Confidence: 0.790354097142857

 $00:06:17.703 \longrightarrow 00:06:18.968$  than would have been expected,

NOTE Confidence: 0.790354097142857

 $00:06:18.970 \dashrightarrow 00:06:20.770$  and you can see there are also some other.

NOTE Confidence: 0.790354097142857

 $00:06:20.770 \longrightarrow 00:06:21.530$  Some conditions,

NOTE Confidence: 0.790354097142857

 $00:06:21.530 \rightarrow 00:06:23.050$  including neuromuscular diseases and

NOTE Confidence: 0.790354097142857

 $00:06:23.050 \rightarrow 00:06:25.527$  a few people who had acute psychosis

NOTE Confidence: 0.790354097142857

00:06:25.527 --> 00:06:27.620 in the sort of Perry COVID setting,

NOTE Confidence: 0.790354097142857

 $00:06:27.620 \longrightarrow 00:06:29.456$  which I'll talk about more later,

NOTE Confidence: 0.790354097142857

 $00{:}06{:}29{.}460 \dashrightarrow 00{:}06{:}31{.}188$  and what we determined was that

NOTE Confidence: 0.790354097142857

 $00:06:31.188 \longrightarrow 00:06:33.084$  there were sort of two major

NOTE Confidence: 0.790354097142857

 $00:06:33.084 \rightarrow 00:06:35.118$  categories of conditions that we saw.

NOTE Confidence: 0.790354097142857

00:06:35.120 --> 00:06:36.692 One were cerebral vascular

NOTE Confidence: 0.790354097142857

 $00:06:36.692 \rightarrow 00:06:38.657$  injury or stroke and and,

NOTE Confidence: 0.790354097142857

 $00{:}06{:}38.660 \dashrightarrow 00{:}06{:}40.628$  and this was something that was

- NOTE Confidence: 0.790354097142857
- $00:06:40.630 \rightarrow 00:06:42.555$  known to be potentially associated
- NOTE Confidence: 0.790354097142857
- $00{:}06{:}42.555 \dashrightarrow 00{:}06{:}44.480$  with clotting factors that are
- NOTE Confidence: 0.790354097142857
- 00:06:44.543 --> 00:06:46.498 elevated in people with COVID-19,
- NOTE Confidence: 0.790354097142857
- $00{:}06{:}46{.}500 \dashrightarrow 00{:}06{:}47{.}970$  but also due to additional
- NOTE Confidence: 0.790354097142857
- $00{:}06{:}47.970 \dashrightarrow 00{:}06{:}49.146$  research investigation we did
- NOTE Confidence: 0.790354097142857
- $00:06:49.146 \longrightarrow 00:06:50.637$  in some of these patients,
- NOTE Confidence: 0.790354097142857
- $00:06:50.640 \longrightarrow 00:06:51.680$  we found that this also
- NOTE Confidence: 0.790354097142857
- $00:06:51.680 \dashrightarrow 00:06:52.720$  seemed to be associated with.
- NOTE Confidence: 0.790354097142857
- $00:06:52.720 \longrightarrow 00:06:54.944$  Endothelial inflammation and activation
- NOTE Confidence: 0.790354097142857
- $00:06:54.944 \dashrightarrow 00:06:58.573$  in the setting of acute COVID-19 and
- NOTE Confidence: 0.790354097142857
- $00:06:58.573 \rightarrow 00:07:00.917$  the rest of the conditions that we saw.
- NOTE Confidence: 0.790354097142857
- $00:07:00.920 \dashrightarrow 00:07:02.560$  Although they were quite diverse,
- NOTE Confidence: 0.790354097142857
- $00{:}07{:}02.560 \dashrightarrow 00{:}07{:}04.498$  we ended up considering them to
- NOTE Confidence: 0.790354097142857
- $00{:}07{:}04.498 \dashrightarrow 00{:}07{:}06.414$  fall mostly in the categories
- NOTE Confidence: 0.790354097142857
- $00{:}07{:}06.414 \dashrightarrow 00{:}07{:}08.614$  of immune mediated neurologic
- NOTE Confidence: 0.790354097142857

00:07:08.614 --> 00:07:10.264 and psychiatric conditions,

NOTE Confidence: 0.790354097142857

 $00{:}07{:}10.270 \dashrightarrow 00{:}07{:}12.139$  and that was mostly based on the

NOTE Confidence: 0.790354097142857

 $00:07:12.139 \rightarrow 00:07:13.619$  types of presentations we're seeing.

NOTE Confidence: 0.790354097142857

 $00:07:13.620 \longrightarrow 00:07:14.900$  Things like key on beret,

NOTE Confidence: 0.790354097142857

00:07:14.900 --> 00:07:17.905 things like what look like

NOTE Confidence: 0.790354097142857

00:07:17.905 --> 00:07:19.936 autoimmune myositis and the

NOTE Confidence: 0.790354097142857

 $00{:}07{:}19{.}936 \dashrightarrow 00{:}07{:}22{.}001$  neurologic conditions seem to be

NOTE Confidence: 0.790354097142857

 $00:07:22.001 \rightarrow 00:07:23.730$  associated potentially with immune.

NOTE Confidence: 0.790354097142857

 $00{:}07{:}23.730 \dashrightarrow 00{:}07{:}26.570$  Some inflammation.

NOTE Confidence: 0.790354097142857

 $00{:}07{:}26{.}570 \dashrightarrow 00{:}07{:}28{.}187$  This is a really nice example of

NOTE Confidence: 0.790354097142857

 $00{:}07{:}28.187 \dashrightarrow 00{:}07{:}29.559$  such an immune mediated course

NOTE Confidence: 0.790354097142857

 $00{:}07{:}29.559 \dashrightarrow 00{:}07{:}31.129$  or something that we decided

NOTE Confidence: 0.790354097142857

00:07:31.129 --> 00:07:32.570 was probably immune mediated,

NOTE Confidence: 0.790354097142857

 $00{:}07{:}32.570 \dashrightarrow 00{:}07{:}35.216$  so this was a 70 year old woman who

NOTE Confidence: 0.790354097142857

 $00:07:35.216 \longrightarrow 00:07:37.146$  presented to you in March of 2020.

NOTE Confidence: 0.790354097142857

 $00:07:37.150 \dashrightarrow 00:07:38.722$  This was before we were screening

 $00:07:38.722 \rightarrow 00:07:40.572$  everyone for COVID when they came into

NOTE Confidence: 0.790354097142857

 $00:07:40.572 \rightarrow 00:07:42.222$  the hospital and she actually presented

NOTE Confidence: 0.790354097142857

 $00:07:42.222 \dashrightarrow 00:07:43.950$  with confusion and a witness seizure.

NOTE Confidence: 0.790354097142857

 $00:07:43.950 \rightarrow 00:07:46.218$  And so she she actually didn't have

NOTE Confidence: 0.790354097142857

 $00{:}07{:}46.218 \dashrightarrow 00{:}07{:}48.632$  fever cough and a positive news or

NOTE Confidence: 0.790354097142857

 $00:07:48.632 \rightarrow 00:07:50.690$  fringilla swab for COVID until Ford

NOTE Confidence: 0.790354097142857

 $00:07:50.762 \rightarrow 00:07:52.987$  four days into her hospitalization.

NOTE Confidence: 0.790354097142857

 $00{:}07{:}52{.}990 \dashrightarrow 00{:}07{:}54{.}862$  So prior to that she had an MRI and

NOTE Confidence: 0.790354097142857

 $00{:}07{:}54.862 \dashrightarrow 00{:}07{:}56.938$  the MRI images are shown on the right.

NOTE Confidence: 0.790354097142857

 $00:07:56.940 \rightarrow 00:07:58.816$  This is obviously a fairly abnormal MRI,

NOTE Confidence: 0.790354097142857

 $00:07:58.820 \dashrightarrow 00:08:00.884$  but I think these are really this is

NOTE Confidence: 0.790354097142857

 $00{:}08{:}00{.}884$  -->  $00{:}08{:}02{.}648$  Shane's brain atrophy and she has a

NOTE Confidence: 0.790354097142857

 $00:08:02.648 \dashrightarrow 00:08:03.853$  really chronic microvascular changes

NOTE Confidence: 0.790354097142857

 $00:08:03.853 \longrightarrow 00:08:06.459$  and she had a history of risk factors NOTE Confidence: 0.790354097142857

 $00:08:06.459 \rightarrow 00:08:08.319$  for significant microvascular disease,

 $00:08:08.320 \longrightarrow 00:08:10.120$  but her LP was completely

NOTE Confidence: 0.790354097142857

 $00{:}08{:}10{.}120 \dashrightarrow 00{:}08{:}11{.}920$  benign and two white cells,

NOTE Confidence: 0.790354097142857

00:08:11.920 --> 00:08:14.345 normal protein of PCR's for

NOTE Confidence: 0.790354097142857

 $00:08:14.345 \longrightarrow 00:08:16.285$  viruses were not detected.

NOTE Confidence: 0.790354097142857

00:08:16.290 --> 00:08:18.378 Once we found out that she had acute COVID,

NOTE Confidence: 0.842571092142857

 $00{:}08{:}18{.}380 \dashrightarrow 00{:}08{:}21{.}068$  we also were able to do research testing

NOTE Confidence: 0.842571092142857

00:08:21.068 --> 00:08:23.092 and looking for COVID in her CSS.

NOTE Confidence: 0.842571092142857

00:08:23.092 --> 00:08:25.270 SRS could be 2 in her CSF by PCR

NOTE Confidence: 0.842571092142857

 $00{:}08{:}25{.}342 \dashrightarrow 00{:}08{:}28{.}027$  metagenomic sequencing and viral culture.

NOTE Confidence: 0.842571092142857

 $00{:}08{:}28{.}030 \dashrightarrow 00{:}08{:}30{.}137$  And the virus did not was not

NOTE Confidence: 0.842571092142857

00:08:30.137 --> 00:08:32.109 detected by any of these means.

NOTE Confidence: 0.842571092142857

 $00{:}08{:}32{.}110 \dashrightarrow 00{:}08{:}34{.}427$  However, when we used more sort of

NOTE Confidence: 0.842571092142857

 $00:08:34.427 \rightarrow 00:08:36.556$  research testing to look at inflammatory

NOTE Confidence: 0.842571092142857

 $00:08:36.556 \rightarrow 00:08:39.048$  cytokines in the CSF of this patient,

NOTE Confidence: 0.842571092142857

 $00:08:39.050 \rightarrow 00:08:41.605$  what we found was that compared to

NOTE Confidence: 0.842571092142857

 $00:08:41.605 \rightarrow 00:08:43.894$  pre pandemic control samples that we

- NOTE Confidence: 0.842571092142857
- $00:08:43.894 \rightarrow 00:08:46.150$  had that were age matched controls.
- NOTE Confidence: 0.842571092142857
- 00:08:46.150 --> 00:08:48.080 This patient, whose CSF cytokines
- NOTE Confidence: 0.842571092142857
- $00:08:48.080 \rightarrow 00:08:50.420$  are shown in the orange bars,
- NOTE Confidence: 0.842571092142857
- $00:08:50.420 \rightarrow 00:08:52.156$  had evidence of neuroinflammation
- NOTE Confidence: 0.842571092142857
- $00{:}08{:}52{.}156 \dashrightarrow 00{:}08{:}55{.}874$  and in fact some of this seem to be
- NOTE Confidence: 0.842571092142857
- $00:08:55.874 \rightarrow 00:08:58.282$  similar to the the patterns of CSF.
- NOTE Confidence: 0.842571092142857
- $00:08:58.290 \longrightarrow 00:09:00.348$  Cytokines are similar to the plasma.
- NOTE Confidence: 0.842571092142857
- 00:09:00.350 00:09:01.658 But a couple of these markers,
- NOTE Confidence: 0.842571092142857
- $00:09:01.660 \longrightarrow 00:09:03.430$  and in particular MCP one,
- NOTE Confidence: 0.842571092142857
- $00:09:03.430 \longrightarrow 00:09:05.470$  was quite elevated in the CSF
- NOTE Confidence: 0.842571092142857
- $00:09:05.470 \longrightarrow 00:09:06.490$  and this patient,
- NOTE Confidence: 0.842571092142857
- $00:09:06.490 \rightarrow 00:09:08.746$  although it was not elevated in the plasma.
- NOTE Confidence: 0.842571092142857
- $00:09:08.750 \dashrightarrow 00:09:10.676$  So this was the first clue that we had
- NOTE Confidence: 0.842571092142857
- $00:09:10.676 \dashrightarrow 00:09:12.820$  that made the underlying some of these
- NOTE Confidence: 0.842571092142857
- $00:09:12.820 \rightarrow 00:09:14.480$  encephalopathies that we were seeing.
- NOTE Confidence: 0.842571092142857

- $00:09:14.480 \longrightarrow 00:09:14.921$  Potentially,
- NOTE Confidence: 0.842571092142857
- 00:09:14.921 --> 00:09:16.685 it wasn't necessarily viral
- NOTE Confidence: 0.842571092142857
- $00:09:16.685 \rightarrow 00:09:18.890$  encephalitis in the common sense,
- NOTE Confidence: 0.842571092142857
- $00:09:18.890 \rightarrow 00:09:20.510$  where you see viral replication
- NOTE Confidence: 0.842571092142857
- $00:09:20.510 \longrightarrow 00:09:21.806$  in the nervous system,
- NOTE Confidence: 0.842571092142857
- $00{:}09{:}21.810 \dashrightarrow 00{:}09{:}23.595$  but instead this was some kind of
- NOTE Confidence: 0.842571092142857
- 00:09:23.595 --> 00:09:24.960 an immune mediated phenomenon,
- NOTE Confidence: 0.842571092142857
- $00:09:24.960 \longrightarrow 00:09:27.081$  despite the fact that she had no
- NOTE Confidence: 0.842571092142857
- $00:09:27.081 \dashrightarrow 00:09:29.069$  increase in her CSF white cells.
- NOTE Confidence: 0.842571092142857
- $00:09:29.070 \rightarrow 00:09:31.005$  And this is a sort of busy looking slide,
- NOTE Confidence: 0.842571092142857
- $00:09:31.010 \longrightarrow 00:09:32.552$  but it's just a reminder for
- NOTE Confidence: 0.842571092142857
- $00:09:32.552 \rightarrow 00:09:34.229$  me to point out that many,
- NOTE Confidence: 0.842571092142857
- $00:09:34.230 \longrightarrow 00:09:36.590$  many of the reports that have come out
- NOTE Confidence: 0.842571092142857
- $00:09:36.590 \rightarrow 00:09:38.751$  that have been case reports clinically
- NOTE Confidence: 0.842571092142857
- $00:09:38.751 \dashrightarrow 00:09:41.056$  described patients during acute COVID-19
- NOTE Confidence: 0.842571092142857
- $00:09:41.056 \rightarrow 00:09:44.004$  that have neurologic and then also I

- NOTE Confidence: 0.842571092142857
- $00:09:44.004 \rightarrow 00:09:45.734$  think psychiatric conditions that can
- NOTE Confidence: 0.842571092142857
- $00:09:45.734 \rightarrow 00:09:48.249$  best be attributed to immune pairing,
- NOTE Confidence: 0.842571092142857
- 00:09:48.250 --> 00:09:51.988 infectious or autoimmune kinds of ideologies,
- NOTE Confidence: 0.842571092142857
- $00:09:51.990 \rightarrow 00:09:54.170$  so acute necrotizing encephalopathy,
- NOTE Confidence: 0.842571092142857
- 00:09:54.170 --> 00:09:55.805 Guillain Barre syndrome,
- NOTE Confidence: 0.842571092142857
- 00:09:55.810 --> 00:09:56.530 acute flossin,
- NOTE Confidence: 0.842571092142857
- $00:09:56.530 \rightarrow 00:09:57.970$  my leitis and many,
- NOTE Confidence: 0.842571092142857
- $00:09:57.970 \longrightarrow 00:09:59.626$  many cases that we've seen of.
- NOTE Confidence: 0.842571092142857
- $00{:}09{:}59{.}630 \dashrightarrow 00{:}10{:}02{.}936$  I'm small fiber sensory neuropathy or
- NOTE Confidence: 0.842571092142857
- $00:10:02.940 \longrightarrow 00:10:05.232$  neuropathy's have all been described in
- NOTE Confidence: 0.842571092142857
- 00:10:05.232 --> 00:10:08.099 the sort of Perry acute COVID period,
- NOTE Confidence: 0.842571092142857
- $00{:}10{:}08{.}100 \dashrightarrow 00{:}10{:}11{.}375$  and many of these cases have
- NOTE Confidence: 0.842571092142857
- $00{:}10{:}11{.}375 \dashrightarrow 00{:}10{:}12{.}860$  had normal workups.
- NOTE Confidence: 0.842571092142857
- 00:10:12.860 --> 00:10:15.830 No CSF pleocytosis normal protein levels,
- NOTE Confidence: 0.842571092142857
- $00{:}10{:}15{.}830 \dashrightarrow 00{:}10{:}18{.}386$  but the clinical phenomena are are
- NOTE Confidence: 0.842571092142857

 $00:10:18.386 \longrightarrow 00:10:21.616$  really what we see typically in

NOTE Confidence: 0.842571092142857

00:10:21.616 --> 00:10:24.508 postinfectious immune mediated disorders.

NOTE Confidence: 0.842571092142857

00:10:24.510 --> 00:10:25.752 I also wanted to touch on

NOTE Confidence: 0.842571092142857

 $00{:}10{:}25.752 \dashrightarrow 00{:}10{:}26.580$  the issue of stroke,

NOTE Confidence: 0.842571092142857

 $00{:}10{:}26.580 \dashrightarrow 00{:}10{:}28.372$  which was another major category that we

NOTE Confidence: 0.842571092142857

 $00{:}10{:}28.372 \dashrightarrow 00{:}10{:}30.659$  saw and in in our hospitalized patients.

NOTE Confidence: 0.842571092142857

 $00:10:30.660 \longrightarrow 00:10:32.260$  And this was actually very

NOTE Confidence: 0.842571092142857

 $00:10:32.260 \longrightarrow 00:10:33.860$  very early on the pandemic.

NOTE Confidence: 0.842571092142857

 $00{:}10{:}33.860 \dashrightarrow 00{:}10{:}36.352$  There was a report that was super

NOTE Confidence: 0.842571092142857

 $00{:}10{:}36.352 \dashrightarrow 00{:}10{:}38.215$  frightening of young people under age

NOTE Confidence: 0.842571092142857

 $00{:}10{:}38{.}215 \dashrightarrow 00{:}10{:}41{.}452$ 50 who had a few or no risk factors

NOTE Confidence: 0.842571092142857

 $00{:}10{:}41{.}452 \dashrightarrow 00{:}10{:}43{.}527$  for stroke presenting with large

NOTE Confidence: 0.842571092142857

 $00{:}10{:}43.527 \dashrightarrow 00{:}10{:}46.084$  vessel in a major strokes in the

NOTE Confidence: 0.842571092142857

 $00:10:46.084 \rightarrow 00:10:48.729$  setting of acute COVID for some people

NOTE Confidence: 0.842571092142857

 $00:10:48.729 \rightarrow 00:10:50.844$  stroke was actually there presenting

NOTE Confidence: 0.842571092142857

 $00:10:50.844 \rightarrow 00:10:53.350$  syndrome or symptom to the hospital.

 $00:10:53.350 \longrightarrow 00:10:54.505$  And there was this sort

NOTE Confidence: 0.842571092142857

00:10:54.505 --> 00:10:55.429 of avalanche of concern.

NOTE Confidence: 0.842571092142857

 $00{:}10{:}55{.}430 \dashrightarrow 00{:}10{:}57{.}113$  There was a lot of press about these cases,

NOTE Confidence: 0.842571092142857

 $00:10:57.120 \longrightarrow 00:10:58.912$  thinking that we were going to see lots

NOTE Confidence: 0.842571092142857

 $00:10:58.912 \rightarrow 00:11:00.669$  and lots of strokes in young people,

NOTE Confidence: 0.842571092142857

 $00{:}11{:}00{.}670 \dashrightarrow 00{:}11{:}03{.}022$  and there are reasons to think that

NOTE Confidence: 0.842571092142857

 $00:11:03.022 \dashrightarrow 00:11:04.944$  people with COVID-19 are at increased

NOTE Confidence: 0.842571092142857

 $00{:}11{:}04{.}944 \dashrightarrow 00{:}11{:}07{.}585$  risk of stroke and this has to do

NOTE Confidence: 0.842571092142857

 $00{:}11{:}07{.}585 \dashrightarrow 00{:}11{:}09{.}388$  with coagulopathies thrombocytopenia.

NOTE Confidence: 0.842571092142857

 $00{:}11{:}09{.}390 \dashrightarrow 00{:}11{:}11{.}616$  Elevation of D dimers and other

NOTE Confidence: 0.842571092142857

00:11:11.616 --> 00:11:13.684 blood measures that are clearly

NOTE Confidence: 0.842571092142857

 $00{:}11{:}13.684 \dashrightarrow 00{:}11{:}16.219$  reflected in the prothrombotic state.

NOTE Confidence: 0.854677013809524

 $00{:}11{:}16{.}220 \dashrightarrow 00{:}11{:}18{.}758$  And the fact that there are ACE 2 receptors

NOTE Confidence: 0.854677013809524

 $00{:}11{:}18.758 \dashrightarrow 00{:}11{:}20.931$  which are the receptors that are necessary

NOTE Confidence: 0.854677013809524

 $00{:}11{:}20{.}931 \dashrightarrow 00{:}11{:}23{.}490$  for the virus to entry on the surface

 $00:11:23.490 \rightarrow 00:11:25.140$  of endothelial cells and pericytes,

NOTE Confidence: 0.854677013809524

 $00{:}11{:}25{.}140 \dashrightarrow 00{:}11{:}27{.}702$  that line the blood vessels and

NOTE Confidence: 0.854677013809524

 $00:11:27.702 \longrightarrow 00:11:29.388$  cells theoretically could be leading

NOTE Confidence: 0.854677013809524

 $00:11:29.388 \rightarrow 00:11:31.394$  to vascular inflammation and changes.

NOTE Confidence: 0.854677013809524

 $00{:}11{:}31{.}394 \dashrightarrow 00{:}11{:}34{.}010$  So this was a major concern

NOTE Confidence: 0.854677013809524

 $00{:}11{:}34.088 \dashrightarrow 00{:}11{:}35.918$  based on this first paper.

NOTE Confidence: 0.854677013809524

00:11:35.920 --> 00:11:37.460 But I think that what was really

NOTE Confidence: 0.854677013809524

00:11:37.460 --> 00:11:38.660 interesting to learn and I think,

NOTE Confidence: 0.854677013809524

00:11:38.660 - 00:11:41.420 was borne out by our studies as well,

NOTE Confidence: 0.854677013809524

 $00:11:41.420 \longrightarrow 00:11:43.620$  is that in fact,

NOTE Confidence: 0.854677013809524

 $00{:}11{:}43.620 \dashrightarrow 00{:}11{:}46.342$  in the the most sort of comprehensive

NOTE Confidence: 0.854677013809524

 $00{:}11{:}46{.}342 \dashrightarrow 00{:}11{:}48{.}653$  studies have suggested that stroke in young

NOTE Confidence: 0.854677013809524

 $00:11:48.653 \rightarrow 00:11:51.120$  people is not a big feature of COVID-19.

NOTE Confidence: 0.854677013809524

 $00:11:51.120 \rightarrow 00:11:51.774$  Thank goodness.

NOTE Confidence: 0.854677013809524

 $00:11:51.774 \longrightarrow 00:11:52.101$  However,

NOTE Confidence: 0.854677013809524

 $00{:}11{:}52{.}101 \dashrightarrow 00{:}11{:}54{.}063$  there are increased rates of stroke

 $00:11:54.063 \rightarrow 00:11:56.576$  in people living with people who have COVID,

NOTE Confidence: 0.854677013809524

 $00{:}11{:}56{.}580 \dashrightarrow 00{:}11{:}59{.}108$  so some of the best data that has

NOTE Confidence: 0.854677013809524

 $00:11:59.108 \rightarrow 00:12:00.897$  really characterized in their logic

NOTE Confidence: 0.854677013809524

 $00:12:00.897 \rightarrow 00:12:02.349$  and psychiatric complications of

NOTE Confidence: 0.854677013809524

 $00{:}12{:}02{.}349 \dashrightarrow 00{:}12{:}04{.}620$  cute COVID has come out of the UK.

NOTE Confidence: 0.854677013809524

 $00{:}12{:}04.620 \dashrightarrow 00{:}12{:}06.006$  And it's really because of course.

NOTE Confidence: 0.854677013809524

 $00:12:06.010 \longrightarrow 00:12:07.100$  They are able to do,

NOTE Confidence: 0.854677013809524

 $00:12:07.100 \longrightarrow 00:12:09.098$  you know they have a unified

NOTE Confidence: 0.854677013809524

 $00{:}12{:}09{.}098 \dashrightarrow 00{:}12{:}11{.}694$  healthcare system and also a very very

NOTE Confidence: 0.854677013809524

 $00:12:11.694 \rightarrow 00:12:13.294$  connected healthcare system where

NOTE Confidence: 0.854677013809524

 $00{:}12{:}13.294 \dashrightarrow 00{:}12{:}15.348$  hospital records are shared between

NOTE Confidence: 0.854677013809524

 $00{:}12{:}15{.}348 \dashrightarrow 00{:}12{:}17{.}333$  all of their different institutions

NOTE Confidence: 0.854677013809524

 $00{:}12{:}17{.}333 \dashrightarrow 00{:}12{:}19{.}618$  and data is collected in uniform

NOTE Confidence: 0.854677013809524

00:12:19.618 --> 00:12:21.106 ways across their institutions,

NOTE Confidence: 0.854677013809524

 $00{:}12{:}21{.}110 \dashrightarrow 00{:}12{:}22{.}685$  and so they're able to collect data

00:12:22.685 --> 00:12:24.470 in a very far standardized way.

NOTE Confidence: 0.854677013809524

 $00{:}12{:}24.470 \dashrightarrow 00{:}12{:}26.166$  And this was one of the first reports

NOTE Confidence: 0.854677013809524

 $00:12:26.166 \longrightarrow 00:12:27.512$  that came out of what's called

NOTE Confidence: 0.854677013809524

00:12:27.512 --> 00:12:29.000 the Coro Nerve study in the UK,

NOTE Confidence: 0.854677013809524

 $00:12:29.000 \rightarrow 00:12:30.815$  where essentially they surveyed many

NOTE Confidence: 0.854677013809524

 $00:12:30.815 \rightarrow 00:12:33.742$  many hospitals in the UK system for any

NOTE Confidence: 0.854677013809524

 $00:12:33.742 \rightarrow 00:12:36.199$  reported cases of people who had neurologic.

NOTE Confidence: 0.854677013809524

 $00:12:36.200 \rightarrow 00:12:38.186$  Diseases and they saw sort of

NOTE Confidence: 0.854677013809524

 $00:12:38.186 \rightarrow 00:12:40.140$  similar cases that were reported.

NOTE Confidence: 0.854677013809524

00:12:40.140 --> 00:12:40.560 Of course,

NOTE Confidence: 0.854677013809524

 $00{:}12{:}40.560 \dashrightarrow 00{:}12{:}41.820$  there's bias is what gets reported,

NOTE Confidence: 0.854677013809524

 $00:12:41.820 \longrightarrow 00:12:43.120$  what gets looked at,

NOTE Confidence: 0.854677013809524

 $00:12:43.120 \rightarrow 00:12:45.070$  but they also saw many cerebrovascular

NOTE Confidence: 0.854677013809524

 $00:12:45.134 \rightarrow 00:12:47.304$  events in many cases of altered mental

NOTE Confidence: 0.854677013809524

 $00{:}12{:}47{.}304 \dashrightarrow 00{:}12{:}49{.}050$  status and what was interesting here

NOTE Confidence: 0.854677013809524

 $00:12:49.050 \rightarrow 00:12:51.385$  is that when they looked at the age

 $00:12:51.385 \rightarrow 00:12:53.071$  ranges of who was getting these

NOTE Confidence: 0.854677013809524

 $00:12:53.071 \rightarrow 00:12:54.740$  conditions in this particular study,

NOTE Confidence: 0.854677013809524

 $00:12:54.740 \longrightarrow 00:12:56.762$  what they found was that although

NOTE Confidence: 0.854677013809524

 $00{:}12{:}56.762 \dashrightarrow 00{:}12{:}58.472$  cerebral vascular disease shown in

NOTE Confidence: 0.854677013809524

 $00{:}12{:}58{.}472 \dashrightarrow 00{:}13{:}00{.}308$  these blue columns was actually much

NOTE Confidence: 0.854677013809524

 $00{:}13{:}00{.}308 \dashrightarrow 00{:}13{:}02{.}102$  more predominant in older ages and

NOTE Confidence: 0.854677013809524

 $00:13:02.102 \longrightarrow 00:13:04.343$  picked between ages of 71 and 80.

NOTE Confidence: 0.854677013809524

 $00{:}13{:}04{.}343 \dashrightarrow 00{:}13{:}06{.}248$  What they term neuro psychiatric.

NOTE Confidence: 0.854677013809524

00:13:06.250 --> 00:13:08.746 That really included altered mental status,

NOTE Confidence: 0.854677013809524

00:13:08.750 --> 00:13:09.917 peripheral nerve disorders,

NOTE Confidence: 0.854677013809524

 $00{:}13{:}09{.}917 \dashrightarrow 00{:}13{:}12{.}640$  and then some cases of things like

NOTE Confidence: 0.854677013809524

 $00{:}13{:}12.705 \dashrightarrow 00{:}13{:}14.461$  psychosis were actually happening,

NOTE Confidence: 0.854677013809524

00:13:14.461 - 00:13:16.446 sort of throughout the lifespan,

NOTE Confidence: 0.854677013809524

 $00{:}13{:}16{.}450 \dashrightarrow 00{:}13{:}17{.}302$  and in fact,

NOTE Confidence: 0.854677013809524

 $00:13:17.302 \longrightarrow 00:13:19.290$  one might even say that they were

 $00:13:19.360 \longrightarrow 00:13:21.618$  more common in people ages 21 to 60.

