WEBVTT

NOTE duration:"00:44:38.2800000"

NOTE recognizability:0.554

NOTE language:en-us

NOTE Confidence: 0.58605236

 $00:00:00.000 \rightarrow 00:00:03.555$ Be here and share my work with you guys.

NOTE Confidence: 0.58605236

 $00{:}00{:}03.560 \dashrightarrow 00{:}00{:}10.640$ Let's see. Does that still look OK?

NOTE Confidence: 0.58605236

00:00:10.640 --> 00:00:12.946 It does, yes. All right, Great.

NOTE Confidence: 0.58605236

00:00:12.946 --> 00:00:17.512 Thank you. So I think we'll start out

NOTE Confidence: 0.58605236

 $00{:}00{:}17.512 \dashrightarrow 00{:}00{:}20.893$ with some problems and hurdles and

NOTE Confidence: 0.58605236

 $00{:}00{:}20.893 \dashrightarrow 00{:}00{:}23.358$ the neuroimaging field in psychiatry,

NOTE Confidence: 0.58605236

 $00:00:23.360 \dashrightarrow 00:00:26.576$ I think this is probably relevant if we NOTE Confidence: 0.58605236

00:00:26.576 --> 00:00:29.732 think of the clinicians in the audience NOTE Confidence: 0.58605236

 $00:00:29.732 \rightarrow 00:00:32.247$ deciding whether there's ever going

NOTE Confidence: 0.58605236

 $00:00:32.247 \dashrightarrow 00:00:35.488$ to be any horizon in which imaging is NOTE Confidence: 0.58605236

 $00{:}00{:}35{.}488 \dashrightarrow 00{:}00{:}37{.}840$ actually useful in their clinical practice.

NOTE Confidence: 0.58605236

 $00{:}00{:}37.840 \dashrightarrow 00{:}00{:}41.074$ I would argue that it isn't typically.

NOTE Confidence: 0.58605236

 $00:00:41.080 \longrightarrow 00:00:45.320$ And so some of the hurdles and

 $00:00:45.320 \rightarrow 00:00:48.840$ and problems in the field include

NOTE Confidence: 0.58605236

 $00{:}00{:}48.840 \dashrightarrow 00{:}00{:}51.884$ a lot of various issues, right.

NOTE Confidence: 0.58605236

 $00{:}00{:}51.884 \dashrightarrow 00{:}00{:}55.880$ Some of them have to do with really finding

NOTE Confidence: 0.58605236

 $00:00:55.978 \longrightarrow 00:00:59.358$ no clear neurobiological evidence that

NOTE Confidence: 0.58605236

 $00{:}00{:}59{.}360 \dashrightarrow 00{:}01{:}01{.}600$ you know fits with the DSM categories.

NOTE Confidence: 0.58605236

00:01:01.600 --> 00:01:04.400 We have correlations with symptoms

NOTE Confidence: 0.58605236

 $00{:}01{:}04{.}400 \dashrightarrow 00{:}01{:}07{.}340$ and other behavioral scales tend

NOTE Confidence: 0.58605236

 $00:01:07.340 \longrightarrow 00:01:10.840$ to be difficult to replicate.

NOTE Confidence: 0.58605236

00:01:10.840 --> 00:01:13.576 We don't use imaging and clinical

NOTE Confidence: 0.58605236

 $00{:}01{:}13.576 \dashrightarrow 00{:}01{:}16.370$ decision making on the the reliability

NOTE Confidence: 0.58605236

 $00{:}01{:}16.370 \dashrightarrow 00{:}01{:}19.450$ of many of the imaging measures we

NOTE Confidence: 0.58605236

00:01:19.450 --> 00:01:22.056 use are suspect and need improvement.

NOTE Confidence: 0.58605236

 $00{:}01{:}22.056 \dashrightarrow 00{:}01{:}25.052$ So we have all these recent publications

NOTE Confidence: 0.58605236

 $00{:}01{:}25{.}052 \dashrightarrow 00{:}01{:}27{.}422$ right in the last few years that

NOTE Confidence: 0.58605236

 $00:01:27.422 \longrightarrow 00:01:29.644$ that are really causing us to re

NOTE Confidence: 0.58605236

 $00{:}01{:}29{.}644 \dashrightarrow 00{:}01{:}31{.}974$ evaluate what we're doing and and what

00:01:31.974 --> 00:01:34.312 kind of horizon we have for making

NOTE Confidence: 0.58605236

00:01:34.312 --> 00:01:36.399 imaging more useful in psychiatry.

NOTE Confidence: 0.4773955

 $00{:}01{:}38.760 \dashrightarrow 00{:}01{:}41.370$ Even though as we are able to share more

NOTE Confidence: 0.4773955

 $00{:}01{:}41{.}370 \dashrightarrow 00{:}01{:}44{.}045$ data with one another and try to look at

NOTE Confidence: 0.4773955

00:01:44.045 --> 00:01:46.366 big scale approaches with typically large

NOTE Confidence: 0.4773955

 $00{:}01{:}46.366 \dashrightarrow 00{:}01{:}49.896$ and studies when you combine them this way.

NOTE Confidence: 0.4773955

 $00{:}01{:}49.896 \dashrightarrow 00{:}01{:}53.452$ There have been some hits to finding

NOTE Confidence: 0.4773955

 $00:01:53.452 \rightarrow 00:01:56.638$ biomarkers and biotypes in recent years,

NOTE Confidence: 0.4773955

 $00{:}01{:}56{.}640 \dashrightarrow 00{:}01{:}59{.}310$ including this paper and many hundreds

NOTE Confidence: 0.4773955

 $00:01:59.310 \longrightarrow 00:02:02.255$ of patients finding minimal evidence for

NOTE Confidence: 0.4773955

00:02:02.255 --> 00:02:05.000 depression abnormality using structural MRI,

NOTE Confidence: 0.4773955

00:02:05.000 --> 00:02:06.996 DTI, task resting state,

NOTE Confidence: 0.4773955

 $00{:}02{:}06{.}996 \dashrightarrow 00{:}02{:}11{.}491$ not being able to find a clear signature

NOTE Confidence: 0.4773955

 $00:02:11.491 \dashrightarrow 00:02:15.280$ that hears our depression imaging marker.

NOTE Confidence: 0.4773955

 $00:02:15.280 \longrightarrow 00:02:18.280$ All right, so that's that's problematic.

 $00:02:18.280 \rightarrow 00:02:20.696$ But this may be more familiar with the

NOTE Confidence: 0.4773955

 $00{:}02{:}20.696 \dashrightarrow 00{:}02{:}22.736$ clinician for the clinicians who don't

NOTE Confidence: 0.4773955

 $00{:}02{:}22{.}736 \dashrightarrow 00{:}02{:}25{.}320$ typically pay as much attention to imaging,

NOTE Confidence: 0.4773955

 $00{:}02{:}25{.}320 \dashrightarrow 00{:}02{:}27{.}588$ which is that the diagnosis itself

NOTE Confidence: 0.4773955

 $00:02:27.588 \dashrightarrow 00:02:30.919$ in a lot of cases is not optimal.

NOTE Confidence: 0.4773955

00:02:30.920 --> 00:02:33.504 And so if you feed in something that's

NOTE Confidence: 0.4773955

 $00:02:33.504 \rightarrow 00:02:35.945$ kind of nebulous and not very precise

NOTE Confidence: 0.4773955

 $00:02:35.945 \longrightarrow 00:02:39.004$ and then you try to create a precise

NOTE Confidence: 0.4773955

 $00{:}02{:}39{.}004 \dashrightarrow 00{:}02{:}41{.}951$ measurement of that with an imaging marker,

NOTE Confidence: 0.4773955

 $00:02:41.960 \dashrightarrow 00:02:43.820$ of course you know there's there's

NOTE Confidence: 0.4773955

 $00:02:43.820 \dashrightarrow 00:02:46.680$ going to be a real difficulty there.

NOTE Confidence: 0.4773955

 $00:02:46.680 \rightarrow 00:02:50.124$ We can't even agree amongst one another

NOTE Confidence: 0.4773955

 $00{:}02{:}50{.}124 \dashrightarrow 00{:}02{:}53{.}240$ from clinician to clinician what the

NOTE Confidence: 0.4773955

 $00:02:53.240 \dashrightarrow 00:02:56.036$ right diagnosis is for a patient.

NOTE Confidence: 0.4773955

 $00{:}02{:}56{.}040 \dashrightarrow 00{:}02{:}56{.}964$ So these are hurdles.

NOTE Confidence: 0.4773955

 $00:02:56.964 \rightarrow 00:02:58.680$ I don't have answers for all these,

- NOTE Confidence: 0.4773955
- 00:02:58.680 --> 00:03:01.656 but I I feel like it's it's important

 $00{:}03{:}01{.}656 \dashrightarrow 00{:}03{:}04{.}701$ to bring up some of the struggles

NOTE Confidence: 0.4773955

 $00:03:04.701 \longrightarrow 00:03:06.033$ and the challenges.

NOTE Confidence: 0.4773955

 $00{:}03{:}06{.}040 \dashrightarrow 00{:}03{:}07{.}665$ I'll say on the neuroscience

NOTE Confidence: 0.4773955

 $00:03:07.665 \rightarrow 00:03:08.640$ side with imaging.

NOTE Confidence: 0.4773955

 $00{:}03{:}08{.}640 \dashrightarrow 00{:}03{:}12{.}098$ There are other issues when we think

NOTE Confidence: 0.4773955

00:03:12.098 --> 00:03:14.821 about making bridges to patients

NOTE Confidence: 0.4773955

 $00:03:14.821 \longrightarrow 00:03:16.248$ centered decision making.

NOTE Confidence: 0.4773955

 $00:03:16.248 \longrightarrow 00:03:19.640$ One of them is that you can have.

NOTE Confidence: 0.4773955

 $00:03:19.640 \longrightarrow 00:03:21.474$ So this is a paper by my

NOTE Confidence: 0.4773955

00:03:21.480 --> 00:03:22.992 friend John Medallia,

NOTE Confidence: 0.4773955

 $00:03:22.992 \dashrightarrow 00:03:25.660$ who was saying that as neuroscientists,

NOTE Confidence: 0.4773955

 $00{:}03{:}25{.}660 \dashrightarrow 00{:}03{:}28{.}579$ we have these average brains and we've

NOTE Confidence: 0.4773955

 $00:03:28.579 \longrightarrow 00:03:31.078$ all seen pictures of these and they

NOTE Confidence: 0.4773955

 $00:03:31.078 \longrightarrow 00:03:33.272$ have features that in aggregate have

- $00:03:33.272 \rightarrow 00:03:35.960$ never been observed in any single patient.
- NOTE Confidence: 0.4773955
- $00{:}03{:}35{.}960 \dashrightarrow 00{:}03{:}38{.}090$ And and so that's problematic if
- NOTE Confidence: 0.4773955
- $00{:}03{:}38{.}090 \dashrightarrow 00{:}03{:}40{.}090$ you're looking at an average brain
- NOTE Confidence: 0.4773955
- $00:03:40.090 \dashrightarrow 00:03:41.640$ image and you're thinking about,
- NOTE Confidence: 0.4773955
- $00:03:41.640 \longrightarrow 00:03:41.896$ oh,
- NOTE Confidence: 0.4773955
- 00:03:41.896 --> 00:03:42.152 OK,
- NOTE Confidence: 0.4773955
- $00:03:42.152 \rightarrow 00:03:44.720$ how can I make the use of this for applying
- NOTE Confidence: 0.4773955
- $00:03:44.720 \longrightarrow 00:03:46.800$ to this patient who's in front of me?
- NOTE Confidence: 0.4773955
- $00{:}03{:}46{.}800 \dashrightarrow 00{:}03{:}48{.}474$ This is problematic.
- NOTE Confidence: 0.4773955
- $00:03:48.474 \dashrightarrow 00:03:52.380$ Reinforcing this idea is a paper by
- NOTE Confidence: 0.4773955
- $00:03:52.483 \dashrightarrow 00:03:54.940$ Deanna Barch from many years ago,
- NOTE Confidence: 0.4773955
- $00:03:54.940 \longrightarrow 00:03:56.515$ more than 10 years ago,
- NOTE Confidence: 0.4773955
- $00:03:56.520 \rightarrow 00:03:58.840$ and there have been other instances of this.
- NOTE Confidence: 0.4773955
- $00:03:58.840 \rightarrow 00:04:01.514$ On the left side you see something
- NOTE Confidence: 0.4773955
- $00{:}04{:}01{.}514 \dashrightarrow 00{:}04{:}03{.}682$ that's used very widely in
- NOTE Confidence: 0.4773955
- $00:04:03.682 \rightarrow 00:04:06.037$ cognitive neuroscience which is in

- NOTE Confidence: 0.4773955
- $00:04:06.040 \rightarrow 00:04:08.120$ designed to capture working memory,

 $00{:}04{:}08{.}120 \dashrightarrow 00{:}04{:}09{.}680$ other attentional kind of factors.

NOTE Confidence: 0.4773955

 $00:04:09.680 \dashrightarrow 00:04:12.720$ So this is an N back task where you have

NOTE Confidence: 0.4773955

 $00:04:12.802 \rightarrow 00:04:15.994$ more working memory load compared to less.

NOTE Confidence: 0.4773955

00:04:16.000 --> 00:04:17.918 What areas pop up in the brain,

NOTE Confidence: 0.4773955

 $00:04:17.920 \longrightarrow 00:04:19.918$ which ones are strongly active And

NOTE Confidence: 0.4773955

 $00:04:19.918 \longrightarrow 00:04:22.740$ on the left, the left set of images

NOTE Confidence: 0.4773955

 $00:04:22.740 \longrightarrow 00:04:24.875$ are the average brain maps, right?

NOTE Confidence: 0.4773955

 $00:04:24.875 \rightarrow 00:04:26.765$ This is what we normally report

NOTE Confidence: 0.4773955

00:04:26.765 --> 00:04:28.826 in my own work as well, right?

NOTE Confidence: 0.4773955

 $00:04:28.826 \longrightarrow 00:04:29.942$ This is what we usually show

NOTE Confidence: 0.4773955

 $00:04:29.942 \longrightarrow 00:04:30.960$ in an imaging experiment.

NOTE Confidence: 0.4773955

 $00:04:30.960 \longrightarrow 00:04:32.096$ This is the output.

NOTE Confidence: 0.4773955

 $00{:}04{:}32.096 \dashrightarrow 00{:}04{:}33.516$ If on the other hand,

NOTE Confidence: 0.4773955

 $00{:}04{:}33{.}520 \dashrightarrow 00{:}04{:}35{.}030$ instead of taking the average

 $00:04:35.030 \longrightarrow 00:04:36.238$ from the same contrast,

NOTE Confidence: 0.4773955

 $00:04:36.240 \longrightarrow 00:04:37.998$ if instead on the right side,

NOTE Confidence: 0.4773955

00:04:38.000 --> 00:04:40.046 you pay more attention to how

NOTE Confidence: 0.4773955

00:04:40.046 --> 00:04:41.936 many individuals in that group

NOTE Confidence: 0.4773955

 $00:04:41.936 \longrightarrow 00:04:43.756$ are showing strong activation,

NOTE Confidence: 0.4773955

 $00:04:43.760 \dashrightarrow 00:04:45.400$ the map looks a little bit different there.

NOTE Confidence: 0.4773955

00:04:45.400 -> 00:04:46.540 There's some overlaps,

NOTE Confidence: 0.4773955

 $00{:}04{:}46{.}540 \dashrightarrow 00{:}04{:}48{.}440$ but there's also some differences.

NOTE Confidence: 0.59921736

00:04:48.440 --> 00:04:50.000 If you look closely right,

NOTE Confidence: 0.59921736

 $00:04:50.000 \rightarrow 00:04:51.360$ it's it's much more sparse.

NOTE Confidence: 0.59921736

 $00{:}04{:}51{.}360 \dashrightarrow 00{:}04{:}52{.}650$ There's some areas that look

NOTE Confidence: 0.59921736

 $00:04:52.650 \longrightarrow 00:04:54.477$ like they have a lot more going

NOTE Confidence: 0.59921736

 $00:04:54.477 \longrightarrow 00:04:56.157$ on than on the left side maps.

NOTE Confidence: 0.59921736

 $00:04:56.160 \dashrightarrow 00:04:57.960$ And I would argue something on

NOTE Confidence: 0.59921736

 $00{:}04{:}57{.}960 \dashrightarrow 00{:}05{:}00{.}087$ the right side is more relevant

NOTE Confidence: 0.59921736

 $00:05:00.087 \rightarrow 00:05:01.799$ to the individual patients.

- NOTE Confidence: 0.59921736
- $00:05:01.800 \longrightarrow 00:05:02.872$ On the left side,

 $00:05:02.872 \rightarrow 00:05:04.212$ especially with small end studies

NOTE Confidence: 0.59921736

 $00:05:04.212 \longrightarrow 00:05:05.684$ which are typical in imaging

NOTE Confidence: 0.59921736

 $00:05:05.684 \rightarrow 00:05:06.836$ because it's so expensive.

NOTE Confidence: 0.59921736

 $00{:}05{:}06{.}840 \dashrightarrow 00{:}05{:}10{.}252$ You can you can throw off the average

NOTE Confidence: 0.59921736

 $00{:}05{:}10.252 \dashrightarrow 00{:}05{:}12.004$ map by having a few individuals

NOTE Confidence: 0.59921736

 $00:05:12.004 \rightarrow 00:05:13.520$ showing lots of activation.

NOTE Confidence: 0.59921736

 $00:05:13.520 \dashrightarrow 00:05:15.464$ Whereas on the right side we're

NOTE Confidence: 0.59921736

 $00:05:15.464 \dashrightarrow 00:05:16.760$ probably looking for something

NOTE Confidence: 0.59921736

00:05:16.813 --> 00:05:18.640 that's very reliable in say a patient

NOTE Confidence: 0.59921736

 $00{:}05{:}18.640 \dashrightarrow 00{:}05{:}20.759$ group and we want to know like is

NOTE Confidence: 0.59921736

 $00{:}05{:}20.759 \dashrightarrow 00{:}05{:}22.620$ the typical patient going to show a NOTE Confidence: 0.59921736

1011 Connuclice: 0.05521150

 $00{:}05{:}22.620 \dashrightarrow 00{:}05{:}24.360$ bunch of activation in this spot.

NOTE Confidence: 0.59921736

 $00{:}05{:}24{.}360 \dashrightarrow 00{:}05{:}26{.}874$ So these are ideas about forming

NOTE Confidence: 0.59921736

00:05:26.874 --> 00:05:29.480 bridges between what we normally do NOTE Confidence: 0.59921736

 $00:05:29.480 \rightarrow 00:05:32.036$ in imaging and thinking about how

NOTE Confidence: 0.59921736

 $00:05:32.036 \rightarrow 00:05:36.960$ imaging can be applied more to individuals.

NOTE Confidence: 0.59921736

 $00:05:36.960 \dashrightarrow 00:05:39.984$ Another thing to bring up since I'm

NOTE Confidence: 0.59921736

 $00{:}05{:}39{.}984 \dashrightarrow 00{:}05{:}43{.}246$ doing TMS depression is there's a lot

NOTE Confidence: 0.59921736

 $00:05:43.246 \longrightarrow 00:05:45.130$ of excitement building especially

NOTE Confidence: 0.59921736

 $00{:}05{:}45{.}130 \dashrightarrow 00{:}05{:}48{.}077$ from Nolan Williams work at Stanford NOTE Confidence: 0.59921736

 $00{:}05{:}48.080 \dashrightarrow 00{:}05{:}51.020$ that left led to an FDA approval

NOTE Confidence: 0.59921736

 $00:05:51.020 \rightarrow 00:05:54.212$ for a new way of doing TMS for

NOTE Confidence: 0.59921736

 $00{:}05{:}54{.}212 \dashrightarrow 00{:}05{:}55{.}400$ treatment resistant depression.

NOTE Confidence: 0.59921736

 $00{:}05{:}55{.}400 \dashrightarrow 00{:}05{:}57{.}892$ And so we have the distressed patient

NOTE Confidence: 0.59921736

 $00:05:57.892 \rightarrow 00:06:02.264$ or a we apply even a really amazing

NOTE Confidence: 0.59921736

 $00:06:02.264 \longrightarrow 00:06:05.120$ clinically effective stimulation

NOTE Confidence: 0.59921736

00:06:05.120 --> 00:06:08.880 protocol in studies seeing like 80%

NOTE Confidence: 0.59921736

 $00:06:08.880 \rightarrow 00:06:10.720$ remission in treatment resistant depression.

NOTE Confidence: 0.59921736

 $00:06:10.720 \longrightarrow 00:06:12.380$ Obviously a really important tool

NOTE Confidence: 0.59921736

 $00:06:12.380 \longrightarrow 00:06:14.827$ right for for adding for that very

- NOTE Confidence: 0.59921736
- 00:06:14.827 --> 00:06:16.632 ill patient group that doesn't

 $00:06:16.632 \longrightarrow 00:06:17.715$ respond to medication.

NOTE Confidence: 0.59921736

 $00:06:17.720 \rightarrow 00:06:21.560$ So you do the stimulation protocol,

NOTE Confidence: 0.59921736

 $00:06:21.560 \rightarrow 00:06:23.360$ you measure the treatment response.

NOTE Confidence: 0.59921736

 $00:06:23.360 \longrightarrow 00:06:25.236$ A bunch of the patients do well.

NOTE Confidence: 0.59921736

00:06:25.240 --> 00:06:27.200 Some of the patients don't change very much,

NOTE Confidence: 0.59921736

 $00:06:27.200 \dashrightarrow 00:06:29.198$ some of the patients do worse.

NOTE Confidence: 0.59921736

 $00{:}06{:}29{.}200 \dashrightarrow 00{:}06{:}31{.}080$ And you're left struggling saying,

NOTE Confidence: 0.59921736

 $00:06:31.080 \longrightarrow 00:06:33.236$ well, what do we do about that?

NOTE Confidence: 0.59921736

 $00{:}06{:}33.240 \dashrightarrow 00{:}06{:}34.872$ What do we do about the patients who

NOTE Confidence: 0.59921736

 $00:06:34.872 \longrightarrow 00:06:37.280$ don't do well, The ones that do great,

NOTE Confidence: 0.59921736

 $00{:}06{:}37.280 \dashrightarrow 00{:}06{:}38.452$ like, OK, problem solved,

NOTE Confidence: 0.59921736

 $00{:}06{:}38{.}452 \dashrightarrow 00{:}06{:}40{.}643$ but what about for all the patients

NOTE Confidence: 0.59921736

 $00:06:40.643 \rightarrow 00:06:42.478$ that don't do especially well?

NOTE Confidence: 0.59921736

 $00{:}06{:}42.480 \dashrightarrow 00{:}06{:}45.678$ I would argue that you stimulated

 $00:06:45.680 \longrightarrow 00:06:48.880$ based on an imaging marker.

NOTE Confidence: 0.59921736

 $00{:}06{:}48.880 \dashrightarrow 00{:}06{:}51.582$ You don't know what TMS actually did

NOTE Confidence: 0.59921736

 $00{:}06{:}51{.}582 \dashrightarrow 00{:}06{:}54{.}338$ to that imaging marker and that may

NOTE Confidence: 0.59921736

 $00:06:54.338 \rightarrow 00:06:57.360$ be critical in figuring out why patients,

NOTE Confidence: 0.59921736

 $00{:}06{:}57{.}360 \dashrightarrow 00{:}06{:}58{.}452$ some patients don't respond.

NOTE Confidence: 0.59921736

 $00:06:58.452 \longrightarrow 00:07:00.560$ But if we don't do brain imaging,

NOTE Confidence: 0.59921736

 $00:07:00.560 \longrightarrow 00:07:02.996$ we don't do any brain based measurement,

NOTE Confidence: 0.59921736

 $00:07:03.000 \rightarrow 00:07:05.401$ then it's gonna be really hard to

NOTE Confidence: 0.59921736

 $00{:}07{:}05{.}401 \dashrightarrow 00{:}07{:}07{.}480$ unpack that and further refine

NOTE Confidence: 0.59921736

 $00{:}07{:}07{.}480 \dashrightarrow 00{:}07{:}09{.}472$ the treatment and optimize it at

NOTE Confidence: 0.59921736

 $00:07:09.472 \longrightarrow 00:07:10.800$ the individual patient level.

NOTE Confidence: 0.6194585

00:07:13.200 --> 00:07:15.360 So we'll enter TMS, FM, RI

NOTE Confidence: 0.6194585

 $00:07:17.880 \dashrightarrow 00:07:20.420$ where I think it's especially

NOTE Confidence: 0.6194585

 $00{:}07{:}20{.}420 \dashrightarrow 00{:}07{:}22{.}960$ relevant and appropriate to think

NOTE Confidence: 0.6194585

 $00{:}07{:}23.041 \dashrightarrow 00{:}07{:}25.411$ of how imaging may be relevant

NOTE Confidence: 0.6194585

00:07:25.411 -> 00:07:27.960 to the practice of psychiatry.

- NOTE Confidence: 0.6194585
- $00:07:27.960 \rightarrow 00:07:31.100$ We have this very straightforward

 $00:07:31.100 \dashrightarrow 00:07:34.240$ brain based intervention with TMS.

NOTE Confidence: 0.6194585

00:07:34.240 --> 00:07:35.104 You might argue, oh,

NOTE Confidence: 0.6194585

 $00:07:35.104 \rightarrow 00:07:36.680$ all of our interventions are brain based,

NOTE Confidence: 0.6194585

 $00{:}07{:}36{.}680 \dashrightarrow 00{:}07{:}40{.}355$ but when it comes to making a

NOTE Confidence: 0.6194585

00:07:40.360 --> 00:07:42.740 very specific hypothesis about a

NOTE Confidence: 0.6194585

 $00{:}07{:}42.740 \dashrightarrow 00{:}07{:}45.566$ particular brain area or circuit that

NOTE Confidence: 0.6194585

00:07:45.566 --> 00:07:47.780 you think is critical for patient

NOTE Confidence: 0.6194585

 $00:07:47.780 \dashrightarrow 00:07:49.680$ alleviation of symptoms with TMS,

NOTE Confidence: 0.6194585

 $00{:}07{:}49.680 \dashrightarrow 00{:}07{:}51.725$ you have to choose something, right?

NOTE Confidence: 0.6194585

 $00{:}07{:}51.725 \dashrightarrow 00{:}07{:}54.155$ So really linking that brain area

NOTE Confidence: 0.6194585

00:07:54.155 --> 00:07:56.812 to a clinical outcome is very sort

NOTE Confidence: 0.6194585

 $00{:}07{:}56.812 \dashrightarrow 00{:}07{:}59.260$ of required with TMS and I and I

NOTE Confidence: 0.6194585

00:07:59.338 --> 00:08:01.997 would argue since you have that that

NOTE Confidence: 0.6194585

 $00{:}08{:}01{.}997 \dashrightarrow 00{:}08{:}03{.}585$ understanding or that background

 $00:08:03.585 \dashrightarrow 00:08:06.571$ and the relevance of the brain

NOTE Confidence: 0.6194585

 $00:08:06.571 \longrightarrow 00:08:08.435$ for this particular intervention,

NOTE Confidence: 0.6194585

 $00{:}08{:}08{.}440$ --> $00{:}08{:}12{.}822$ this may be the the most straightforward NOTE Confidence: 0.6194585

00:08:12.822 --> 00:08:15.559 reasonable proving ground for putting

NOTE Confidence: 0.6194585

00:08:15.559 --> 00:08:18.433 imaging in a treatment context in

NOTE Confidence: 0.6194585

 $00{:}08{:}18{.}433 \dashrightarrow 00{:}08{:}20{.}919$ psychiatry and showing that there is NOTE Confidence: 0.6194585

 $00:08:20.920 \longrightarrow 00:08:24.900$ some utility of the imaging for for

NOTE Confidence: 0.6194585

 $00{:}08{:}24.900 \dashrightarrow 00{:}08{:}28.200$ the actual treatment or intervention.

NOTE Confidence: 0.6194585

00:08:28.200 --> 00:08:28.850 All right.

NOTE Confidence: 0.6194585

00:08:28.850 --> 00:08:31.652 So more about TMSF MRI fMRI BOLD

NOTE Confidence: 0.6194585

 $00{:}08{:}31.652 \dashrightarrow 00{:}08{:}35.168$ response takes a little while to

NOTE Confidence: 0.6194585

 $00:08:35.168 \rightarrow 00:08:37.330$ really show a strong signal when

NOTE Confidence: 0.6194585

 $00:08:37.330 \dashrightarrow 00:08:39.605$ you have some kind of psychological

NOTE Confidence: 0.6194585

 $00{:}08{:}39{.}605 \dashrightarrow 00{:}08{:}42{.}326$ event which you know is is one of

NOTE Confidence: 0.6194585

 $00{:}08{:}42.326 \dashrightarrow 00{:}08{:}44.455$ its shortcomings if you want to

NOTE Confidence: 0.6194585

 $00:08:44.455 \rightarrow 00:08:46.400$ capture things moving really quickly.