NOTE Confidence: 0.854677013809524

 $00{:}13{:}21.618 \dashrightarrow 00{:}13{:}23.593$  So I think this is the first clue

NOTE Confidence: 0.854677013809524

 $00:13:23.593 \rightarrow 00:13:25.613$  that there obviously are different

NOTE Confidence: 0.854677013809524

00:13:25.613 --> 00:13:27.229 types of ideologies underlying.

NOTE Confidence: 0.854677013809524

00:13:27.230 --> 00:13:29.258 They may just super vascular complications,

NOTE Confidence: 0.854677013809524

 $00:13:29.260 \rightarrow 00:13:31.126$  and some of these other complications.

NOTE Confidence: 0.854677013809524

 $00{:}13{:}31{.}130 \dashrightarrow 00{:}13{:}32{.}834$  And it was also our first clue that

NOTE Confidence: 0.854677013809524

 $00:13:32.834 \rightarrow 00:13:34.590$  some of these major complications of

NOTE Confidence: 0.854677013809524

 $00:13:34.590 \rightarrow 00:13:36.498$  COVID-19 may not only be affecting.

NOTE Confidence: 0.854677013809524

00:13:36.500 --> 00:13:38.866 Elderly people who are at highest risk NOTE Confidence: 0.854677013809524

 $00{:}13{:}38{.}866 \dashrightarrow 00{:}13{:}41{.}529$  of death from COVID but actually are

NOTE Confidence: 0.854677013809524

 $00{:}13{:}41{.}529 \dashrightarrow 00{:}13{:}43{.}905$  also affecting people at younger ages.

NOTE Confidence: 0.854677013809524

 $00{:}13{:}43{.}910 \dashrightarrow 00{:}13{:}45{.}410$  This is another beautiful study

NOTE Confidence: 0.854677013809524

 $00:13:45.410 \longrightarrow 00:13:47.300$  from the UK Koro Nerve group,

NOTE Confidence: 0.854677013809524

00:13:47.300 --> 00:13:49.360 though this UK surveillance study.

NOTE Confidence: 0.854677013809524

 $00:13:49.360 \longrightarrow 00:13:51.262$  So this was a slightly larger

- NOTE Confidence: 0.854677013809524
- $00:13:51.262 \rightarrow 00:13:52.530$  population that they published
- NOTE Confidence: 0.854677013809524
- $00:13:52.589 \longrightarrow 00:13:54.239$  later where they again looked at
- NOTE Confidence: 0.854677013809524
- $00:13:54.239 \longrightarrow 00:13:56.594$  people who had been reported to have
- NOTE Confidence: 0.854677013809524
- 00:13:56.594 --> 00:13:58.194 neurologic or psychiatric conditions
- NOTE Confidence: 0.854677013809524
- 00:13:58.200 --> 00:14:00.930 around the time of acute COVID-19,
- NOTE Confidence: 0.938186078333333
- $00:14:00.930 \longrightarrow 00:14:02.580$  and they did something very clever,
- NOTE Confidence: 0.938186078333333
- $00:14:02.580 \rightarrow 00:14:04.988$  which is they tried to look to see
- NOTE Confidence: 0.938186078333333
- $00{:}14{:}04{.}988 \dashrightarrow 00{:}14{:}07{.}413$  when the onset of these different
- NOTE Confidence: 0.938186078333333
- $00{:}14{:}07{.}413 \dashrightarrow 00{:}14{:}10.060$  conditions were with respect to onset
- NOTE Confidence: 0.938186078333333
- 00:14:10.060 --> 00:14:12.360 of respiratory symptoms of COVID.
- NOTE Confidence: 0.938186078333333
- $00:14:12.360 \longrightarrow 00:14:14.424$  So on the Y axis in this figure.
- NOTE Confidence: 0.938186078333333
- 00:14:14.430 --> 00:14:16.684 The zero point would be the onset
- NOTE Confidence: 0.938186078333333
- $00{:}14{:}16{.}684 \dashrightarrow 00{:}14{:}18{.}558$  of respiratory symptoms and then the NOTE Confidence: 0.938186078333333
- $00:14:18.558 \rightarrow 00:14:20.532$  widest point on the violin plot would
- NOTE Confidence: 0.938186078333333
- 00:14:20.597 --> 00:14:22.541 be the main time that the onset
- NOTE Confidence: 0.938186078333333

 $00:14:22.541 \longrightarrow 00:14:24.404$  of this particular condition had

NOTE Confidence: 0.938186078333333

 $00:14:24.404 \rightarrow 00:14:26.694$  risen in these different patients,

NOTE Confidence: 0.938186078333333

 $00:14:26.700 \longrightarrow 00:14:28.653$  and I think what this does is it gives NOTE Confidence: 0.938186078333333

 $00:14:28.653 \rightarrow 00:14:31.603$  us a little bit of insight into again

NOTE Confidence: 0.938186078333333

00:14:31.603 --> 00:14:32.749 potentially diverse pathophysiologies

NOTE Confidence: 0.938186078333333

 $00{:}14{:}32{.}750 \dashrightarrow 00{:}14{:}35{.}030$  of these different types of conditions,

NOTE Confidence: 0.938186078333333

 $00{:}14{:}35{.}030 \dashrightarrow 00{:}14{:}37{.}670$  and So what they found was that in

NOTE Confidence: 0.938186078333333

 $00:14:37.670 \longrightarrow 00:14:39.482$  29% of people there were actually

NOTE Confidence: 0.938186078333333

 $00{:}14{:}39{.}482 \dashrightarrow 00{:}14{:}41{.}707$  neuro or sex symptoms that predated

NOTE Confidence: 0.938186078333333

00:14:41.707 --> 00:14:42.667 respiratory symptoms.

NOTE Confidence: 0.938186078333333

 $00:14:42.670 \longrightarrow 00:14:43.937$  And when you look at the figure,

NOTE Confidence: 0.938186078333333

 $00:14:43.940 \longrightarrow 00:14:45.825$  it actually is primarily this

NOTE Confidence: 0.938186078333333

 $00{:}14{:}45.825 \dashrightarrow 00{:}14{:}46.956$  river vascular complications.

NOTE Confidence: 0.938186078333333

 $00:14:46.960 \rightarrow 00:14:51.069$  Starting very early and then our preceding

NOTE Confidence: 0.938186078333333

 $00{:}14{:}51.069 \dashrightarrow 00{:}14{:}53.028$  the relative respiratory symptoms.

NOTE Confidence: 0.938186078333333

 $00:14:53.028 \rightarrow 00:14:55.764$  Then there were another group of

- NOTE Confidence: 0.938186078333333
- $00:14:55.770 \rightarrow 00:14:58.236$  symptoms that were actually seen after
- NOTE Confidence: 0.938186078333333
- $00:14:58.236 \rightarrow 00:14:59.880$  the initial respiratory conditions.
- NOTE Confidence: 0.938186078333333
- $00:14:59.880 \longrightarrow 00:15:01.389$  Severe respiratory system
- NOTE Confidence: 0.938186078333333
- $00:15:01.389 \longrightarrow 00:15:02.898$  condition improved again.
- NOTE Confidence: 0.938186078333333
- $00{:}15{:}02{.}900 \dashrightarrow 00{:}15{:}03{.}952$  These were hospitalized patients,
- NOTE Confidence: 0.938186078333333
- $00:15:03.952 \rightarrow 00:15:05.821$  so many of these people were coming
- NOTE Confidence: 0.938186078333333
- $00:15:05.821 \longrightarrow 00:15:07.056$  in with shortness of breath.
- NOTE Confidence: 0.938186078333333
- 00:15:07.060 --> 00:15:09.040 Oxygen needs that kind of thing,
- NOTE Confidence: 0.938186078333333
- $00:15:09.040 \longrightarrow 00:15:12.211$  but a good proportion of people actually
- NOTE Confidence: 0.938186078333333
- $00:15:12.211 \rightarrow 00:15:15.341$  develop their symptoms up to two weeks
- NOTE Confidence: 0.938186078333333
- $00{:}15{:}15{.}341 \dashrightarrow 00{:}15{:}17{.}885$  after the respiratory symptoms had started.
- NOTE Confidence: 0.938186078333333
- $00:15:17.890 \longrightarrow 00:15:19.122$  And this was interesting,
- NOTE Confidence: 0.938186078333333
- $00:15:19.122 \rightarrow 00:15:21.910$  because these seem to be in what they
- NOTE Confidence: 0.938186078333333
- $00:15:21.910 \longrightarrow 00:15:24.115$  termed central inflammatory psychiatric and
- NOTE Confidence: 0.938186078333333
- $00:15:24.115 \rightarrow 00:15:26.490$  peripheral nerve types of complications.
- NOTE Confidence: 0.938186078333333

- $00:15:26.490 \longrightarrow 00:15:27.170$  And again this is,
- NOTE Confidence: 0.938186078333333
- 00:15:27.170 --> 00:15:27.510 I think,
- NOTE Confidence: 0.938186078333333
- $00:15:27.510 \rightarrow 00:15:29.406$  reflective of what we've seen clinically,
- NOTE Confidence: 0.938186078333333
- $00:15:29.410 \longrightarrow 00:15:32.042$  and it suggests again that these are
- NOTE Confidence: 0.938186078333333
- $00{:}15{:}32{.}042 \dashrightarrow 00{:}15{:}34{.}405$  likely immune mediated phenomena that are
- NOTE Confidence: 0.938186078333333
- $00:15:34.405 \rightarrow 00:15:37.128$  somehow a response to the viral infection,
- NOTE Confidence: 0.938186078333333
- $00:15:37.130 \rightarrow 00:15:39.834$  but maybe not directly caused by the virus.
- NOTE Confidence: 0.938186078333333
- 00:15:39.840 --> 00:15:40.348 So again,
- NOTE Confidence: 0.938186078333333
- $00:15:40.348 \longrightarrow 00:15:42.806$  this is another clue to kind of help us
- NOTE Confidence: 0.938186078333333
- $00:15:42.806 \rightarrow 00:15:44.984$  understand the etiology of these disorders.
- NOTE Confidence: 0.938186078333333
- $00{:}15{:}44{.}990 \dashrightarrow 00{:}15{:}46{.}796$  But what I've been telling you were
- NOTE Confidence: 0.938186078333333
- 00:15:46.796 --> 00:15:47.930 basically all clinical reports
- NOTE Confidence: 0.938186078333333
- $00{:}15{:}47{.}930 \dashrightarrow 00{:}15{:}49{.}378$  and this has to do with the fact
- NOTE Confidence: 0.938186078333333
- $00{:}15{:}49{.}378 \dashrightarrow 00{:}15{:}50{.}529$  that clinical data was collected.
- NOTE Confidence: 0.938186078333333
- $00:15:50.530 \longrightarrow 00:15:51.128$  Of course,
- NOTE Confidence: 0.938186078333333
- $00:15:51.128 \longrightarrow 00:15:53.221$  in all of these patients who were

- NOTE Confidence: 0.938186078333333
- $00:15:53.221 \longrightarrow 00:15:54.514$  hospitalized but there weren't
- NOTE Confidence: 0.938186078333333
- $00:15:54.514 \rightarrow 00:15:56.082$  really systematic research studies
- NOTE Confidence: 0.938186078333333
- $00{:}15{:}56{.}082 \dashrightarrow 00{:}15{:}57{.}650$  done at that time.
- NOTE Confidence: 0.938186078333333
- $00:15:57.650 \rightarrow 00:15:59.970$  And what we have learned,
- NOTE Confidence: 0.938186078333333
- $00:15:59.970 \longrightarrow 00:16:00.334$  though,
- NOTE Confidence: 0.938186078333333
- $00{:}16{:}00{.}334 \dashrightarrow 00{:}16{:}02{.}882$  are that even small numbers of of
- NOTE Confidence: 0.938186078333333
- $00:16:02.882 \rightarrow 00:16:04.641$  systematic research can be helpful
- NOTE Confidence: 0.938186078333333
- $00:16:04.641 \rightarrow 00:16:06.246$  in trying to understand HIV.
- NOTE Confidence: 0.938186078333333
- 00:16:06.250 --> 00:16:09.466 I'm sorry, acute COVID-19 era pathogenesis,
- NOTE Confidence: 0.938186078333333
- 00:16:09.470 --> 00:16:11.726 and I just wanted to do a really
- NOTE Confidence: 0.938186078333333
- 00:16:11.726 --> 00:16:13.168 quick review of the virus.
- NOTE Confidence: 0.938186078333333
- $00:16:13.170 \longrightarrow 00:16:14.955$  For those of you who are not
- NOTE Confidence: 0.938186078333333
- $00:16:14.955 \rightarrow 00:16:15.465$  completely tired.
- NOTE Confidence: 0.938186078333333
- $00:16:15.470 \longrightarrow 00:16:16.526$  Is remembering exactly what
- NOTE Confidence: 0.938186078333333
- $00:16:16.526 \longrightarrow 00:16:17.846$  the structure is of cart.
- NOTE Confidence: 0.938186078333333

 $00:16:17.850 \longrightarrow 00:16:19.674$  Stars could be 2 and what the viral

NOTE Confidence: 0.938186078333333

00:16:19.674 --> 00:16:21.320 life cycle is probably most of us

NOTE Confidence: 0.938186078333333

 $00:16:21.320 \rightarrow 00:16:23.252$  know this way more than we would ever

NOTE Confidence: 0.938186078333333

 $00:16:23.252 \rightarrow 00:16:24.981$  want to know anything about a virus,

NOTE Confidence: 0.938186078333333

 $00{:}16{:}24{.}990 \dashrightarrow 00{:}16{:}28{.}000$  but just as a reminder.

NOTE Confidence: 0.938186078333333

 $00:16:28.000 \rightarrow 00:16:29.220$  We've known since very,

NOTE Confidence: 0.938186078333333

 $00:16:29.220 \longrightarrow 00:16:31.613$  very early in the pandemic that this is

NOTE Confidence: 0.938186078333333

 $00:16:31.613 \rightarrow 00:16:34.060$  a very simple virus with a single RNA strand.

NOTE Confidence: 0.938186078333333

00:16:34.060 --> 00:16:34.584 Very,

NOTE Confidence: 0.938186078333333

 $00:16:34.584 \rightarrow 00:16:38.020$  very few proteins encoded and the

NOTE Confidence: 0.938186078333333

 $00:16:38.020 \longrightarrow 00:16:41.370$  virus is surrounded by a.

NOTE Confidence: 0.938186078333333

 $00:16:41.370 \longrightarrow 00:16:43.800$  Declare capsid and then a.

NOTE Confidence: 0.938186078333333

00:16:43.800 --> 00:16:45.678 Sorry it's bye bye and envelope

NOTE Confidence: 0.938186078333333

 $00{:}16{:}45{.}678 \dashrightarrow 00{:}16{:}47{.}596$  proteins and then there are spike

NOTE Confidence: 0.938186078333333

 $00:16:47.596 \rightarrow 00:16:49.408$  trimers that emerge from the surface

NOTE Confidence: 0.938186078333333

 $00:16:49.408 \longrightarrow 00:16:51.277$  of the virus and these spike

- NOTE Confidence: 0.938186078333333
- $00{:}16{:}51{.}277 \dashrightarrow 00{:}16{:}53{.}089$  trimers are again what the most
- NOTE Confidence: 0.835962504285714
- $00{:}16{:}53.090 \dashrightarrow 00{:}16{:}56.240$  of our RNA antibodies are directed against.
- NOTE Confidence: 0.835962504285714
- 00:16:56.240 --> 00:16:57.800 I'm sorry vaccinations are
- NOTE Confidence: 0.835962504285714
- $00:16:57.800 \longrightarrow 00:16:58.970$  directed against these.
- NOTE Confidence: 0.835962504285714
- $00{:}16{:}58{.}970 \dashrightarrow 00{:}17{:}02{.}039$  Spike trimers are.
- NOTE Confidence: 0.835962504285714
- 00:17:02.040 --> 00:17:03.408 Basically, what's needed to
- NOTE Confidence: 0.835962504285714
- $00:17:03.408 \longrightarrow 00:17:05.460$  be recognized by a host cell,
- NOTE Confidence: 0.835962504285714
- $00:17:05.460 \longrightarrow 00:17:07.748$  so the ACE 2 receptor on the surface
- NOTE Confidence: 0.835962504285714
- $00{:}17{:}07{.}748 \dashrightarrow 00{:}17{:}09{.}615$  of mammalian cells is recognized as
- NOTE Confidence: 0.835962504285714
- 00:17:09.615 --> 00:17:12.056 the spike trimmer of the virus and it
- NOTE Confidence: 0.835962504285714
- $00:17:12.056 \rightarrow 00:17:14.152$  allows for entry of virus into a cell.
- NOTE Confidence: 0.835962504285714
- 00:17:14.160 --> 00:17:16.715 So the presence of ACE 2 receptors
- NOTE Confidence: 0.835962504285714
- 00:17:16.715 --> 00:17:19.318 and then other related receptors and NOTE Confidence: 0.835962504285714
- $00:17:19.318 \longrightarrow 00:17:22.060$  other proteins that allow for binding NOTE Confidence: 0.835962504285714
- $00:17:22.060 \rightarrow 00:17:24.883$  and entry of the virus is really what NOTE Confidence: 0.835962504285714

 $00:17:24.883 \rightarrow 00:17:26.929$  determines the cellular tropism of this

NOTE Confidence: 0.835962504285714

 $00{:}17{:}26{.}929 \dashrightarrow 00{:}17{:}28{.}929$  virus and determines what types of

NOTE Confidence: 0.835962504285714

 $00:17:28.929 \dashrightarrow 00:17:31.150$  cells and tissues the virus can enter.

NOTE Confidence: 0.835962504285714

 $00{:}17{:}31{.}150 \dashrightarrow 00{:}17{:}32{.}152$  And then I also wanted to

NOTE Confidence: 0.835962504285714

 $00:17:32.152 \longrightarrow 00:17:33.410$  remind you with a figure on the.

NOTE Confidence: 0.835962504285714

 $00:17:33.410 \rightarrow 00:17:35.723$  Right, but the viral life cycle is for SARS,

NOTE Confidence: 0.835962504285714

 $00{:}17{:}35{.}730 \dashrightarrow 00{:}17{:}38{.}930$  Co V2 and essentially this is an RNA

NOTE Confidence: 0.835962504285714

 $00:17:38.930 \rightarrow 00:17:41.425$  virus that uses the host cytoplasmic

NOTE Confidence: 0.835962504285714

00:17:41.425 --> 00:17:43.900 cell machinery to replicate itself.

NOTE Confidence: 0.835962504285714

00:17:43.900 --> 00:17:45.523 So unlike HIV,

NOTE Confidence: 0.835962504285714

 $00{:}17{:}45{.}523 \dashrightarrow 00{:}17{:}48{.}332$  another RNA virus which actually uses

NOTE Confidence: 0.835962504285714

 $00:17:48.332 \rightarrow 00:17:49.908$  reverse transcriptase to integrate

NOTE Confidence: 0.835962504285714

00:17:49.908 --> 00:17:52.049 its genome into our host genome,

NOTE Confidence: 0.835962504285714

 $00{:}17{:}52.050 \dashrightarrow 00{:}17{:}54.290$  which is why this is a chronic and

NOTE Confidence: 0.835962504285714

 $00:17:54.290 \longrightarrow 00:17:55.310$  essentially incurable disease,

NOTE Confidence: 0.835962504285714

 $00:17:55.310 \longrightarrow 00:17:57.361$  except for three people out of 75
NOTE Confidence: 0.835962504285714

00:17:57.361 - 00:17:59.770 million people have had it in SARS, Co.

NOTE Confidence: 0.835962504285714

 $00:17:59.770 \longrightarrow 00:18:00.150$  V2.

NOTE Confidence: 0.835962504285714

 $00:18:00.150 \rightarrow 00:18:02.430$  The virus does not become hopefully

NOTE Confidence: 0.835962504285714

 $00:18:02.512 \longrightarrow 00:18:04.267$  as far as we understand.

NOTE Confidence: 0.835962504285714

 $00:18:04.270 \longrightarrow 00:18:04.910$  Chronic illness.

NOTE Confidence: 0.835962504285714

 $00{:}18{:}04{.}910 \dashrightarrow 00{:}18{:}07{.}150$  It's an acute illness that uses the

NOTE Confidence: 0.835962504285714

 $00:18:07.150 \longrightarrow 00:18:09.387$  host machinery to make more of itself.

NOTE Confidence: 0.835962504285714

 $00:18:09.390 \rightarrow 00:18:11.675$  But eventually, when the immune

NOTE Confidence: 0.835962504285714

 $00:18:11.675 \rightarrow 00:18:14.066$  system can kill the infected cells,

NOTE Confidence: 0.835962504285714

 $00:18:14.066 \longrightarrow 00:18:16.280$  then the virus will die out.

NOTE Confidence: 0.835962504285714

 $00:18:16.280 \longrightarrow 00:18:18.368$  So what do we know about how this

NOTE Confidence: 0.835962504285714

 $00{:}18{:}18{.}368 \dashrightarrow 00{:}18{:}20{.}459$  virus might affect the nervous system?

NOTE Confidence: 0.835962504285714

00:18:20.460 --> 00:18:22.516 And some of it is indicated by some

NOTE Confidence: 0.835962504285714

 $00{:}18{:}22.516 \dashrightarrow 00{:}18{:}24.853$  of it initially was indicated by what

NOTE Confidence: 0.835962504285714

 $00:18:24.853 \rightarrow 00:18:27.180$  we knew by prior similar viruses.

NOTE Confidence: 0.835962504285714

- 00:18:27.180 --> 00:18:28.006 So SARS,
- NOTE Confidence: 0.835962504285714
- 00:18:28.006 --> 00:18:30.897 Co V2 has a lot of nucleotide
- NOTE Confidence: 0.835962504285714
- 00:18:30.897 00:18:33.430 identity to prior coronaviruses.
- NOTE Confidence: 0.835962504285714
- 00:18:33.430 --> 00:18:34.558 In particular SARS,
- NOTE Confidence: 0.835962504285714
- $00{:}18{:}34{.}558 \dashrightarrow 00{:}18{:}36{.}814$  Co V1 and the mayor's virus.
- NOTE Confidence: 0.835962504285714
- $00{:}18{:}36{.}820 \dashrightarrow 00{:}18{:}38{.}780$  This is important because there
- NOTE Confidence: 0.835962504285714
- $00:18:38.780 \longrightarrow 00:18:40.348$  were actually known neurologic
- NOTE Confidence: 0.835962504285714
- $00:18:40.348 \rightarrow 00:18:41.680$  complications even though very,
- NOTE Confidence: 0.835962504285714
- $00:18:41.680 \rightarrow 00:18:43.610$  very few people worldwide contracted
- NOTE Confidence: 0.835962504285714
- $00:18:43.610 \longrightarrow 00:18:45.154$  either of those infections.
- NOTE Confidence: 0.835962504285714
- $00:18:45.160 \rightarrow 00:18:47.029$  But some of what we knew originally
- NOTE Confidence: 0.835962504285714
- $00{:}18{:}47.029 \dashrightarrow 00{:}18{:}47.563$  about how.
- NOTE Confidence: 0.835962504285714
- 00:18:47.570 --> 00:18:49.375 Starts Kaviti might affect the
- NOTE Confidence: 0.835962504285714
- 00:18:49.375 --> 00:18:51.180 nervous system was learned from
- NOTE Confidence: 0.835962504285714
- $00{:}18{:}51{.}246 \dashrightarrow 00{:}18{:}53{.}126$  these earlier outbreaks and what
- NOTE Confidence: 0.835962504285714
- $00:18:53.126 \longrightarrow 00:18:54.630$  was understood from them.

- NOTE Confidence: 0.835962504285714
- $00{:}18{:}54{.}630 \dashrightarrow 00{:}18{:}56{.}807$  And one of the early concerns was
- NOTE Confidence: 0.835962504285714
- 00:18:56.807 00:18:59.361 whether or not stars could be 2 might
- NOTE Confidence: 0.835962504285714
- $00{:}18{:}59{.}361 \dashrightarrow 00{:}19{:}01{.}630$  enter and infect cells in the brain.
- NOTE Confidence: 0.835962504285714
- $00:19:01.630 \rightarrow 00:19:03.583$  So why would we think that could be possible?
- NOTE Confidence: 0.835962504285714
- $00:19:03.590 \longrightarrow 00:19:03.859$  Well,
- NOTE Confidence: 0.835962504285714
- $00:19:03.859 \longrightarrow 00:19:05.473$  one thing that's known is that
- NOTE Confidence: 0.835962504285714
- $00:19:05.473 \longrightarrow 00:19:06.970$  stars that ACE 2 receptors,
- NOTE Confidence: 0.835962504285714
- $00:19:06.970 \longrightarrow 00:19:07.442$  which again,
- NOTE Confidence: 0.835962504285714
- $00:19:07.442 \longrightarrow 00:19:08.150$  as I mentioned,
- NOTE Confidence: 0.835962504285714
- 00:19:08.150 --> 00:19:10.411 allow for entry of virus into cells
- NOTE Confidence: 0.835962504285714
- $00:19:10.411 \rightarrow 00:19:12.483$  and into tissues are actually located
- NOTE Confidence: 0.835962504285714
- $00:19:12.483 \longrightarrow 00:19:14.912$  on multiple cell types in the body,
- NOTE Confidence: 0.835962504285714
- $00:19:14.920 \longrightarrow 00:19:17.164$  and although there are very very
- NOTE Confidence: 0.835962504285714
- $00{:}19{:}17{.}164 \dashrightarrow 00{:}19{:}19{.}781$  common in the nasopharynx and in the
- NOTE Confidence: 0.835962504285714
- $00:19:19.781 \rightarrow 00:19:21.887$  alveolar epithelial cells of the lung,
- NOTE Confidence: 0.835962504285714

 $00:19:21.890 \longrightarrow 00:19:24.404$  probably explaining why most of those

NOTE Confidence: 0.835962504285714

00:19:24.404 - 00:19:27.149 are these major major target organs,

NOTE Confidence: 0.835962504285714

 $00:19:27.150 \rightarrow 00:19:29.446$  other target organs also include the kidney,

NOTE Confidence: 0.835962504285714

 $00:19:29.450 \longrightarrow 00:19:31.210$  the intestines, the blood vessels,

NOTE Confidence: 0.835962504285714

 $00:19:31.210 \longrightarrow 00:19:32.998$  and the nervous system.

NOTE Confidence: 0.835962504285714

00:19:32.998 --> 00:19:35.380 And as again, we all learn very,

NOTE Confidence: 0.835962504285714

 $00:19:35.380 \longrightarrow 00:19:36.680$  very quickly in the first

NOTE Confidence: 0.835962504285714

 $00:19:36.680 \longrightarrow 00:19:37.810$  months of the pandemic,

NOTE Confidence: 0.835962504285714

 $00:19:37.810 \longrightarrow 00:19:40.001$  all of these organs can actually be

NOTE Confidence: 0.835962504285714

 $00:19:40.001 \rightarrow 00:19:42.158$  affected in people with acute COVID-19.

NOTE Confidence: 0.835962504285714

 $00:19:42.160 \longrightarrow 00:19:43.860$  And what we didn't know,

NOTE Confidence: 0.835962504285714

00:19:43.860 --> 00:19:44.323 however,

NOTE Confidence: 0.835962504285714

 $00:19:44.323 \longrightarrow 00:19:46.175$  is which actual cells

NOTE Confidence: 0.835962504285714

 $00{:}19{:}46.175 \dashrightarrow 00{:}19{:}48.490$  of the brain express ACE

NOTE Confidence: 0.794358251166667

 $00{:}19{:}48.574 \dashrightarrow 00{:}19{:}51.532$  2 receptors and on the right you can see a

NOTE Confidence: 0.794358251166667

 $00:19:51.532 \rightarrow 00:19:54.585$  very nice in silico analysis looking for the

NOTE Confidence: 0.794358251166667

 $00:19:54.585 \rightarrow 00:19:56.940$  distribution of genes relevant to severe.

NOTE Confidence: 0.794358251166667

 $00:19:56.940 \rightarrow 00:20:00.846$  So stars Kobe 2IN different cell types in the

NOTE Confidence: 0.794358251166667

 $00{:}20{:}00{.}846 \dashrightarrow 00{:}20{:}03{.}143$  brain and what you can see is that ACE 2.

NOTE Confidence: 0.794358251166667

 $00:20:03.150 \longrightarrow 00:20:05.780$  Actually seems to have only

NOTE Confidence: 0.794358251166667

 $00{:}20{:}05.780 \dashrightarrow 00{:}20{:}07.884$  modest expression in neurons.

NOTE Confidence: 0.794358251166667

 $00:20:07.890 \longrightarrow 00:20:10.014$  It does seem to have higher

NOTE Confidence: 0.794358251166667

 $00:20:10.014 \rightarrow 00:20:11.076$  expression in oligodendrocytes,

NOTE Confidence: 0.794358251166667

 $00:20:11.080 \rightarrow 00:20:13.488$  but some of these other proteins that

NOTE Confidence: 0.794358251166667

 $00:20:13.488 \longrightarrow 00:20:15.696$  are important for viral entry are

NOTE Confidence: 0.794358251166667

 $00:20:15.696 \rightarrow 00:20:17.910$  also are highly expressed in neurons,

NOTE Confidence: 0.794358251166667

 $00:20:17.910 \longrightarrow 00:20:19.884$  suggesting that there may be some

NOTE Confidence: 0.794358251166667

00:20:19.884 --> 00:20:23.390 vulnerability of neurons to SARS, Co V2,

NOTE Confidence: 0.794358251166667

 $00{:}20{:}23{.}390 \dashrightarrow 00{:}20{:}25{.}707$  but but we don't have strong expression

NOTE Confidence: 0.794358251166667

 $00{:}20{:}25{.}707 \dashrightarrow 00{:}20{:}28{.}569$  of ACE 2 on the surface of neurons.