 $00:08:46.400 \rightarrow 00:08:49.472$ But it has a major advantage for me

NOTE Confidence: 0.6194585

 $00{:}08{:}49{.}472 \dashrightarrow 00{:}08{:}51{.}917$ delivering pulses of TMS in the scanner,

NOTE Confidence: 0.6194585

 $00{:}08{:}51{.}920 \dashrightarrow 00{:}08{:}54{.}456$ because I can send a pulse of TMS

NOTE Confidence: 0.6194585

00:08:54.456 --> 00:08:57.141 through the circuit and I can turn

NOTE Confidence: 0.6194585

 $00{:}08{:}57{.}141 \dashrightarrow 00{:}08{:}59{.}116$ on the scanner without correcting

NOTE Confidence: 0.6194585

00:08:59.189 --> 00:09:01.856 the image and capture a really nice

NOTE Confidence: 0.6194585

 $00{:}09{:}01{.}856 \dashrightarrow 00{:}09{:}04{.}568$ evokes response in the rest of the

NOTE Confidence: 0.6194585

 $00{:}09{:}04.568 \dashrightarrow 00{:}09{:}07.685$ brain that follows from the causal

NOTE Confidence: 0.6194585

00:09:07.685 --> 00:09:09.865 stimulation through that pathway

NOTE Confidence: 0.6194585

 $00:09:09.865 \dashrightarrow 00:09:13.112$ in a way that traditional imaging

NOTE Confidence: 0.6194585

 $00:09:13.112 \dashrightarrow 00:09:15.684$ doesn't have within its toolbox.

NOTE Confidence: 0.6194585

 $00{:}09{:}15.684 \dashrightarrow 00{:}09{:}17.716$ So we do that.

NOTE Confidence: 0.6194585

00:09:17.720 $\operatorname{-->}$ 00:09:20.368 We started this was work that I did

NOTE Confidence: 0.6194585

 $00:09:20.368 \dashrightarrow 00:09:23.516$ with the media and back at Stanford said,

NOTE Confidence: 0.6194585

 $00:09:23.520 \longrightarrow 00:09:24.384$ all right, well,

 $00:09:24.384 \longrightarrow 00:09:25.824$ we have these canonical resting

NOTE Confidence: 0.6194585

 $00:09:25.824 \rightarrow 00:09:26.400$ state networks.

NOTE Confidence: 0.6194585

 $00:09:26.400 \rightarrow 00:09:27.880$ They're all based on correlations.

NOTE Confidence: 0.6194585

 $00{:}09{:}27.880 \dashrightarrow 00{:}09{:}30.142$ Let's throw some little like causal

NOTE Confidence: 0.6194585

 $00:09:30.142 \rightarrow 00:09:33.044$ pings into this situation by stimulating

NOTE Confidence: 0.6194585

 $00:09:33.044 \rightarrow 00:09:37.160$ ostensible nodes of a resting state network.

NOTE Confidence: 0.6194585

00:09:37.160 -> 00:09:38.399 And we want to prove a couple

NOTE Confidence: 0.6194585

 $00:09:38.399 \longrightarrow 00:09:38.753$ different things.

NOTE Confidence: 0.6194585

 $00{:}09{:}38.760 \dashrightarrow 00{:}09{:}39.480$ We want to say, well,

NOTE Confidence: 0.6194585

 $00:09:39.480 \longrightarrow 00:09:42.350$ if you hit one node of a

NOTE Confidence: 0.6194585

 $00:09:42.350 \longrightarrow 00:09:44.679$ network with TMS at a time,

NOTE Confidence: 0.6194585

00:09:44.680 --> 00:09:44.936 right?

NOTE Confidence: 0.6194585

 $00:09:44.936 \rightarrow 00:09:47.560$ So if we ping that with a pulse of TMS,

NOTE Confidence: 0.6194585

 $00{:}09{:}47.560 \dashrightarrow 00{:}09{:}49.360$ can we actually engage the network,

NOTE Confidence: 0.6194585

 $00:09:49.360 \rightarrow 00:09:51.982$ can we do network level circuit engagement

NOTE Confidence: 0.6194585

00:09:51.982 --> 00:09:54.470 just by hitting one spot And we found

 $00:09:54.531 \rightarrow 00:09:56.554$ evidence that we could in a couple

NOTE Confidence: 0.6194585

 $00{:}09{:}56{.}554 \dashrightarrow 00{:}09{:}58{.}479$ of different task positive networks.

NOTE Confidence: 0.6194585

 $00:09:58.480 \longrightarrow 00:09:59.720$ So that's really reassuring.

NOTE Confidence: 0.6194585

 $00:09:59.720 \rightarrow 00:10:02.029$ I suggest they we are engaging

NOTE Confidence: 0.6194585

 $00:10:02.029 \rightarrow 00:10:03.984$ networks even though we're stimulating

NOTE Confidence: 0.6194585

 $00{:}10{:}03{.}984 \dashrightarrow 00{:}10{:}06{.}200$ a single brain area at a time.

NOTE Confidence: 0.6194585

 $00{:}10{:}06{.}200 \dashrightarrow 00{:}10{:}07{.}682$ The other thing that we wanted

NOTE Confidence: 0.6194585

 $00:10:07.682 \rightarrow 00:10:09.820$ to do had more to do with turning

NOTE Confidence: 0.6194585

 $00{:}10{:}09{.}820 \dashrightarrow 00{:}10{:}11{.}980$ the correlations from resting

NOTE Confidence: 0.6194585

 $00:10:11.980 \longrightarrow 00:10:14.680$ state into more causal maps.

NOTE Confidence: 0.6194585

 $00:10:14.680 \longrightarrow 00:10:17.281$ And so we we sought to ping the task

NOTE Confidence: 0.6194585

 $00{:}10{:}17{.}281 \dashrightarrow 00{:}10{:}19{.}470$ positive networks and based on the

NOTE Confidence: 0.6194585

 $00:10:19.470 \rightarrow 00:10:22.080$ correlations in the past people thought OK,

NOTE Confidence: 0.6194585

 $00{:}10{:}22.080 \dashrightarrow 00{:}10{:}24.160$ well there's this antagonistic

NOTE Confidence: 0.6194585

 $00{:}10{:}24.160 \dashrightarrow 00{:}10{:}25.706$ relationship between the test

 $00{:}10{:}25.706 \dashrightarrow 00{:}10{:}27.758$ positive networks and the DMN but

NOTE Confidence: 0.6194585

 $00{:}10{:}27.758 \dashrightarrow 00{:}10{:}29.724$ it's not easy to causally test

NOTE Confidence: 0.6194585

 $00:10:29.724 \longrightarrow 00:10:31.720$ that non invasively in a human.

NOTE Confidence: 0.6194585

 $00{:}10{:}31.720 \dashrightarrow 00{:}10{:}33.550$ So we pinned some of these

NOTE Confidence: 0.6194585

 $00{:}10{:}33.550 \dashrightarrow 00{:}10{:}34.770$ test positive networks and

NOTE Confidence: 0.7076512

 $00{:}10{:}34.829 \dashrightarrow 00{:}10{:}37.083$ looked at the evoke response in the

NOTE Confidence: 0.7076512

 $00{:}10{:}37{.}083 \dashrightarrow 00{:}10{:}39{.}319$ default mode network and we supported the,

NOTE Confidence: 0.7076512

 $00:10:39.320 \longrightarrow 00:10:41.560$ you know the idea in the field that they had.

NOTE Confidence: 0.7076512

00:10:41.560 --> 00:10:43.360 There are some antagonistic

NOTE Confidence: 0.7076512

 $00:10:43.360 \rightarrow 00:10:45.160$ relationships between these networks.

NOTE Confidence: 0.7076512

 $00{:}10{:}45{.}160 \dashrightarrow 00{:}10{:}46{.}966$ The DMN turns off in response to

NOTE Confidence: 0.7076512

00:10:46.966 --> 00:10:49.280 a ping of a test positive network.

NOTE Confidence: 0.7076512

 $00{:}10{:}49{.}280 \dashrightarrow 00{:}10{:}52{.}165$ So we're adding this causal argument to

NOTE Confidence: 0.7076512

 $00:10:52.165 \rightarrow 00:10:54.265$ what's traditional been traditionally

NOTE Confidence: 0.7076512

 $00{:}10{:}54.265 \dashrightarrow 00{:}10{:}56.799$ been just time series correlations.

NOTE Confidence: 0.5931011

 $00:10:59.000 \rightarrow 00:11:01.744$ When I arrived at Penn about eight years

 $00{:}11{:}01{.}744 \dashrightarrow 00{:}11{:}04{.}857$ ago and this priority to focus on some of

NOTE Confidence: 0.5931011

00:11:04.857 --> 00:11:08.264 the deep rain regions that we thought were

NOTE Confidence: 0.5931011

 $00:11:08.264 \rightarrow 00:11:11.000$ most relevant for anxiety and depression,

NOTE Confidence: 0.5931011

 $00:11:11.000 \rightarrow 00:11:12.665$ starting with the subtennial cingular

NOTE Confidence: 0.5931011

 $00{:}11{:}12.665 \dashrightarrow 00{:}11{:}14.640$ cortex and the amygdala and said,

NOTE Confidence: 0.5931011

00:11:14.640 - 00:11:16.635 well, these are deeper in the brain.

NOTE Confidence: 0.5931011

00:11:16.640 --> 00:11:19.314 You can't stimulate them directly with TMS,

NOTE Confidence: 0.5931011

 $00{:}11{:}19{.}320 \dashrightarrow 00{:}11{:}21{.}318$ but through those these network approaches,

NOTE Confidence: 0.5931011

 $00{:}11{:}21{.}320 \dashrightarrow 00{:}11{:}24{.}074$ can you stimulate one of the nodes in the

NOTE Confidence: 0.5931011

 $00{:}11{:}24.074 \dashrightarrow 00{:}11{:}26.221$ cortical surface and show evidence that

NOTE Confidence: 0.5931011

 $00{:}11{:}26{.}221 \dashrightarrow 00{:}11{:}28{.}920$ you can engage these deeper brain regions?

NOTE Confidence: 0.5931011

00:11:28.920 --> 00:11:34.248 And if so how do we how do we think

NOTE Confidence: 0.5931011

 $00{:}11{:}34{.}248 \dashrightarrow 00{:}11{:}36{.}888$ that this happens at the circuit level?

NOTE Confidence: 0.5931011

 $00:11:36.888 \longrightarrow 00:11:38.760$ How do you kind of prioritize

NOTE Confidence: 0.5931011

 $00:11:38.823 \rightarrow 00:11:40.718$ which brain areas to stimulate?

 $00{:}11{:}40{.}720 \dashrightarrow 00{:}11{:}43{.}812$ And so we we collect baseline resting

NOTE Confidence: 0.5931011

 $00{:}11{:}43.812 \dashrightarrow 00{:}11{:}46.156$ connectivity from individuals and

NOTE Confidence: 0.5931011

 $00{:}11{:}46.156$ --> $00{:}11{:}49.484$ we choose stimulation sites on the NOTE Confidence: 0.5931011

 $00:11:49.484 \rightarrow 00:11:52.190$ cortex and try stimulating them and NOTE Confidence: 0.5931011

 $00{:}11{:}52{.}190 \dashrightarrow 00{:}11{:}54{.}599$ evoking responses deeper in the brain NOTE Confidence: 0.5931011

 $00{:}11{:}54{.}600 \dashrightarrow 00{:}11{:}56{.}760$ what the imaging sequence looks like. NOTE Confidence: 0.5931011

 $00{:}11{:}56{.}760$ --> $00{:}11{:}58{.}853$ We have these interleaved kind of gaps NOTE Confidence: 0.5931011

 $00{:}11{:}58.853 \dashrightarrow 00{:}12{:}00.775$ in between the F MRI recordings where

NOTE Confidence: 0.5931011

00:12:00.775 --> 00:12:03.079 we can put in a ping of the circuit

NOTE Confidence: 0.5931011

 $00{:}12{:}03.080 \dashrightarrow 00{:}12{:}04.760$ and this is not neuromodulation,

NOTE Confidence: 0.5931011

 $00:12:04.760 \longrightarrow 00:12:06.440$ this is not repetitive TMS.

NOTE Confidence: 0.5931011

 $00:12:06.440 \longrightarrow 00:12:08.858$ This is just sending individual pings

NOTE Confidence: 0.5931011

 $00{:}12{:}08.858 \dashrightarrow 00{:}12{:}11.847$ through that circuit a bunch of times just

NOTE Confidence: 0.5931011

 $00{:}12{:}11.847 \dashrightarrow 00{:}12{:}14.495$ like any other task evoked brain response.

NOTE Confidence: 0.5931011

00:12:14.495 --> 00:12:17.165 It's also similar in our minds

NOTE Confidence: 0.5931011

 $00{:}12{:}17.165 \dashrightarrow 00{:}12{:}19.440$ to motor evoke potential.

- NOTE Confidence: 0.5931011
- $00:12:19.440 \rightarrow 00:12:21.108$ So you're just engaging the circuit
- NOTE Confidence: 0.5931011
- 00:12:21.108 --> 00:12:22.596 and the strength of engagement
- NOTE Confidence: 0.5931011
- $00:12:22.596 \longrightarrow 00:12:24.196$ of the circuit is measured.
- NOTE Confidence: 0.5931011
- $00:12:24.200 \rightarrow 00:12:25.556$ Instead of in a finger twitch,
- NOTE Confidence: 0.5931011
- $00{:}12{:}25{.}560 \dashrightarrow 00{:}12{:}28{.}437$ it's measured in an fMRI BOLD response.
- NOTE Confidence: 0.5931011
- $00{:}12{:}28{.}440 \dashrightarrow 00{:}12{:}30{.}654$ But conceptually we see them very
- NOTE Confidence: 0.5931011
- $00:12:30.654 \rightarrow 00:12:33.391$ similarly that if the circuit is really
- NOTE Confidence: 0.5931011
- $00:12:33.391 \rightarrow 00:12:36.163$ intact for an individual through the this
- NOTE Confidence: 0.5931011
- $00:12:36.234 \rightarrow 00:12:38.719$ cortical node that we're stimulating,
- NOTE Confidence: 0.5931011
- $00:12:38.720 \longrightarrow 00:12:40.628$ then your evoked response deeper in
- NOTE Confidence: 0.5931011
- $00{:}12{:}40.628 \dashrightarrow 00{:}12{:}42.999$ the brain should be especially strong.
- NOTE Confidence: 0.5931011
- $00{:}12{:}43.000 \dashrightarrow 00{:}12{:}45.624$ So that's how we measure it and what we
- NOTE Confidence: 0.5931011
- $00{:}12{:}45{.}624 \dashrightarrow 00{:}12{:}47{.}592$ capture is the whole brain response.
- NOTE Confidence: 0.5931011
- $00{:}12{:}47.600 \dashrightarrow 00{:}12{:}51.758$ So this this is not only like
- NOTE Confidence: 0.5931011
- $00:12:51.760 \rightarrow 00:12:52.560$ direct pathways,
- NOTE Confidence: 0.5931011

 $00:12:52.560 \rightarrow 00:12:55.360$ we're getting a bunch of these like

NOTE Confidence: 0.5931011

 $00{:}12{:}55{.}360 \dashrightarrow 00{:}12{:}58{.}136$ downstream multi synaptic kind of responses

NOTE Confidence: 0.5931011

 $00{:}12{:}58{.}136 \dashrightarrow 00{:}13{:}01{.}440$ that are downstream of where we stimulate.