NOTE Confidence: 0.794358251166667

 $00:20:28.570 \longrightarrow 00:20:29.767$  How would the virus get to the

NOTE Confidence: 0.794358251166667

 $00:20:29.767 \longrightarrow 00:20:30.720$  brain in the 1st place?

NOTE Confidence: 0.794358251166667

 $00:20:30.720 \longrightarrow 00:20:32.460$  I think this is again something

NOTE Confidence: 0.794358251166667

 $00:20:32.460 \longrightarrow 00:20:34.631$  that that many of the positive sort

NOTE Confidence: 0.794358251166667

00:20:34.631 --> 00:20:36.515 of mechanisms were based on what

NOTE Confidence: 0.794358251166667

 $00{:}20{:}36{.}515 \dashrightarrow 00{:}20{:}38{.}319$  we knew from prior virus es.

NOTE Confidence: 0.794358251166667

 $00{:}20{:}38{.}320 \dashrightarrow 00{:}20{:}40{.}444$  So this is a model that we put together

NOTE Confidence: 0.794358251166667

00:20:40.444 --> 00:20:42.300 back again in March or April 2020,

NOTE Confidence: 0.794358251166667

 $00:20:42.300 \rightarrow 00:20:42.942$  saying well,

NOTE Confidence: 0.794358251166667

 $00:20:42.942 \longrightarrow 00:20:44.868$  one possibility is the virus could

NOTE Confidence: 0.794358251166667

 $00:20:44.868 \rightarrow 00:20:46.706$  potentially get into the brain by

NOTE Confidence: 0.794358251166667

 $00:20:46.706 \rightarrow 00:20:48.131$  haematogenous spread and this model

NOTE Confidence: 0.794358251166667

 $00:20:48.131 \longrightarrow 00:20:49.825$  is based essentially on the model

NOTE Confidence: 0.794358251166667

 $00:20:49.825 \rightarrow 00:20:51.830$  that we know for other viruses,

NOTE Confidence: 0.794358251166667

 $00:20:51.830 \rightarrow 00:20:55.730$  including HIV where viral particles but

NOTE Confidence: 0.794358251166667

 $00:20:55.730 \rightarrow 00:20:59.049$  particularly infect virally infected cells.

NOTE Confidence: 0.794358251166667

 $00:20:59.050 \rightarrow 00:21:01.408$  May traffic through the vascular endothelium

NOTE Confidence: 0.794358251166667

 $00:21:01.408 \longrightarrow 00:21:04.488$  in the blood brain barrier into the brain?

NOTE Confidence: 0.794358251166667

 $00:21:04.490 \longrightarrow 00:21:06.620$  I think that this is something

NOTE Confidence: 0.794358251166667

 $00:21:06.620 \rightarrow 00:21:08.880$  that was a potential hypothesis.

NOTE Confidence: 0.794358251166667

 $00:21:08.880 \rightarrow 00:21:12.910$  It turns out that SARS Co V2 is not really

NOTE Confidence: 0.794358251166667

 $00{:}21{:}12{.}910 \dashrightarrow 00{:}21{:}14{.}794$  readily detectable in the blood and

NOTE Confidence: 0.794358251166667

 $00{:}21{:}14.794 \dashrightarrow 00{:}21{:}17.488$  many people who are very sick with COVID-19.

NOTE Confidence: 0.794358251166667

 $00{:}21{:}17{.}490 \dashrightarrow 00{:}21{:}20{.}258$  So in fact it's there's not as much

NOTE Confidence: 0.794358251166667

 $00{:}21{:}20{.}258 \dashrightarrow 00{:}21{:}23{.}042$  SARS Co V2 viraemia as there is

NOTE Confidence: 0.794358251166667

 $00{:}21{:}23.042 \dashrightarrow 00{:}21{:}24.585$  for example collection of stars.

NOTE Confidence: 0.794358251166667

 $00{:}21{:}24.585 \dashrightarrow 00{:}21{:}26.055$  Kobe 2 virus and things like

NOTE Confidence: 0.794358251166667

00:21:26.055 --> 00:21:27.510 the whole factory epithelium,

NOTE Confidence: 0.794358251166667

 $00{:}21{:}27{.}510 \dashrightarrow 00{:}21{:}29{.}160$  which makes I think this.

NOTE Confidence: 0.794358251166667

00:21:29.160 --> 00:21:31.148 Hematogenous spread a little bit less likely,

NOTE Confidence: 0.794358251166667

00:21:31.150 --> 00:21:32.950 although still a potential in,

NOTE Confidence: 0.794358251166667

 $00{:}21{:}32{.}950 \dashrightarrow 00{:}21{:}34{.}810$  especially may be in people with a

NOTE Confidence: 0.794358251166667

 $00:21:34.810 \longrightarrow 00:21:37.184$  breakdown of the blood brain barrier on

NOTE Confidence: 0.794358251166667

 $00:21:37.184 \rightarrow 00:21:39.308$  the right is another transcranial root,

NOTE Confidence: 0.794358251166667

 $00:21:39.310 \longrightarrow 00:21:41.926$  which I think is potentially sort

NOTE Confidence: 0.794358251166667

 $00:21:41.926 \rightarrow 00:21:44.432$  of more likely if there really is

NOTE Confidence: 0.794358251166667

 $00:21:44.432 \longrightarrow 00:21:46.220$  viral entry into the brain that

NOTE Confidence: 0.794358251166667

 $00:21:46.281 \rightarrow 00:21:48.006$  it could be entering through.

NOTE Confidence: 0.794358251166667

 $00:21:48.010 \longrightarrow 00:21:50.044$  There's robust infection of the system

NOTE Confidence: 0.794358251166667

 $00:21:50.044 \rightarrow 00:21:52.135$  tacular cells and the whole factory

NOTE Confidence: 0.794358251166667

 $00:21:52.135 \longrightarrow 00:21:54.169$  epithelium in the news of pharynx.

NOTE Confidence: 0.794358251166667

 $00:21:54.170 \longrightarrow 00:21:56.543$  This may be related to the anosmia NOTE Confidence: 0.7943582511666667

 $00:21:56.543 \rightarrow 00:21:59.254$  that probably at least half of people NOTE Confidence: 0.7943582511666667

 $00:21:59.254 \rightarrow 00:22:01.284$  experience when they get COVID-19.

NOTE Confidence: 0.794358251166667

 $00:22:01.290 \longrightarrow 00:22:03.740$  And the sub position was is the

NOTE Confidence: 0.794358251166667

 $00:22:03.740 \longrightarrow 00:22:05.266$  potentially the olfactory nerves

NOTE Confidence: 0.794358251166667

 $00:22:05.266 \rightarrow 00:22:07.301$  could then locally become infected

NOTE Confidence: 0.794358251166667

 $00:22:07.301 \longrightarrow 00:22:09.350$  and through retrograde spread

NOTE Confidence: 0.794358251166667

 $00:22:09.350 \rightarrow 00:22:12.425$  through between the synaptic cleft.

NOTE Confidence: 0.794358251166667

 $00{:}22{:}12{.}430 \dashrightarrow 00{:}22{:}14.698$  The virus could then be transmitted into

NOTE Confidence: 0.794358251166667

 $00{:}22{:}14.698 \dashrightarrow 00{:}22{:}16.778$  the olfactory bulb and into the brain.

NOTE Confidence: 0.794358251166667

 $00:22:16.780 \longrightarrow 00:22:19.348$  This has been shown to be possible by

NOTE Confidence: 0.794358251166667

00:22:19.348 --> 00:22:21.419 concerns COVIE 1 using animal models,

NOTE Confidence: 0.794358251166667

 $00{:}22{:}21{.}420 \dashrightarrow 00{:}22{:}23{.}916$  and so this was really a putative mechanism.

NOTE Confidence: 0.794358251166667

 $00{:}22{:}23{.}920 \dashrightarrow 00{:}22{:}25{.}495$  But what's the evidence that stars could

NOTE Confidence: 0.794358251166667

 $00:22:25.495 \rightarrow 00:22:27.520$  be to you actually gets into the brain?

NOTE Confidence: 0.794358251166667

 $00:22:27.520 \longrightarrow 00:22:29.386$  I think there's really not a

NOTE Confidence: 0.794358251166667

 $00:22:29.386 \longrightarrow 00:22:30.630$  lot of evidence so.

NOTE Confidence: 0.794358251166667

 $00{:}22{:}30{.}630 \dashrightarrow 00{:}22{:}32{.}694$  There have been a number of studies that

NOTE Confidence: 0.794358251166667

 $00{:}22{:}32.694 \dashrightarrow 00{:}22{:}35.069$  have used small samples of looking for stars.

NOTE Confidence: 0.794358251166667

 $00{:}22{:}35{.}070 \dashrightarrow 00{:}22{:}37{.}350$  Kobe 2 for example in CSF fluid and

NOTE Confidence: 0.794358251166667

 $00{:}22{:}37{.}350 \dashrightarrow 00{:}22{:}39{.}624$  all of you know that super spinal

NOTE Confidence: 0.794358251166667

 $00{:}22{:}39{.}624 \dashrightarrow 00{:}22{:}41{.}254$  fluid is not the same

NOTE Confidence: 0.828827753913044

 $00{:}22{:}41{.}326 \dashrightarrow 00{:}22{:}43{.}355$  as the brain. It's not telling us about

NOTE Confidence: 0.828827753913044

 $00:22:43.355 \rightarrow 00:22:44.909$  what's happening in the deep brain

NOTE Confidence: 0.828827753913044

00:22:44.909 --> 00:22:47.205 parenchyma, but in many many acute NOTE Confidence: 0.828827753913044

 $00:22:47.205 \rightarrow 00:22:49.573$  viral infections of viral particles are

NOTE Confidence: 0.828827753913044

 $00{:}22{:}49{.}573 \dashrightarrow 00{:}22{:}51{.}775$  readily detected in the spinal fluid

NOTE Confidence: 0.828827753913044

 $00{:}22{:}51.775 \dashrightarrow 00{:}22{:}54.208$  in the setting of brain infection,

NOTE Confidence: 0.828827753913044

 $00:22:54.210 \longrightarrow 00:22:56.070$  acute HIV being something I've been

NOTE Confidence: 0.828827753913044

 $00:22:56.070 \rightarrow 00:22:58.349$  studying for 20 years is a good example.

NOTE Confidence: 0.828827753913044

 $00{:}22{:}58{.}350 \dashrightarrow 00{:}23{:}01{.}090$  We're about 80 or 90% of people during acute.

NOTE Confidence: 0.828827753913044

00:23:01.090 --> 00:23:01.810 Striking infection,

NOTE Confidence: 0.828827753913044

 $00:23:01.810 \longrightarrow 00:23:03.502$  even without any symptoms,

NOTE Confidence: 0.828827753913044

 $00:23:03.502 \longrightarrow 00:23:05.194$  have readily detectable HIV

NOTE Confidence: 0.828827753913044

 $00{:}23{:}05{.}194 \dashrightarrow 00{:}23{:}07{.}290$  RNA in the spinal fluid.

NOTE Confidence: 0.828827753913044

 $00:23:07.290 \longrightarrow 00:23:08.518$  But interestingly,

NOTE Confidence: 0.828827753913044

 $00:23:08.518 \rightarrow 00:23:11.588$  in people with acute COVID-19,

NOTE Confidence: 0.828827753913044

00:23:11.590 --> 00:23:13.130 particularly looking at people

- NOTE Confidence: 0.828827753913044
- 00:23:13.130 -> 00:23:14.285 with neurologic symptoms,
- NOTE Confidence: 0.828827753913044
- $00:23:14.290 \longrightarrow 00:23:15.662$  there have been very,
- NOTE Confidence: 0.828827753913044
- $00:23:15.662 \longrightarrow 00:23:17.377$  very little a few reports
- NOTE Confidence: 0.828827753913044
- $00{:}23{:}17.377 \dashrightarrow 00{:}23{:}19.268$  suggesting that one can detect SARS.
- NOTE Confidence: 0.828827753913044
- 00:23:19.270 --> 00:23:19.780 Kobe 2,
- NOTE Confidence: 0.828827753913044
- $00:23:19.780 \longrightarrow 00:23:21.565$  So this was a small study of
- NOTE Confidence: 0.828827753913044
- 00:23:21.565 --> 00:23:23.597 just six people by my colleagues
- NOTE Confidence: 0.828827753913044
- $00{:}23{:}23{.}597 \dashrightarrow 00{:}23{:}25{.}500$  in Sweden where they looked at
- NOTE Confidence: 0.828827753913044
- 00:23:25.500 --> 00:23:27.064 CSF markers of inflammation,
- NOTE Confidence: 0.828827753913044
- 00:23:27.064 --> 00:23:29.830 and they also try to detect SARS,
- NOTE Confidence: 0.828827753913044
- 00:23:29.830 --> 00:23:31.478 Co V2 by PCR.
- NOTE Confidence: 0.828827753913044
- 00:23:31.478 > 00:23:33.997 And in this study they found very,
- NOTE Confidence: 0.828827753913044
- 00:23:33.997 > 00:23:35.731 very low level detection by PCR
- NOTE Confidence: 0.828827753913044
- $00:23:35.731 \longrightarrow 00:23:37.497$  in half of the participants,
- NOTE Confidence: 0.828827753913044
- 00:23:37.500 -> 00:23:38.980 but they essentially felt that
- NOTE Confidence: 0.828827753913044

 $00{:}23{:}38{.}980 \dashrightarrow 00{:}23{:}41{.}020$  based on the levels of detection

NOTE Confidence: 0.828827753913044

 $00{:}23{:}41{.}020 \dashrightarrow 00{:}23{:}43{.}648$  and their subsequent work that this

NOTE Confidence: 0.828827753913044

00:23:43.648 --> 00:23:45.400 was probably just contamination

NOTE Confidence: 0.828827753913044

00:23:45.400 - 00:23:47.941 and they later did a review article

NOTE Confidence: 0.828827753913044

 $00:23:47.941 \longrightarrow 00:23:49.846$  where they actually looked at all

NOTE Confidence: 0.828827753913044

 $00:23:49.846 \longrightarrow 00:23:51.478$  of the published reports to date,

NOTE Confidence: 0.828827753913044

 $00{:}23{:}51{.}480 \dashrightarrow 00{:}23{:}54{.}040$  which had been almost 450 reports to date.

NOTE Confidence: 0.828827753913044

00:23:54.040 --> 00:23:56.476 Looking for PCR detection of SARS,

NOTE Confidence: 0.828827753913044

00:23:56.480 --> 00:24:00.332 Co V2 in CSF in people with acute COVID-19,

NOTE Confidence: 0.828827753913044

 $00:24:00.340 \rightarrow 00:24:01.860$  mostly with severe disease.

NOTE Confidence: 0.828827753913044

 $00:24:01.860 \rightarrow 00:24:03.760$  Almost all with neurologic symptoms,

NOTE Confidence: 0.828827753913044

 $00:24:03.760 \longrightarrow 00:24:05.350$  which should be the indication

NOTE Confidence: 0.828827753913044

 $00:24:05.350 \longrightarrow 00:24:06.812$  for lumbar puncture and starts.

NOTE Confidence: 0.828827753913044

 $00:24:06.812 \longrightarrow 00:24:08.318$  Kovi 2 was only detected in

NOTE Confidence: 0.828827753913044

 $00:24:08.318 \longrightarrow 00:24:10.039$  less than 3% of those cases,

NOTE Confidence: 0.828827753913044

 $00{:}24{:}10.039 \dashrightarrow 00{:}24{:}12.510$  so I think this is very convincing

- NOTE Confidence: 0.828827753913044
- $00:24:12.582 \rightarrow 00:24:14.616$  evidence that direct viral invasion,
- NOTE Confidence: 0.828827753913044
- $00{:}24{:}14.616 \dashrightarrow 00{:}24{:}16.476$  main and and replication within
- NOTE Confidence: 0.828827753913044
- $00{:}24{:}16{.}476 \dashrightarrow 00{:}24{:}18{.}910$  the CNS may not be a major
- NOTE Confidence: 0.828827753913044
- $00:24:18.910 \rightarrow 00:24:20.214$  driver of neurologic symptoms.
- NOTE Confidence: 0.828827753913044
- $00{:}24{:}20{.}220 \dashrightarrow 00{:}24{:}20{.}752$  However,
- NOTE Confidence: 0.828827753913044
- $00{:}24{:}20.752 \dashrightarrow 00{:}24{:}23.944$  this study shows elevations of immune
- NOTE Confidence: 0.828827753913044
- $00:24:23.944 \rightarrow 00:24:26.220$  activation biomarkers in the CSF,
- NOTE Confidence: 0.828827753913044
- $00:24:26.220 \longrightarrow 00:24:27.505$  so similar to the patient
- NOTE Confidence: 0.828827753913044
- $00:24:27.505 \longrightarrow 00:24:28.790$  case that I showed you,
- NOTE Confidence: 0.828827753913044
- $00:24:28.790 \longrightarrow 00:24:30.850$  they found elevation of CSF,
- NOTE Confidence: 0.828827753913044
- $00:24:30.850 \rightarrow 00:24:33.534$  neoprene and beta microglobulin.
- NOTE Confidence: 0.828827753913044
- $00:24:33.534 \rightarrow 00:24:37.102$  Metro biomarkers of myeloid inflammation in
- NOTE Confidence: 0.828827753913044
- $00{:}24{:}37{.}102 \dashrightarrow 00{:}24{:}38{.}798$  all of the individuals that they looked at.
- NOTE Confidence: 0.828827753913044
- $00:24:38.800 \longrightarrow 00:24:40.678$  The dotted line here being the
- NOTE Confidence: 0.828827753913044
- $00{:}24{:}40.678 \dashrightarrow 00{:}24{:}42.350$  normal levels and healthy controls,
- NOTE Confidence: 0.828827753913044

 $00:24:42.350 \longrightarrow 00:24:44.905$  and they also found a hint of

NOTE Confidence: 0.828827753913044

 $00{:}24{:}44{.}905 \dashrightarrow 00{:}24{:}46{.}866$  neuronal injury in a few of

NOTE Confidence: 0.828827753913044

 $00:24:46.866 \longrightarrow 00:24:48.396$  the people during this time.

NOTE Confidence: 0.828827753913044

 $00:24:48.400 \rightarrow 00:24:50.452$  And I'll come back to this in a minute,

NOTE Confidence: 0.828827753913044

 $00:24:50.460 \longrightarrow 00:24:53.500$  so this was really the first clue that

NOTE Confidence: 0.828827753913044

 $00:24:53.500 \rightarrow 00:24:55.319$  that neuroinflammation was predominant.

NOTE Confidence: 0.828827753913044

 $00{:}24{:}55{.}320 \dashrightarrow 00{:}24{:}58{.}008$  Even without detection in viral PCR.

NOTE Confidence: 0.828827753913044

00:24:58.008 --> 00:24:58.336 Now,

NOTE Confidence: 0.828827753913044

 $00:24:58.336 \rightarrow 00:25:00.960$  this is a beautiful study led by actually

NOTE Confidence: 0.828827753913044

 $00:25:01.029 \rightarrow 00:25:03.539$  today's neurology grand rounds speaker.

NOTE Confidence: 0.828827753913044

 $00{:}25{:}03.540 \dashrightarrow 00{:}25{:}05.472$ Shibani Mukherjee and colleagues

NOTE Confidence: 0.828827753913044

 $00:25:05.472 \longrightarrow 00:25:07.688$  from MGH where they looked at

NOTE Confidence: 0.828827753913044

 $00:25:07.688 \rightarrow 00:25:09.560$  larger numbers of people so they

NOTE Confidence: 0.828827753913044

 $00:25:09.621 \longrightarrow 00:25:11.667$  had 27 people and they collected

NOTE Confidence: 0.828827753913044

00:25:11.667 --> 00:25:13.450 CSF during acute COVID-19 again,

NOTE Confidence: 0.828827753913044

 $00{:}25{:}13.450 \dashrightarrow 00{:}25{:}15.376$  people who had LP's for neurologic

- NOTE Confidence: 0.828827753913044
- $00{:}25{:}15{.}376 \dashrightarrow 00{:}25{:}17{.}553$  indications and so this is not a
- NOTE Confidence: 0.828827753913044
- 00:25:17.553 --> 00:25:18.938 survey and everyone with COVID,
- NOTE Confidence: 0.828827753913044
- $00:25:18.940 \longrightarrow 00:25:20.998$  but it's actually people who had
- NOTE Confidence: 0.828827753913044
- $00:25:20.998 \rightarrow 00:25:23.140$  distinct neurologic disease and they did.
- NOTE Confidence: 0.828827753913044
- $00{:}25{:}23.140 \dashrightarrow 00{:}25{:}24.990$  QT PCR and metagenomic sequencing
- NOTE Confidence: 0.828827753913044
- $00{:}25{:}24{.}990 \dashrightarrow 00{:}25{:}27{.}439$  in all 27 samples and did not
- NOTE Confidence: 0.828827753913044
- $00{:}25{:}27{.}439 \dashrightarrow 00{:}25{:}29{.}727$  find detection of SARS Co V2 in
- NOTE Confidence: 0.828827753913044
- $00{:}25{:}29{.}727 \dashrightarrow 00{:}25{:}30{.}867$  any of the samples.
- NOTE Confidence: 0.828827753913044
- 00:25:30.870 --> 00:25:31.336 However,
- NOTE Confidence: 0.828827753913044
- $00{:}25{:}31{.}336 \dashrightarrow 00{:}25{:}34{.}598$  they did find elevation of CSF inflammatory.
- NOTE Confidence: 0.828827753913044
- 00:25:34.600 --> 00:25:37.025 Markers in the COVID-19 patients
- NOTE Confidence: 0.828827753913044
- $00{:}25{:}37.025 \dashrightarrow 00{:}25{:}40.320$  that are shown with the red dots,
- NOTE Confidence: 0.828827753913044
- $00:25:40.320 \rightarrow 00:25:42.378$  particularly a couple of the markers,
- NOTE Confidence: 0.735505144285714
- $00{:}25{:}42{.}380 \dashrightarrow 00{:}25{:}48{.}925$  including MCP one and CSF mcglen beta,
- NOTE Confidence: 0.735505144285714
- $00:25:48.930 \rightarrow 00:25:53.234$  compared to healthy controls I wanna I'll 6.
- NOTE Confidence: 0.735505144285714

 $00:25:53.240 \rightarrow 00:25:54.806$  And interestingly, in this study they

NOTE Confidence: 0.735505144285714

 $00{:}25{:}54.806 \dashrightarrow 00{:}25{:}56.421$  also looked at other viral infections

NOTE Confidence: 0.735505144285714

00:25:56.421 --> 00:25:58.248 and compared the levels here in West NOTE Confidence: 0.735505144285714

 $00:25:58.248 \rightarrow 00:26:00.069$  Nile virus was the only one that had

NOTE Confidence: 0.735505144285714

 $00:26:00.069 \rightarrow 00:26:01.904$  higher levels in some of these markers.

NOTE Confidence: 0.735505144285714

 $00:26:01.904 \rightarrow 00:26:03.304$  So again, this is suggesting and

NOTE Confidence: 0.735505144285714

 $00:26:03.304 \longrightarrow 00:26:04.804$  I should say that most of these

NOTE Confidence: 0.735505144285714

 $00:26:04.804 \rightarrow 00:26:06.280$  people had normal CSF white counts,

NOTE Confidence: 0.735505144285714

 $00{:}26{:}06{.}280 \dashrightarrow 00{:}26{:}07{.}884$  so they didn't have.

NOTE Confidence: 0.735505144285714

00:26:07.884 --> 00:26:09.889 Will work evidence of Pleocytosis,

NOTE Confidence: 0.735505144285714

 $00{:}26{:}09{.}890 \dashrightarrow 00{:}26{:}11{.}800$  but they had subtle neuroinflammation.

NOTE Confidence: 0.85082046875

 $00:26:13.920 \longrightarrow 00:26:15.768$  Interestingly, there has been

NOTE Confidence: 0.85082046875

 $00:26:15.768 \longrightarrow 00:26:18.540$  look at other types of markers

NOTE Confidence: 0.85082046875

00:26:18.621 --> 00:26:21.009 in CSF in acute COVID patients,

NOTE Confidence: 0.85082046875

 $00:26:21.010 \longrightarrow 00:26:22.774$  and this paper was recently published

NOTE Confidence: 0.85082046875

 $00{:}26{:}22{.}774 \dashrightarrow 00{:}26{:}25{.}075$  in about a lot of attention because

- NOTE Confidence: 0.85082046875
- $00{:}26{:}25.075 \dashrightarrow 00{:}26{:}26.855$  it demonstrates the fact that
- NOTE Confidence: 0.85082046875
- $00{:}26{:}26{.}855 \dashrightarrow 00{:}26{:}29{.}018$  markers that are associated with
- NOTE Confidence: 0.85082046875
- $00{:}26{:}29.018 \dashrightarrow 00{:}26{:}30.874$  neurodegeneration in Alzheimer's disease
- NOTE Confidence: 0.85082046875
- $00:26:30.874 \rightarrow 00:26:32.854$  were actually abnormal in people
- NOTE Confidence: 0.85082046875
- $00{:}26{:}32.854 \dashrightarrow 00{:}26{:}34.942$  who had COVID were hospitalized with
- NOTE Confidence: 0.85082046875
- $00:26:34.942 \rightarrow 00:26:37.067$  acute COVID and neurologic symptoms.
- NOTE Confidence: 0.85082046875
- 00:26:37.070 00:26:38.732 So again, here are the COVID
- NOTE Confidence: 0.85082046875
- $00:26:38.732 \longrightarrow 00:26:40.510$  patients are shown in the orange,
- NOTE Confidence: 0.85082046875
- $00{:}26{:}40.510 \dashrightarrow 00{:}26{:}43.720$  and it's showing reductions in soluble.
- NOTE Confidence: 0.85082046875
- 00:26:43.720 --> 00:26:46.290 A panel of precursor protein
- NOTE Confidence: 0.85082046875
- $00:26:46.290 \longrightarrow 00:26:49.368$  and amyloid beta in people with
- NOTE Confidence: 0.85082046875
- 00:26:49.368 --> 00:26:51.420 COVID-19 during acute disease.
- NOTE Confidence: 0.85082046875
- $00{:}26{:}51{.}420 \dashrightarrow 00{:}26{:}52{.}818$  This has been a little bit
- NOTE Confidence: 0.85082046875
- $00:26:52.818 \rightarrow 00:26:54.282$  interpreted to say that maybe this
- NOTE Confidence: 0.85082046875
- $00:26:54.282 \longrightarrow 00:26:55.716$  is setting these people up for
- NOTE Confidence: 0.85082046875

00:26:55.720 --> 00:26:56.806 Alzheimer's type neurodegeneration,

NOTE Confidence: 0.85082046875

 $00{:}26{:}56{.}806 \dashrightarrow 00{:}26{:}58{.}616$  but I was interpret this

NOTE Confidence: 0.85082046875

 $00:26:58.616 \longrightarrow 00:27:00.160$  to say that actually,

NOTE Confidence: 0.85082046875

 $00:27:00.160 \longrightarrow 00:27:02.720$  in most acute infectious,

NOTE Confidence: 0.85082046875

 $00:27:02.720 \longrightarrow 00:27:04.640$  acute viral conditions,

NOTE Confidence: 0.85082046875

 $00{:}27{:}04.640 \dashrightarrow 00{:}27{:}06.502$  you can see these kinds of changes

NOTE Confidence: 0.85082046875

 $00{:}27{:}06.502 \dashrightarrow 00{:}27{:}08.231$  that resolve after acute infection and

NOTE Confidence: 0.85082046875

 $00:27:08.231 \rightarrow 00:27:10.268$  this is something that we've also seen

NOTE Confidence: 0.85082046875

 $00{:}27{:}10{.}328$  -->  $00{:}27{:}12{.}188$  and published in acute HIV infection,

NOTE Confidence: 0.85082046875

 $00:27:12.190 \longrightarrow 00:27:14.050$  so hopefully this doesn't actually.

NOTE Confidence: 0.85082046875

 $00:27:14.050 \longrightarrow 00:27:15.820$  Mean that there are going

NOTE Confidence: 0.85082046875

 $00:27:15.820 \longrightarrow 00:27:17.236$  to be Alzheimer's disease.

NOTE Confidence: 0.85082046875

 $00{:}27{:}17{.}240 \dashrightarrow 00{:}27{:}19{.}186$  You know Avalanche coming in our future.