NOTE Confidence: 0.5931011

 $00:13:01.440 \longrightarrow 00:13:03.771$ But you can still make a causal

NOTE Confidence: 0.5931011

 $00{:}13{:}03{.}771 \dashrightarrow 00{:}13{:}05{.}694$ argument because we stimulated at

NOTE Confidence: 0.5931011

 $00{:}13{:}05{.}694 \dashrightarrow 00{:}13{:}07{.}839$ a particular node cortically and

NOTE Confidence: 0.5931011

 $00:13:07.840 \longrightarrow 00:13:10.120$ generated these whole brain responses.

NOTE Confidence: 0.5931011

 $00{:}13{:}10{.}120 \dashrightarrow 00{:}13{:}12{.}960$ I think we could learn a lot about

NOTE Confidence: 0.5931011

 $00:13:12.960 \rightarrow 00:13:16.164$ how the signal kind of propagates and

NOTE Confidence: 0.5931011

 $00{:}13{:}16{.}164 \dashrightarrow 00{:}13{:}19{.}163$ engages the brain from different places

NOTE Confidence: 0.5931011

00:13:19.163 --> 00:13:22.719 that we can stimulate on the surface.

NOTE Confidence: 0.5931011

 $00{:}13{:}22.720 \dashrightarrow 00{:}13{:}23.264$ Also,

NOTE Confidence: 0.5931011

 $00:13:23.264 \rightarrow 00:13:26.044$ just to say that imaging right

NOTE Confidence: 0.5931011

 $00:13:26.044 \longrightarrow 00:13:27.554$ has come a long way.

NOTE Confidence: 0.5931011

 $00:13:27.560 \rightarrow 00:13:30.280$ There's a lot of different methods and tools,

NOTE Confidence: 0.5931011

 $00:13:30.280 \rightarrow 00:13:33.480$ and when it comes to trying to stimulate

- NOTE Confidence: 0.5931011
- 00:13:33.480 --> 00:13:35.228 a particular cortical location,

 $00:13:35.228 \longrightarrow 00:13:37.937$ there are a lot of variations

NOTE Confidence: 0.5931011

00:13:37.937 --> 00:13:39.959 that you could apply right you.

NOTE Confidence: 0.5931011

 $00:13:39.960 \rightarrow 00:13:42.630$ You could choose a cortical target

NOTE Confidence: 0.5931011

00:13:42.630 --> 00:13:45.680 based on DTI, FM, RI, task, resting,

NOTE Confidence: 0.5931011

00:13:45.680 --> 00:13:46.135 ASL.

NOTE Confidence: 0.5931011

 $00{:}13{:}46{.}135 \dashrightarrow 00{:}13{:}49{.}320$ Whatever your kind of pet measure is,

NOTE Confidence: 0.5931011

00:13:49.320 --> 00:13:52.400 you can look out for hypothesis about

NOTE Confidence: 0.5931011

 $00{:}13{:}52{.}400 \dashrightarrow 00{:}13{:}55{.}800$ at lases and how the brain is organized NOTE Confidence: 0.5931011

 $00{:}13{:}55{.}800 \dashrightarrow 00{:}13{:}58{.}685$ into networks and you can test them

NOTE Confidence: 0.5931011

 $00{:}13{:}58.685 \dashrightarrow 00{:}14{:}01.080$ like causally by picking these spots.

NOTE Confidence: 0.5931011

 $00{:}14{:}01{.}080 \dashrightarrow 00{:}14{:}03{.}229$ So we will collect a a baseline

NOTE Confidence: 0.5931011

 $00:14:03.229 \rightarrow 00:14:04.863$ imaging set of data, right?

NOTE Confidence: 0.5931011

00:14:04.863 --> 00:14:07.287 We put the patients in front of a

NOTE Confidence: 0.5931011

 $00{:}14{:}07{.}287 \dashrightarrow 00{:}14{:}09{.}303$ camera and we mark some fiducial

 $00{:}14{:}09{.}303 \dashrightarrow 00{:}14{:}11{.}749$ points on their scalp and then we can

NOTE Confidence: 0.5931011

 $00{:}14{:}11.749 \dashrightarrow 00{:}14{:}13.890$ line up and find out exactly where

NOTE Confidence: 0.5931011

 $00{:}14{:}13.890 \dashrightarrow 00{:}14{:}15.540$ we're stimulating relative to their

NOTE Confidence: 0.47924274

00:14:15.600 --> 00:14:17.765 brain. And you can also stick

NOTE Confidence: 0.47924274

 $00{:}14{:}17.765 \dashrightarrow 00{:}14{:}19.840$ to your target really well by

NOTE Confidence: 0.47924274

 $00{:}14{:}19{.}840 \dashrightarrow 00{:}14{:}21{.}982$ holding your TMS coil and getting NOTE Confidence: 0.47924274

 $00{:}14{:}21{.}982 \dashrightarrow 00{:}14{:}24{.}191$ this feedback from the camera on

NOTE Confidence: 0.47924274

 $00{:}14{:}24{.}191 \dashrightarrow 00{:}14{:}25{.}976$ which brain area you're overlying

NOTE Confidence: 0.47924274

 $00{:}14{:}25{.}976 \dashrightarrow 00{:}14{:}27{.}880$ while you do stimulation.

NOTE Confidence: 0.47924274

 $00{:}14{:}27{.}880 \dashrightarrow 00{:}14{:}30{.}040$ So that's the neuro

NOTE Confidence: 0.47924274

00:14:30.040 --> 00:14:31.999 navigated part in the scanner

NOTE Confidence: 0.4464437

00:14:34.600 --> 00:14:35.848 not showing these data.

NOTE Confidence: 0.4464437

 $00{:}14{:}35{.}848 \dashrightarrow 00{:}14{:}38{.}158$ But we did a smaller pilot study

NOTE Confidence: 0.4464437

 $00:14:38.158 \longrightarrow 00:14:40.776$ in 14 subjects where we looked at

NOTE Confidence: 0.4464437

 $00{:}14{:}40.776 \dashrightarrow 00{:}14{:}42.340$ resting connectivity based pings

NOTE Confidence: 0.4464437

 $00{:}14{:}42{.}340 \dashrightarrow 00{:}14{:}44{.}288$ and found subtennial and amygdala

- NOTE Confidence: 0.4464437
- $00:14:44.288 \rightarrow 00:14:46.080$ engagement through those pathways.

00:14:46.080 --> 00:14:48.234 I'll show you the replication 'cause

NOTE Confidence: 0.4464437

 $00:14:48.234 \rightarrow 00:14:50.275$ they're in bigger cohorts and we

NOTE Confidence: 0.4464437

 $00:14:50.275 \longrightarrow 00:14:52.920$ explored a little bit more kind of

NOTE Confidence: 0.4464437

 $00{:}14{:}52{.}920 \dashrightarrow 00{:}14{:}55{.}880$ evidence for which target is doing what.

NOTE Confidence: 0.4464437

 $00:14:55.880 \longrightarrow 00:14:58.519$ So this is in 32 healthy subjects.

NOTE Confidence: 0.4464437

 $00:14:58.520 \rightarrow 00:15:00.650$ We did the resting fMRI

NOTE Confidence: 0.4464437

 $00:15:00.650 \longrightarrow 00:15:01.848$ guided stimulation right,

NOTE Confidence: 0.4464437

 $00:15:01.848 \rightarrow 00:15:04.152$ based on the subgenual connectivity and

NOTE Confidence: 0.4464437

 $00:15:04.152 \rightarrow 00:15:06.200$ we stimulated through those pathways.

NOTE Confidence: 0.4464437

 $00:15:06.200 \longrightarrow 00:15:08.084$ We had a control region and

NOTE Confidence: 0.4464437

 $00{:}15{:}08{.}084 \dashrightarrow 00{:}15{:}10{.}078$ motor cortex and we say, hey,

NOTE Confidence: 0.4464437

 $00{:}15{:}10.078 \dashrightarrow 00{:}15{:}12.466$ can we reliably ping this target

NOTE Confidence: 0.4464437

 $00:15:12.466 \longrightarrow 00:15:14.919$ in through these circuits?

NOTE Confidence: 0.4464437

 $00{:}15{:}14.920 \dashrightarrow 00{:}15{:}17.097$ And we found that there was evidence

 $00:15:17.097 \rightarrow 00:15:19.548$ we could engage the subgenual singlet

NOTE Confidence: 0.4464437

 $00:15:19.548 \longrightarrow 00:15:21.833$ better than the control region,

NOTE Confidence: 0.4464437

 $00{:}15{:}21.840 \dashrightarrow 00{:}15{:}23.692$ suggesting that there's some

NOTE Confidence: 0.4464437

 $00:15:23.692 \rightarrow 00:15:25.544$ pathway specificity in choosing

NOTE Confidence: 0.4464437

 $00{:}15{:}25{.}544 \dashrightarrow 00{:}15{:}27{.}172$ these individualized resting guided

NOTE Confidence: 0.4464437

 $00{:}15{:}27{.}172 \dashrightarrow 00{:}15{:}29{.}398$ targets and that when we ping them,

NOTE Confidence: 0.4464437

 $00:15:29.400 \longrightarrow 00:15:31.475$ we can reliably engage that

NOTE Confidence: 0.4464437

 $00:15:31.475 \rightarrow 00:15:32.720$ deeper brain region.

NOTE Confidence: 0.516610831538462

 $00:15:35.440 \longrightarrow 00:15:39.016$ All right. So another replication and

NOTE Confidence: 0.516610831538462

 $00:15:39.016 \rightarrow 00:15:42.480$ extension that we tried is to say,

NOTE Confidence: 0.516610831538462

 $00:15:42.480 \longrightarrow 00:15:45.565$ well, all the clinical folks

NOTE Confidence: 0.516610831538462

00:15:45.565 --> 00:15:48.066 especially are looking at anti

NOTE Confidence: 0.516610831538462

 $00:15:48.066 \rightarrow 00:15:49.754$ correlated brain stimulation targets.

NOTE Confidence: 0.516610831538462

 $00:15:49.760 \longrightarrow 00:15:51.296$ That's including the same

NOTE Confidence: 0.516610831538462

 $00{:}15{:}51.296 \dashrightarrow 00{:}15{:}52.980$ protocol and there's pretty nice

NOTE Confidence: 0.516610831538462

 $00:15:52.980 \longrightarrow 00:15:54.280$ clinical evidence for that.

 $00:15:54.280 \rightarrow 00:15:56.666$ You look for the subgenual negative

NOTE Confidence: 0.516610831538462

 $00:15:56.666 \longrightarrow 00:15:58.690$ functional connectivity partner on

NOTE Confidence: 0.516610831538462

 $00:15:58.690 \rightarrow 00:16:01.398$ the brain service and you stimulate

NOTE Confidence: 0.516610831538462

 $00:16:01.398 \longrightarrow 00:16:03.093$ that clinically and show that

NOTE Confidence: 0.516610831538462

 $00{:}16{:}03.093 \dashrightarrow 00{:}16{:}04.469$ there's a relationship between

NOTE Confidence: 0.516610831538462

 $00{:}16{:}04{.}469 \dashrightarrow 00{:}16{:}06{.}287$ how patients do and the strength

NOTE Confidence: 0.516610831538462

 $00:16:06.287 \rightarrow 00:16:07.919$ of connectivity to that pathway.

NOTE Confidence: 0.516610831538462

 $00:16:07.920 \longrightarrow 00:16:10.758$ So that that's really nice evidence.

NOTE Confidence: 0.516610831538462

00:16:10.760 --> 00:16:13.960 But we wanted to see if it's really

NOTE Confidence: 0.516610831538462

 $00:16:13.960 \longrightarrow 00:16:16.840$ important that you get the anti correlated

NOTE Confidence: 0.516610831538462

 $00:16:16.840 \longrightarrow 00:16:19.130$ spot or what actually happens if you

NOTE Confidence: 0.516610831538462

 $00{:}16{:}19{.}130 \dashrightarrow 00{:}16{:}20{.}920$ look at a positively correlated spot.

NOTE Confidence: 0.516610831538462

 $00:16:20.920 \longrightarrow 00:16:23.104$ And there's some data from Corey

NOTE Confidence: 0.516610831538462

00:16:23.104 --> 00:16:25.540 Keller ET all doing some electrical

NOTE Confidence: 0.516610831538462

 $00{:}16{:}25{.}540 \dashrightarrow 00{:}16{:}27{.}815$ stimulation and trying to map

 $00{:}16{:}27.815 \dashrightarrow 00{:}16{:}30.160$ those networks from Reston State.

NOTE Confidence: 0.516610831538462

 $00:16:30.160 \rightarrow 00:16:33.275$ And it looks like the positively correlated

NOTE Confidence: 0.516610831538462

 $00{:}16{:}33.275 \dashrightarrow 00{:}16{:}36.055$ ones are a better fit for the stimulation,

NOTE Confidence: 0.516610831538462

00:16:36.055 --> 00:16:36.645 you know,

NOTE Confidence: 0.516610831538462

 $00{:}16{:}36{.}645 \dashrightarrow 00{:}16{:}39{.}160$ related effects in the brain sort of thought,

NOTE Confidence: 0.516610831538462

 $00:16:39.160 \longrightarrow 00:16:39.432$ hey,

NOTE Confidence: 0.516610831538462

 $00{:}16{:}39{.}432 \dashrightarrow 00{:}16{:}41{.}336$ what we should we should at least

NOTE Confidence: 0.516610831538462

 $00:16:41.336 \rightarrow 00:16:42.861$ look into the positive connectivity

NOTE Confidence: 0.516610831538462

 $00{:}16{:}42.861 \dashrightarrow 00{:}16{:}45.719$ spots and see what we get in terms of

NOTE Confidence: 0.516610831538462

 $00{:}16{:}45.719 \dashrightarrow 00{:}16{:}47.675$ the evoked response in the subgenual.