NOTE Confidence: 0.85082046875

 $00:27:19.190 \rightarrow 00:27:21.314$  Although we can talk about that at the end,

NOTE Confidence: 0.85082046875

 $00{:}27{:}21{.}320 \dashrightarrow 00{:}27{:}23{.}826$  but I think that these kinds of

NOTE Confidence: 0.85082046875

00:27:23.826 --> 00:27:26.010 perturbations and amyloid processing and

- NOTE Confidence: 0.85082046875
- $00:27:26.010 \rightarrow 00:27:28.262$  neuronal processes maybe something better.
- NOTE Confidence: 0.85082046875
- $00:27:28.262 \longrightarrow 00:27:30.282$  Hint that there's been some
- NOTE Confidence: 0.85082046875
- 00:27:30.282 --> 00:27:32.149 injury during acute infection.
- NOTE Confidence: 0.85082046875
- $00:27:32.150 \rightarrow 00:27:34.150$  So this is really elegant work and this
- NOTE Confidence: 0.85082046875
- $00:27:34.150 \longrightarrow 00:27:36.006$  is being led by my colleague here.
- NOTE Confidence: 0.85082046875
- 00:27:36.010 --> 00:27:36.828 Shelly Farhadian,
- NOTE Confidence: 0.85082046875
- $00:27:36.828 \longrightarrow 00:27:39.691$  who is a faculty member in infectious
- NOTE Confidence: 0.85082046875
- $00:27:39.691 \longrightarrow 00:27:41.804$  disease who's also really a
- NOTE Confidence: 0.85082046875
- $00{:}27{:}41.804 \dashrightarrow 00{:}27{:}43.440$  stellar investigator and clinician
- NOTE Confidence: 0.85082046875
- $00:27:43.440 \longrightarrow 00:27:45.560$  in neuro infectious disease.
- NOTE Confidence: 0.85082046875
- 00:27:45.560 --> 00:27:47.795 And Shelly really took forward
- NOTE Confidence: 0.85082046875
- 00:27:47.795 --> 00:27:49.583 the opportunity to characterize
- NOTE Confidence: 0.85082046875
- $00:27:49.583 \rightarrow 00:27:51.270$  in a research level,
- NOTE Confidence: 0.85082046875
- $00{:}27{:}51{.}270 \dashrightarrow 00{:}27{:}53{.}188$  some of the clinical patients that we're
- NOTE Confidence: 0.85082046875
- $00{:}27{:}53.188 \dashrightarrow 00{:}27{:}55.490$  seeing on the Neuro COVID console service.
- NOTE Confidence: 0.85082046875

 $00:27:55.490 \longrightarrow 00:27:58.298$  So when patients did have CSF

NOTE Confidence: 0.85082046875

00:27:58.298 --> 00:28:00.170 collection for clinical reasons,

NOTE Confidence: 0.85082046875

00:28:00.170 --> 00:28:02.280 Shelly scrambled to do, really.

NOTE Confidence: 0.85082046875

 $00:28:02.280 \longrightarrow 00:28:04.260$  Real time studies on the CSF,

NOTE Confidence: 0.85082046875

 $00:28:04.260 \rightarrow 00:28:05.820$  including things like single cell RNA,

NOTE Confidence: 0.85082046875

 $00:28:05.820 \longrightarrow 00:28:08.228$  seek on fresh samples to try to

NOTE Confidence: 0.85082046875

 $00{:}28{:}08{.}228 \dashrightarrow 00{:}28{:}10{.}052$  characterize in great detail what

NOTE Confidence: 0.85082046875

 $00{:}28{:}10.052 \dashrightarrow 00{:}28{:}11.867$  some of the immune perturbations

NOTE Confidence: 0.85082046875

 $00{:}28{:}11{.}867 \dashrightarrow 00{:}28{:}14{.}000$  might be in these patients.

NOTE Confidence: 0.85082046875

 $00:28:14.000 \longrightarrow 00:28:16.928$  And so in this first six

NOTE Confidence: 0.85082046875

00:28:16.928 --> 00:28:18.880 patients that were evaluated,

NOTE Confidence: 0.85082046875

 $00{:}28{:}18{.}880 \dashrightarrow 00{:}28{:}20{.}650$  they she and other colleagues

NOTE Confidence: 0.85082046875

 $00{:}28{:}20.650 \dashrightarrow 00{:}28{:}22.560$  here at Yale looked for stars.

NOTE Confidence: 0.85082046875

00:28:22.560 --> 00:28:23.760 Kobe 2 by PCR,

NOTE Confidence: 0.85082046875

 $00:28:23.760 \longrightarrow 00:28:25.392$  metagenomics and culture did

NOTE Confidence: 0.85082046875

 $00:28:25.392 \rightarrow 00:28:27.840$  not find any evidence of virus,

- NOTE Confidence: 0.85082046875
- 00:28:27.840 --> 00:28:29.930 but did find really intriguing
- NOTE Confidence: 0.85082046875
- $00{:}28{:}29{.}930 \dashrightarrow 00{:}28{:}32{.}350$  alternate immune responses in the CSF.
- NOTE Confidence: 0.85082046875
- $00:28:32.350 \longrightarrow 00:28:33.846$  And what we did is that we looked
- NOTE Confidence: 0.85082046875
- $00:28:33.846 \longrightarrow 00:28:35.262$  at the patients who had COVID-19
- NOTE Confidence: 0.85082046875
- $00:28:35.262 \rightarrow 00:28:36.507$  and again on the left.
- NOTE Confidence: 0.85082046875
- $00{:}28{:}36{.}510 \dashrightarrow 00{:}28{:}38{.}358$  These are shown in purple compared
- NOTE Confidence: 0.85082046875
- $00:28:38.358 \longrightarrow 00:28:40.261$  them to pre pandemic CSF and
- NOTE Confidence: 0.85082046875
- $00{:}28{:}40{.}261 \dashrightarrow 00{:}28{:}42{.}079$  blood controls that we had been
- NOTE Confidence: 0.85082046875
- $00:28:42.079 \longrightarrow 00:28:43.530$  collecting for other studies.
- NOTE Confidence: 0.85082046875
- 00:28:43.530 --> 00:28:45.828 Healthy people who were age matched
- NOTE Confidence: 0.85082046875
- $00:28:45.830 \longrightarrow 00:28:47.522$  and what she found was increased
- NOTE Confidence: 0.85082046875
- 00:28:47.522 --> 00:28:49.322 CSF cytokines in the CSF compared
- NOTE Confidence: 0.85082046875
- $00{:}28{:}49{.}322 \dashrightarrow 00{:}28{:}50{.}246$  to the controls.
- NOTE Confidence: 0.85082046875
- $00:28:50.250 \rightarrow 00:28:51.805$  But what was really interesting
- NOTE Confidence: 0.85082046875
- $00:28:51.805 \rightarrow 00:28:53.741$  here is that she specifically found
- NOTE Confidence: 0.85082046875

 $00{:}28{:}53{.}741 \dashrightarrow 00{:}28{:}55{.}697$  a distinct pattern between the CSF

NOTE Confidence: 0.85082046875

 $00:28:55.697 \rightarrow 00:28:57.499$  cytokine elevations and those in blood,

NOTE Confidence: 0.85082046875

 $00:28:57.500 \rightarrow 00:28:59.165$  suggesting that there was actually

NOTE Confidence: 0.85082046875

 $00:28:59.165 \rightarrow 00:29:00.164$  a compartmentalized response.

NOTE Confidence: 0.85082046875

 $00{:}29{:}00{.}170 \dashrightarrow 00{:}29{:}01{.}758$  This wasn't necessarily just

NOTE Confidence: 0.85082046875

 $00:29:01.758 \longrightarrow 00:29:03.346$  a spillover of inflammation.

NOTE Confidence: 0.85082046875

00:29:03.350 --> 00:29:04.496 Systemic circulation,

NOTE Confidence: 0.85082046875

 $00:29:04.496 \rightarrow 00:29:07.361$  but instead was actually potentially

NOTE Confidence: 0.85082046875

 $00{:}29{:}07{.}361 \dashrightarrow 00{:}29{:}10{.}703$  a local response related to local

NOTE Confidence: 0.85082046875

 $00:29:10.703 \rightarrow 00:29:12.755$  cells and local perturbations.

NOTE Confidence: 0.85082046875

 $00{:}29{:}12.760 \dashrightarrow 00{:}29{:}14.235$  Another thing that she detected

NOTE Confidence: 0.85082046875

 $00:29:14.235 \longrightarrow 00:29:16.461$  by single cell RNA seek was a

NOTE Confidence: 0.85082046875

00:29:16.461 --> 00:29:17.157 increased frequency.

NOTE Confidence: 0.817463569444445

 $00{:}29{:}17.160 \dashrightarrow 00{:}29{:}20.229$  B cells in the CSF and so this led

NOTE Confidence: 0.817463569444445

 $00{:}29{:}20{.}229 \dashrightarrow 00{:}29{:}22{.}936$  to an interrogation of antibody

NOTE Confidence: 0.81746356944445

 $00:29:22.936 \rightarrow 00:29:25.848$  responses in the CSF and really,

- NOTE Confidence: 0.817463569444445
- 00:29:25.848 --> 00:29:26.820 really interesting work.
- NOTE Confidence: 0.817463569444445
- $00:29:26.820 \longrightarrow 00:29:29.459$  Again led by Shelly and other colleagues
- NOTE Confidence: 0.817463569444445
- $00{:}29{:}29{.}459 \dashrightarrow 00{:}29{:}32{.}880$  here at Yale and also collaborators at UCSF.
- NOTE Confidence: 0.817463569444445
- $00:29:32.880 \longrightarrow 00:29:35.040$  Using some really novel ways to
- NOTE Confidence: 0.817463569444445
- 00:29:35.040 --> 00:29:37.220 detect whole panels of anti SARS,
- NOTE Confidence: 0.817463569444445
- $00:29:37.220 \longrightarrow 00:29:38.192$  Kobe 2 antibodies.
- NOTE Confidence: 0.817463569444445
- $00:29:38.192 \rightarrow 00:29:40.460$  They were able to describe the fact
- NOTE Confidence: 0.817463569444445
- 00:29:40.520 --> 00:29:42.704 that anti SARS Co<br/> V2 antibodies were
- NOTE Confidence: 0.817463569444445
- $00:29:42.704 \rightarrow 00:29:45.260$  detected in CSF and all of these patients,
- NOTE Confidence: 0.817463569444445
- $00:29:45.260 \rightarrow 00:29:47.000$  but actually some of the antibodies
- NOTE Confidence: 0.817463569444445
- 00:29:47.000 --> 00:29:48.769 were distinct from the patterns of
- NOTE Confidence: 0.817463569444445
- $00{:}29{:}48.769 \dashrightarrow 00{:}29{:}50.419$  the antibodies that were found in
- NOTE Confidence: 0.817463569444445
- $00{:}29{:}50{.}419 \dashrightarrow 00{:}29{:}52{.}079$  the blood in the same patients.
- NOTE Confidence: 0.817463569444445
- $00{:}29{:}52.080 \dashrightarrow 00{:}29{:}53.079$  And in fact,
- NOTE Confidence: 0.817463569444445
- $00{:}29{:}53.079 \dashrightarrow 00{:}29{:}54.744$  when some of these antibodies
- NOTE Confidence: 0.817463569444445

 $00:29:54.744 \rightarrow 00:29:56.840$  remain into monoclonal antibodies,

NOTE Confidence: 0.817463569444445

 $00{:}29{:}56.840 \dashrightarrow 00{:}30{:}00{.}032$  they were found in a novel auto

NOTE Confidence: 0.817463569444445

 $00:30:00.032 \longrightarrow 00:30:02.047$  antibody discovery method to

NOTE Confidence: 0.817463569444445

 $00:30:02.047 \longrightarrow 00:30:03.727$  actually be autoreactive.

NOTE Confidence: 0.817463569444445

 $00{:}30{:}03{.}730 \dashrightarrow 00{:}30{:}04.969$  To brain tissue.

NOTE Confidence: 0.817463569444445

 $00{:}30{:}04{.}969 \dashrightarrow 00{:}30{:}07{.}458$  So these are again hints that

NOTE Confidence: 0.817463569444445

 $00:30:07.458 \longrightarrow 00:30:09.954$  not only is there a generalized

NOTE Confidence: 0.817463569444445

 $00:30:09.954 \rightarrow 00:30:11.890$  neuroinflammation and antibody formation,

NOTE Confidence: 0.817463569444445

 $00{:}30{:}11.890 \dashrightarrow 00{:}30{:}14.067$  but some of these antibodies that are

NOTE Confidence: 0.817463569444445

 $00:30:14.067 \rightarrow 00:30:15.988$  developing maybe in response to SARS,

NOTE Confidence: 0.817463569444445

 $00{:}30{:}15{.}990 \dashrightarrow 00{:}30{:}18{.}510$  Co V2 are actually auto reacting or

NOTE Confidence: 0.817463569444445

 $00{:}30{:}18{.}510 \dashrightarrow 00{:}30{:}20{.}019$  autoimmune antibodies that could

NOTE Confidence: 0.817463569444445

 $00:30:20.019 \dashrightarrow 00:30:21.859$  be attacking the nervous system.

NOTE Confidence: 0.863128735

 $00:30:24.060 \rightarrow 00:30:26.460$  So what have we learned from autopsy tissue?

NOTE Confidence: 0.863128735

 $00:30:26.460 \longrightarrow 00:30:28.140$  And I think that this is again,

NOTE Confidence: 0.863128735

 $00:30:28.140 \longrightarrow 00:30:29.376$  it's come out and fix and

- NOTE Confidence: 0.863128735
- $00:30:29.376 \longrightarrow 00:30:30.699$  starts over the last two years.
- NOTE Confidence: 0.863128735
- $00{:}30{:}30{.}700 \dashrightarrow 00{:}30{:}33{.}322$  Is these autopsy series looking at
- NOTE Confidence: 0.863128735
- 00:30:33.322 --> 00:30:36.350 people who died with acute COVID-19?
- NOTE Confidence: 0.863128735
- $00:30:36.350 \longrightarrow 00:30:37.122$  Always have of course,
- NOTE Confidence: 0.863128735
- $00:30:37.122 \longrightarrow 00:30:38.762$  all the caveats of the fact that they
- NOTE Confidence: 0.863128735
- $00:30:38.762 \rightarrow 00:30:40.070$  will affect people who have really,
- NOTE Confidence: 0.863128735
- $00:30:40.070 \rightarrow 00:30:43.269$  really severe disease who died from COVID.
- NOTE Confidence: 0.863128735
- $00:30:43.270 \longrightarrow 00:30:44.845$  And many of these people
- NOTE Confidence: 0.863128735
- $00{:}30{:}44.845 \dashrightarrow 00{:}30{:}46.105$  had prolonged ICU stays.
- NOTE Confidence: 0.863128735
- 00:30:46.110 --> 00:30:47.688 Many of them had, you know,
- NOTE Confidence: 0.863128735
- $00{:}30{:}47.690 \dashrightarrow 00{:}30{:}49.490$  hypertension, heart failure, hypoxemia,
- NOTE Confidence: 0.863128735
- $00{:}30{:}49{.}490 \dashrightarrow 00{:}30{:}52{.}830$  and you can see here for example.
- NOTE Confidence: 0.863128735
- $00:30:52.830 \longrightarrow 00:30:55.182$  This is a group of patients that
- NOTE Confidence: 0.863128735
- $00{:}30{:}55{.}182 \dashrightarrow 00{:}30{:}57{.}570$  were collected again at MGH.
- NOTE Confidence: 0.863128735
- $00:30:57.570 \longrightarrow 00:30:58.710$  18 people.
- NOTE Confidence: 0.863128735

 $00:30:58.710 \longrightarrow 00:31:01.629$  Most of these people did not have

NOTE Confidence: 0.863128735

 $00:31:01.629 \rightarrow 00:31:02.880$  significant neurological symptoms,

NOTE Confidence: 0.863128735

 $00:31:02.880 \longrightarrow 00:31:04.390$  but they, but they died.

NOTE Confidence: 0.863128735

 $00:31:04.390 \longrightarrow 00:31:06.160$  All of them had hypoxic ischemic

NOTE Confidence: 0.863128735

 $00{:}31{:}06{.}160 \dashrightarrow 00{:}31{:}07{.}340$  in jury in the brain.

NOTE Confidence: 0.863128735

 $00{:}31{:}07{.}340 \dashrightarrow 00{:}31{:}09{.}363$  But I think what's important in this

NOTE Confidence: 0.863128735

 $00{:}31{:}09{.}363 \dashrightarrow 00{:}31{:}11{.}805$  study is that this study was particularly

NOTE Confidence: 0.863128735

00:31:11.805 --> 00:31:13.700 looking for detection of virus,

NOTE Confidence: 0.863128735

 $00:31:13.700 \dashrightarrow 00:31:15.536$  and they did different methods of

NOTE Confidence: 0.863128735

 $00{:}31{:}15{.}536 \dashrightarrow 00{:}31{:}17{.}084$  detection trying to determine whether

NOTE Confidence: 0.863128735

 $00:31:17.084 \rightarrow 00:31:18.710$  or not there was actually SARS.

NOTE Confidence: 0.863128735

 $00{:}31{:}18{.}710 \dashrightarrow 00{:}31{:}20{.}775$  Kobe 2IN the brains of these people

NOTE Confidence: 0.863128735

 $00:31:20.775 \rightarrow 00:31:23.225$  who were very very severely ill with

NOTE Confidence: 0.863128735

00:31:23.225 --> 00:31:24.484 COVID-19 using immunohistochemistry.

NOTE Confidence: 0.863128735

00:31:24.484 --> 00:31:27.578 They did not detect virus in neurons,

NOTE Confidence: 0.863128735

 $00:31:27.580 \longrightarrow 00:31:28.504$  glial and ileum,

- NOTE Confidence: 0.863128735
- 00:31:28.504 --> 00:31:30.660 or immune cells in any structures of
- NOTE Confidence: 0.863128735
- $00:31:30.719 \rightarrow 00:31:33.430$  the brain. In any of these individuals.
- NOTE Confidence: 0.863128735
- $00{:}31{:}33{.}430 \dashrightarrow 00{:}31{:}36{.}182$  When they used PCR and looking just for
- NOTE Confidence: 0.863128735
- $00:31:36.182 \rightarrow 00:31:38.589$  fragments of the nucleocapsid protein,
- NOTE Confidence: 0.863128735
- $00{:}31{:}38{.}590 \dashrightarrow 00{:}31{:}40{.}186$  they did find positive findings in
- NOTE Confidence: 0.863128735
- $00{:}31{:}40{.}186 \dashrightarrow 00{:}31{:}42{.}293$  six of the 52 different blocks that
- NOTE Confidence: 0.863128735
- $00:31:42.293 \longrightarrow 00:31:44.582$  they looked at and sort of equivocal.
- NOTE Confidence: 0.863128735
- 00:31:44.590 --> 00:31:46.570 Very low, low level findings,
- NOTE Confidence: 0.863128735
- $00{:}31{:}46{.}570 \dashrightarrow 00{:}31{:}48{.}538$  and in some this is consistent
- NOTE Confidence: 0.863128735
- $00:31:48.538 \longrightarrow 00:31:49.522$  with other studies.
- NOTE Confidence: 0.863128735
- $00{:}31{:}49{.}530 \dashrightarrow 00{:}31{:}50{.}934$  There's also a really nice study
- NOTE Confidence: 0.863128735
- $00{:}31{:}50{.}934 \dashrightarrow 00{:}31{:}53{.}141$  out of the NIH that also looked at a
- NOTE Confidence: 0.863128735
- $00{:}31{:}53{.}141 \dashrightarrow 00{:}31{:}54{.}877$  number of people that again did not
- NOTE Confidence: 0.863128735
- $00:31:54.877 \dashrightarrow 00:31:58.470$  detect intact virus in any of the patients,
- NOTE Confidence: 0.863128735
- $00{:}31{:}58{.}470 \dashrightarrow 00{:}32{:}00{.}138$  so this would suggest again that
- NOTE Confidence: 0.863128735

00:32:00.138 --> 00:32:01.610 if you had replicating virus,

NOTE Confidence: 0.863128735

 $00:32:01.610 \longrightarrow 00:32:02.510$  typical viral encephalitis.

NOTE Confidence: 0.863128735

00:32:02.510 --> 00:32:04.610 You find a lot of intact virus,

NOTE Confidence: 0.863128735

 $00:32:04.610 \longrightarrow 00:32:06.540$  and that's not being found.

NOTE Confidence: 0.863128735

 $00{:}32{:}06{.}540 \dashrightarrow 00{:}32{:}08{.}724$  This is another study in another group.

NOTE Confidence: 0.863128735

 $00{:}32{:}08{.}730 \dashrightarrow 00{:}32{:}11.674$  This is a group out of Germany that

NOTE Confidence: 0.863128735

 $00:32:11.674 \rightarrow 00:32:13.841$  has published reports suggesting that

NOTE Confidence: 0.863128735

 $00:32:13.841 \rightarrow 00:32:17.600$  they can detect intact virus in some people,

NOTE Confidence: 0.863128735

 $00:32:17.600 \dashrightarrow 00:32:19.060$  but but what's really remarkable

NOTE Confidence: 0.863128735

 $00{:}32{:}19{.}060 \dashrightarrow 00{:}32{:}21{.}278$  about this study is the the wides pread

NOTE Confidence: 0.863128735

 $00{:}32{:}21.278 \dashrightarrow 00{:}32{:}23.714$  inflammation that was reported in this study.

NOTE Confidence: 0.863128735

 $00:32:23.720 \longrightarrow 00:32:24.492$  So again,

NOTE Confidence: 0.863128735

 $00{:}32{:}24.492 \dashrightarrow 00{:}32{:}27.194$  this is autopsy data from 43 patients.

NOTE Confidence: 0.863128735

 $00:32:27.200 \longrightarrow 00:32:29.876$  Each column in this figure is

NOTE Confidence: 0.863128735

 $00:32:29.876 \dashrightarrow 00:32:32.260$  showing you the the demographic

NOTE Confidence: 0.863128735

 $00:32:32.260 \dashrightarrow 00:32:34.860$  information for an individual donor

- NOTE Confidence: 0.863128735
- $00:32:34.860 \longrightarrow 00:32:37.750$  who died of acute COVID-19.
- NOTE Confidence: 0.863128735
- $00{:}32{:}37{.}750 \dashrightarrow 00{:}32{:}40{.}279$  And then you can see on the left the
- NOTE Confidence: 0.863128735
- $00:32:40.279 \rightarrow 00:32:42.197$  different brain regions that were
- NOTE Confidence: 0.863128735
- $00:32:42.197 \longrightarrow 00:32:44.275$  examined and what this large portion
- NOTE Confidence: 0.863128735
- $00{:}32{:}44.275 \dashrightarrow 00{:}32{:}46.893$  of the chart is showing is microglial
- NOTE Confidence: 0.863128735
- $00{:}32{:}46.893 \dashrightarrow 00{:}32{:}49.473$  activation wides pread in the brains of
- NOTE Confidence: 0.863128735
- $00:32:49.473 \rightarrow 00:32:52.187$  almost every single one of these donors?
- NOTE Confidence: 0.863128735
- $00:32:52.190 \dashrightarrow 00:32:53.738$  So microglial activation there
- NOTE Confidence: 0.863128735
- 00:32:53.738 --> 00:32:56.060 was also a very similar graph
- NOTE Confidence: 0.863128735
- $00:32:56.129 \dashrightarrow 00:32:58.306$  shown for CD8T cell infiltration.
- NOTE Confidence: 0.863128735
- 00:32:58.306 --> 00:32:59.370 Now again,
- NOTE Confidence: 0.863128735
- $00{:}32{:}59{.}370 \dashrightarrow 00{:}33{:}02{.}170$  in the setting of acute illness and death,
- NOTE Confidence: 0.863128735
- $00:33:02.170 \longrightarrow 00:33:04.006$  all sorts of hypoxic ischemic injury.
- NOTE Confidence: 0.863128735
- $00:33:04.010 \rightarrow 00:33:06.368$  Maybe we expect some microglial activation,
- NOTE Confidence: 0.863128735
- $00:33:06.370 \longrightarrow 00:33:07.660$  but this seemed to be to.
- NOTE Confidence: 0.863128735

 $00:33:07.660 \rightarrow 00:33:09.184$  This pathology group seem to be

NOTE Confidence: 0.863128735

 $00{:}33{:}09{.}184 \dashrightarrow 00{:}33{:}10.782$  way out of proportion to what

NOTE Confidence: 0.863128735

 $00:33:10.782 \longrightarrow 00:33:11.838$  they would have expected,

NOTE Confidence: 0.863128735

 $00{:}33{:}11{.}840 \dashrightarrow 00{:}33{:}14{.}328$  and compared to other types of donors who

NOTE Confidence: 0.863128735

 $00{:}33{:}14.328 \dashrightarrow 00{:}33{:}17.058$  also of course died with a cute illnesses

NOTE Confidence: 0.86507961826087

00:33:17.060 -> 00:33:18.350 and everything in this graph

NOTE Confidence: 0.86507961826087

 $00:33:18.350 \longrightarrow 00:33:20.678$  that is not blue is shown to be

NOTE Confidence: 0.86507961826087

 $00:33:20.678 \rightarrow 00:33:21.990$  abnormal microglial activation in

NOTE Confidence: 0.86507961826087

 $00{:}33{:}21{.}990 \dashrightarrow 00{:}33{:}23{.}780$  the bottom part of the figure.

NOTE Confidence: 0.86507961826087

 $00{:}33{:}23.780 \dashrightarrow 00{:}33{:}26.784$  I'm showing you in purple the few

NOTE Confidence: 0.86507961826087

 $00:33:26.784 \longrightarrow 00:33:28.596$  brains in which they could base.

NOTE Confidence: 0.86507961826087

 $00{:}33{:}28.600 \dashrightarrow 00{:}33{:}31.440$  They identified stars Kobe 2 RNA or in

NOTE Confidence: 0.86507961826087

 $00:33:31.440 \longrightarrow 00:33:34.576$  a few more brains of positive SARS.

NOTE Confidence: 0.86507961826087

 $00{:}33{:}34{.}580 \dashrightarrow 00{:}33{:}37{.}268$  Co V2 proteins such as nucleocapsid

NOTE Confidence: 0.86507961826087

 $00{:}33{:}37{.}268 \dashrightarrow 00{:}33{:}38{.}612$  or spike protein.

NOTE Confidence: 0.86507961826087

 $00:33:38.620 \dashrightarrow 00:33:40.360$  And what's really remarkable here

- NOTE Confidence: 0.86507961826087
- $00:33:40.360 \longrightarrow 00:33:42.934$  is that the high levels of neural
- NOTE Confidence: 0.86507961826087
- 00:33:42.934 --> 00:33:44.474 inflammation do not necessarily
- NOTE Confidence: 0.86507961826087
- $00:33:44.474 \rightarrow 00:33:46.466$  cluster only in those people
- NOTE Confidence: 0.86507961826087
- 00:33:46.466 00:33:48.030 who had detectable virus,
- NOTE Confidence: 0.86507961826087
- $00{:}33{:}48.030 \dashrightarrow 00{:}33{:}49.976$  but in fact is wides pread even in
- NOTE Confidence: 0.86507961826087
- $00:33:49.976 \longrightarrow 00:33:51.859$  people with no detectable virus.
- NOTE Confidence: 0.86507961826087
- $00:33:51.860 \rightarrow 00:33:54.668$  So again, what's been emerging is
- NOTE Confidence: 0.86507961826087
- $00:33:54.668 \dashrightarrow 00:33:56.540$  high levels of neuroinflammation.
- NOTE Confidence: 0.86507961826087
- $00{:}33{:}56{.}540 \dashrightarrow 00{:}33{:}59{.}557$  In the absence of major viral replication.
- NOTE Confidence: 0.86507961826087
- $00:33:59.560 \longrightarrow 00:34:00.918$  And this is one more study that
- NOTE Confidence: 0.86507961826087
- 00:34:00.918 --> 00:34:01.500 I just revealed.
- NOTE Confidence: 0.86507961826087
- $00{:}34{:}01{.}500 \dashrightarrow 00{:}34{:}02{.}412$  One more thing,
- NOTE Confidence: 0.86507961826087
- $00{:}34{:}02{.}412 \dashrightarrow 00{:}34{:}04{.}236$  I think that's truly important about
- NOTE Confidence: 0.86507961826087
- $00:34:04.236 \longrightarrow 00:34:06.058$  the neuropathology of COVID-19.
- NOTE Confidence: 0.86507961826087
- 00:34:06.060 --> 00:34:07.676 Again, an autopsy study.
- NOTE Confidence: 0.86507961826087

 $00:34:07.676 \rightarrow 00:34:11.139$  Many of these people died with sudden death,

NOTE Confidence: 0.86507961826087

 $00{:}34{:}11{.}140 \dashrightarrow 00{:}34{:}13{.}492$  so they were cases of people

NOTE Confidence: 0.86507961826087

 $00:34:13.492 \longrightarrow 00:34:15.060$  who were corner cases,

NOTE Confidence: 0.86507961826087

 $00:34:15.060 \rightarrow 00:34:18.730$  so they weren't necessarily hospitalized.

NOTE Confidence: 0.86507961826087

 $00{:}34{:}18.730 \dashrightarrow 00{:}34{:}22.032$  These individuals did not have any other

NOTE Confidence: 0.86507961826087

 $00{:}34{:}22.032 \dashrightarrow 00{:}34{:}23.837$  kind of major respiratory findings.

NOTE Confidence: 0.86507961826087

00:34:23.840 --> 00:34:27.263 They did not have any overt strokes,

NOTE Confidence: 0.86507961826087

 $00{:}34{:}27{.}263 \dashrightarrow 00{:}34{:}29{.}849$  but when brain tissue from these

NOTE Confidence: 0.86507961826087

 $00{:}34{:}29{.}849 \dashrightarrow 00{:}34{:}31{.}954$  individuals was examined both by

NOTE Confidence: 0.86507961826087

 $00:34:31.954 \rightarrow 00:34:34.306$  11 Tesla and Mirai autopsy tissue,

NOTE Confidence: 0.86507961826087

 $00{:}34{:}34{.}310 \dashrightarrow 00{:}34{:}37{.}250$  as well as by histopathologic examination.

NOTE Confidence: 0.86507961826087

00:34:37.250 --> 00:34:40.386 They were found to have microvascular injury,

NOTE Confidence: 0.86507961826087

 $00:34:40.390 \longrightarrow 00:34:43.575$  so if fibringen leakage from

NOTE Confidence: 0.86507961826087

 $00{:}34{:}43{.}575 \dashrightarrow 00{:}34{:}45{.}486$  blood vessels microhemorrhages.