NOTE Confidence: 0.516610831538462

 $00:16:47.680 \rightarrow 00:16:50.040$ So we did that with our typical interleave,

NOTE Confidence: 0.516610831538462

 $00:16:50.040 \longrightarrow 00:16:51.280$ right with our single pulses,

NOTE Confidence: 0.516610831538462

00:16:51.280 --> 00:16:52.306 no neuromodulation,

NOTE Confidence: 0.516610831538462

 $00:16:52.306 \rightarrow 00:16:55.230$ just pinging the circuit and we found

NOTE Confidence: 0.516610831538462

 $00{:}16{:}55{.}230 \dashrightarrow 00{:}16{:}57{.}260$ that for healthy controls this is a

NOTE Confidence: 0.516610831538462

 $00:16:57.326 \rightarrow 00:16:59.566$ replication again that the positive

- NOTE Confidence: 0.516610831538462
- $00:16:59.566 \rightarrow 00:17:01.358$ and negative connectivity spots
- NOTE Confidence: 0.516610831538462
- $00{:}17{:}01{.}358 \dashrightarrow 00{:}17{:}03{.}319$ engage the circuit pretty well.
- NOTE Confidence: 0.516610831538462
- $00:17:03.320 \rightarrow 00:17:06.400$ They they do pretty similarly to one another.
- NOTE Confidence: 0.516610831538462
- $00{:}17{:}06{.}400 \dashrightarrow 00{:}17{:}08{.}528$ So both of them are effective as long
- NOTE Confidence: 0.516610831538462
- $00{:}17{:}08.528 \dashrightarrow 00{:}17{:}10.879$ as you hit a high connectivity peak.
- NOTE Confidence: 0.516610831538462
- 00:17:10.880 --> 00:17:12.872 It doesn't matter so much if it's anti
- NOTE Confidence: 0.516610831538462
- $00:17:12.872 \rightarrow 00:17:14.480$ correlated or positively correlated.
- NOTE Confidence: 0.516610831538462
- $00:17:14.480 \rightarrow 00:17:17.630$ They both seem to do pretty similar
- NOTE Confidence: 0.516610831538462
- $00{:}17{:}17.630 \dashrightarrow 00{:}17{:}20.528$ things and a bit smaller of a
- NOTE Confidence: 0.516610831538462
- 00:17:20.528 --> 00:17:22.160 group of depressed patients.
- NOTE Confidence: 0.516610831538462
- 00:17:22.160 --> 00:17:22.550 However,
- NOTE Confidence: 0.516610831538462
- $00{:}17{:}22.550 \dashrightarrow 00{:}17{:}25.280$ we found that there was a difference.
- NOTE Confidence: 0.516610831538462
- $00{:}17{:}25{.}280 \dashrightarrow 00{:}17{:}27{.}765$ The anti correlated spots still
- NOTE Confidence: 0.516610831538462
- $00{:}17{:}27.765 \dashrightarrow 00{:}17{:}29.753$ engaged the subgenual cingulant.
- NOTE Confidence: 0.516610831538462
- $00:17:29.760 \longrightarrow 00:17:33.000$ So if the subgenual engagement is
- NOTE Confidence: 0.516610831538462

 $00:17:33.000 \rightarrow 00:17:35.531$ really critical for the antidepressant

NOTE Confidence: 0.516610831538462

 $00:17:35.531 \rightarrow 00:17:37.757$ effects of TMS through that pathway,

NOTE Confidence: 0.516610831538462

 $00{:}17{:}37.760 \dashrightarrow 00{:}17{:}39.398$ then this is consistent with that right.

NOTE Confidence: 0.516610831538462

 $00:17:39.400 \longrightarrow 00:17:41.880$ It it suggests that there is a real

NOTE Confidence: 0.516610831538462

 $00:17:41.880 \rightarrow 00:17:43.700$ pathway there in depressed patients

NOTE Confidence: 0.516610831538462

00:17:43.700 --> 00:17:45.992 and perhaps that's why the treatments

NOTE Confidence: 0.516610831538462

 $00:17:45.992 \longrightarrow 00:17:47.560$ work through those pathways.

NOTE Confidence: 0.516610831538462

 $00:17:47.560 \rightarrow 00:17:50.116$ But seeing that there's this difference,

NOTE Confidence: 0.516610831538462

00:17:50.120 --> 00:17:50.658 all right,

NOTE Confidence: 0.516610831538462

 $00{:}17{:}50.658 \dashrightarrow 00{:}17{:}52.003$ there's like a significant difference

NOTE Confidence: 0.516610831538462

 $00:17:52.003 \rightarrow 00:17:53.930$ in the strength of the evoked response

NOTE Confidence: 0.516610831538462

 $00:17:53.930 \longrightarrow 00:17:55.275$ depending on whether it's anti

NOTE Confidence: 0.516610831538462

 $00:17:55.275 \rightarrow 00:17:56.638$ correlated or positively correlated.

NOTE Confidence: 0.516610831538462

 $00:17:56.640 \longrightarrow 00:17:58.080$ The positively correlated ones

NOTE Confidence: 0.516610831538462

 $00:17:58.080 \rightarrow 00:17:59.880$ engage the circuit even more.

NOTE Confidence: 0.516610831538462

00:17:59.880 --> 00:18:00.750 So again,

- NOTE Confidence: 0.516610831538462
- 00:18:00.750 --> 00:18:02.490 if we're really thinking
- NOTE Confidence: 0.516610831538462
- $00:18:02.490 \longrightarrow 00:18:03.360$ that mechanistically,
- NOTE Confidence: 0.516610831538462
- $00:18:03.360 \longrightarrow 00:18:04.972$ engagement of that subgenual
- NOTE Confidence: 0.516610831538462
- $00:18:04.972 \longrightarrow 00:18:06.987$ through the cortical pathway is
- NOTE Confidence: 0.516610831538462
- 00:18:06.987 --> 00:18:08.719 really clinically important,
- NOTE Confidence: 0.516610831538462
- $00{:}18{:}08{.}720 \dashrightarrow 00{:}18{:}11{.}086$ Why not start testing out the positively
- NOTE Confidence: 0.516610831538462
- $00{:}18{:}11.086 \dashrightarrow 00{:}18{:}13.074$ correlated spots and see if our
- NOTE Confidence: 0.516610831538462
- $00:18:13.074 \rightarrow 00:18:14.599$ clinical effects are even better?
- NOTE Confidence: 0.6126814
- 00:18:18.600 --> 00:18:20.098 All right. So I'm going to switch
- NOTE Confidence: 0.6126814
- 00:18:20.098 --> 00:18:21.839 over to the amygdala just briefly.
- NOTE Confidence: 0.6126814
- 00:18:21.840 --> 00:18:23.740 We haven't done any interventions
- NOTE Confidence: 0.6126814
- $00{:}18{:}23.740 \dashrightarrow 00{:}18{:}25.200$ yet through the amygdala pathway,
- NOTE Confidence: 0.6126814
- 00:18:25.200 --> 00:18:27.357 but we wanted to explore a little bit
- NOTE Confidence: 0.6126814
- $00{:}18{:}27{.}357 \dashrightarrow 00{:}18{:}30{.}885$ more about how the amygdala pathway NOTE Confidence: 0.6126814
- 00:18:30.885 --> 00:18:36.533 works and how the TMS stimulation
- NOTE Confidence: 0.6126814

 $00:18:36.533 \rightarrow 00:18:39.598$ propagates from our stimulation site,

NOTE Confidence: 0.6126814

 $00:18:39.600 \longrightarrow 00:18:41.553$ which tended to which tended to be

NOTE Confidence: 0.6126814

 $00{:}18{:}41{.}553 \dashrightarrow 00{:}18{:}42{.}817$ in the ventrilateral prefrontal

NOTE Confidence: 0.6126814

 $00:18:42.817 \rightarrow 00:18:44.677$ cortex and engaging the amygdala.

NOTE Confidence: 0.6126814

 $00:18:44.680 \longrightarrow 00:18:46.543$ So we had a small pilot so that we

NOTE Confidence: 0.6126814

00:18:46.543 --> 00:18:48.746 can engage the amygdala in this case,

NOTE Confidence: 0.6126814

00:18:48.746 --> 00:18:51.490 we're doing that again, the TMS, fMRI,

NOTE Confidence: 0.6126814

 $00:18:51.490 \rightarrow 00:18:54.040$ fMRI connectivity based targeting again.

NOTE Confidence: 0.6126814

 $00{:}18{:}54{.}040 \dashrightarrow 00{:}18{:}56{.}443$ But we also did some DTI at the baseline NOTE Confidence: 0.6126814

 $00{:}18{:}56{.}443 \dashrightarrow 00{:}18{:}59{.}200$ and we wanted to see if there's some

NOTE Confidence: 0.6126814

00:18:59.200 --> 00:19:01.279 relationship between the evoked response,

NOTE Confidence: 0.6126814

 $00{:}19{:}01{.}280 \dashrightarrow 00{:}19{:}04{.}316$ the amygdala and the DTI measure.

NOTE Confidence: 0.6126814

 $00{:}19{:}04{.}320 \dashrightarrow 00{:}19{:}06{.}174$ We found some evidence that there

NOTE Confidence: 0.6126814

 $00:19:06.174 \longrightarrow 00:19:08.080$ there seems to be a pathway,

NOTE Confidence: 0.6126814

 $00{:}19{:}08{.}080 \dashrightarrow 00{:}19{:}10{.}312$ a direct pathway between where we

NOTE Confidence: 0.6126814

 $00{:}19{:}10{.}312 \dashrightarrow 00{:}19{:}12{.}755$ were stimulating in VLPFC and the

 $00{:}19{:}12.755 \dashrightarrow 00{:}19{:}15.050$ downstream amygdala, which is useful.

NOTE Confidence: 0.6126814

00:19:15.050 --> 00:19:18.944 We also showed that the strength of the

NOTE Confidence: 0.6126814

 $00{:}19{:}18{.}944 \dashrightarrow 00{:}19{:}21{.}980$ evoked response to TMS was associated NOTE Confidence: 0.6126814

 $00:19:21.980 \longrightarrow 00:19:25.678$ with the fiber density of that pathway

NOTE Confidence: 0.6126814

 $00{:}19{:}25.680 \dashrightarrow 00{:}19{:}28.120$ at the individual subject level.

NOTE Confidence: 0.6126814

 $00{:}19{:}28{.}120 \dashrightarrow 00{:}19{:}31{.}352$ This supports the idea that TMS likes to

NOTE Confidence: 0.6126814

 $00{:}19{:}31{.}352 \dashrightarrow 00{:}19{:}34{.}147$ flow around along white matter and that

NOTE Confidence: 0.6126814

 $00{:}19{:}34{.}147 \dashrightarrow 00{:}19{:}37{.}025$ this pathway may be a direct pathway

NOTE Confidence: 0.6126814

 $00{:}19{:}37.025 \dashrightarrow 00{:}19{:}40.096$ and that this may partially explain

NOTE Confidence: 0.6126814

 $00:19:40.096 \rightarrow 00:19:43.360$ how TMS actually engages the amygdala.

NOTE Confidence: 0.48297837

00:19:45.640 --> 00:19:46.320 All right. Can you say,

NOTE Confidence: 0.48297837

 $00{:}19{:}46{.}320 \dashrightarrow 00{:}19{:}48{.}600$ well, these are nice tricks.

NOTE Confidence: 0.48297837

 $00{:}19{:}48.600 \dashrightarrow 00{:}19{:}50.238$ You're doing these pings of these circuits.

NOTE Confidence: 0.48297837

 $00{:}19{:}50{.}240 \dashrightarrow 00{:}19{:}51{.}900$ You're showing evoked responses.

NOTE Confidence: 0.48297837

 $00:19:51.900 \rightarrow 00:19:53.560$ That's kind of neat,

 $00:19:53.560 \longrightarrow 00:19:55.948$ but is there any like clinical

NOTE Confidence: 0.48297837

 $00{:}19{:}55{.}948 \dashrightarrow 00{:}19{:}57{.}540$ relevance you're talking earlier

NOTE Confidence: 0.48297837

00:19:57.604 --> 00:19:59.991 about the SYNC protocol and how we

NOTE Confidence: 0.48297837

 $00{:}19{:}59{.}991 \dashrightarrow 00{:}20{:}01{.}782$ don't know anything happening in

NOTE Confidence: 0.48297837

 $00{:}20{:}01.782 \dashrightarrow 00{:}20{:}03.888$ the brain and how's that relevant

NOTE Confidence: 0.48297837

 $00{:}20{:}03.888 \dashrightarrow 00{:}20{:}06.608$ for the any clinical effects.

NOTE Confidence: 0.48297837

 $00{:}20{:}06{.}608 \dashrightarrow 00{:}20{:}10{.}147$ The first we're looking at TMSF MRI in

NOTE Confidence: 0.48297837

 $00:20:10.147 \longrightarrow 00:20:12.800$ this more clinically relevant context,

NOTE Confidence: 0.48297837

 $00{:}20{:}12.800 \dashrightarrow 00{:}20{:}14.906$ but it's this requires a little

NOTE Confidence: 0.48297837

 $00{:}20{:}14.906 \dashrightarrow 00{:}20{:}15.959$ bit of explanation.

NOTE Confidence: 0.48297837

 $00:20:15.960 \longrightarrow 00:20:18.120$ We didn't do this full clinical

NOTE Confidence: 0.48297837

 $00:20:18.120 \rightarrow 00:20:20.599$ trial with the pings along the way.

NOTE Confidence: 0.48297837

 $00{:}20{:}20{.}600 \dashrightarrow 00{:}20{:}23{.}957$ We tried to take some bit of a shortcut,

NOTE Confidence: 0.48297837

 $00{:}20{:}23{.}960 \dashrightarrow 00{:}20{:}26{.}408$ which is to test the circuit

NOTE Confidence: 0.48297837

00:20:26.408 --> 00:20:28.040 hypothesis in a faster

NOTE Confidence: 0.76734865

 $00:20:30.760 \longrightarrow 00:20:32.680$ like design. Yeah.

 $00:20:32.680 \rightarrow 00:20:36.836$ So one of the difficulties of doing

NOTE Confidence: 0.76734865

 $00{:}20{:}36{.}840 \dashrightarrow 00{:}20{:}39{.}269$ a treatment with TMS is that they

NOTE Confidence: 0.76734865

 $00:20:39.269 \longrightarrow 00:20:41.696$ typically take long time like even the

NOTE Confidence: 0.76734865

00:20:41.696 --> 00:20:44.160 SYNC protocol that only takes one week,

NOTE Confidence: 0.76734865

 $00:20:44.160 \longrightarrow 00:20:46.048$ you have to do 10 sessions per day

NOTE Confidence: 0.76734865

 $00{:}20{:}46.048 \dashrightarrow 00{:}20{:}48.618$ and then we have the four to six week

NOTE Confidence: 0.76734865

 $00:20:48.618 \longrightarrow 00:20:50.175$ traditional clinical TMS for depression

NOTE Confidence: 0.76734865

 $00{:}20{:}50{.}175 \dashrightarrow 00{:}20{:}52{.}352$ protocol and that takes a long time.

NOTE Confidence: 0.76734865

 $00:20:52.360 \longrightarrow 00:20:53.032$ So we thought, OK,

NOTE Confidence: 0.76734865

 $00:20:53.032 \rightarrow 00:20:54.240$ can we speed this up at all?

NOTE Confidence: 0.76734865

 $00:20:54.240 \longrightarrow 00:20:56.400$ Let's let's try to pack in a fair

NOTE Confidence: 0.76734865

 $00{:}20{:}56{.}400 \dashrightarrow 00{:}20{:}58{.}638$ amount of stimulation in three days.