NOTE Confidence: 0.86507961826087

 $00:34:45.490 \rightarrow 00:34:47.910$  And large collections of perivascular

NOTE Confidence: 0.86507961826087

 $00:34:47.910 \rightarrow 00:34:51.503$  macrophages so the hint here was that

- NOTE Confidence: 0.86507961826087
- $00:34:51.503 \rightarrow 00:34:54.730$  even in people who don't have overt strokes,
- NOTE Confidence: 0.86507961826087
- $00:34:54.730 \longrightarrow 00:34:56.110$  microvascular injury microvascular
- NOTE Confidence: 0.86507961826087
- $00:34:56.110 \rightarrow 00:34:59.330$  changes may be also underlying some of
- NOTE Confidence: 0.86507961826087
- $00:34:59.393 \rightarrow 00:35:01.811$  the neurologic types of consequences that
- NOTE Confidence: 0.86507961826087
- $00:35:01.811 \rightarrow 00:35:04.750$  we're seeing in people with acute COVID-19.
- NOTE Confidence: 0.86507961826087
- $00:35:04.750 \dashrightarrow 00:35:05.025$  Again,
- NOTE Confidence: 0.86507961826087
- 00:35:05.025 --> 00:35:06.675 this study did not detect SARS
- NOTE Confidence: 0.86507961826087
- 00:35:06.675 --> 00:35:08.849 Co V2 in any of their brains
- NOTE Confidence: 0.86507961826087
- $00{:}35{:}08{.}849 \dashrightarrow 00{:}35{:}10{.}781$  segments looked at and this group.
- NOTE Confidence: 0.86507961826087
- $00:35:10.790 \longrightarrow 00:35:13.002$  This is from a group of based
- NOTE Confidence: 0.86507961826087
- 00:35:13.002 --> 00:35:13.950 primarily at NIH.
- NOTE Confidence: 0.86507961826087
- $00{:}35{:}13.950 \dashrightarrow 00{:}35{:}16.278$  They continue to do studies and do not.
- NOTE Confidence: 0.86507961826087
- $00{:}35{:}16.280 \dashrightarrow 00{:}35{:}18.770$  Find any virus in the brain.
- NOTE Confidence: 0.86507961826087
- 00:35:18.770 $\operatorname{-->}$ 00:35:21.137 So I I think the final thing to talk
- NOTE Confidence: 0.86507961826087
- $00:35:21.137 \longrightarrow 00:35:23.531$  about in terms of pathology are some
- NOTE Confidence: 0.86507961826087

 $00:35:23.531 \rightarrow 00:35:25.480$  of these neuronal injury markers.

NOTE Confidence: 0.86507961826087

 $00{:}35{:}25{.}480 \dashrightarrow 00{:}35{:}27{.}840$  So I mentioned neuroinflammation.

NOTE Confidence: 0.86507961826087

 $00{:}35{:}27.840 \dashrightarrow 00{:}35{:}30.290$  I mentioned the fact that there doesn't

NOTE Confidence: 0.86507961826087

 $00:35:30.290 \rightarrow 00:35:32.210$  seem to be robust active replication,

NOTE Confidence: 0.86507961826087

 $00:35:32.210 \rightarrow 00:35:34.910$  but there may be microvascular injury,

NOTE Confidence: 0.86507961826087

 $00:35:34.910 \rightarrow 00:35:37.022$  but is there actually brain injury

NOTE Confidence: 0.86507961826087

 $00:35:37.022 \rightarrow 00:35:39.209$  in these patients during acute COVID?

NOTE Confidence: 0.86507961826087

 $00:35:39.210 \longrightarrow 00:35:40.302$  And this is a little bit of

NOTE Confidence: 0.86507961826087

 $00{:}35{:}40{.}302 \dashrightarrow 00{:}35{:}41{.}609$  a of a concerning study,

NOTE Confidence: 0.86507961826087

 $00{:}35{:}41.610 \dashrightarrow 00{:}35{:}43.794$  I think we have a lot more information

NOTE Confidence: 0.86507961826087

 $00:35:43.794 \rightarrow 00:35:45.469$  that we need to look into,

NOTE Confidence: 0.86507961826087

00:35:45.470 -> 00:35:48.046 but this is a group that had large

NOTE Confidence: 0.86507961826087

00:35:48.046 --> 00:35:50.919 numbers of people who had acute COVID-19.

NOTE Confidence: 0.86507961826087

 $00:35:50.920 \dashrightarrow 00:35:53.797$  So 246 people who were hospitalized with

NOTE Confidence: 0.86507961826087

 $00{:}35{:}53.797 \dashrightarrow 00{:}35{:}56.748$  acute COVID-19 this is from NYU in New York.

NOTE Confidence: 0.86507961826087

 $00:35:56.750 \dashrightarrow 00:35:59.042$  And samples were collected from the

- NOTE Confidence: 0.86507961826087
- $00{:}35{:}59{.}042 \dashrightarrow 00{:}36{:}01{.}386$  blood for these individuals and then
- NOTE Confidence: 0.86507961826087
- $00:36:01.386 \rightarrow 00:36:03.266$  highly sensitive assays were used
- NOTE Confidence: 0.86507961826087
- $00:36:03.266 \rightarrow 00:36:05.170$  to measure neuronal injury markers
- NOTE Confidence: 0.86507961826087
- $00:36:05.170 \longrightarrow 00:36:07.306$  that are leaking into the blood.
- NOTE Confidence: 0.86507961826087
- $00{:}36{:}07{.}310 \dashrightarrow 00{:}36{:}08{.}590$  So these include neurofilament
- NOTE Confidence: 0.86507961826087
- $00:36:08.590 \longrightarrow 00:36:09.550$  light chain was,
- NOTE Confidence: 0.86507961826087
- $00:36:09.550 \rightarrow 00:36:11.608$  which is a biomarker of axonal injury.
- NOTE Confidence: 0.86507961826087
- 00:36:11.610 --> 00:36:13.030 Glial fibrillary acid protein,
- NOTE Confidence: 0.86507961826087
- $00:36:13.030 \longrightarrow 00:36:15.160$  which is a marker of astrocyte
- NOTE Confidence: 0.86507961826087
- 00:36:15.221 --> 00:36:17.946 injury and ECHL one which is also
- NOTE Confidence: 0.86507961826087
- $00:36:17.946 \longrightarrow 00:36:20.200$  a neuron specific protein and what
- NOTE Confidence: 0.86507961826087
- $00{:}36{:}20{.}200 \dashrightarrow 00{:}36{:}22{.}545$  this group found was that NFL and
- NOTE Confidence: 0.86507961826087
- $00{:}36{:}22{.}545 \dashrightarrow 00{:}36{:}25{.}191$  GF AP were quite elevated in the
- NOTE Confidence: 0.86507961826087
- $00{:}36{:}25{.}191 \dashrightarrow 00{:}36{:}26{.}679$  blood in these acute
- NOTE Confidence: 0.786990786590909
- $00:36:26.762 \longrightarrow 00:36:27.880$  COVID patients.
- NOTE Confidence: 0.786990786590909

 $00:36:27.880 \rightarrow 00:36:29.915$  These were not necessarily people

NOTE Confidence: 0.786990786590909

 $00{:}36{:}29{.}915 \dashrightarrow 00{:}36{:}31{.}543$  who had neurologic conditions,

NOTE Confidence: 0.786990786590909

 $00{:}36{:}31{.}550 \dashrightarrow 00{:}36{:}34{.}274$  they just took all comers and what

NOTE Confidence: 0.786990786590909

 $00:36:34.274 \rightarrow 00:36:36.259$  was interesting was that these

NOTE Confidence: 0.786990786590909

 $00{:}36{:}36{.}259 \dashrightarrow 00{:}36{:}38{.}474$  measures were actually quite a bit

NOTE Confidence: 0.786990786590909

 $00{:}36{:}38{.}474 \dashrightarrow 00{:}36{:}40{.}394$  higher than even those found in

NOTE Confidence: 0.786990786590909

 $00:36:40.394 \rightarrow 00:36:42.378$  people with Alzheimer's disease.

NOTE Confidence: 0.786990786590909

 $00:36:42.380 \longrightarrow 00:36:43.985$  So again, what the implications

NOTE Confidence: 0.786990786590909

 $00:36:43.985 \longrightarrow 00:36:46.077$  of this might be for people

NOTE Confidence: 0.786990786590909

00:36:46.077 --> 00:36:47.757 who survive acute COVID-19,

NOTE Confidence: 0.786990786590909

 $00:36:47.760 \longrightarrow 00:36:49.538$  I think is a really important question,

NOTE Confidence: 0.786990786590909

00:36:49.540 --> 00:36:51.880 but it's a really clinically unknown

NOTE Confidence: 0.786990786590909

 $00{:}36{:}51.880 \dashrightarrow 00{:}36{:}54.064$  and I will say that during acute

NOTE Confidence: 0.786990786590909

 $00{:}36{:}54.064 \dashrightarrow 00{:}36{:}56.067$  HIV infection we also see elevations

NOTE Confidence: 0.786990786590909

 $00:36:56.067 \rightarrow 00:36:58.150$  of things like NFL and GFAP.

NOTE Confidence: 0.786990786590909

00:36:58.150 - > 00:37:00.610 Ubiquitously in people who do not
- NOTE Confidence: 0.786990786590909
- 00:37:00.610 00:37:02.540 have any neurologic symptoms,
- NOTE Confidence: 0.786990786590909
- $00{:}37{:}02.540 \dashrightarrow 00{:}37{:}04.238$  and we haven't seen an avalanche
- NOTE Confidence: 0.786990786590909
- $00{:}37{:}04{.}238 \dashrightarrow 00{:}37{:}05{.}799$  of things of nerve degenerative
- NOTE Confidence: 0.786990786590909
- $00{:}37{:}05{.}799 \dashrightarrow 00{:}37{:}07{.}634$  disease such as Alzheimer's and
- NOTE Confidence: 0.786990786590909
- $00:37:07.634 \rightarrow 00:37:09.880$  people who've had HIV for 40 years,
- NOTE Confidence: 0.786990786590909
- $00{:}37{:}09{.}880 \dashrightarrow 00{:}37{:}11{.}512$  so I think what this means
- NOTE Confidence: 0.786990786590909
- $00:37:11.512 \rightarrow 00:37:12.600$  clinically is is unclear,
- NOTE Confidence: 0.786990786590909
- $00:37:12.600 \longrightarrow 00:37:14.592$  but it does suggest that there's
- NOTE Confidence: 0.786990786590909
- $00:37:14.592 \rightarrow 00:37:15.920$  some neuronal injury during
- NOTE Confidence: 0.786990786590909
- $00:37:15.983 \longrightarrow 00:37:17.478$  the time of acute COVID-19.
- NOTE Confidence: 0.786990786590909
- $00:37:17.480 \dashrightarrow 00:37:20.048$  So all of this leads to this sort
- NOTE Confidence: 0.786990786590909
- $00{:}37{:}20.048 \dashrightarrow 00{:}37{:}22.500$  of very oversimplified figure,
- NOTE Confidence: 0.786990786590909
- $00:37:22.500 \rightarrow 00:37:24.124$  which is actually a beautiful figure put
- NOTE Confidence: 0.786990786590909
- $00{:}37{:}24.124 \dashrightarrow 00{:}37{:}27.340$  together by the science illustrators.
- NOTE Confidence: 0.786990786590909
- $00:37:27.340 \rightarrow 00:37:27.740$  That summarizes,
- NOTE Confidence: 0.786990786590909

 $00:37:27.740 \longrightarrow 00:37:29.340$  I think what I've told you so far,

NOTE Confidence: 0.786990786590909

 $00{:}37{:}29{.}340 \dashrightarrow 00{:}37{:}31{.}244$  so we think in the upper left that

NOTE Confidence: 0.786990786590909

 $00:37:31.244 \rightarrow 00:37:32.771$  there's really generalized inflammation

NOTE Confidence: 0.786990786590909

 $00:37:32.771 \rightarrow 00:37:34.775$  and generalizing neural inflammation.

NOTE Confidence: 0.786990786590909

 $00{:}37{:}34.780 \dashrightarrow 00{:}37{:}36.108$  Immune cells,

NOTE Confidence: 0.786990786590909

 $00:37:36.108 \rightarrow 00:37:39.060$  including monocytes and CD8T cells and CD.

NOTE Confidence: 0.786990786590909

00:37:39.060 --> 00:37:39.540 Four cells,

NOTE Confidence: 0.786990786590909

 $00:37:39.540 \rightarrow 00:37:42.498$  probably traffic into the nervous system.

NOTE Confidence: 0.786990786590909

 $00:37:42.500 \longrightarrow 00:37:43.545$  You don't necessarily have to

NOTE Confidence: 0.786990786590909

 $00{:}37{:}43.545 \dashrightarrow 00{:}37{:}44.932$  have a broken down blood brain

NOTE Confidence: 0.786990786590909

00:37:44.932 --> 00:37:46.140 barrier for cellular trafficking,

NOTE Confidence: 0.786990786590909

00:37:46.140 --> 00:37:46.616 of course,

NOTE Confidence: 0.786990786590909

 $00:37:46.616 \longrightarrow 00:37:48.282$  but there may be some blood brain

NOTE Confidence: 0.786990786590909

 $00:37:48.282 \rightarrow 00:37:49.259$  barrier injury as well,

NOTE Confidence: 0.786990786590909

 $00:37:49.260 \rightarrow 00:37:51.120$  and then cytokines and antibodies

NOTE Confidence: 0.786990786590909

 $00:37:51.120 \longrightarrow 00:37:53.724$  also seem to be diffusing into the

- NOTE Confidence: 0.786990786590909
- $00:37:53.724 \rightarrow 00:37:55.758$  nervous system and into the brain.
- NOTE Confidence: 0.786990786590909
- $00:37:55.760 \rightarrow 00:37:57.870$  There is also antibody production.
- NOTE Confidence: 0.786990786590909
- $00{:}37{:}57{.}870 \dashrightarrow 00{:}37{:}59{.}338$  Which may be exacerbating
- NOTE Confidence: 0.786990786590909
- $00:37:59.338 \longrightarrow 00:38:00.439$  the nerve inflammation,
- NOTE Confidence: 0.786990786590909
- $00:38:00.440 \longrightarrow 00:38:02.150$  and there seems to be production
- NOTE Confidence: 0.786990786590909
- 00:38:02.150 --> 00:38:03.610 of antibodies both to SARS,
- NOTE Confidence: 0.786990786590909
- $00{:}38{:}03{.}610 \dashrightarrow 00{:}38{:}06{.}133$  Co V2 that are entering the brain and
- NOTE Confidence: 0.786990786590909
- $00:38:06.133 \rightarrow 00:38:07.548$  persisting potentially in the brain,
- NOTE Confidence: 0.786990786590909
- $00{:}38{:}07{.}550 \dashrightarrow 00{:}38{:}09{.}034$  and then also autoantibodies.
- NOTE Confidence: 0.786990786590909
- 00:38:09.034 --> 00:38:10.518 There's limited presence of
- NOTE Confidence: 0.786990786590909
- $00:38:10.518 \longrightarrow 00:38:12.501$  the viral proteins or a viral
- NOTE Confidence: 0.786990786590909
- $00{:}38{:}12{.}501 \dashrightarrow 00{:}38{:}14{.}265$  particles in the neurons based on
- NOTE Confidence: 0.786990786590909
- $00:38:14.323 \rightarrow 00:38:16.208$  all the current detection methods,
- NOTE Confidence: 0.786990786590909
- $00{:}38{:}16{.}210 \dashrightarrow 00{:}38{:}17{.}848$  although you know more research has
- NOTE Confidence: 0.786990786590909
- $00{:}38{:}17{.}848 \dashrightarrow 00{:}38{:}20{.}080$  to be done and there seems to be at
- NOTE Confidence: 0.786990786590909

 $00:38:20.080 \rightarrow 00:38:22.199$  least some level of microvascular injury.

NOTE Confidence: 0.786990786590909

00:38:22.200 --> 00:38:23.844 Some of this may be related

NOTE Confidence: 0.786990786590909

00:38:23.844 --> 00:38:24.666 to endothelial injury,

NOTE Confidence: 0.786990786590909

 $00:38:24.670 \rightarrow 00:38:27.248$  some of it's related to micro clotting.

NOTE Confidence: 0.786990786590909

 $00:38:27.248 \longrightarrow 00:38:29.462$  And some of this may also

NOTE Confidence: 0.786990786590909

 $00{:}38{:}29{.}462 \dashrightarrow 00{:}38{:}30{.}810$  be underlying disease.

NOTE Confidence: 0.786990786590909

 $00:38:30.810 \rightarrow 00:38:32.784$  Which of these mechanisms are primarily

NOTE Confidence: 0.786990786590909

 $00:38:32.784 \rightarrow 00:38:35.198$  leading to the signs of neuronal injury?

NOTE Confidence: 0.786990786590909

 $00{:}38{:}35{.}200 \dashrightarrow 00{:}38{:}37{.}250$  I think are not certain.

NOTE Confidence: 0.786990786590909

 $00:38:37.250 \longrightarrow 00:38:38.834$  But I think that it's important

NOTE Confidence: 0.786990786590909

 $00{:}38{:}38{.}834 \dashrightarrow 00{:}38{:}40{.}654$  to think that there are also

NOTE Confidence: 0.786990786590909

 $00:38:40.654 \rightarrow 00:38:42.429$  susceptibility factors such as genetic,

NOTE Confidence: 0.786990786590909

 $00:38:42.430 \dashrightarrow 00:38:43.502$  pre-existing comorbidities,

NOTE Confidence: 0.786990786590909

 $00:38:43.502 \rightarrow 00:38:47.254$  and immune status that may be contributing.

NOTE Confidence: 0.786990786590909

 $00{:}38{:}47{.}260 \dashrightarrow 00{:}38{:}49{.}618$  So I'm gonna spend the rest

NOTE Confidence: 0.786990786590909

 $00:38:49.618 \rightarrow 00:38:52.239$  of my talk really focused on.

- NOTE Confidence: 0.786990786590909
- 00:38:52.240 --> 00:38:53.740 The mystery of long COVID,
- NOTE Confidence: 0.786990786590909
- $00:38:53.740 \rightarrow 00:38:55.476$  and I suspect that for most people,
- NOTE Confidence: 0.786990786590909
- $00:38:55.480 \longrightarrow 00:38:56.746$  this is the part that they
- NOTE Confidence: 0.786990786590909
- $00:38:56.746 \rightarrow 00:38:57.900$  really have heard less about,
- NOTE Confidence: 0.786990786590909
- $00:38:57.900 \dashrightarrow 00:38:59.860$  and I'm I'm hoping that to show a
- NOTE Confidence: 0.786990786590909
- $00:38:59.860 \longrightarrow 00:39:01.748$  little bit of light on this so very
- NOTE Confidence: 0.786990786590909
- $00:39:01.748 \longrightarrow 00:39:03.398$  early on in the pandemic there's
- NOTE Confidence: 0.786990786590909
- $00:39:03.398 \dashrightarrow 00:39:05.504$  there was some kind of popular
- NOTE Confidence: 0.786990786590909
- 00:39:05.504 --> 00:39:07.116 press reporting of people saying,
- NOTE Confidence: 0.786990786590909
- 00:39:07.116 --> 00:39:07.720 you know,
- NOTE Confidence: 0.786990786590909
- $00:39:07.720 \rightarrow 00:39:09.918$  I really am having trouble with this
- NOTE Confidence: 0.786990786590909
- $00{:}39{:}09{.}918 \dashrightarrow 00{:}39{:}11.868$  feeling that I have dementia and
- NOTE Confidence: 0.786990786590909
- $00:39:11.868 \longrightarrow 00:39:14.066$  this term brain fog has come out.
- NOTE Confidence: 0.786990786590909
- $00:39{:}14.070 \dashrightarrow 00{:}39{:}15.850$  There's also being more scientific
- NOTE Confidence: 0.786990786590909
- $00:39:15.850 \rightarrow 00:39:17.630$  reports talking about these issues,
- NOTE Confidence: 0.899939165

 $00:39:17.630 \rightarrow 00:39:20.926$  and now it's really emerged that there are

NOTE Confidence: 0.899939165

 $00{:}39{:}20{.}926 \dashrightarrow 00{:}39{:}23{.}607$  persistent issues relating to mental health.

NOTE Confidence: 0.899939165

 $00:39:23.610 \dashrightarrow 00:39:26.082$  Affective disorders psychiatric

NOTE Confidence: 0.899939165

 $00:39:26.082 \rightarrow 00:39:28.287$  psychosis disorders, cardiovascular,

NOTE Confidence: 0.899939165

 $00{:}39{:}28{.}287 \dashrightarrow 00{:}39{:}31{.}629$  etc that are really persisting after

NOTE Confidence: 0.899939165

 $00:39:31.629 \dashrightarrow 00:39:34.566$  COVID-19 and so really what we have.

NOTE Confidence: 0.899939165

 $00{:}39{:}34{.}570 \dashrightarrow 00{:}39{:}37{.}261$  What we have done is again as I mentioned

NOTE Confidence: 0.899939165

 $00:39:37.261 \rightarrow 00:39:39.983$  for the first wave we initially have

NOTE Confidence: 0.899939165

 $00{:}39{:}39{.}983 \dashrightarrow 00{:}39{:}42{.}448$  learned about this through a clinical

NOTE Confidence: 0.899939165

 $00:39:42.448 \rightarrow 00:39:44.920$  response and along with a really

NOTE Confidence: 0.899939165

 $00:39{:}44.920 \dashrightarrow 00{:}39{:}46.688$  fantastic partners associated with

NOTE Confidence: 0.899939165

 $00:39:46.688 \rightarrow 00:39:48.564$  running this multidisciplinary COVID-19

NOTE Confidence: 0.899939165

 $00:39{:}48.564 \dashrightarrow 00{:}39{:}50.936$  recovery clinic which is directed

NOTE Confidence: 0.899939165

00:39:50.936 --> 00:39:53.086 by Jennifer Plastics and pulmonary.

NOTE Confidence: 0.899939165

00:39:53.090 --> 00:39:55.578 And colleagues and psychiatry,

NOTE Confidence: 0.899939165

00:39:55.578 --> 00:39:58.688 Dr Klingensmith and Doctor Fisher.

- NOTE Confidence: 0.899939165
- $00:39:58.690 \rightarrow 00:40:00.652$  We have been involved in seeing
- NOTE Confidence: 0.899939165
- 00:40:00.652 --> 00:40:02.420 people who have recovered from
- NOTE Confidence: 0.899939165
- $00{:}40{:}02{.}420 \dashrightarrow 00{:}40{:}04{.}425$  COVID-19 but have lingering symptoms,
- NOTE Confidence: 0.899939165
- $00:40:04.430 \longrightarrow 00:40:06.110$  and by October 2020 it became
- NOTE Confidence: 0.899939165
- $00:40:06.110 \longrightarrow 00:40:08.266$  clear that there was really a large
- NOTE Confidence: 0.899939165
- 00:40:08.266 --> 00:40:10.216 demand for people who are having
- NOTE Confidence: 0.899939165
- 00:40:10.216 --> 00:40:11.610 persistent neurologic issues,
- NOTE Confidence: 0.899939165
- $00:40:11.610 \rightarrow 00:40:13.650$  and so again with my wonderful
- NOTE Confidence: 0.899939165
- 00:40:13.650 --> 00:40:15.010 fellow stone Lindsay Farhadian.
- NOTE Confidence: 0.899939165
- $00{:}40{:}15.010 \dashrightarrow 00{:}40{:}17.845$  I'm let Lindsey and McAlpine began
- NOTE Confidence: 0.899939165
- $00:40:17.845 \longrightarrow 00:40:19.855$  to run this clinic that's focused
- NOTE Confidence: 0.899939165
- 00:40:19.855 --> 00:40:22.082 on these disorders and what you can
- NOTE Confidence: 0.899939165
- $00:40:22.082 \rightarrow 00:40:23.816$  see here are the chief complaints
- NOTE Confidence: 0.899939165
- $00:40:23.878 \longrightarrow 00:40:26.065$  of the people who the 1st 300 or so
- NOTE Confidence: 0.899939165
- 00:40:26.065 -> 00:40:28.330 people who came into our clinic.
- NOTE Confidence: 0.899939165

 $00:40:28.330 \longrightarrow 00:40:29.802$  Again, there's a separate.

NOTE Confidence: 0.899939165

00:40:29.802 --> 00:40:30.906 Psychiatry referral clinics.

NOTE Confidence: 0.899939165

00:40:30.910 --> 00:40:32.692 So we were not primarily seeing

NOTE Confidence: 0.899939165

 $00:40:32.692 \rightarrow 00:40:34.779$  people who are having severe anxiety,

NOTE Confidence: 0.899939165

00:40:34.780 --> 00:40:36.226 depression, PTSD, psychosis.

NOTE Confidence: 0.899939165

 $00:40:36.226 \longrightarrow 00:40:38.859$  These kinds of things so you can

NOTE Confidence: 0.899939165

 $00:40:38.859 \longrightarrow 00:40:40.584$  see that 60% of these people are

NOTE Confidence: 0.899939165

 $00:40:40.584 \rightarrow 00:40:41.864$  coming in with cognitive impairment,

NOTE Confidence: 0.899939165

 $00{:}40{:}41.870 \dashrightarrow 00{:}40{:}43.962$  others with neuromuscular complaints

NOTE Confidence: 0.899939165

 $00:40:43.962 \longrightarrow 00:40:45.008$  and headache.

NOTE Confidence: 0.899939165

 $00{:}40{:}45{.}010 \dashrightarrow 00{:}40{:}46{.}570$  And a few things have emerged

NOTE Confidence: 0.899939165

 $00{:}40{:}46{.}570 \dashrightarrow 00{:}40{:}47{.}610$  that have been interesting.

NOTE Confidence: 0.899939165

00:40:47.610 --> 00:40:49.014 First of all, surprisingly,

NOTE Confidence: 0.899939165

 $00:40:49.014 \longrightarrow 00:40:50.067$  in the clinic,

NOTE Confidence: 0.899939165

 $00{:}40{:}50{.}070 \dashrightarrow 00{:}40{:}52{.}770$  the median age is less than 50 years old.

NOTE Confidence: 0.899939165

 $00:40:52.770 \rightarrow 00:40:54.930$  So rather than what we might have expected,

- NOTE Confidence: 0.899939165
- $00:40:54.930 \longrightarrow 00:40:57.142$  which is people who would have the
- NOTE Confidence: 0.899939165
- $00{:}40{:}57.142 \dashrightarrow 00{:}40{:}59.340$  most severe course of acute COVID-19
- NOTE Confidence: 0.899939165
- 00:40:59.340 --> 00:41:01.310 like being hospitalized had had
- NOTE Confidence: 0.899939165
- $00:41:01.310 \longrightarrow 00:41:03.165$  prolonged severe illness related to
- NOTE Confidence: 0.899939165
- 00:41:03.165 --> 00:41:05.169 their risk factors of being older
- NOTE Confidence: 0.899939165
- $00:41:05.169 \rightarrow 00:41:07.420$  and having a lot of comorbidities,
- NOTE Confidence: 0.899939165
- $00:41:07.420 \longrightarrow 00:41:09.516$  we were actually seeing a lot of people
- NOTE Confidence: 0.899939165
- 00:41:09.516 --> 00:41:11.330 who were young and the other really
- NOTE Confidence: 0.899939165
- 00:41:11.330 --> 00:41:12.530 remarkable finding in this clinic,
- NOTE Confidence: 0.899939165
- $00:41:12.530 \rightarrow 00:41:14.185$  and this is completely echoing
- NOTE Confidence: 0.899939165
- $00:41:14.185 \longrightarrow 00:41:15.178$  what's being found.
- NOTE Confidence: 0.899939165
- $00{:}41{:}15{.}180 \dashrightarrow 00{:}41{:}17{.}646$  Worldwide and people who are presenting
- NOTE Confidence: 0.899939165
- 00:41:17.646 --> 00:41:19.830 lingering symptoms after COVID.
- NOTE Confidence: 0.899939165
- $00{:}41{:}19{.}830 \dashrightarrow 00{:}41{:}21{.}447$  Is that the vast majority of people
- NOTE Confidence: 0.899939165
- $00{:}41{:}21{.}447 \dashrightarrow 00{:}41{:}23.057$  who are coming into our clinic
- NOTE Confidence: 0.899939165

- $00:41:23.057 \rightarrow 00:41:24.217$  now with lingering symptoms,
- NOTE Confidence: 0.899939165
- $00{:}41{:}24{.}220 \dashrightarrow 00{:}41{:}25{.}999$  were never hospitalized.
- NOTE Confidence: 0.899939165
- $00:41:25.999 \longrightarrow 00:41:29.780$  So while 19% did have ICU admission,
- NOTE Confidence: 0.899939165
- $00:41:29.780 \longrightarrow 00:41:33.130$  67% of people completely convalesced at home,
- NOTE Confidence: 0.899939165
- $00:41:33.130 \rightarrow 00:41:36.378$  reflecting the fact that they had mild COVID.
- NOTE Confidence: 0.899939165
- $00:41:36.380 \longrightarrow 00:41:39.120$  So what does that mean?
- NOTE Confidence: 0.899939165
- $00:41:39.120 \longrightarrow 00:41:40.160$  What are some of the?
- NOTE Confidence: 0.899939165
- $00:41:40.160 \longrightarrow 00:41:41.959$  What are some of the stories that
- NOTE Confidence: 0.899939165
- $00:41:41.959 \longrightarrow 00:41:43.310$  we had with patients?
- NOTE Confidence: 0.899939165
- $00:41:43.310 \rightarrow 00:41:45.776$  Well, here are just some examples.
- NOTE Confidence: 0.899939165
- $00:41:45.780 \longrightarrow 00:41:47.341$  So one of the types of syndromes
- NOTE Confidence: 0.899939165
- $00:41:47.341 \longrightarrow 00:41:48.952$  that we've seen are people who
- NOTE Confidence: 0.899939165
- $00:41:48.952 \rightarrow 00:41:50.144$  are having cognitive problems,
- NOTE Confidence: 0.899939165
- $00{:}41{:}50{.}150 \dashrightarrow 00{:}41{:}53{.}238$  and this is an example of a patient.
- NOTE Confidence: 0.899939165
- $00:41:53.240 \rightarrow 00:41:55.712$  They they presented to us saying that they
- NOTE Confidence: 0.899939165
- $00:41:55.712 \rightarrow 00:41:57.879$  were having trouble remembering tasks,

- NOTE Confidence: 0.899939165
- $00:41:57.880 \rightarrow 00:41:59.664$  conversations needing a notepad
- NOTE Confidence: 0.899939165
- $00{:}41{:}59.664 \dashrightarrow 00{:}42{:}02.340$  to write things down during calls,
- NOTE Confidence: 0.899939165
- $00:42:02.340 \rightarrow 00:42:03.488$  writing emails and correspondence,
- NOTE Confidence: 0.899939165
- $00:42:03.488 \rightarrow 00:42:05.900$  taking two to three times as long as usual,
- NOTE Confidence: 0.899939165
- $00:42:05.900 \rightarrow 00:42:07.216$  and one of the things that brought
- NOTE Confidence: 0.899939165
- $00{:}42{:}07{.}216 \dashrightarrow 00{:}42{:}08{.}100$  them into our clinic.
- NOTE Confidence: 0.899939165
- $00:42:08.100 \longrightarrow 00:42:09.666$  Finally is that they were unable
- NOTE Confidence: 0.899939165
- $00:42:09.666 \rightarrow 00:42:11.480$  to follow a recipe to bake bread,
- NOTE Confidence: 0.899939165
- $00{:}42{:}11{.}480 \dashrightarrow 00{:}42{:}13{.}736$  and this is a physician who of course
- NOTE Confidence: 0.899939165
- 00:42:13.736 --> 00:42:16.137 you know all of these things would
- NOTE Confidence: 0.899939165
- $00:42:16.137 \rightarrow 00:42:17.912$  be second nature and unthinkable
- NOTE Confidence: 0.824273793181818
- $00{:}42{:}17.980 \dashrightarrow 00{:}42{:}19.896$  before COVID-19 another patient reflected
- NOTE Confidence: 0.824273793181818
- $00{:}42{:}19.896 \dashrightarrow 00{:}42{:}21.888$  sort of another category of people
- NOTE Confidence: 0.824273793181818
- $00{:}42{:}21.888 \dashrightarrow 00{:}42{:}23.860$  that we're seeing which is head ache.
- NOTE Confidence: 0.824273793181818
- $00:42:23.860 \rightarrow 00:42:25.796$  And for some people this has been happening
- NOTE Confidence: 0.824273793181818

 $00:42:25.796 \longrightarrow 00:42:27.569$  in people who had severe headache as

NOTE Confidence: 0.824273793181818

 $00{:}42{:}27.569 \dashrightarrow 00{:}42{:}29.220$  part of their initial COVID illness.