NOTE Confidence: 0.76734865

 $00{:}20{:}58.640 \dashrightarrow 00{:}21{:}00.824$ And we thought that that's probably

NOTE Confidence: 0.76734865

 $00:21:00.824 \longrightarrow 00:21:02.691$ enough to start modulating the

NOTE Confidence: 0.76734865

 $00{:}21{:}02{.}691$ --> $00{:}21{:}04.755$ target and to start pushing symptoms,

 $00:21:04.760 \rightarrow 00:21:06.560$ but it's not a full clinical trial yet.

NOTE Confidence: 0.48220587

00:21:08.720 --> 00:21:10.960 Also in the other TMS studies,

NOTE Confidence: 0.48220587

 $00:21:10.960 \rightarrow 00:21:12.955$ imaging has been sort of an afterthought.

NOTE Confidence: 0.48220587

 $00:21:12.960 \longrightarrow 00:21:15.030$ And the case here, we're really

NOTE Confidence: 0.48220587

 $00{:}21{:}15{.}030 \dashrightarrow 00{:}21{:}17{.}518$ making a priority of how well we

NOTE Confidence: 0.48220587

 $00{:}21{:}17{.}518$ --> $00{:}21{:}19{.}588$ engage this target that we're aiming NOTE Confidence: 0.48220587

00:21:19.588 --> 00:21:22.053 for and showing evidence that TMS of

NOTE Confidence: 0.48220587

 $00{:}21{:}22.053 \dashrightarrow 00{:}21{:}24.563$ MRI can be useful here to show that

NOTE Confidence: 0.48220587

 $00{:}21{:}24{.}563 \dashrightarrow 00{:}21{:}26{.}520$ there's a change in the pathway.

NOTE Confidence: 0.48220587

 $00{:}21{:}26{.}520 \dashrightarrow 00{:}21{:}28{.}795$ And then usually the imaging in other NOTE Confidence: 0.48220587

 $00{:}21{:}28.795 \dashrightarrow 00{:}21{:}30.445$ TMS studies has been correlational

NOTE Confidence: 0.48220587

00:21:30.445 --> 00:21:32.893 and we want to throw in our TMS

NOTE Confidence: 0.48220587

 $00:21:32.962 \longrightarrow 00:21:35.066$ of MRI and see if if there's any

NOTE Confidence: 0.48220587

 $00{:}21{:}35{.}066 \dashrightarrow 00{:}21{:}36{.}984$ utility in looking at it there.

NOTE Confidence: 0.48220587

 $00:21:36.984 \rightarrow 00:21:39.060$ There's of course the patient provider

NOTE Confidence: 0.48220587

 $00{:}21{:}39{.}125 \dashrightarrow 00{:}21{:}41{.}240$ burden of the traditional protocols.
- NOTE Confidence: 0.48220587
- $00:21:41.240 \rightarrow 00:21:43.680$ We wanna do this in a very short,

00:21:43.680 --> 00:21:45.510 like straightforward way

NOTE Confidence: 0.48220587

 $00:21:45.510 \rightarrow 00:21:48.560$ with only a single protocol.

NOTE Confidence: 0.48220587

 $00{:}21{:}48.560 \dashrightarrow 00{:}21{:}50.680$ Also throw in this little bit about sham.

NOTE Confidence: 0.48220587

 $00{:}21{:}50{.}680 \dashrightarrow 00{:}21{:}52{.}800$ You can't do sham stimulation in the scanner.

NOTE Confidence: 0.48220587

 $00:21:52.800 \rightarrow 00:21:55.232$ There isn't a commercially

NOTE Confidence: 0.48220587

 $00:21:55.232 \rightarrow 00:21:58.280$ available stimulator for doing that.

NOTE Confidence: 0.48220587

 $00{:}21{:}58{.}280 \dashrightarrow 00{:}22{:}00{.}728$ And I'll also say clinically there's

NOTE Confidence: 0.48220587

 $00{:}22{:}00{.}728 \dashrightarrow 00{:}22{:}02{.}730$ at least some considerations with

NOTE Confidence: 0.48220587

 $00:22:02.730 \longrightarrow 00:22:04.536$ doing sham that you know does

NOTE Confidence: 0.48220587

 $00:22:04.536 \longrightarrow 00:22:06.639$ not reach the brain effectively.

NOTE Confidence: 0.48220587

 $00{:}22{:}06{.}640 \dashrightarrow 00{:}22{:}09{.}076$ And so asking the patients to

NOTE Confidence: 0.48220587

 $00{:}22{:}09{.}076 \dashrightarrow 00{:}22{:}12{.}451$ wait that out and like have these

NOTE Confidence: 0.48220587

 $00{:}22{:}12.451 \dashrightarrow 00{:}22{:}13.979$ extended symptom assessments,

NOTE Confidence: 0.48220587

 $00{:}22{:}13.979 \dashrightarrow 00{:}22{:}16.912$ you know that they're not getting an

00:22:16.912 --> 00:22:18.589 efficacious treatment that's that's

NOTE Confidence: 0.48220587

 $00:22:18.589 \rightarrow 00:22:21.826$ just another hurdle to considering

NOTE Confidence: 0.48220587

 $00:22:21.826 \longrightarrow 00:22:23.956$ adding sham to TMS studies.

NOTE Confidence: 0.48220587

 $00:22:23.960 \longrightarrow 00:22:26.696$ And I'll say in this case we can

NOTE Confidence: 0.48220587

 $00{:}22{:}26.696 \dashrightarrow 00{:}22{:}28.773$ still show some control conditions

NOTE Confidence: 0.48220587

 $00{:}22{:}28.773 \dashrightarrow 00{:}22{:}31.832$ which is that we have a circuit

NOTE Confidence: 0.48220587

00:22:31.840 --> 00:22:33.296 specific circuit in mind.

NOTE Confidence: 0.48220587

 $00{:}22{:}33{.}296 \dashrightarrow 00{:}22{:}35{.}480$ We also have a specific symptom

NOTE Confidence: 0.48220587

 $00{:}22{:}35{.}546 \dashrightarrow 00{:}22{:}37{.}078$ in mind with depression.

NOTE Confidence: 0.48220587

00:22:37.080 --> 00:22:38.160 And so I'll show you some,

NOTE Confidence: 0.48220587

 $00{:}22{:}38.160 \dashrightarrow 00{:}22{:}41.016$ some evidence of how well we did with

NOTE Confidence: 0.48220587

 $00:22:41.016 \rightarrow 00:22:43.558$ the circuit and symptom specificity.

NOTE Confidence: 0.48220587

00:22:43.560 --> 00:22:46.000 All right. This is, this is our design.

NOTE Confidence: 0.48220587

 $00:22:46.000 \rightarrow 00:22:50.040$ So we collect a baseline scan,

NOTE Confidence: 0.48220587

 $00{:}22{:}50{.}040 \dashrightarrow 00{:}22{:}52{.}440$ we use that to determine the

NOTE Confidence: 0.48220587

 $00:22:52.440 \rightarrow 00:22:53.240$ connectivity targets.

- NOTE Confidence: 0.48220587
- $00:22:53.240 \longrightarrow 00:22:55.240$ So they're personalized high

 $00:22:55.240 \rightarrow 00:22:56.240$ connectivity peaks,

NOTE Confidence: 0.48220587

00:22:56.240 --> 00:22:59.840 positive connectivity peaks with Subgenual.

NOTE Confidence: 0.48220587

 $00:22:59.840 \rightarrow 00:23:02.750$ We also collect an amygdala seated

NOTE Confidence: 0.48220587

 $00:23:02.750 \rightarrow 00:23:05.380$ connectivity profile for a second

NOTE Confidence: 0.48220587

 $00{:}23{:}05{.}380 \dashrightarrow 00{:}23{:}08{.}980$ stimulation site and then before the

NOTE Confidence: 0.48220587

 $00{:}23{:}08{.}980 \dashrightarrow 00{:}23{:}12{.}900$ intervention we pin the circuit in

NOTE Confidence: 0.48220587

 $00:23:12.900 \longrightarrow 00:23:15.288$ both kind of connectivity targets

NOTE Confidence: 0.48220587

 $00{:}23{:}15{.}288 \dashrightarrow 00{:}23{:}17{.}460$ and then we do our intervention

NOTE Confidence: 0.48220587

 $00{:}23{:}17{.}521 \dashrightarrow 00{:}23{:}19{.}544$ over the three days and then we

NOTE Confidence: 0.48220587

 $00:23:19.544 \rightarrow 00:23:20.840$ ping the circuit again.

NOTE Confidence: 0.48220587

00:23:20.840 --> 00:23:22.116 So pretty straightforward, right?

NOTE Confidence: 0.48220587

 $00{:}23{:}22{.}116 \dashrightarrow 00{:}23{:}25{.}152$ We do a pre and post measure and we're

NOTE Confidence: 0.48220587

 $00{:}23{:}25{.}152 \dashrightarrow 00{:}23{:}26{.}922$ focusing on this subgeneral pathway

NOTE Confidence: 0.48220587

 $00{:}23{:}26{.}922 \dashrightarrow 00{:}23{:}29{.}305$ to see if we can link the TMS up

 $00:23:29.305 \rightarrow 00:23:31.236$ from Rye with some clinical change.

NOTE Confidence: 0.48220587

 $00{:}23{:}31{.}236 \dashrightarrow 00{:}23{:}33{.}708$ And I call the intermittent date

NOTE Confidence: 0.48220587

00:23:33.708 --> 00:23:35.126 of birth stimulation protocol.

NOTE Confidence: 0.48220587

 $00{:}23{:}35{.}126 \dashrightarrow 00{:}23{:}37{.}107$ I call it an intervention because I

NOTE Confidence: 0.48220587

 $00{:}23{:}37{.}107 \dashrightarrow 00{:}23{:}39{.}036$ know it's not a full treatment protocol.

NOTE Confidence: 0.48220587

00:23:39.040 --> 00:23:42.533 I know this is not like the

NOTE Confidence: 0.48220587

00:23:42.533 --> 00:23:44.808 maximally effective dose of applying

NOTE Confidence: 0.48220587

 $00:23:44.808 \longrightarrow 00:23:46.760$ TMS to affect depression,

NOTE Confidence: 0.48220587

00:23:46.760 --> 00:23:49.144 but I was hoping that it would move

NOTE Confidence: 0.48220587

 $00{:}23{:}49{.}144 \dashrightarrow 00{:}23{:}51{.}399$ it enough that we can capture this

NOTE Confidence: 0.48220587

 $00{:}23{:}51{.}400 \dashrightarrow 00{:}23{:}54{.}676$ more acute response and link the TMS,

NOTE Confidence: 0.48220587

 $00:23:54.680 \rightarrow 00:23:57.116$ HEP, MRI to a clinical change.

NOTE Confidence: 0.48220587

 $00{:}23{:}57{.}120 \dashrightarrow 00{:}23{:}58{.}767$ So that's what we set out to do when

NOTE Confidence: 0.48220587

 $00:23:58.767 \rightarrow 00:24:00.597$ we actually deliver the intervention.

NOTE Confidence: 0.48220587

 $00:24:00.600 \rightarrow 00:24:02.235$ They're not in the scanner, right?

NOTE Confidence: 0.48220587

 $00{:}24{:}02{.}235 \dashrightarrow 00{:}24{:}04{.}115$ We just do the pings before and after.

- NOTE Confidence: 0.48220587
- $00:24:04.120 \longrightarrow 00:24:04.906$ So the intervention,

 $00:24:04.906 \longrightarrow 00:24:06.216$ they're sitting in front of

NOTE Confidence: 0.48220587

 $00{:}24{:}06{.}216$ --> $00{:}24{:}07{.}639$ a neuro navigation camera.

NOTE Confidence: 0.48220587

00:24:07.640 --> 00:24:09.795 We're getting 2400 pulses of

NOTE Confidence: 0.48220587

 $00{:}24{:}09.795 \dashrightarrow 00{:}24{:}11.950$ intermittent date of births per

NOTE Confidence: 0.48220587

 $00{:}24{:}12.024 \dashrightarrow 00{:}24{:}13.475$ day for three consecutive days and

NOTE Confidence: 0.48220587

 $00:24:13.475 \rightarrow 00:24:15.276$ then we ping them in the scanner

NOTE Confidence: 0.48220587

 $00{:}24{:}15{.}276 \dashrightarrow 00{:}24{:}16{.}556$ again the day after that.

NOTE Confidence: 0.5028308

00:24:19.320 --> 00:24:22.744 So we found evidence that there is an

NOTE Confidence: 0.5028308

 $00{:}24{:}22{.}744 \dashrightarrow 00{:}24{:}24{.}923$ association between the strength of

NOTE Confidence: 0.5028308

 $00{:}24{:}24{.}923 \dashrightarrow 00{:}24{:}27{.}401$ the ping the evoked response before

NOTE Confidence: 0.5028308

 $00{:}24{:}27{.}401 \dashrightarrow 00{:}24{:}30{.}740$ the intervention and how well they do NOTE Confidence: 0.5028308

 $00:24:30.740 \rightarrow 00:24:32.670$ clinically with depression improvement.

NOTE Confidence: 0.5028308

00:24:32.670 --> 00:24:37.400 And it's very supportive of this of our

NOTE Confidence: 0.5028308

 $00{:}24{:}37{.}400 \dashrightarrow 00{:}24{:}41{.}240$ hypothesis that engaging the subgenual is NOTE Confidence: 0.5028308

 $00:24:41.240 \rightarrow 00:24:43.864$ really relevant for depression improvement.

NOTE Confidence: 0.5028308

 $00{:}24{:}43.864 \dashrightarrow 00{:}24{:}47.640$ And so we found some evidence of that.

NOTE Confidence: 0.5028308

 $00:24:47.640 \longrightarrow 00:24:49.732$ We also did the ping after all, right.

NOTE Confidence: 0.5028308

 $00{:}24{:}49{.}732 \dashrightarrow 00{:}24{:}50{.}764$ So we did the pre and

NOTE Confidence: 0.5028308

 $00:24:50.764 \longrightarrow 00:24:51.679$ post change and the ping,

NOTE Confidence: 0.5028308

 $00{:}24{:}51{.}680 \dashrightarrow 00{:}24{:}55{.}220$ the evoked response change was also

NOTE Confidence: 0.5028308

 $00:24:55.220 \longrightarrow 00:24:57.692$ associated with depression improvement.

NOTE Confidence: 0.5028308

 $00{:}24{:}57.692 \dashrightarrow 00{:}25{:}01.146$ So showing evidence that TMS fMRI

NOTE Confidence: 0.5028308

 $00{:}25{:}01{.}146 \dashrightarrow 00{:}25{:}03{.}744$ not only tells you something about

NOTE Confidence: 0.5028308

 $00{:}25{:}03.744 \dashrightarrow 00{:}25{:}05.534$ circuit integrity that's relevant

NOTE Confidence: 0.5028308

 $00:25:05.534 \rightarrow 00:25:06.872$ to improvement clinically,

NOTE Confidence: 0.5028308

 $00{:}25{:}06.872 \dashrightarrow 00{:}25{:}09.824$ but it also measures a change in

NOTE Confidence: 0.5028308

 $00{:}25{:}09{.}824 \dashrightarrow 00{:}25{:}11{.}804$ the communication in that pathway

NOTE Confidence: 0.5028308

 $00{:}25{:}11.804 \dashrightarrow 00{:}25{:}14.008$ that we hope happens when we apply

NOTE Confidence: 0.5028308

00:25:14.008 --> 00:25:16.240 TMS and get a clinical apply.

NOTE Confidence: 0.35288116

00:25:19.880 --> 00:25:21.430 Now I'll jump back into

- NOTE Confidence: 0.35288116
- $00:25:21.430 \longrightarrow 00:25:22.360$ the circuit specificities.

00:25:22.360 --> 00:25:23.385 We're like you don't have

NOTE Confidence: 0.35288116

 $00:25:23.385 \longrightarrow 00:25:24.000$ a control condition,

NOTE Confidence: 0.35288116

00:25:24.000 --> 00:25:25.637 you didn't do a sham control, right.

NOTE Confidence: 0.35288116

 $00{:}25{:}25{.}637 \dashrightarrow 00{:}25{:}27{.}576$ We didn't even have another active site

NOTE Confidence: 0.35288116

 $00{:}25{:}27.576 \dashrightarrow 00{:}25{:}29.717$ that we delivered the intervention to.

NOTE Confidence: 0.35288116

 $00{:}25{:}29{.}720 \dashrightarrow 00{:}25{:}33{.}208$ But what we did have is two different

NOTE Confidence: 0.35288116

 $00{:}25{:}33{.}208 \dashrightarrow 00{:}25{:}35{.}013$ stimulation pathways and two

NOTE Confidence: 0.35288116

 $00{:}25{:}35{.}013 \dashrightarrow 00{:}25{:}36{.}691$ different downstream targets that

NOTE Confidence: 0.35288116

 $00:25:36.691 \rightarrow 00:25:39.193$ we can measure evoked responses in.

NOTE Confidence: 0.35288116

 $00{:}25{:}39{.}200 \dashrightarrow 00{:}25{:}41.006$ So we looked at the amygdala evoked

NOTE Confidence: 0.35288116

 $00{:}25{:}41.006 \dashrightarrow 00{:}25{:}42.647$ response and the subgenual evoked

NOTE Confidence: 0.35288116

 $00{:}25{:}42{.}647 \dashrightarrow 00{:}25{:}44{.}682$ response through the amygdala functional

NOTE Confidence: 0.35288116

 $00{:}25{:}44.682 \dashrightarrow 00{:}25{:}46.869$ connectivity pathway and the subgenual

NOTE Confidence: 0.35288116

 $00{:}25{:}46.869 \dashrightarrow 00{:}25{:}48.240$ functional connectivity pathway.

 $00{:}25{:}48{.}240 \dashrightarrow 00{:}25{:}50{.}382$ And so our hypothesis was only the

NOTE Confidence: 0.35288116

 $00{:}25{:}50{.}382 \dashrightarrow 00{:}25{:}52{.}391$ solid blue line that's the place

NOTE Confidence: 0.35288116

 $00{:}25{:}52{.}391 \dashrightarrow 00{:}25{:}54{.}226$ where we delivered the intervention NOTE Confidence: 0.35288116

 $00:25:54.226 \dashrightarrow 00:25:56.556$ and that's our downstream target.

NOTE Confidence: 0.35288116

 $00{:}25{:}56{.}560 \dashrightarrow 00{:}25{:}58{.}904$ We we thought that if if if our

NOTE Confidence: 0.35288116

 $00:25:58.904 \rightarrow 00:26:00.759$ hypothesis is right that engaging NOTE Confidence: 0.35288116

 $00{:}26{:}00{.}759 \dashrightarrow 00{:}26{:}02{.}749$ that target and modulating that

NOTE Confidence: 0.35288116

 $00:26:02.749 \longrightarrow 00:26:05.424$ target is the is the one most

NOTE Confidence: 0.35288116

 $00{:}26{:}05{.}424 \dashrightarrow 00{:}26{:}06{.}872$ relevant to depression change,

NOTE Confidence: 0.35288116

 $00{:}26{:}06{.}880 \dashrightarrow 00{:}26{:}08{.}620$ then that's the only evoked response

NOTE Confidence: 0.35288116

 $00{:}26{:}08{.}620 \dashrightarrow 00{:}26{:}10{.}195$ response that will be associated

NOTE Confidence: 0.35288116

00:26:10.195 --> 00:26:11.619 with depression improvement and

NOTE Confidence: 0.35288116

 $00:26:11.619 \longrightarrow 00:26:13.399$ that's indeed what we found.

NOTE Confidence: 0.35288116

 $00{:}26{:}13.400 \dashrightarrow 00{:}26{:}15.518$ So we found some circuit specificity

NOTE Confidence: 0.35288116

 $00:26:15.518 \rightarrow 00:26:17.640$ some region of interest specificity

NOTE Confidence: 0.33387774

 $00{:}26{:}20.680 \dashrightarrow 00{:}26{:}23.680$ also say that anxiety improved

 $00:26:23.680 \longrightarrow 00:26:25.534$ even though we were aiming at

NOTE Confidence: 0.33387774

 $00{:}26{:}25{.}534 \dashrightarrow 00{:}26{:}27{.}320$ the at the depression pathway.

NOTE Confidence: 0.33387774

00:26:27.320 --> 00:26:29.795 Anxiety improvement was not associated

NOTE Confidence: 0.33387774

 $00{:}26{:}29.795 \dashrightarrow 00{:}26{:}32.941$ with change in subgenual evoked response

NOTE Confidence: 0.33387774

 $00{:}26{:}32{.}941 \dashrightarrow 00{:}26{:}35{.}317$ only depression improvement loss.

NOTE Confidence: 0.33387774

 $00{:}26{:}35{.}320 \dashrightarrow 00{:}26{:}38{.}287$ Now let's show some degree of symptom

NOTE Confidence: 0.33387774

 $00:26:38.287 \rightarrow 00:26:40.522$ specificity and relevance to that

NOTE Confidence: 0.33387774

 $00:26:40.522 \rightarrow 00:26:43.040$ pathway with the subgenual stimulant.

NOTE Confidence: 0.31938392

 $00{:}26{:}45{.}680 \dashrightarrow 00{:}26{:}47{.}717$ Also say that we cast a pretty

NOTE Confidence: 0.31938392

00:26:47.717 -> 00:26:50.119 wide net we took in any patients.

NOTE Confidence: 0.31938392

00:26:50.120 --> 00:26:52.320 Actually we wanted to prioritize

NOTE Confidence: 0.31938392

 $00{:}26{:}52{.}320 \dashrightarrow 00{:}26{:}53{.}640$ our medicated patients,

NOTE Confidence: 0.31938392

 $00{:}26{:}53.640 \dashrightarrow 00{:}26{:}55.488$ which are not the difficult patients

NOTE Confidence: 0.31938392

 $00{:}26{:}55{.}488 \dashrightarrow 00{:}26{:}57{.}352$ in the TMS clinical studies because

NOTE Confidence: 0.31938392

 $00:26:57.352 \rightarrow 00:26:59.640$ we wanted to kind of clean our brain

 $00:26:59.700 \rightarrow 00:27:01.590$ response as our first stab at linking

NOTE Confidence: 0.31938392

 $00{:}27{:}01.590 \dashrightarrow 00{:}27{:}03.420$ TMS up from my clinical outcome.

NOTE Confidence: 0.31938392

00:27:03.420 --> 00:27:05.800 But we did get some treatment resistant

NOTE Confidence: 0.31938392

 $00{:}27{:}05{.}800 \dashrightarrow 00{:}27{:}07{.}918$ patients that have not responded to

NOTE Confidence: 0.31938392

 $00{:}27{:}07{.}920 \dashrightarrow 00{:}27{:}09{.}772$ multiple rounds of antidepressant

NOTE Confidence: 0.31938392

 $00{:}27{:}09{.}772 \dashrightarrow 00{:}27{:}12{.}550$ medication and they tended to have

NOTE Confidence: 0.31938392

 $00{:}27{:}12.626 \dashrightarrow 00{:}27{:}14.601$ stronger higher levels of depression

NOTE Confidence: 0.31938392

 $00:27:14.601 \longrightarrow 00:27:17.400$ which is the blue bar on the left

NOTE Confidence: 0.31938392

 $00{:}27{:}17{.}400 \dashrightarrow 00{:}27{:}19{.}716$ compared to the non treatment resistant.

NOTE Confidence: 0.31938392

 $00{:}27{:}19.720 \dashrightarrow 00{:}27{:}22.456$ But their clinical response to the

NOTE Confidence: 0.31938392

 $00:27:22.456 \rightarrow 00:27:24.633$ intervention was very similar, right?

NOTE Confidence: 0.31938392

00:27:24.633 --> 00:27:28.320 You can see the non TRD and the TRD ones,

NOTE Confidence: 0.31938392

 $00{:}27{:}28.320 \dashrightarrow 00{:}27{:}30.420$ they respond equally well

NOTE Confidence: 0.31938392

 $00{:}27{:}30{.}420 \dashrightarrow 00{:}27{:}32{.}520$ to this brief intervention.

NOTE Confidence: 0.34967873

 $00{:}27{:}35{.}800 \dashrightarrow 00{:}27{:}38{.}005$ I will say I mentioned that we

NOTE Confidence: 0.34967873

00:27:38.005 --> 00:27:39.710 collected whole brain data, right?

 $00:27:39.710 \longrightarrow 00:27:42.050$ And so I'm talking all about

NOTE Confidence: 0.34967873

 $00{:}27{:}42.050 \dashrightarrow 00{:}27{:}43.648$ the subgenual cingulate and a

NOTE Confidence: 0.34967873

 $00:27:43.648 \longrightarrow 00:27:45.158$ little bit about the amygdala.

NOTE Confidence: 0.34967873

 $00{:}27{:}45.160 \dashrightarrow 00{:}27{:}46.740$ Maybe the subgenual cingulate

NOTE Confidence: 0.34967873

 $00:27:46.740 \longrightarrow 00:27:48.715$ is not even a hotspot,

NOTE Confidence: 0.34967873

 $00{:}27{:}48.720 \dashrightarrow 00{:}27{:}50.596$ you're aiming for it, you engaged it,

NOTE Confidence: 0.34967873

 $00{:}27{:}50.600 \dashrightarrow 00{:}27{:}51.856$ you showed these relationships.

NOTE Confidence: 0.34967873

 $00:27:51.856 \longrightarrow 00:27:54.478$ But if you looked at the evoked response

NOTE Confidence: 0.34967873

 $00{:}27{:}54.478 \dashrightarrow 00{:}27{:}56.837$ changes through the rest of the brain,

NOTE Confidence: 0.34967873

 $00:27:56.840 \longrightarrow 00:27:58.320$ probably some other parts

NOTE Confidence: 0.34967873

 $00:27:58.320 \longrightarrow 00:28:00.066$ of the network are yes,

NOTE Confidence: 0.34967873

 $00{:}28{:}00{.}066 \dashrightarrow 00{:}28{:}01{.}396$ is relevant, may be more relevant.

NOTE Confidence: 0.34967873

 $00{:}28{:}01{.}400 \dashrightarrow 00{:}28{:}03{.}434$ So we looked at the rest of the brain,

NOTE Confidence: 0.34967873

 $00{:}28{:}03{.}440 \dashrightarrow 00{:}28{:}05{.}120$ we looked at the evoked response

NOTE Confidence: 0.34967873

 $00:28:05.120 \rightarrow 00:28:07.400$ change map and the symptom improvement.

 $00{:}28{:}07{.}400 \dashrightarrow 00{:}28{:}08{.}972$ So this is different from other

NOTE Confidence: 0.34967873

 $00{:}28{:}08{.}972 \dashrightarrow 00{:}28{:}10.672$ brain images that you may have

NOTE Confidence: 0.34967873

 $00:28:10.672 \rightarrow 00:28:12.157$ seen that are just correlational.

NOTE Confidence: 0.34967873

 $00:28:12.160 \rightarrow 00:28:15.368$ These are the evoked response changes, right?

NOTE Confidence: 0.34967873

 $00{:}28{:}15{.}368 \dashrightarrow 00{:}28{:}19{.}653$ So a very unique measurement and I

NOTE Confidence: 0.34967873

 $00{:}28{:}19.653 \dashrightarrow 00{:}28{:}21.759$ will say for a depression change,

NOTE Confidence: 0.34967873

 $00{:}28{:}21.760 \dashrightarrow 00{:}28{:}23.440$ the subgenual came up as a hotspot.

NOTE Confidence: 0.34967873

00:28:23.440 --> 00:28:24.840 It was, it's definitely solid,

NOTE Confidence: 0.34967873

 $00{:}28{:}24{.}840 \dashrightarrow 00{:}28{:}26{.}200$ it's definitely a reasonable target.

NOTE Confidence: 0.34967873

00:28:26.200 --> 00:28:27.154 But of course,

NOTE Confidence: 0.34967873

 $00{:}28{:}27{.}154 \dashrightarrow 00{:}28{:}29{.}062$ other brain areas are also changing

NOTE Confidence: 0.34967873

 $00{:}28{:}29.062 \dashrightarrow 00{:}28{:}31.688$ and then are relevant to depression

NOTE Confidence: 0.34967873

00:28:31.688 --> 00:28:33.035 improvement like hippocampus,

NOTE Confidence: 0.34967873

 $00:28:33.040 \longrightarrow 00:28:33.750$ posterior singlet.

NOTE Confidence: 0.34967873

 $00{:}28{:}33{.}750 \dashrightarrow 00{:}28{:}35{.}880$ A bunch of these other brain

NOTE Confidence: 0.34967873

 $00:28:35.880 \longrightarrow 00:28:37.503$ areas also come along.

 $00:28:37.503 \rightarrow 00:28:40.450$ And then we we recognized that the

NOTE Confidence: 0.34967873

 $00{:}28{:}40{.}536 \dashrightarrow 00{:}28{:}43{.}368$ evoked response in the subgenual was

NOTE Confidence: 0.34967873

00:28:43.368 --> 00:28:45.688 not relevant for anxiety improvement,

NOTE Confidence: 0.34967873

00:28:45.688 --> 00:28:47.998 even though anxiety did improve.

NOTE Confidence: 0.34967873

 $00:28:48.000 \rightarrow 00:28:49.520$ So we looked at the other parts of the brain.