NOTE Confidence: 0.824273793181818

 $00{:}42{:}29{.}220 \dashrightarrow 00{:}42{:}32{.}363$  But head aches then lasting daily for months

NOTE Confidence: 0.824273793181818

 $00:42:32.363 \rightarrow 00:42:35.647$  and months and fearing with their jobs.

NOTE Confidence: 0.824273793181818

 $00{:}42{:}35{.}650 \dashrightarrow 00{:}42{:}38{.}370$  We've also had numbers of people who are

NOTE Confidence: 0.824273793181818

 $00:42:38.370 \rightarrow 00:42:40.509$  having patchy sensory abnormalities,

NOTE Confidence: 0.824273793181818

 $00:42:40.510 \rightarrow 00:42:41.788$  and this is something that unfortunately,

NOTE Confidence: 0.824273793181818

 $00:42:41.790 \rightarrow 00:42:43.006$  we're continuing to see.

NOTE Confidence: 0.824273793181818

 $00:42:43.006 \rightarrow 00:42:46.150$  We just have a patient who had a breakthrough

NOTE Confidence: 0.824273793181818

 $00{:}42{:}46.150 \dashrightarrow 00{:}42{:}48.240$  infection of Omicron after complete

NOTE Confidence: 0.824273793181818

 $00:42:48.240 \rightarrow 00:42:50.456$  vaccination and booster who's having

NOTE Confidence: 0.824273793181818

 $00:42:50.456 \rightarrow 00:42:52.656$  patchy sensory changes after COVID-19.

NOTE Confidence: 0.824273793181818

 $00:42:52.660 \rightarrow 00:42:53.260$  And finally,

NOTE Confidence: 0.824273793181818

 $00{:}42{:}53.260 \dashrightarrow 00{:}42{:}55.660$  this is a case that's well known to

NOTE Confidence: 0.824273793181818

 $00:42:55.727 \rightarrow 00:42:57.863$  many people in psychiatry because we

NOTE Confidence: 0.824273793181818

 $00:42:57.863 \rightarrow 00:43:00.170$  share taking care of this patient.

 $00:43:00.170 \longrightarrow 00:43:01.850$  People such as this gentleman a 30

NOTE Confidence: 0.824273793181818

 $00:43:01.850 \longrightarrow 00:43:04.057$  year old man with no past psychiatric

NOTE Confidence: 0.824273793181818

00:43:04.057 --> 00:43:05.489 history who developed paranoia,

NOTE Confidence: 0.824273793181818

 $00:43:05.490 \longrightarrow 00:43:05.839$  delusions,

NOTE Confidence: 0.824273793181818

 $00:43:05.839 \rightarrow 00:43:08.282$  hypersomnolence in a few weeks after COVID-19

NOTE Confidence: 0.824273793181818

 $00:43:08.282 \rightarrow 00:43:10.650$  that was refractory to anti psychotics.

NOTE Confidence: 0.824273793181818

 $00{:}43{:}10.650 \dashrightarrow 00{:}43{:}12.562$  So these are some of the sort of

NOTE Confidence: 0.824273793181818

 $00:43:12.562 \longrightarrow 00:43:13.708$  individual stories and I'll tell

NOTE Confidence: 0.824273793181818

 $00{:}43{:}13.708 \dashrightarrow 00{:}43{:}15.478$  you that the more and more you hear

NOTE Confidence: 0.824273793181818

 $00:43:15.478 \longrightarrow 00:43:17.410$  from people around the world who are

NOTE Confidence: 0.824273793181818

 $00:43:17.410 \longrightarrow 00:43:19.110$  experiencing lung COVID the more and

NOTE Confidence: 0.824273793181818

 $00{:}43{:}19{.}110 \dashrightarrow 00{:}43{:}21{.}245$  more you hear stories that are very

NOTE Confidence: 0.824273793181818

 $00{:}43{:}21{.}245 \dashrightarrow 00{:}43{:}23{.}435$  very similar to these individual tales.

NOTE Confidence: 0.824273793181818

 $00{:}43{:}23{.}440 \dashrightarrow 00{:}43{:}25{.}904$  So what do we know from research standpoint

NOTE Confidence: 0.824273793181818

 $00:43:25.904 \rightarrow 00:43:28.130$  about this condition about long COVID,

 $00:43:28.130 \longrightarrow 00:43:29.754$  though some of the best data has

NOTE Confidence: 0.824273793181818

 $00:43:29.754 \rightarrow 00:43:31.140$  actually come from the community,

NOTE Confidence: 0.824273793181818

 $00{:}43{:}31{.}140 \dashrightarrow 00{:}43{:}33{.}275$  and this has really been a remarkable

NOTE Confidence: 0.824273793181818

 $00:43:33.275 \rightarrow 00:43:35.899$  effort from a group called the patient

NOTE Confidence: 0.824273793181818

 $00{:}43{:}35{.}899 \dashrightarrow 00{:}43{:}37{.}959$  LED Resource Consortium for COVID-19.

NOTE Confidence: 0.824273793181818

 $00{:}43{:}37{.}960 \dashrightarrow 00{:}43{:}41{.}061$  Some of the people in this consortium

NOTE Confidence: 0.824273793181818

 $00:43:41.061 \rightarrow 00:43:43.200$  are actually neuroscientists originally,

NOTE Confidence: 0.824273793181818

 $00:43:43.200 \rightarrow 00:43:45.288$  many people or people who have

NOTE Confidence: 0.824273793181818

 $00{:}43{:}45{.}288 \dashrightarrow 00{:}43{:}47{.}060$  been in researching other ways.

NOTE Confidence: 0.824273793181818

 $00{:}43{:}47.060 \dashrightarrow 00{:}43{:}48.620$  But once they experienced kovid and

NOTE Confidence: 0.824273793181818

 $00{:}43{:}48.620 \dashrightarrow 00{:}43{:}50.551$  then had a what they called long

NOTE Confidence: 0.824273793181818

 $00:43:50.551 \rightarrow 00:43:52.231$  COVID symptoms and the term long

NOTE Confidence: 0.824273793181818

 $00{:}43{:}52{.}231 \dashrightarrow 00{:}43{:}53{.}836$  COVID has really come from the.

NOTE Confidence: 0.824273793181818

 $00:43:53.840 \rightarrow 00:43:55.500$  Community,

NOTE Confidence: 0.824273793181818

00:43:55.500 --> 00:43:57.216 they have really come forward to

NOTE Confidence: 0.824273793181818

 $00:43:57.216 \rightarrow 00:43:59.530$  try to be advocates and involved in

00:43:59.530 --> 00:44:01.385 research and setting research agendas,

NOTE Confidence: 0.824273793181818

 $00:44:01.390 \rightarrow 00:44:04.100$  so this is a study that has a lot of caveats.

NOTE Confidence: 0.824273793181818

00:44:04.100 --> 00:44:05.000 Online survey.

NOTE Confidence: 0.824273793181818

00:44:05.000 --> 00:44:06.800 Not everyone was documented

NOTE Confidence: 0.824273793181818

00:44:06.800 --> 00:44:08.600 to actually have COVID,

NOTE Confidence: 0.824273793181818

 $00:44:08.600 \longrightarrow 00:44:10.880$  but it is a survey that I think

NOTE Confidence: 0.824273793181818

 $00:44:10.880 \longrightarrow 00:44:12.618$  reflects what the current knowledge

NOTE Confidence: 0.824273793181818

00:44:12.618 --> 00:44:14.814 is of us long COVID worldwide.

NOTE Confidence: 0.824273793181818

 $00{:}44{:}14.820 \dashrightarrow 00{:}44{:}16.696$  So this is something that revealed a

NOTE Confidence: 0.824273793181818

 $00:44:16.696 \rightarrow 00:44:18.519$  couple of really important messages.

NOTE Confidence: 0.824273793181818

00:44:18.520 --> 00:44:19.564 First of all,

NOTE Confidence: 0.824273793181818

 $00:44:19.564 \longrightarrow 00:44:21.304$  this is people reporting their

NOTE Confidence: 0.824273793181818

 $00:44:21.304 \rightarrow 00:44:23.142$  average number of symptoms over

NOTE Confidence: 0.824273793181818

 $00:44:23.142 \rightarrow 00:44:24.947$  seven months after having COVID.

NOTE Confidence: 0.824273793181818

 $00{:}44{:}24{.}950 \dashrightarrow 00{:}44{:}26{.}910$  And what you can see here is that

00:44:26.910 --> 00:44:28.883 while many many people have recovery

NOTE Confidence: 0.824273793181818

 $00{:}44{:}28{.}883 \dashrightarrow 00{:}44{:}30{.}663$  overtime with gradual decrement in

NOTE Confidence: 0.824273793181818

00:44:30.663 - 00:44:32.807 the number of symptoms over months,

NOTE Confidence: 0.824273793181818

 $00:44:32.810 \longrightarrow 00:44:35.386$  there's a large number of people in

NOTE Confidence: 0.824273793181818

 $00:44:35.386 \longrightarrow 00:44:37.950$  this reported study that actually had

NOTE Confidence: 0.824273793181818

 $00{:}44{:}37{.}950 \dashrightarrow 00{:}44{:}40{.}260$  frequent and numerous symptoms lasting

NOTE Confidence: 0.824273793181818

 $00:44:40.260 \dashrightarrow 00:44:42.997$  seven months and longer after COVID-19.

NOTE Confidence: 0.824273793181818

 $00:44:43.000 \longrightarrow 00:44:44.130$  And what really came out

NOTE Confidence: 0.824273793181818

 $00:44:44.130 \longrightarrow 00:44:45.034$  in this initial report,

NOTE Confidence: 0.824273793181818

 $00:44:45.040 \rightarrow 00:44:47.455$  which I think is really extremely important,

NOTE Confidence: 0.824273793181818

 $00:44:47.460 \longrightarrow 00:44:48.504$  is that many,

NOTE Confidence: 0.824273793181818

 $00{:}44{:}48{.}504 \dashrightarrow 00{:}44{:}50{.}592$  many of the symptoms people are

NOTE Confidence: 0.824273793181818

 $00:44:50.592 \rightarrow 00:44:52.740$  having are considered what they

NOTE Confidence: 0.824273793181818

 $00:44:52.740 \rightarrow 00:44:54.900$  consider to be neuro psychiatric.

NOTE Confidence: 0.824273793181818

 $00:44:54.900 \rightarrow 00:44:57.267$  So you can see at the top what they

NOTE Confidence: 0.824273793181818

00:44:57.267 --> 00:44:59.408 call brain fog, memory issues,

- NOTE Confidence: 0.824273793181818
- $00:44:59.408 \rightarrow 00:45:02.278$  sensory changes in the middle,
- NOTE Confidence: 0.824273793181818
- $00:45:02.280 \longrightarrow 00:45:05.118$  and then what they call headache
- NOTE Confidence: 0.824273793181818
- $00{:}45{:}05{.}118 \dashrightarrow 00{:}45{:}06{.}064$  and insomnia.
- NOTE Confidence: 0.824273793181818
- 00:45:06.070 --> 00:45:07.915 Being major features of some
- NOTE Confidence: 0.824273793181818
- $00{:}45{:}07{.}915 \dashrightarrow 00{:}45{:}09{.}760$  of these most lasting symptoms
- NOTE Confidence: 0.874153357368421
- $00{:}45{:}09{.}832 \dashrightarrow 00{:}45{:}11{.}962$  after COVID and I think has
- NOTE Confidence: 0.874153357368421
- $00:45:11.962 \longrightarrow 00:45:13.027$  really drawn attention.
- NOTE Confidence: 0.874153357368421
- $00:45:13.030 \longrightarrow 00:45:15.564$  And what is a is an incredibly
- NOTE Confidence: 0.874153357368421
- 00:45:15.564 --> 00:45:17.070 important problem for many,
- NOTE Confidence: 0.874153357368421
- $00{:}45{:}17.070 \dashrightarrow 00{:}45{:}18.710$  many people worldwide and trying
- NOTE Confidence: 0.874153357368421
- $00:45:18.710 \longrightarrow 00:45:20.813$  to understand what may be the
- NOTE Confidence: 0.874153357368421
- $00:45:20.813 \longrightarrow 00:45:21.970$  ideologies that challenges.
- NOTE Confidence: 0.874153357368421
- $00:45:21.970 \longrightarrow 00:45:23.870$  There's really been very little
- NOTE Confidence: 0.874153357368421
- 00:45:23.870 --> 00:45:25.375 systematic research into the
- NOTE Confidence: 0.874153357368421
- $00{:}45{:}25{.}375 \dashrightarrow 00{:}45{:}27{.}247$  ideologies of these conditions so far.
- NOTE Confidence: 0.874153357368421

00:45:27.250 --> 00:45:28.990 There's major research efforts worldwide,

NOTE Confidence: 0.874153357368421

 $00{:}45{:}28{.}990 \dashrightarrow 00{:}45{:}30{.}866$  of course, so this is a study

NOTE Confidence: 0.874153357368421

 $00:45:30.866 \rightarrow 00:45:32.450$  that's a little interesting.

NOTE Confidence: 0.874153357368421

 $00:45:32.450 \rightarrow 00:45:35.422$  It's a study that came out a few months ago,

NOTE Confidence: 0.874153357368421

 $00{:}45{:}35{.}422 \dashrightarrow 00{:}45{:}37{.}180$  and there's actually been a follow-up

NOTE Confidence: 0.874153357368421

 $00{:}45{:}37{.}237 \dashrightarrow 00{:}45{:}39{.}182$  PET study really finding similar

NOTE Confidence: 0.874153357368421

 $00:45:39.182 \rightarrow 00:45:41.127$  findings by another group independently.

NOTE Confidence: 0.874153357368421

 $00:45:41.130 \longrightarrow 00:45:43.686$  This is a group that looked at 45 people.

NOTE Confidence: 0.874153357368421

 $00:45:43.690 \rightarrow 00:45:45.818$  Had persistent cognitive symptoms

NOTE Confidence: 0.874153357368421

 $00{:}45{:}45{.}818 \dashrightarrow 00{:}45{:}48{.}478$  or psychiatric symptoms and median

NOTE Confidence: 0.874153357368421

 $00{:}45{:}48{.}478 \dashrightarrow 00{:}45{:}51{.}469$  of three months after COVID-19 and

NOTE Confidence: 0.874153357368421

 $00:45:51.469 \longrightarrow 00:45:53.623$  what they found was that there

NOTE Confidence: 0.874153357368421

 $00:45:53.623 \rightarrow 00:45:54.700$  was regional hypometabolism.

NOTE Confidence: 0.874153357368421

00:45:54.700 --> 00:45:56.704 Looking at FDG pet compared to

NOTE Confidence: 0.874153357368421

 $00:45:56.704 \rightarrow 00:45:58.428$  pretty well matched healthy controls

NOTE Confidence: 0.874153357368421

 $00:45:58.428 \rightarrow 00:46:00.396$  and what was interesting in this

 $00:46:00.396 \rightarrow 00:46:02.634$  finding is that the metabolic values

NOTE Confidence: 0.874153357368421

 $00:46:02.634 \rightarrow 00:46:04.222$  actually associated with symptoms

NOTE Confidence: 0.874153357368421

 $00:46:04.222 \longrightarrow 00:46:06.320$  in this fairly small study,

NOTE Confidence: 0.874153357368421

 $00:46:06.320 \longrightarrow 00:46:07.670$  we don't know,

NOTE Confidence: 0.874153357368421

 $00:46:07.670 \longrightarrow 00:46:08.350$  of course,

NOTE Confidence: 0.874153357368421

 $00{:}46{:}08{.}350 \dashrightarrow 00{:}46{:}10{.}390$  is whether some of these regional

NOTE Confidence: 0.874153357368421

00:46:10.390 --> 00:46:11.977 hypometabolism I'm from metabolism

NOTE Confidence: 0.874153357368421

00:46:11.977 --> 00:46:13.252 differences were actually

NOTE Confidence: 0.874153357368421

 $00:46:13.252 \longrightarrow 00:46:14.527$  present before COVID.

NOTE Confidence: 0.874153357368421

 $00{:}46{:}14.530 \dashrightarrow 00{:}46{:}16.810$  And whether they were somehow people

NOTE Confidence: 0.874153357368421

00:46:16.810 --> 00:46:19.100 who were sensitive to having some

NOTE Confidence: 0.874153357368421

 $00{:}46{:}19{.}100 \dashrightarrow 00{:}46{:}21{.}356$  of these syndromes after COVID so

NOTE Confidence: 0.874153357368421

 $00{:}46{:}21.356 \dashrightarrow 00{:}46{:}23.312$  a really beautiful study that was

NOTE Confidence: 0.874153357368421

 $00{:}46{:}23.312 \dashrightarrow 00{:}46{:}24.673$  actually just officially published

NOTE Confidence: 0.874153357368421

 $00{:}46{:}24.673 \dashrightarrow 00{:}46{:}26.599$  last week that was actually reported

 $00:46:26.599 \rightarrow 00:46:28.756$  as a preprint last summer gets around

NOTE Confidence: 0.874153357368421

 $00{:}46{:}28.756 \dashrightarrow 00{:}46{:}30.940$  a little bit of that issue so this

NOTE Confidence: 0.874153357368421

 $00:46:31.006 \rightarrow 00:46:33.463$  is a study that takes advantage of

NOTE Confidence: 0.874153357368421

 $00:46:33.463 \rightarrow 00:46:34.903$  the absolutely fantastic resource

NOTE Confidence: 0.874153357368421

 $00:46:34.903 \longrightarrow 00:46:36.538$  of the UK biobank study.

NOTE Confidence: 0.874153357368421

 $00{:}46{:}36{.}540 \dashrightarrow 00{:}46{:}38{.}610$  Many of you may know about UK biobank study.

NOTE Confidence: 0.874153357368421

 $00:46:38.610 \longrightarrow 00:46:41.646$  It's basically a long term surveillance

NOTE Confidence: 0.874153357368421

 $00:46:41.646 \rightarrow 00:46:43.860$  population based study that collects.

NOTE Confidence: 0.874153357368421

 $00{:}46{:}43.860 \dashrightarrow 00{:}46{:}46.275$  All sorts of samples and data from

NOTE Confidence: 0.874153357368421

 $00:46:46.275 \rightarrow 00:46:47.901$  thousands of people throughout the

NOTE Confidence: 0.874153357368421

00:46:47.901 -> 00:46:50.492 UK over years and it's this has been

NOTE Confidence: 0.874153357368421

 $00{:}46{:}50{.}492 \dashrightarrow 00{:}46{:}52{.}247$  an amazing resource for studying,

NOTE Confidence: 0.874153357368421

 $00:46:52.250 \longrightarrow 00:46:52.954$  for example,

NOTE Confidence: 0.874153357368421

 $00:46:52.954 \rightarrow 00:46:54.714$  genetic diseases and rare disorders,

NOTE Confidence: 0.874153357368421

 $00:46:54.720 \longrightarrow 00:46:56.200$  and they collect things like

NOTE Confidence: 0.874153357368421

 $00:46:56.200 \longrightarrow 00:46:58.160$  echoes in a subset of people.

00:46:58.160 --> 00:47:00.170 They collect all sorts of blood

NOTE Confidence: 0.874153357368421

 $00{:}47{:}00{.}170 \dashrightarrow 00{:}47{:}02{.}725$  and CSF and other data and other

NOTE Confidence: 0.874153357368421

 $00{:}47{:}02.725 \dashrightarrow 00{:}47{:}05.155$  people limited neuro psych data in

NOTE Confidence: 0.874153357368421

 $00{:}47{:}05{.}155 \dashrightarrow 00{:}47{:}07{.}782$  all of the participants and then

NOTE Confidence: 0.874153357368421

 $00{:}47{:}07{.}782 \dashrightarrow 00{:}47{:}09{.}487$  in some subsets of participants

NOTE Confidence: 0.874153357368421

 $00:47:09.487 \longrightarrow 00:47:11.319$  they do serial MRI imaging.

NOTE Confidence: 0.874153357368421

 $00:47:11.320 \longrightarrow 00:47:12.608$  And so this is a wonderful study,

NOTE Confidence: 0.874153357368421

 $00:47:12.610 \longrightarrow 00:47:14.146$  but didn't manage of the fact

NOTE Confidence: 0.874153357368421

 $00:47:14.146 \longrightarrow 00:47:15.474$  that they identified that they

NOTE Confidence: 0.874153357368421

 $00:47:15.474 \rightarrow 00:47:16.719$  had participants in the UK.

NOTE Confidence: 0.874153357368421

 $00{:}47{:}16.720 \dashrightarrow 00{:}47{:}19.975$  Biobank study that had SARS Co V2

NOTE Confidence: 0.874153357368421

 $00{:}47{:}19{.}975 \dashrightarrow 00{:}47{:}22{.}460$  positive tests between their prior

NOTE Confidence: 0.874153357368421

 $00{:}47{:}22.460 \dashrightarrow 00{:}47{:}24.955$  scan in their usual surveillance

NOTE Confidence: 0.874153357368421

 $00{:}47{:}24.955 \dashrightarrow 00{:}47{:}27.784$  system and then their follow up

NOTE Confidence: 0.874153357368421

 $00:47:27.784 \longrightarrow 00:47:30.167$  scan and they were able to do a

 $00:47:30.167 \rightarrow 00:47:31.716$  really really deep chart analysis

NOTE Confidence: 0.874153357368421

 $00:47:31.716 \rightarrow 00:47:34.268$  to identify what I think is a fairly

NOTE Confidence: 0.874153357368421

00:47:34.331 --> 00:47:36.086 convincing group of 384 controls

NOTE Confidence: 0.874153357368421

 $00:47:36.086 \rightarrow 00:47:38.350$  that really do not seem to have had

NOTE Confidence: 0.874153357368421

 $00{:}47{:}38{.}417 \dashrightarrow 00{:}47{:}40{.}734$  COVID based on lab tests and other

NOTE Confidence: 0.874153357368421

 $00{:}47{:}40.734 \dashrightarrow 00{:}47{:}42.320$  data that's available in there.

NOTE Confidence: 0.874153357368421

 $00{:}47{:}42.320 \dashrightarrow 00{:}47{:}44.609$  Charts which can be linked to the

NOTE Confidence: 0.874153357368421

 $00:47:44.609 \rightarrow 00:47:46.460$  UK Biobank database and when they

NOTE Confidence: 0.874153357368421

 $00{:}47{:}46{.}460 \dashrightarrow 00{:}47{:}48{.}200$  did this comparison and these people

NOTE Confidence: 0.874153357368421

 $00{:}47{:}48.200 \dashrightarrow 00{:}47{:}50.411$  were also very well matched in terms

NOTE Confidence: 0.874153357368421

 $00{:}47{:}50{.}411 \dashrightarrow 00{:}47{:}52{.}449$  intervals between scans and other factors.

NOTE Confidence: 0.874153357368421

 $00{:}47{:}52{.}450 \dashrightarrow 00{:}47{:}54{.}452$  They found focal loss of Gray matter

NOTE Confidence: 0.874153357368421

 $00{:}47{:}54{.}452 \dashrightarrow 00{:}47{:}56{.}781$  in a variety of brain structures in

NOTE Confidence: 0.874153357368421

00:47:56.781 - 00:47:58.887 those people who would have COVID-19.

NOTE Confidence: 0.874153357368421

 $00:47:58.890 \rightarrow 00:48:01.594$  Now the Gray matter loss was very small

NOTE Confidence: 0.874153357368421

 $00{:}48{:}01{.}594 \dashrightarrow 00{:}48{:}04{.}440$  and and relative to Gray matter loss.

- NOTE Confidence: 0.874153357368421
- $00:48:04.440 \longrightarrow 00:48:06.090$  All of the groups lost Gray
- NOTE Confidence: 0.874153357368421
- $00{:}48{:}06{.}090 \dashrightarrow 00{:}48{:}07{.}190$  matter over the two
- NOTE Confidence: 0.85115896
- $00:48:07.258 \longrightarrow 00:48:08.576$  years. Both the healthy
- NOTE Confidence: 0.85115896
- $00:48:08.576 \rightarrow 00:48:10.186$  controls and the COVID group,
- NOTE Confidence: 0.85115896
- $00{:}48{:}10.190 \dashrightarrow 00{:}48{:}12.774$  but the COVID group lost more Gray matter.
- NOTE Confidence: 0.85115896
- 00:48:12.780 --> 00:48:13.536 Maybe certain regions
- NOTE Confidence: 0.85115896
- $00:48:13.536 \longrightarrow 00:48:14.796$  than the other group did.
- NOTE Confidence: 0.85115896
- $00{:}48{:}14.800 \dashrightarrow 00{:}48{:}16.560$  There were also some disruptions
- NOTE Confidence: 0.85115896
- 00:48:16.560 --> 00:48:17.968 in DTI imaging metrics,
- NOTE Confidence: 0.85115896
- $00{:}48{:}17.970 \dashrightarrow 00{:}48{:}20.400$  suggesting some other structural changes.
- NOTE Confidence: 0.85115896
- $00:48:20.400 \longrightarrow 00:48:21.456$  So what does this tell us?
- NOTE Confidence: 0.85115896
- $00{:}48{:}21.460 \dashrightarrow 00{:}48{:}23.196$  This is not an all title on COVID.
- NOTE Confidence: 0.85115896
- $00{:}48{:}23.200 \dashrightarrow 00{:}48{:}25.512$  We have no idea whether any of these
- NOTE Confidence: 0.85115896
- $00{:}48{:}25{.}512 \dashrightarrow 00{:}48{:}27{.}310$  patients have long COVID symptoms.
- NOTE Confidence: 0.85115896
- $00:48:27.310 \rightarrow 00:48:28.834$  There were some changes in Neuro
- NOTE Confidence: 0.85115896

 $00:48:28.834 \rightarrow 00:48:30.381$  Psych testing overtime in the COVID

NOTE Confidence: 0.85115896

 $00{:}48{:}30{.}381 \dashrightarrow 00{:}48{:}31{.}827$  group compared to the other group,

NOTE Confidence: 0.85115896

00:48:31.830 --> 00:48:33.370 and it wasn't convincingly shown

NOTE Confidence: 0.85115896

 $00:48:33.370 \longrightarrow 00:48:34.910$  to be associated with these

NOTE Confidence: 0.85115896

 $00{:}48{:}34{.}970 \dashrightarrow 00{:}48{:}36{.}358$  changes in brain structure.

NOTE Confidence: 0.85115896

 $00{:}48{:}36{.}360 \dashrightarrow 00{:}48{:}38{.}096$  But I think what this is really

NOTE Confidence: 0.85115896

 $00:48:38.096 \longrightarrow 00:48:39.890$  useful to tell us is there is

NOTE Confidence: 0.85115896

00:48:39.890 --> 00:48:41.378 a footprint of COVID effects in

NOTE Confidence: 0.85115896

00:48:41.436  $\operatorname{-->}$  00:48:43.110 the brain that can be measured,

NOTE Confidence: 0.85115896

00:48:43.110 --> 00:48:44.772 which maybe gives us some more

NOTE Confidence: 0.85115896

 $00{:}48{:}44.772 \dashrightarrow 00{:}48{:}46.442$  targets and even more sort of

NOTE Confidence: 0.85115896

00:48:46.442 --> 00:48:47.948 galvanizes us even more to try

NOTE Confidence: 0.85115896

 $00{:}48{:}47{.}948 \dashrightarrow 00{:}48{:}49{.}547$  to study this question with the

NOTE Confidence: 0.85115896

 $00{:}48{:}49{.}547 \dashrightarrow 00{:}48{:}52{.}350$  kinds of tools that we can use that

NOTE Confidence: 0.85115896

 $00:48:52.350 \rightarrow 00:48:54.810$  we've developed for neuroscience.

NOTE Confidence: 0.85115896

 $00:48:54.810 \longrightarrow 00:48:55.710$  I'll say that there are,

- NOTE Confidence: 0.85115896
- 00:48:55.710 --> 00:48:56.206 you know,
- NOTE Confidence: 0.85115896
- $00:48:56.206 \rightarrow 00:48:57.942$  one hypothesis might be that long COVID
- NOTE Confidence: 0.85115896
- $00{:}48{:}57{.}942 \dashrightarrow 00{:}48{:}59{.}447$  is associated with neuroinflammation and
- NOTE Confidence: 0.85115896
- $00:48:59.447 \rightarrow 00:49:02.210$  this is being sort of put out by many people,
- NOTE Confidence: 0.85115896
- $00:49:02.210 \longrightarrow 00:49:03.098$  including our groups.
- NOTE Confidence: 0.85115896
- $00:49:03.098 \longrightarrow 00:49:04.578$  We don't have really any
- NOTE Confidence: 0.85115896
- $00:49:04.578 \longrightarrow 00:49:05.650$  convincing data for that.
- NOTE Confidence: 0.85115896
- $00{:}49{:}05{.}650 \dashrightarrow 00{:}49{:}07{.}698$  This is a tiny study that looked at
- NOTE Confidence: 0.85115896
- $00{:}49{:}07{.}698 \dashrightarrow 00{:}49{:}09{.}470$  some patients with cancer and World
- NOTE Confidence: 0.85115896
- 00:49:09.470 --> 00:49:11.282 Sloan Kettering and looked at people
- NOTE Confidence: 0.85115896
- $00{:}49{:}11{.}344 \dashrightarrow 00{:}49{:}12{.}934$  who had cancer and neurological
- NOTE Confidence: 0.85115896
- $00{:}49{:}12{.}934 \dashrightarrow 00{:}49{:}14{.}524$  symptoms after COVID that are
- NOTE Confidence: 0.85115896
- $00{:}49{:}14{.}530 \dashrightarrow 00{:}49{:}16{.}616$  shown in the red and then looked
- NOTE Confidence: 0.85115896
- 00:49:16.616 --> 00:49:18.354 at other comparison patients who
- NOTE Confidence: 0.85115896
- $00:49:18.354 \rightarrow 00:49:20.319$  had cancer and neurologic symptoms.
- NOTE Confidence: 0.85115896

 $00{:}49{:}20{.}320 \dashrightarrow 00{:}49{:}22{.}150$  But no kovid and found some

NOTE Confidence: 0.85115896

00:49:22.150 --> 00:49:23.851 higher levels of CSF inflammatory

NOTE Confidence: 0.85115896

 $00{:}49{:}23.851 \dashrightarrow 00{:}49{:}26.305$  markers and those who had COVID.

NOTE Confidence: 0.85115896

00:49:26.310 --> 00:49:26.544 Much,

NOTE Confidence: 0.85115896

 $00{:}49{:}26{.}544 \dashrightarrow 00{:}49{:}28{.}182$  much lower than those people who were

NOTE Confidence: 0.85115896

 $00{:}49{:}28.182 \dashrightarrow 00{:}49{:}29.580$  treated with CAR T cell the rapies,

NOTE Confidence: 0.85115896

 $00:49:29.580 \longrightarrow 00:49:31.460$  so I think it's hard to know really

NOTE Confidence: 0.85115896

 $00:49:31.460 \longrightarrow 00:49:32.918$  how clinically significant this is,

NOTE Confidence: 0.85115896

 $00{:}49{:}32{.}920 \dashrightarrow 00{:}49{:}35{.}209$  but it's a hint that looking for

NOTE Confidence: 0.85115896

00:49:35.209 --> 00:49:37.040 neuroinflammation after Kovac may be helpful.

NOTE Confidence: 0.85115896

 $00:49:37.040 \longrightarrow 00:49:39.300$  Another group has looked prospectively

NOTE Confidence: 0.85115896

 $00{:}49{:}39{.}300 \dashrightarrow 00{:}49{:}42{.}117$  and individuals who had acute COVID-19

NOTE Confidence: 0.85115896

 $00{:}49{:}42.117 \dashrightarrow 00{:}49{:}44.057$  during hospitalization and then

NOTE Confidence: 0.85115896

00:49:44.057 -> 00:49:46.482 were followed over three months,

NOTE Confidence: 0.85115896

 $00:49:46.490 \longrightarrow 00:49:47.790$  and in this group,

NOTE Confidence: 0.85115896

 $00:49:47.790 \longrightarrow 00:49:49.740$  those people who had higher measures

 $00:49:49.807 \rightarrow 00:49:51.702$  of depression and neurocognition 3

NOTE Confidence: 0.85115896

 $00:49:51.702 \rightarrow 00:49:54.130$  months after COVID had higher baseline

NOTE Confidence: 0.85115896

 $00:49:54.130 \longrightarrow 00:49:56.495$  measures of blood inflammatory markers.

NOTE Confidence: 0.85115896

00:49:56.500 - 00:49:58.505 Again suggesting that maybe an

NOTE Confidence: 0.85115896

00:49:58.505 --> 00:50:00.109 inflammatory hit could have

NOTE Confidence: 0.85115896

00:50:00.109 --> 00:50:01.949 resulted in more outcomes later,

NOTE Confidence: 0.85115896

 $00{:}50{:}01{.}950 \dashrightarrow 00{:}50{:}03{.}462$  but of course there's lots of

NOTE Confidence: 0.85115896

 $00{:}50{:}03.462 \dashrightarrow 00{:}50{:}05.136$  cave ats for this kind of study and

NOTE Confidence: 0.85115896

 $00{:}50{:}05{.}136 \dashrightarrow 00{:}50{:}06{.}936$  one issue I think for all of these

NOTE Confidence: 0.85115896

 $00:50:06.936 \longrightarrow 00:50:08.898$  studies that are based in primarily

NOTE Confidence: 0.85115896

 $00{:}50{:}08.898 \dashrightarrow 00{:}50{:}10.502$  hospitalized patients is that it's

NOTE Confidence: 0.85115896

 $00:50:10.502 \rightarrow 00:50:12.368$  really uncertain to know how these

NOTE Confidence: 0.85115896

 $00:50:12.368 \rightarrow 00:50:14.225$  results to people who have milder

NOTE Confidence: 0.85115896

 $00{:}50{:}14.225 \dashrightarrow 00{:}50{:}16.840$  forms of coverage or in their acute illness.

NOTE Confidence: 0.85115896

 $00:50:16.840 \rightarrow 00:50:19.400$  And how they relate to longer term symptoms.

- $00:50:19.400 \longrightarrow 00:50:20.327$  So I mean,
- NOTE Confidence: 0.85115896
- $00:50:20.327 \rightarrow 00:50:22.970$  and by talking about the COVID mine study.
- NOTE Confidence: 0.85115896
- 00:50:22.970 --> 00:50:23.666 And again,
- NOTE Confidence: 0.85115896
- $00:50:23.666 \rightarrow 00:50:26.102$  this is just really a preliminary study
- NOTE Confidence: 0.85115896
- $00{:}50{:}26.102 \dashrightarrow 00{:}50{:}28.929$  that we started over the last year at Yale.
- NOTE Confidence: 0.85115896
- $00{:}50{:}28{.}930 \dashrightarrow 00{:}50{:}31{.}260$  This is in collaboration with
- NOTE Confidence: 0.85115896
- $00{:}50{:}31{.}260 \dashrightarrow 00{:}50{:}33{.}124$ Shelly Farhadian against stellar
- NOTE Confidence: 0.85115896
- $00:50:33.124 \rightarrow 00:50:35.376$  physician investigator here and in
- NOTE Confidence: 0.85115896
- $00{:}50{:}35{.}376$  -->  $00{:}50{:}37{.}156$  new infectious disease and neurology,
- NOTE Confidence: 0.85115896
- $00{:}50{:}37{.}160 \dashrightarrow 00{:}50{:}37{.}811$  and an ID.
- NOTE Confidence: 0.85115896
- $00{:}50{:}37{.}811 \dashrightarrow 00{:}50{:}39{.}330$  And this is a study that's using
- NOTE Confidence: 0.85115896
- $00:50:39.381 \longrightarrow 00:50:41.117$  a lot of the types of tools that
- NOTE Confidence: 0.85115896
- 00:50:41.117 --> 00:50:43.037 we've been using over the years to
- NOTE Confidence: 0.85115896
- $00{:}50{:}43.037 \dashrightarrow 00{:}50{:}44.472$  look for subtle abnormalities and
- NOTE Confidence: 0.793747172222222
- $00:50:44.480 \longrightarrow 00:50:46.630$  people with acute HIV and
- NOTE Confidence: 0.793747172222222
- $00:50:46.630 \longrightarrow 00:50:48.350$  long term treated HIV.

 $00:50:48.350 \rightarrow 00:50:50.220$  And essentially using these same

NOTE Confidence: 0.793747172222222

 $00:50:50.220 \rightarrow 00:50:52.090$  really sense of interrogations to

NOTE Confidence: 0.793747172222222

 $00{:}50{:}52{.}147 \dashrightarrow 00{:}50{:}54{.}366$  look for changes in people who are

NOTE Confidence: 0.793747172222222

 $00:50:54.366 \rightarrow 00:50:55.779$  having neurologic and psychiatric

NOTE Confidence: 0.793747172222222

 $00:50:55.779 \rightarrow 00:50:57.387$  complications months after COVID

NOTE Confidence: 0.793747172222222

 $00:50:57.387 \longrightarrow 00:50:59.792$  and most of these patients are

NOTE Confidence: 0.793747172222222

 $00{:}50{:}59{.}792 \dashrightarrow 00{:}51{:}02{.}144$  referred from our neural COVID clinic

NOTE Confidence: 0.793747172222222

 $00:51:02.150 \dashrightarrow 00:51:03.970$  and we really try to screen them

NOTE Confidence: 0.793747172222222

 $00{:}51{:}03{.}970 \dashrightarrow 00{:}51{:}05{.}837$  to identify people who are having

NOTE Confidence: 0.793747172222222

00:51:05.837 --> 00:51:07.209 central nervous system symptoms,

NOTE Confidence: 0.793747172222222

 $00:51:07.210 \longrightarrow 00:51:08.680$  primarily because those are the

NOTE Confidence: 0.793747172222222

00:51:08.680 --> 00:51:10.350 kinds of tools we're focusing on,

NOTE Confidence: 0.793747172222222

 $00{:}51{:}10{.}350 \dashrightarrow 00{:}51{:}12{.}382$  so you can see that we're using MRI

NOTE Confidence: 0.793747172222222

00:51:12.382 --> 00:51:14.360 brain really kind of detailed neuro

NOTE Confidence: 0.793747172222222

 $00:51:14.360 \longrightarrow 00:51:16.484$  psychiatric batteries of cognition and mood,

00:51:16.490 --> 00:51:17.970 lots of histories and surveys,

NOTE Confidence: 0.793747172222222

 $00:51:17.970 \longrightarrow 00:51:19.460$  lots of information about their.

NOTE Confidence: 0.793747172222222

00:51:19.460 --> 00:51:21.760 Acute illness and their ongoing

NOTE Confidence: 0.793747172222222

 $00:51:21.760 \rightarrow 00:51:24.400$  conditions and then doing very detailed

NOTE Confidence: 0.793747172222222

 $00{:}51{:}24{.}400 \dashrightarrow 00{:}51{:}27{.}888$  blood and CSF studies that range from

NOTE Confidence: 0.793747172222222

 $00{:}51{:}27{.}888 \dashrightarrow 00{:}51{:}29{.}920$  everywhere between immune profiling

NOTE Confidence: 0.793747172222222

 $00{:}51{:}30{.}003 \dashrightarrow 00{:}51{:}32{.}213$  with through single cell studies

NOTE Confidence: 0.793747172222222

00:51:32.213 --> 00:51:34.488 to unique studies of antibodies,

NOTE Confidence: 0.793747172222222

 $00{:}51{:}34{.}488 \dashrightarrow 00{:}51{:}36{.}316$  autoantibodies and really high

NOTE Confidence: 0.793747172222222

 $00:51:36.316 \longrightarrow 00:51:38.220$  level markers are looking for

NOTE Confidence: 0.793747172222222

 $00{:}51{:}38{.}220 \dashrightarrow 00{:}51{:}39{.}476$  evidence of viral persistence.

NOTE Confidence: 0.793747172222222

 $00:51:39.476 \longrightarrow 00:51:41.971$  And I'll just say this is a this

NOTE Confidence: 0.793747172222222

00:51:41.971 --> 00:51:43.346 is a super complicated study

NOTE Confidence: 0.793747172222222

 $00:51:43.346 \dashrightarrow 00:51:45.240$  with lots and lots of expertise.

NOTE Confidence: 0.793747172222222

 $00:51:45.240 \longrightarrow 00:51:48.006$  These are only some of the

NOTE Confidence: 0.793747172222222

 $00:51:48.006 \rightarrow 00:51:49.850$  collaborators unsteady worldwide and.

 $00:51:49.850 \longrightarrow 00:51:51.668$  We'd be really lucky to have

NOTE Confidence: 0.793747172222222

 $00:51:51.668 \rightarrow 00:51:53.016$  collaboration of some investigators

NOTE Confidence: 0.793747172222222

00:51:53.016 --> 00:51:54.488 in Department of Psychiatry.

NOTE Confidence: 0.793747172222222

 $00{:}51{:}54{.}490 \dashrightarrow 00{:}51{:}56{.}190$  Whoever you really interested in

NOTE Confidence: 0.793747172222222

 $00{:}51{:}56{.}190 \dashrightarrow 00{:}51{:}58{.}230$  working together with us on this.

NOTE Confidence: 0.793747172222222

 $00{:}51{:}58{.}230 \dashrightarrow 00{:}51{:}59{.}637$  So I'm just going to show you

NOTE Confidence: 0.793747172222222

00:51:59.637 - 00:52:00.480 some super preliminary data.

NOTE Confidence: 0.793747172222222

 $00{:}52{:}00{.}480 \dashrightarrow 00{:}52{:}01{.}888$  We've presented 1 abstract

NOTE Confidence: 0.793747172222222

 $00{:}52{:}01{.}888 \dashrightarrow 00{:}52{:}03{.}648$  based on this preliminary data,

NOTE Confidence: 0.793747172222222

 $00:52:03.650 \rightarrow 00:52:05.870$  but we're really hoping to have

NOTE Confidence: 0.793747172222222

 $00:52:05.870 \longrightarrow 00:52:08.282$  about 100 patients to pull together

NOTE Confidence: 0.793747172222222

 $00:52:08.282 \longrightarrow 00:52:10.427$  for a more complete approach.

NOTE Confidence: 0.793747172222222

 $00{:}52{:}10{.}430 \dashrightarrow 00{:}52{:}13{.}546$  I partly say that because this is

NOTE Confidence: 0.793747172222222

 $00{:}52{:}13.546 \dashrightarrow 00{:}52{:}15.286$  a very heterogeneous condition and

NOTE Confidence: 0.793747172222222

 $00{:}52{:}15{.}286 \dashrightarrow 00{:}52{:}17{.}351$  I think reporting on small numbers

 $00:52:17.351 \rightarrow 00:52:18.946$  of people will not necessarily

NOTE Confidence: 0.793747172222222

 $00{:}52{:}18{.}946{\:}-{:}{>}00{:}52{:}21{.}098$  give us the answers that we need.

NOTE Confidence: 0.793747172222222

 $00:52:21.100 \longrightarrow 00:52:22.730$  But the first thirty four

NOTE Confidence: 0.793747172222222

00:52:22.730 --> 00:52:24.360 people enrolled in our cohort,

NOTE Confidence: 0.793747172222222

 $00{:}52{:}24{.}360 \dashrightarrow 00{:}52{:}28{.}306$ our young age 5374% women 300

NOTE Confidence: 0.793747172222222

 $00:52:28.306 \longrightarrow 00:52:29.914$  days from symptom onset.

NOTE Confidence: 0.793747172222222

 $00{:}52{:}29{.}920 \dashrightarrow 00{:}52{:}32{.}958$  So almost a year after acute COVID,

NOTE Confidence: 0.793747172222222

 $00:52:32.960 \rightarrow 00:52:35.300$  74% of them convalesced at home,

NOTE Confidence: 0.793747172222222

 $00{:}52{:}35{.}300 \dashrightarrow 00{:}52{:}37{.}274$  and the vast majority of them came

NOTE Confidence: 0.793747172222222

 $00:52:37.274 \rightarrow 00:52:39.850$  to us and rolled in our study

NOTE Confidence: 0.793747172222222

 $00{:}52{:}39{.}850 \dashrightarrow 00{:}52{:}41{.}514$  because of cognitive impairment.

NOTE Confidence: 0.793747172222222

 $00:52:41.520 \rightarrow 00:52:44.660 59\%$  also have mood symptoms,

NOTE Confidence: 0.793747172222222

 $00:52:44.660 \rightarrow 00:52:46.753$  and we're comparing them to pre pandemic

NOTE Confidence: 0.793747172222222

 $00:52:46.753 \rightarrow 00:52:48.619$  controls in the data that I'm going

NOTE Confidence: 0.793747172222222

 $00{:}52{:}48.619 \dashrightarrow 00{:}52{:}50.958$  to show you in the next couple of slides,

NOTE Confidence: 0.793747172222222

 $00:52:50.960 \longrightarrow 00:52:52.651$  who were of a similar age, but.

 $00{:}52{:}52{.}651 \dashrightarrow 00{:}52{:}54{.}215$  Different gender because most

NOTE Confidence: 0.793747172222222

 $00{:}52{:}54{.}215 \dashrightarrow 00{:}52{:}56{.}170$  of our controls are men.

NOTE Confidence: 0.793747172222222

 $00{:}52{:}56{.}170 \dashrightarrow 00{:}52{:}57{.}773$  So what are the kinds of symptoms

NOTE Confidence: 0.793747172222222

 $00:52:57.773 \rightarrow 00:52:59.348$  these patients had during acute COVID?

NOTE Confidence: 0.793747172222222

 $00{:}52{:}59{.}350 \dashrightarrow 00{:}53{:}02{.}073$  You can see it's all across the

NOTE Confidence: 0.793747172222222

 $00{:}53{:}02{.}073 \dashrightarrow 00{:}53{:}04{.}339$  books and some of them had.

NOTE Confidence: 0.793747172222222

 $00:53:04.340 \longrightarrow 00:53:05.390$  Most of them had cough,

NOTE Confidence: 0.793747172222222

 $00{:}53{:}05{.}390 \dashrightarrow 00{:}53{:}06{.}545$  fever and headache.

NOTE Confidence: 0.793747172222222

 $00:53:06.545 \rightarrow 00:53:09.240$  Many of them also had other symptoms.

NOTE Confidence: 0.793747172222222

 $00:53:09.240 \rightarrow 00:53:10.220$  Many people ask me well,

NOTE Confidence: 0.793747172222222

 $00:53:10.220 \rightarrow 00:53:11.796$  did everybody have loss of taste and smell?

NOTE Confidence: 0.793747172222222

 $00{:}53{:}11.800 \dashrightarrow 00{:}53{:}14.080$  Know in our study only 40% of these

NOTE Confidence: 0.793747172222222

 $00{:}53{:}14.080 \dashrightarrow 00{:}53{:}16.300$  people who are having long term

NOTE Confidence: 0.793747172222222

00:53:16.300 --> 00:53:18.357 symptoms actually had a nausea or

NOTE Confidence: 0.793747172222222

 $00{:}53{:}18.357 \dashrightarrow 00{:}53{:}20.148$  or thus ia during acute COVID and

 $00:53:20.148 \longrightarrow 00:53:21.516$  what are the symptoms that they

NOTE Confidence: 0.793747172222222

 $00:53:21.516 \longrightarrow 00:53:22.460$  are now presenting with?

NOTE Confidence: 0.793747172222222

 $00:53:22.460 \longrightarrow 00:53:24.971$  We do a very very detailed survey of what

NOTE Confidence: 0.793747172222222

00:53:24.971 --> 00:53:27.457 kinds of symptoms people are experiencing,

NOTE Confidence: 0.793747172222222

 $00:53:27.460 \longrightarrow 00:53:29.340$  so you'll see lots of things on here.

NOTE Confidence: 0.793747172222222

 $00:53:29.340 \longrightarrow 00:53:30.735$  I think we've actually left

NOTE Confidence: 0.793747172222222

00:53:30.735 --> 00:53:32.466 off psychosis which a couple of

NOTE Confidence: 0.793747172222222

00:53:32.466 --> 00:53:33.876 people have also had psychosis,

NOTE Confidence: 0.793747172222222

 $00:53:33.880 \longrightarrow 00:53:34.780$  but you can see that.

NOTE Confidence: 0.793747172222222

 $00:53:34.780 \longrightarrow 00:53:36.970$  The majority of people are now

NOTE Confidence: 0.793747172222222

00:53:36.970 --> 00:53:38.430 having what they describe

NOTE Confidence: 0.811268676153846

00:53:38.503 --> 00:53:40.664 as cognitive impairment, anxiety,

NOTE Confidence: 0.811268676153846

 $00:53:40.664 \rightarrow 00:53:43.040$  depression, fatigue and headache,

NOTE Confidence: 0.811268676153846

 $00{:}53{:}43.040 \dashrightarrow 00{:}53{:}44.896$  and then some of these patients also have

NOTE Confidence: 0.811268676153846

 $00{:}53{:}44.896 \dashrightarrow 00{:}53{:}46.829$  some of these other types of symptoms.

NOTE Confidence: 0.832369560769231

 $00{:}53{:}48.850 \dashrightarrow 00{:}53{:}50.170$  So what I'm going to show you were

 $00:53:50.170 \rightarrow 00:53:51.598$  just some really preliminary findings,

NOTE Confidence: 0.832369560769231

 $00:53:51.600 \rightarrow 00:53:52.758$  and in all of these figures,

NOTE Confidence: 0.832369560769231

 $00:53:52.760 \rightarrow 00:53:54.950$  the post COVID participants again

NOTE Confidence: 0.832369560769231

00:53:54.950 --> 00:53:57.632 about a year after having COVID-19

NOTE Confidence: 0.832369560769231

 $00{:}53{:}57{.}632 \dashrightarrow 00{:}54{:}00{.}340$  a median time are shown in the red

NOTE Confidence: 0.832369560769231

 $00{:}54{:}00{.}340 \dashrightarrow 00{:}54{:}02{.}280$  and our pre pandemic control samples

NOTE Confidence: 0.832369560769231

 $00:54:02.280 \rightarrow 00:54:04.270$  who are basically healthy controls

NOTE Confidence: 0.832369560769231

 $00{:}54{:}04{.}270 \dashrightarrow 00{:}54{:}06{.}882$  that were recruited for each of these

NOTE Confidence: 0.832369560769231

 $00{:}54{:}06{.}882 \dashrightarrow 00{:}54{:}08{.}424$  studies are shown in the orange and

NOTE Confidence: 0.832369560769231

00:54:08.424 --> 00:54:10.308 what you can see here is we've looked

NOTE Confidence: 0.832369560769231

00:54:10.308 --> 00:54:11.838 at sort of different categories of

NOTE Confidence: 0.832369560769231

00:54:11.885 --> 00:54:13.369 markers and preliminary studies.

NOTE Confidence: 0.832369560769231

00:54:13.370 --> 00:54:15.170 These are immune measures that we

NOTE Confidence: 0.832369560769231

00:54:15.170 --> 00:54:16.695 wondered whether might be abnormal

NOTE Confidence: 0.832369560769231

00:54:16.695 - 00:54:18.309 in the people who had COVID.

 $00:54:18.310 \longrightarrow 00:54:20.934$  And you can see that the only one

NOTE Confidence: 0.832369560769231

 $00:54:20.934 \rightarrow 00:54:22.486$  that's persistently abnormal a year

NOTE Confidence: 0.832369560769231

 $00:54:22.486 \dashrightarrow 00:54:24.870$  after COVID seems to be the D dimer,

NOTE Confidence: 0.832369560769231

 $00:54:24.870 \rightarrow 00:54:26.630$  which is only slightly elevated

NOTE Confidence: 0.832369560769231

 $00{:}54{:}26{.}630 \dashrightarrow 00{:}54{:}29{.}162$  and seems to be driven by small

NOTE Confidence: 0.832369560769231

 $00:54:29.162 \rightarrow 00:54:30.814$  numbers of people. Do you die?

NOTE Confidence: 0.832369560769231

 $00{:}54{:}30{.}814 \dashrightarrow 00{:}54{:}32{.}002$  Mark is a sort of general

NOTE Confidence: 0.832369560769231

 $00:54:32.002 \rightarrow 00:54:32.940$  acute phase reactant,

NOTE Confidence: 0.832369560769231

 $00{:}54{:}32{.}940 \dashrightarrow 00{:}54{:}34{.}872$  but it's also of course a marker

NOTE Confidence: 0.832369560769231

 $00:54:34.872 \rightarrow 00:54:36.569$  of clotting and microphone by,

NOTE Confidence: 0.832369560769231

 $00{:}54{:}36{.}570 \dashrightarrow 00{:}54{:}38{.}025$  so that's potentially a little

NOTE Confidence: 0.832369560769231

 $00:54:38.025 \rightarrow 00:54:40.049$  hint of what could be going on.

NOTE Confidence: 0.832369560769231

 $00{:}54{:}40{.}050 \dashrightarrow 00{:}54{:}42{.}378$  And then we've also had a nice collaboration

NOTE Confidence: 0.832369560769231

 $00{:}54{:}42{.}378 \dashrightarrow 00{:}54{:}44{.}928$  to look at neuronal and a strocyte markers,

NOTE Confidence: 0.832369560769231

 $00:54:44.930 \rightarrow 00:54:47.218$  and what we were surprised to find is

NOTE Confidence: 0.832369560769231

 $00:54:47.218 \rightarrow 00:54:49.137$  that although most of these neuronal.
- NOTE Confidence: 0.832369560769231
- $00{:}54{:}49{.}140 \dashrightarrow 00{:}54{:}51{.}947$  Matt astrocyte markers NFL and Tau were
- NOTE Confidence: 0.832369560769231
- $00{:}54{:}51{.}947 \dashrightarrow 00{:}54{:}54{.}558$  normal or similar between the groups.
- NOTE Confidence: 0.832369560769231
- $00:54:54.560 \longrightarrow 00:54:56.583$  We did find a hint of a strocyte
- NOTE Confidence: 0.832369560769231
- $00:54:56.583 \rightarrow 00:54:59.038$  injury in the blood and these people
- NOTE Confidence: 0.832369560769231
- $00:54:59.038 \rightarrow 00:55:01.312$  with long term symptoms after COVID.
- NOTE Confidence: 0.832369560769231
- $00:55:01.320 \longrightarrow 00:55:02.700$  What exactly that means and where
- NOTE Confidence: 0.832369560769231
- $00:55:02.700 \rightarrow 00:55:04.260$  this GF AP is coming from?
- NOTE Confidence: 0.832369560769231
- $00:55:04.260 \rightarrow 00:55:05.534$  Is it definitely coming from the brain,
- NOTE Confidence: 0.832369560769231
- $00:55:05.540 \longrightarrow 00:55:07.256$  or could it be coming from
- NOTE Confidence: 0.832369560769231
- $00:55:07.256 \rightarrow 00:55:08.680$  peripheral nerves in some way?
- NOTE Confidence: 0.832369560769231
- $00:55:08.680 \longrightarrow 00:55:10.000$  Or some other kind of cell
- NOTE Confidence: 0.832369560769231
- $00:55:10.000 \rightarrow 00:55:11.359$  tech that we're not aware of?
- NOTE Confidence: 0.832369560769231
- $00:55:11.360 \longrightarrow 00:55:12.832$  Is it interesting question?
- NOTE Confidence: 0.832369560769231
- $00{:}55{:}12.832 \dashrightarrow 00{:}55{:}15.471$  But this would be interpreted as actually
- NOTE Confidence: 0.832369560769231
- $00{:}55{:}15{.}471 \dashrightarrow 00{:}55{:}17{.}643$  being injury to a strocytes in the
- NOTE Confidence: 0.832369560769231

 $00:55:17.643 \rightarrow 00:55:20.208$  brain that we're detecting in the blood.

NOTE Confidence: 0.832369560769231

 $00{:}55{:}20{.}210 \dashrightarrow 00{:}55{:}21{.}536$  We've also looked at spinal fluid

NOTE Confidence: 0.832369560769231

 $00:55:21.536 \longrightarrow 00:55:23.010$  in all of these individuals,

NOTE Confidence: 0.832369560769231

 $00:55:23.010 \rightarrow 00:55:24.648$  so again these are really generous

NOTE Confidence: 0.832369560769231

 $00{:}55{:}24.648 \dashrightarrow 00{:}55{:}25.740$  participants who are coming

NOTE Confidence: 0.832369560769231

 $00:55:25.791 \rightarrow 00:55:26.847$  in for lumbar punctures,

NOTE Confidence: 0.832369560769231

 $00:55:26.850 \longrightarrow 00:55:28.040$  and you can see here that the

NOTE Confidence: 0.832369560769231

 $00{:}55{:}28.040 \dashrightarrow 00{:}55{:}28.989$  white cell counts are normal.

NOTE Confidence: 0.832369560769231

 $00{:}55{:}28{.}990 \dashrightarrow 00{:}55{:}30{.}215$  This is consistent with all

NOTE Confidence: 0.832369560769231

 $00:55:30.215 \rightarrow 00:55:30.950$  the clinical experience,

NOTE Confidence: 0.832369560769231

 $00:55:30.950 \longrightarrow 00:55:32.414$  even during acute COVID.

NOTE Confidence: 0.832369560769231

 $00:55:32.414 \rightarrow 00:55:34.610$  The protein albumin ratio when marker

NOTE Confidence: 0.832369560769231

 $00{:}55{:}34.670 \dashrightarrow 00{:}55{:}36.500$  blood brain barrier are normal.

NOTE Confidence: 0.832369560769231

 $00{:}55{:}36{.}500 \dashrightarrow 00{:}55{:}38{.}552$  We did find a higher percentage

NOTE Confidence: 0.832369560769231

 $00:55:38.552 \rightarrow 00:55:40.770$  of monocytes in the CSF and

NOTE Confidence: 0.832369560769231

 $00{:}55{:}40.770 \dashrightarrow 00{:}55{:}42.690$  individuals that have are still

- NOTE Confidence: 0.832369560769231
- $00:55:42.690 \rightarrow 00:55:44.190$  experiencing symptoms after COVID,
- NOTE Confidence: 0.832369560769231
- $00:55:44.190 \longrightarrow 00:55:45.840$  so we're investigating that with more
- NOTE Confidence: 0.832369560769231
- $00:55:45.840 \rightarrow 00:55:47.350$  detailed solely on their studies,
- NOTE Confidence: 0.832369560769231
- $00{:}55{:}47{.}350 \dashrightarrow 00{:}55{:}49{.}492$  but it may be a hint that there's still
- NOTE Confidence: 0.832369560769231
- $00{:}55{:}49{.}492 \dashrightarrow 00{:}55{:}51{.}358$  some cellular immune perturbation.
- NOTE Confidence: 0.832369560769231
- $00:55:51.360 \rightarrow 00:55:53.838$  And finally, looking at the neuronal
- NOTE Confidence: 0.832369560769231
- $00:55:53.838 \rightarrow 00:55:55.077$  and astrocyte measures,
- NOTE Confidence: 0.832369560769231
- $00:55:55.080 \rightarrow 00:55:57.420$  we do see elevations in GF,
- NOTE Confidence: 0.832369560769231
- $00{:}55{:}57{.}420 \dashrightarrow 00{:}56{:}00{.}957$  AP and NFL in a couple of the people,
- NOTE Confidence: 0.832369560769231
- 00:56:00.960 --> 00:56:03.310 but we're not seeing significantly
- NOTE Confidence: 0.832369560769231
- $00:56:03.310 \longrightarrow 00:56:05.320$  different levels in the CSF.
- NOTE Confidence: 0.832369560769231
- $00{:}56{:}05{.}320 \dashrightarrow 00{:}56{:}06{.}475$  In these people,
- NOTE Confidence: 0.832369560769231
- $00{:}56{:}06{.}480 \dashrightarrow 00{:}56{:}08{.}820$  we're seeing a hint to elevations
- NOTE Confidence: 0.832369560769231
- 00:56:08.820 --> 00:56:10.380 and CSF S tream,
- NOTE Confidence: 0.832369560769231
- $00{:}56{:}10{.}380 \dashrightarrow 00{:}56{:}13{.}236$  which is a microglial activation marker,
- NOTE Confidence: 0.832369560769231

 $00:56:13.240 \longrightarrow 00:56:14.716$  but again, you can see why.

NOTE Confidence: 0.832369560769231

00:56:14.720 --> 00:56:16.670 I feel strongly that before we

NOTE Confidence: 0.832369560769231

 $00:56:16.670 \longrightarrow 00:56:18.898$  report any of this to the world,

NOTE Confidence: 0.832369560769231

 $00:56:18.900 \rightarrow 00:56:20.120$  we really need more people.

NOTE Confidence: 0.832369560769231

 $00:56:20.120 \longrightarrow 00:56:21.728$  You can see there's a lot of heterogeneity.

NOTE Confidence: 0.832369560769231

 $00{:}56{:}21.730 \dashrightarrow 00{:}56{:}23.970$  Here and we need to understand what

NOTE Confidence: 0.832369560769231

 $00:56:23.970 \rightarrow 00:56:25.724$  are these patterns are persisting

NOTE Confidence: 0.832369560769231

 $00:56:25.724 \rightarrow 00:56:27.544$  in larger numbers of people.

NOTE Confidence: 0.822511573333333

00:56:27.550 --> 00:56:28.000 Interestingly,

NOTE Confidence: 0.822511573333333

 $00:56:28.000 \rightarrow 00:56:30.637$  we're seeing persistence of SARS, Co.

NOTE Confidence: 0.822511573333333

 $00{:}56{:}30{.}637 \dashrightarrow 00{:}56{:}33{.}346$  V2 antibodies in the CSF and almost

NOTE Confidence: 0.822511573333333

 $00:56:33.346 \dashrightarrow 00:56:35.420$  everybody that we're looking at.

NOTE Confidence: 0.822511573333333

 $00:56:35.420 \rightarrow 00:56:37.388$  You expect the anti spike antibody

NOTE Confidence: 0.822511573333333

 $00:56:37.388 \longrightarrow 00:56:40.169$  on the top to be positive and

NOTE Confidence: 0.822511573333333

 $00:56:40.169 \rightarrow 00:56:42.080$  everyone who's vaccinated and it

NOTE Confidence: 0.822511573333333

 $00:56:42.080 \longrightarrow 00:56:43.865$  does seem to be positive but the

- NOTE Confidence: 0.822511573333333
- $00:56:43.865 \rightarrow 00:56:45.924$  anti nucleocapsid antibody is not

 $00{:}56{:}45{.}924 \dashrightarrow 00{:}56{:}48{.}099$  something that turns positive with

NOTE Confidence: 0.822511573333333

 $00:56:48.099 \rightarrow 00:56:49.807$  vaccination and that is persistently

NOTE Confidence: 0.822511573333333

 $00:56:49.807 \rightarrow 00:56:51.898$  positive in the CSF and the blood.

NOTE Confidence: 0.822511573333333

 $00:56:51.898 \longrightarrow 00:56:53.566$  And and most of the people

NOTE Confidence: 0.822511573333333

 $00:56:53.566 \longrightarrow 00:56:54.620$  that we've looked at,

NOTE Confidence: 0.822511573333333

 $00:56:54.620 \longrightarrow 00:56:57.524$  so it's kind of interesting to see that

NOTE Confidence: 0.822511573333333

 $00:56:57.524 \rightarrow 00:57:00.040$  these antiviral antibodies are persisting,

NOTE Confidence: 0.822511573333333

 $00{:}57{:}00{.}040 \dashrightarrow 00{:}57{:}02{.}122$  and we're doing now additional studies

NOTE Confidence: 0.822511573333333

 $00:57:02.122 \rightarrow 00:57:03.950$  to look for evidence of autoimmunity.

NOTE Confidence: 0.822511573333333

00:57:03.950 - 00:57:06.143 So I'm going to end by a comparison

NOTE Confidence: 0.822511573333333

 $00{:}57{:}06{.}143 \dashrightarrow 00{:}57{:}08{.}045$  between two virus es that now I've

NOTE Confidence: 0.822511573333333

 $00:57:08.045 \longrightarrow 00:57:09.679$  been studied for a long time.

NOTE Confidence: 0.822511573333333

00:57:09.680 --> 00:57:10.884 Just to give you a sense of

NOTE Confidence: 0.822511573333333

 $00:57:10.884 \rightarrow 00:57:11.560$  how stars could be,

 $00:57:11.560 \longrightarrow 00:57:13.330$  2 might be different than other

NOTE Confidence: 0.822511573333333

 $00{:}57{:}13.330 \dashrightarrow 00{:}57{:}14.510$  virus es that we understand.

NOTE Confidence: 0.822511573333333

00:57:14.510 --> 00:57:16.980 So in general acute HIV,

NOTE Confidence: 0.822511573333333

 $00:57:16.980 \longrightarrow 00:57:18.070$  which is really something that

NOTE Confidence: 0.822511573333333

 $00:57:18.070 \dashrightarrow 00:57:19.420$  we've been studying for many years,

NOTE Confidence: 0.822511573333333

 $00{:}57{:}19{.}420 \dashrightarrow 00{:}57{:}21{.}842$  looking at the first weeks and months NOTE Confidence: 0.822511573333333

00:57:21.842 - 00:57:25.010 after initial HIV entry into the body,

NOTE Confidence: 0.822511573333333

 $00:57:25.010 \rightarrow 00:57:27.596$  is associated with robust viral invasion.

NOTE Confidence: 0.822511573333333

 $00{:}57{:}27{.}600 \dashrightarrow 00{:}57{:}30{.}400$  This can be detected in the CSF.

NOTE Confidence: 0.822511573333333

 $00:57:30.400 \longrightarrow 00:57:32.157$  This can be detected in the brain,

NOTE Confidence: 0.822511573333333

 $00{:}57{:}32{.}160 \dashrightarrow 00{:}57{:}33{.}774$  whereas servers could be 2 does

NOTE Confidence: 0.822511573333333

 $00:57:33.774 \longrightarrow 00:57:35.580$  not seem to have significant.

NOTE Confidence: 0.822511573333333

 $00{:}57{:}35{.}580 \dashrightarrow 00{:}57{:}36{.}126$  Viral invasion,

NOTE Confidence: 0.822511573333333

 $00:57:36.126 \longrightarrow 00:57:38.310$  at least it does not seem to be

NOTE Confidence: 0.822511573333333

 $00:57:38.376 \rightarrow 00:57:40.296$  something that's detectable at the level

NOTE Confidence: 0.822511573333333

 $00{:}57{:}40.296 \dashrightarrow 00{:}57{:}42.858$  of CSF or most brain tissue studies.

 $00:57:42.860 \rightarrow 00:57:43.326$  However,

NOTE Confidence: 0.822511573333333

 $00{:}57{:}43.326 \dashrightarrow 00{:}57{:}46.122$  both viruses seem to be associated

NOTE Confidence: 0.822511573333333

 $00:57:46.122 \longrightarrow 00:57:48.600$  with immune cell trafficking to

NOTE Confidence: 0.822511573333333

00:57:48.600 - 00:57:51.095 the CNS and immune activation,

NOTE Confidence: 0.822511573333333

 $00{:}57{:}51{.}100 \dashrightarrow 00{:}57{:}52{.}186$  so generalized neuroinflammation

NOTE Confidence: 0.822511573333333

00:57:52.186 --> 00:57:53.996 I mentioned the fact that

NOTE Confidence: 0.822511573333333

 $00:57:53.996 \dashrightarrow 00:57:55.559$  there's changes in siding kinds.

NOTE Confidence: 0.822511573333333

 $00{:}57{:}55{.}560 \dashrightarrow 00{:}57{:}58{.}748$  There's also microglial activation

NOTE Confidence: 0.822511573333333

 $00:57:58.748 \longrightarrow 00:58:01.936$  in brain autopsy tissues.

NOTE Confidence: 0.822511573333333

 $00{:}58{:}01{.}940 \dashrightarrow 00{:}58{:}03{.}450$  Autoimmune responses do occur in

NOTE Confidence: 0.822511573333333

 $00:58:03.450 \rightarrow 00:58:05.266$  some people with acute HIV and

NOTE Confidence: 0.822511573333333

00:58:05.266 --> 00:58:06.988 it's kind of one of those hallmarks

NOTE Confidence: 0.822511573333333

 $00{:}58{:}06{.}988 \dashrightarrow 00{:}58{:}08{.}664$  that you teach residents to look

NOTE Confidence: 0.822511573333333

 $00{:}58{:}08.664 \dashrightarrow 00{:}58{:}10.356$  for acute HIV and some body with

NOTE Confidence: 0.822511573333333

 $00{:}58{:}10{.}360 \dashrightarrow 00{:}58{:}12{.}270$  Jan Murray and emergency room.

 $00{:}58{:}12.270 \dashrightarrow 00{:}58{:}14.670$  But in fact this seems to be something

NOTE Confidence: 0.822511573333333

 $00:58:14.670 \rightarrow 00:58:16.858$  we're seeing frequently in acute COVID.

NOTE Confidence: 0.822511573333333

00:58:16.860 - 00:58:18.337 And is that because we just have

NOTE Confidence: 0.822511573333333

 $00{:}58{:}18{.}337 \dashrightarrow 00{:}58{:}19{.}818$  billions of cases of COVID worldwide,

NOTE Confidence: 0.822511573333333

 $00:58:19.820 \rightarrow 00:58:21.620$  so we're seeing these conditions more?

NOTE Confidence: 0.822511573333333

 $00:58:21.620 \dashrightarrow 00:58:22.995$  Or is there actually something

NOTE Confidence: 0.822511573333333

 $00{:}58{:}22{.}995 \dashrightarrow 00{:}58{:}24{.}770$  about this virus that is more

NOTE Confidence: 0.822511573333333

 $00:58:24.770 \rightarrow 00:58:26.170$  prone to trigger autoimmunity?

NOTE Confidence: 0.822511573333333

 $00{:}58{:}26{.}170 \dashrightarrow 00{:}58{:}28{.}039$  And so I think it's a super

NOTE Confidence: 0.822511573333333

 $00:58:28.039 \rightarrow 00:58:28.573$  important question.

NOTE Confidence: 0.822511573333333

 $00{:}58{:}28{.}580 \dashrightarrow 00{:}58{:}30{.}035$  Acute thrombosis and stroke is

NOTE Confidence: 0.822511573333333

00:58:30.035 --> 00:58:31.848 a feature of acute COVID which

NOTE Confidence: 0.822511573333333

 $00:58:31.848 \longrightarrow 00:58:33.348$  is different than acute HIV.

NOTE Confidence: 0.822511573333333

 $00:58:33.350 \rightarrow 00:58:35.384$  So it really relates to something

NOTE Confidence: 0.822511573333333

 $00:58:35.384 \rightarrow 00:58:37.708$  particular about how this virus activates

NOTE Confidence: 0.822511573333333

 $00:58:37.708 \rightarrow 00:58:39.968$  endothelial cells and clotting systems.

- NOTE Confidence: 0.822511573333333
- $00:58:39.970 \longrightarrow 00:58:42.268$  Nerdy generation seems to be detectable
- NOTE Confidence: 0.822511573333333
- $00:58:42.268 \dashrightarrow 00:58:44.650$  in some people with acute COVID.
- NOTE Confidence: 0.822511573333333
- $00{:}58{:}44{.}650 \dashrightarrow 00{:}58{:}47{.}530$  We also see this in acute infection with HIV.
- NOTE Confidence: 0.822511573333333
- $00:58:47.530 \longrightarrow 00:58:48.965$  So what are going to be the
- NOTE Confidence: 0.822511573333333
- 00:58:48.965 --> 00:58:49.950 long term consequences of this?
- NOTE Confidence: 0.822511573333333
- 00:58:49.950 --> 00:58:51.470 I think we don't know.
- NOTE Confidence: 0.822511573333333
- 00:58:51.470 -> 00:58:52.990 Clearly HIV is a persistent
- NOTE Confidence: 0.822511573333333
- $00:58:52.990 \rightarrow 00:58:54.819$  infection as I explained the viral
- NOTE Confidence: 0.822511573333333
- $00:58:54.819 \longrightarrow 00:58:56.569$  life cycle is one that you get
- NOTE Confidence: 0.822511573333333
- $00:58:56.569 \rightarrow 00:58:58.493$  long term infection of host cells
- NOTE Confidence: 0.822511573333333
- $00:58:58.493 \rightarrow 00:59:00.203$  because the virus integrates its
- NOTE Confidence: 0.822511573333333
- $00:59:00.203 \longrightarrow 00:59:01.978$  genome into our host cells.
- NOTE Confidence: 0.822511573333333
- $00:59:01.978 \longrightarrow 00:59:03.763$  This is hopefully not true.
- NOTE Confidence: 0.822511573333333
- 00:59:03.770 --> 00:59:04.994 Instars kovi 2.
- NOTE Confidence: 0.822511573333333
- $00:59:04.994 \dashrightarrow 00:59:07.442$  We don't even see initial infection,
- NOTE Confidence: 0.822511573333333

 $00:59:07.450 \rightarrow 00:59:09.310$  so hopefully it's not persistent infection,

NOTE Confidence: 0.822511573333333

 $00{:}59{:}09{.}310 \dashrightarrow 00{:}59{:}11{.}347$  but that doesn't mean there isn't persistent.

NOTE Confidence: 0.822511573333333

 $00{:}59{:}11{.}350 \dashrightarrow 00{:}59{:}13{.}348$  Antigen presence and I think that's

NOTE Confidence: 0.822511573333333

 $00:59:13.348 \longrightarrow 00:59:14.680$  a really important distinction

NOTE Confidence: 0.822511573333333

 $00:59:14.734 \dashrightarrow 00:59:16.349$  and important area for research.

NOTE Confidence: 0.84228417

 $00{:}59{:}16.350 \dashrightarrow 00{:}59{:}18.065$  Long term neurologic suquilla is

NOTE Confidence: 0.84228417

 $00:59:18.065 \rightarrow 00:59:19.780$  clearly something that happens when

NOTE Confidence: 0.84228417

 $00:59:19.831 \longrightarrow 00:59:21.643$  you set up infection and inflammation

NOTE Confidence: 0.84228417

 $00{:}59{:}21.643 \dashrightarrow 00{:}59{:}23.110$  in reservoirs in acute HIV,

NOTE Confidence: 0.84228417

 $00:59:23.110 \dashrightarrow 00:59:24.657$  but I think the question of whether

NOTE Confidence: 0.84228417

 $00:59:24.657 \dashrightarrow 00:59:26.847$  or not this is going to be a long term NOTE Confidence: 0.84228417

 $00:59:26.847 \rightarrow 00:59:28.216$  problem and people with acute stars

NOTE Confidence: 0.84228417

 $00{:}59{:}28.216 \dashrightarrow 00{:}59{:}30.850$  could be too still needs to be answered.

NOTE Confidence: 0.84228417

00:59:30.850 --> 00:59:32.026 So I'm going to end by just saying,

NOTE Confidence: 0.84228417

 $00{:}59{:}32{.}030 \dashrightarrow 00{:}59{:}33{.}590$  you know, these are the gaps and questions.

NOTE Confidence: 0.84228417

 $00:59:33.590 \longrightarrow 00:59:35.207$  Why do we still need to learn?

 $00:59:35.210 \rightarrow 00:59:36.800$  I think the really pressing questions

NOTE Confidence: 0.84228417

 $00{:}59{:}36{.}800 \dashrightarrow 00{:}59{:}38{.}732$  now relate to long COVID and these

NOTE Confidence: 0.84228417

 $00:59:38.732 \dashrightarrow 00:59:40.650$  lingering effects of people who are really

NOTE Confidence: 0.84228417

 $00{:}59{:}40.705 \dashrightarrow 00{:}59{:}42.409$  having trouble getting back to work.

NOTE Confidence: 0.84228417

00:59:42.410 --> 00:59:44.380 I'm having trouble functioning having

NOTE Confidence: 0.84228417

 $00:59:44.380 \dashrightarrow 00:59:47.669$  very little to turn in terms of the rapies,

NOTE Confidence: 0.84228417

 $00{:}59{:}47.670 \dashrightarrow 00{:}59{:}49.931$  so we need to understand the biological

NOTE Confidence: 0.84228417

 $00:59:49.931 \rightarrow 00:59:52.169$  mechanisms of these long ongoing symptoms.

NOTE Confidence: 0.84228417

 $00{:}59{:}52{.}170 \dashrightarrow 00{:}59{:}54{.}585$  One possibility is this is due to

NOTE Confidence: 0.84228417

 $00:59:54.585 \rightarrow 00:59:56.550$  injury occurred during two infection.

NOTE Confidence: 0.84228417

 $00:59:56.550 \longrightarrow 00:59:58.182$  I will say I do not think this

NOTE Confidence: 0.84228417

 $00{:}59{:}58{.}182 \dashrightarrow 00{:}59{:}59{.}090$  is the problem.

NOTE Confidence: 0.84228417

00:59:59.090 - 01:00:01.386 I think many people who have severe

NOTE Confidence: 0.84228417

01:00:01.386 --> 01:00:03.522 disease during acute infection recover

NOTE Confidence: 0.84228417

 $01{:}00{:}03.522 \dashrightarrow 01{:}00{:}05.834$  completely and then some people who have

 $01{:}00{:}05.834 \dashrightarrow 01{:}00{:}08.382$  mild disease who don't seem to have had

NOTE Confidence: 0.84228417

 $01{:}00{:}08.382 \dashrightarrow 01{:}00{:}10.022$  neurologic symptoms even during that

NOTE Confidence: 0.84228417

 $01:00:10.022 \rightarrow 01:00:12.389$  time seemed to have persistent symptoms.

NOTE Confidence: 0.84228417

 $01:00:12.390 \longrightarrow 01:00:13.758$  But of course we need to

NOTE Confidence: 0.84228417

 $01:00:13.758 \longrightarrow 01:00:14.670$  be studying that more.

NOTE Confidence: 0.84228417

 $01{:}00{:}14.670 \dashrightarrow 01{:}00{:}17.010$  Another possibility is ongoing perturbations

NOTE Confidence: 0.84228417

 $01:00:17.010 \rightarrow 01:00:19.350$  and inflammation and immune responses,

NOTE Confidence: 0.84228417

 $01{:}00{:}19.350 \dashrightarrow 01{:}00{:}21.492$  and I think this is one of the major

NOTE Confidence: 0.84228417

01:00:21.492 --> 01:00:22.948 hypothesis for long COVID overall,

NOTE Confidence: 0.84228417

 $01{:}00{:}22.950 \dashrightarrow 01{:}00{:}24.222$  and I think as it relates

NOTE Confidence: 0.84228417

 $01:00:24.222 \rightarrow 01:00:25.070$  to the nervous system,

NOTE Confidence: 0.84228417

 $01{:}00{:}25{.}070 \dashrightarrow 01{:}00{:}26{.}252$  we have a lot of evidence

NOTE Confidence: 0.84228417

 $01{:}00{:}26.252 \dashrightarrow 01{:}00{:}27.310$  that that might be true.

NOTE Confidence: 0.84228417

 $01{:}00{:}27.310 \dashrightarrow 01{:}00{:}29.776$  Can there be a vascular inflammation

NOTE Confidence: 0.84228417

 $01{:}00{:}29.776 \dashrightarrow 01{:}00{:}31.420$  or microvascular compromise that's

NOTE Confidence: 0.84228417

 $01:00:31.485 \longrightarrow 01:00:33.195$  continuing to have impacts on

- NOTE Confidence: 0.84228417
- $01{:}00{:}33.195 \dashrightarrow 01{:}00{:}35.321$  blood flow and brain function even

01:00:35.321 --> 01:00:37.106 after recovery from acute COVID?

NOTE Confidence: 0.84228417

01:00:37.110 --> 01:00:37.790 And finally,

NOTE Confidence: 0.84228417

 $01:00:37.790 \longrightarrow 01:00:39.830$  is there a possibility that there's

NOTE Confidence: 0.84228417

 $01:00:39.830 \longrightarrow 01:00:41.735$  low level viral antigen either

NOTE Confidence: 0.84228417

 $01:00:41.735 \longrightarrow 01:00:43.279$  in the endothelial cells?

NOTE Confidence: 0.84228417

 $01{:}00{:}43.280 \dashrightarrow 01{:}00{:}45.604$  Wanting them to blood vessels in the

NOTE Confidence: 0.84228417

01:00:45.604 --> 01:00:48.077 brain or actually in brain tissue itself,

NOTE Confidence: 0.84228417

 $01{:}00{:}48.080 \dashrightarrow 01{:}00{:}50.232$  and I think this is still an area

NOTE Confidence: 0.84228417

 $01:00:50.232 \dashrightarrow 01:00:52.000$  that needs to be investigated.

NOTE Confidence: 0.84228417

01:00:52.000 --> 01:00:53.320 And I'll end by talking about,

NOTE Confidence: 0.84228417

 $01{:}00{:}53{.}320 \dashrightarrow 01{:}00{:}54{.}120$  you know this is a.

NOTE Confidence: 0.84228417

 $01:00:54.120 \rightarrow 01:00:55.836$  This is a pretty vulnerable population.

NOTE Confidence: 0.84228417

01:00:55.840 --> 01:00:57.268 I spent my career taking care

NOTE Confidence: 0.84228417

 $01:00:57.268 \rightarrow 01:00:58.220$  of people with HIV.

- 01:00:58.220 --> 01:00:59.069 And you know,
- NOTE Confidence: 0.84228417
- $01:00:59.069 \longrightarrow 01:00:59.918$  this is it's.
- NOTE Confidence: 0.84228417
- $01{:}00{:}59{.}920 \dashrightarrow 01{:}01{:}02{.}139$  It's been a highly recognized for a
- NOTE Confidence: 0.84228417
- 01:01:02.139 $\dashrightarrow>$ 01:01:04.150 really long time that people living
- NOTE Confidence: 0.84228417
- 01:01:04.150 --> 01:01:06.460 with HIV are vulnerable to lots and
- NOTE Confidence: 0.84228417
- $01{:}01{:}06.522 \dashrightarrow 01{:}01{:}08.490$  lots of different social and other
- NOTE Confidence: 0.84228417
- $01{:}01{:}08.490 \dashrightarrow 01{:}01{:}10.622$  kinds of challenges that make living NOTE Confidence: 0.84228417
- 01:01:10.622 --> 01:01:12.462 with illness even more difficult.
- NOTE Confidence: 0.84228417
- $01{:}01{:}12{.}470 \dashrightarrow 01{:}01{:}14{.}294$  And I would say that there are ways NOTE Confidence: 0.84228417
- $01{:}01{:}14{.}294 \dashrightarrow 01{:}01{:}16{.}420$  in which long COVID also has a lot
- NOTE Confidence: 0.84228417
- $01{:}01{:}16.420 \dashrightarrow 01{:}01{:}17.920$  of personal challenges for people.
- NOTE Confidence: 0.84228417
- 01:01:17.920 --> 01:01:19.132 There's stigma associated with
- NOTE Confidence: 0.84228417
- 01:01:19.132 --> 01:01:19.738 this condition.
- NOTE Confidence: 0.84228417
- $01{:}01{:}19.740 \dashrightarrow 01{:}01{:}20.985$  There's a lack of understanding
- NOTE Confidence: 0.84228417
- 01:01:20.985 --> 01:01:22.230 a lot of people are.
- NOTE Confidence: 0.84228417
- $01:01:22.230 \rightarrow 01:01:23.990$  Really frustrated and how a lack of hope

- NOTE Confidence: 0.84228417
- $01{:}01{:}23.990 \dashrightarrow 01{:}01{:}25.489$  that things are going to get better,
- NOTE Confidence: 0.84228417
- $01:01:25.490 \longrightarrow 01:01:27.002$  so I think this is really why we
- NOTE Confidence: 0.84228417
- 01:01:27.002 --> 01:01:28.743 have such a research mandate to try
- NOTE Confidence: 0.84228417
- $01{:}01{:}28.743 \dashrightarrow 01{:}01{:}30.053$  to understand this condition and
- NOTE Confidence: 0.84228417
- 01:01:30.098 --> 01:01:31.946 hopefully see that it resolves over time,
- NOTE Confidence: 0.84228417
- $01{:}01{:}31{.}950 \dashrightarrow 01{:}01{:}34{.}281$  but if not to develop their the rapeutic
- NOTE Confidence: 0.84228417
- $01{:}01{:}34.281 \dashrightarrow 01{:}01{:}36.074$  interventions that are targeted to
- NOTE Confidence: 0.84228417
- $01{:}01{:}36.074 \dashrightarrow 01{:}01{:}37.914$  and really writing these conditions.
- NOTE Confidence: 0.84228417
- $01{:}01{:}37{.}920 \dashrightarrow 01{:}01{:}41{.}440$  So end by thanking all of our colleagues.
- NOTE Confidence: 0.84228417
- $01:01:41.440 \longrightarrow 01:01:43.176$  Thank you so much for the invitation.
- NOTE Confidence: 0.84228417
- $01:01:43.180 \longrightarrow 01:01:44.926$  Thank you in participant to the
- NOTE Confidence: 0.84228417
- $01{:}01{:}44.926 \dashrightarrow 01{:}01{:}46.090$  general study participants who
- NOTE Confidence: 0.804293125333333
- $01:01:46.145 \longrightarrow 01:01:47.790$  were coming in for these studies in
- NOTE Confidence: 0.804293125333333
- $01:01:47.790 \longrightarrow 01:01:49.532$  the setting of all the uncertainty
- NOTE Confidence: 0.804293125333333
- $01{:}01{:}49.532 \dashrightarrow 01{:}01{:}50.848$  they're experiencing and to
- NOTE Confidence: 0.804293125333333

01:01:50.848 $\operatorname{-->}$ 01:01:52.893 particularly to Shelly and Lindsey who

NOTE Confidence: 0.804293125333333

 $01:01:52.893 \dashrightarrow 01:01:55.350$  are Co directing the study with me.

NOTE Confidence: 0.804293125333333

01:01:55.350 --> 01:01:57.464 I will stop sharing so that I

NOTE Confidence: 0.804293125333333

 $01{:}01{:}57{.}464 \dashrightarrow 01{:}01{:}59{.}409$  can see people for questions.

NOTE Confidence: 0.804293125333333

 $01{:}01{:}59{.}410 \dashrightarrow 01{:}02{:}01{.}996$  Thanks so much for the attention.