NOTE Confidence: 0.34967873

 $00{:}28{:}49{.}520 \dashrightarrow 00{:}28{:}52{.}250$ We found that there's a an adjacent

NOTE Confidence: 0.34967873

00:28:52.250 --> 00:28:54.497 region of intermedial prefrontal cortex

NOTE Confidence: 0.34967873

 $00:28:54.497 \rightarrow 00:28:57.200$ that changed in response to stimulation,

NOTE Confidence: 0.34967873

 $00{:}28{:}57{.}200 \dashrightarrow 00{:}29{:}00{.}130$ some other regions and posterior

NOTE Confidence: 0.34967873

 $00:29:00.130 \longrightarrow 00:29:01.878$ cingulate orbital frontal cortex.

NOTE Confidence: 0.34967873

 $00{:}29{:}01{.}878 \dashrightarrow 00{:}29{:}04{.}194$ So there are other regions that

NOTE Confidence: 0.34967873

 $00{:}29{:}04.194 \dashrightarrow 00{:}29{:}06.637$ seem to have been modulated and that

NOTE Confidence: 0.34967873

 $00:29:06.640 \longrightarrow 00:29:09.160$ are relevant to anxiety change.

NOTE Confidence: 0.34967873

 $00:29:09.160 \longrightarrow 00:29:11.470$ I would say these maps could be

NOTE Confidence: 0.34967873

 $00{:}29{:}11.470 \dashrightarrow 00{:}29{:}13.369$ really useful because these can

- 00:29:13.369 00:29:14.638 generate new hypothesis.
- NOTE Confidence: 0.34967873
- 00:29:14.640 --> 00:29:16.038 If you're, if you say OK,
- NOTE Confidence: 0.34967873
- $00:29:16.040 \longrightarrow 00:29:17.368$ well we want to,
- NOTE Confidence: 0.34967873
- $00{:}29{:}17.368 \dashrightarrow 00{:}29{:}19.826$ we want we want another pathway that
- NOTE Confidence: 0.34967873
- 00:29:19.826 --> 00:29:22.196 might be more relevant for anxiety.
- NOTE Confidence: 0.34967873
- $00:29:22.200 \longrightarrow 00:29:22.968$ So we can say,
- NOTE Confidence: 0.34967873
- 00:29:22.968 --> 00:29:23.160 OK,
- NOTE Confidence: 0.34967873
- $00{:}29{:}23.160 \dashrightarrow 00{:}29{:}25.024$ we can see these regions and look for
- NOTE Confidence: 0.34967873
- 00:29:25.024 --> 00:29:26.126 connectivity targets at the surface
- NOTE Confidence: 0.34967873
- $00:29:26.126 \rightarrow 00:29:27.505$ or we can try to capture something
- NOTE Confidence: 0.34967873
- $00{:}29{:}27{.}547 \dashrightarrow 00{:}29{:}28{.}777$ that's more to the surface like
- NOTE Confidence: 0.34967873
- 00:29:28.777 --> 00:29:30.132 maybe this orbit of frontal one,
- NOTE Confidence: 0.34967873
- $00:29:30.132 \longrightarrow 00:29:30.664$ you say.
- NOTE Confidence: 0.34967873
- 00:29:30.664 --> 00:29:31.496 All right, well,
- NOTE Confidence: 0.34967873
- $00{:}29{:}31{.}496 \dashrightarrow 00{:}29{:}33{.}568$ that gives us some evidence that this
- NOTE Confidence: 0.34967873
- $00:29:33.568 \rightarrow 00:29:35.959$ is a pathway we want to modulate.

 $00:29:35.960 \rightarrow 00:29:39.370$ And so let's try a treatment or another TMS,

NOTE Confidence: 0.34967873

00:29:39.370 -> 00:29:39.660 FM,

NOTE Confidence: 0.34967873

00:29:39.660 --> 00:29:41.690 RI study focusing on one of these

NOTE Confidence: 0.34967873

 $00:29:41.690 \rightarrow 00:29:43.812$ other cortical targets and see if

NOTE Confidence: 0.34967873

 $00{:}29{:}43.812 \dashrightarrow 00{:}29{:}45.588$ that actually is more effective

NOTE Confidence: 0.34967873

 $00:29:45.588 \rightarrow 00:29:48.080$ as a sa a treatment for anxiety.

NOTE Confidence: 0.42380634

 $00{:}29{:}50{.}800 \dashrightarrow 00{:}29{:}53{.}880$ All right. So I tried to demonstrate

NOTE Confidence: 0.42380634

 $00{:}29{:}53.880 \dashrightarrow 00{:}29{:}56.452$ some evidence that our our positive

NOTE Confidence: 0.42380634

 $00{:}29{:}56{.}452 \dashrightarrow 00{:}29{:}58{.}782$ connectivity targets for the subgenual NOTE Confidence: 0.42380634

 $00:29:58.782 \rightarrow 00:30:02.264$ may be especially clinically relevant,

NOTE Confidence: 0.42380634

 $00{:}30{:}02{.}264 \dashrightarrow 00{:}30{:}05{.}664$ but there's the brief intervention

NOTE Confidence: 0.42380634

 $00{:}30{:}05{.}664 \dashrightarrow 00{:}30{:}10{.}476$ study that may not be as similar to

NOTE Confidence: 0.42380634

 $00{:}30{:}10.476 \dashrightarrow 00{:}30{:}12.361$ traditional RTMS clinical trials.

NOTE Confidence: 0.42380634

 $00{:}30{:}12{.}361 \dashrightarrow 00{:}30{:}14{.}296$ So what about purely based

NOTE Confidence: 0.42380634

 $00:30:14.296 \longrightarrow 00:30:15.720$ on clinical evidence,

 $00:30:15.720 \longrightarrow 00:30:18.400$ what can we show maybe it's

NOTE Confidence: 0.42380634

 $00:30:18.400 \longrightarrow 00:30:19.360$ sort of a distraction.

NOTE Confidence: 0.42380634

00:30:19.360 --> 00:30:21.331 I can come back to it if if there

NOTE Confidence: 0.42380634

 $00:30:21.331 \rightarrow 00:30:22.954$ are questions or people want

NOTE Confidence: 0.42380634

 $00:30:22.954 \longrightarrow 00:30:25.173$ to get into more of the sham

NOTE Confidence: 0.42380634

 $00{:}30{:}25{.}173 \dashrightarrow 00{:}30{:}26{.}440$ consideration etcetera. But

NOTE Confidence: 0.62573975

00:30:28.640 --> 00:30:29.480 I will, I will say,

NOTE Confidence: 0.62573975

 $00:30:29.480 \longrightarrow 00:30:32.835$ I will say that it's harder to

NOTE Confidence: 0.62573975

00:30:32.835 --> 00:30:34.905 get to compare two active sites

NOTE Confidence: 0.62573975

 $00{:}30{:}34{.}905 \dashrightarrow 00{:}30{:}36{.}761$ and get a clinical difference

NOTE Confidence: 0.62573975

 $00{:}30{:}36{.}761 \dashrightarrow 00{:}30{:}39{.}361$ than it is to deliver sham where

NOTE Confidence: 0.62573975

 $00{:}30{:}39{.}361 \dashrightarrow 00{:}30{:}41{.}972$ we know it's not engaging the the

NOTE Confidence: 0.62573975

 $00{:}30{:}41.972 \dashrightarrow 00{:}30{:}43.623$ brain networks or modulating them.

NOTE Confidence: 0.62573975

 $00:30:43.623 \longrightarrow 00:30:46.094$ So let's say it's it's sort of a

NOTE Confidence: 0.62573975

 $00:30:46.094 \rightarrow 00:30:47.864$ higher bar to have another active

NOTE Confidence: 0.62573975

 $00:30:47.864 \rightarrow 00:30:49.806$ site that you think may actually

 $00{:}30{:}49{.}806 \dashrightarrow 00{:}30{:}52{.}482$ help with symptoms and then your

NOTE Confidence: 0.62573975

00:30:52.482 --> 00:30:54.234 personalized fMRI guided target

NOTE Confidence: 0.62573975

 $00:30:54.234 \rightarrow 00:30:56.316$ that you hope is even better.

NOTE Confidence: 0.62573975

 $00{:}30{:}56{.}320 \dashrightarrow 00{:}30{:}59{.}800$ So we tried this out in a cohort

NOTE Confidence: 0.62573975

 $00{:}30{:}59{.}800 \dashrightarrow 00{:}31{:}02{.}800$ of mixed depression and PTSD

NOTE Confidence: 0.62573975

00:31:02.800 --> 00:31:06.625 patients and we chose this positive

NOTE Confidence: 0.62573975

00:31:06.625 --> 00:31:09.156 connectivity target based on their

NOTE Confidence: 0.62573975

00:31:09.156 --> 00:31:11.628 baseline F MRI and we compared

NOTE Confidence: 0.62573975

 $00{:}31{:}11{.}628 \dashrightarrow 00{:}31{:}14{.}521$ that to a six centimeter anterior

NOTE Confidence: 0.62573975

 $00{:}31{:}14{.}521 \dashrightarrow 00{:}31{:}16{.}911$ motor cortex spot that's been

NOTE Confidence: 0.62573975

00:31:16.920 --> 00:31:18.340 looked at clinically in depression

NOTE Confidence: 0.62573975

 $00{:}31{:}18{.}340 \dashrightarrow 00{:}31{:}20{.}040$ and seems to work decently well.

NOTE Confidence: 0.62573975

 $00:31:20.040 \longrightarrow 00:31:22.469$ So we have these two active site NOTE Confidence: 0.62573975

 $00:31:22.469 \dashrightarrow 00:31:24.538$ targets we did between subjects NOTE Confidence: 0.62573975

 $00:31:24.538 \longrightarrow 00:31:27.478$ design on those we have two

00:31:27.478 --> 00:31:30.290 weeks of daily TMS treatment.

NOTE Confidence: 0.62573975

 $00{:}31{:}30{.}290 \dashrightarrow 00{:}31{:}34{.}518$ We added in this funky element where

NOTE Confidence: 0.62573975

00:31:34.518 --> 00:31:37.013 we're trying to engage circuitry

NOTE Confidence: 0.62573975

 $00:31:37.013 \rightarrow 00:31:38.953$ through some psychological tasks

NOTE Confidence: 0.62573975

 $00{:}31{:}38{.}953 \dashrightarrow 00{:}31{:}41{.}167$ and I'm going to skip talking

NOTE Confidence: 0.62573975

00:31:41.167 --> 00:31:44.240 about that because some of the the

NOTE Confidence: 0.62573975

 $00{:}31{:}44{.}240 \dashrightarrow 00{:}31{:}45{.}680$ interactions were not significant.

NOTE Confidence: 0.62573975

 $00{:}31{:}45.680 \dashrightarrow 00{:}31{:}47.944$ We expected them to be with the target

NOTE Confidence: 0.62573975

 $00{:}31{:}47{.}944 \dashrightarrow 00{:}31{:}50{.}035$ and what tasks they were doing there.

NOTE Confidence: 0.62573975

 $00{:}31{:}50{.}035 \dashrightarrow 00{:}31{:}51{.}595$ There's maybe a little bit of signal there.

NOTE Confidence: 0.62573975

 $00{:}31{:}51{.}600 \dashrightarrow 00{:}31{:}53{.}112$ We want to try to follow up on it.

NOTE Confidence: 0.62573975

 $00{:}31{:}53{.}120 \dashrightarrow 00{:}31{:}54{.}848$ But the the basic design here

NOTE Confidence: 0.62573975

 $00:31:54.848 \rightarrow 00:31:56.960$ that I'm going to give you the

NOTE Confidence: 0.62573975

00:31:56.960 --> 00:31:58.754 evidence for as the fMRI guided

NOTE Confidence: 0.62573975

 $00{:}31{:}58.760 \dashrightarrow 00{:}32{:}00{.}320$ versus the six centimeter target

NOTE Confidence: 0.94476616

 $00{:}32{:}02{.}440 \dashrightarrow 00{:}32{:}04{.}420$ and this is what the cortical

- NOTE Confidence: 0.94476616
- $00:32:04.420 \dashrightarrow 00:32:06.839$ sites look like in standard space.

 $00{:}32{:}06{.}840 \dashrightarrow 00{:}32{:}08{.}359$ So you can see the blue ones,

NOTE Confidence: 0.94476616

 $00:32:08.360 \longrightarrow 00:32:09.638$ those are the 6 centimeter ones,

NOTE Confidence: 0.94476616

 $00:32:09.640 \rightarrow 00:32:11.677$ they tend to cluster fairly well together.

NOTE Confidence: 0.94476616

 $00{:}32{:}11.680 \dashrightarrow 00{:}32{:}13.906$ Some people's heads are longer or shorter

NOTE Confidence: 0.94476616

 $00{:}32{:}13.906 \dashrightarrow 00{:}32{:}16.920$ and so you get a little bit of a, you know,

NOTE Confidence: 0.94476616

00:32:16.920 --> 00:32:18.520 spread from anterior to posterior,

NOTE Confidence: 0.94476616

 $00:32:18.520 \rightarrow 00:32:20.200$ whereas the fMRI guided ones,

NOTE Confidence: 0.94476616

 $00{:}32{:}20{.}200 \dashrightarrow 00{:}32{:}22{.}294$ those have a little bit more

NOTE Confidence: 0.94476616

 $00:32:22.294 \rightarrow 00:32:24.080$ variability in where they land.

NOTE Confidence: 0.94476616

 $00{:}32{:}24.080 \dashrightarrow 00{:}32{:}26.327$ So we're looking at a nice consistent

NOTE Confidence: 0.94476616

 $00{:}32{:}26{.}327 \dashrightarrow 00{:}32{:}28{.}663$ cluster that has high positive connectivity

NOTE Confidence: 0.94476616

 $00:32:28.663 \rightarrow 00:32:30.838$ individually guided for that subgenual

NOTE Confidence: 0.94476616

 $00{:}32{:}30{.}838 \dashrightarrow 00{:}32{:}33{.}197$ and you can see there's overlap,

NOTE Confidence: 0.94476616

 $00{:}32{:}33{.}200 \dashrightarrow 00{:}32{:}36{.}518$ There's definitely overlap in standard space.

 $00:32:36.520 \rightarrow 00:32:40.187$ But we still anticipated that the

NOTE Confidence: 0.94476616

 $00{:}32{:}40{.}187 \dashrightarrow 00{:}32{:}42{.}432$ personalization was going to make

NOTE Confidence: 0.94476616

 $00:32:42.432 \dashrightarrow 00:32:45.208$ a difference and help the symptoms NOTE Confidence: 0.94476616

 $00{:}32{:}45{.}208 \dashrightarrow 00{:}32{:}47{.}480$ even more and this is the clinical

NOTE Confidence: 0.94476616

 $00{:}32{:}47{.}480 \dashrightarrow 00{:}32{:}48{.}680$ evidence that that we found.

NOTE Confidence: 0.94476616

 $00{:}32{:}48{.}680 \dashrightarrow 00{:}32{:}51{.}039$ So this from across the weeks with NOTE Confidence: 0.94476616

00:32:51.039 --> 00:32:53.567 a longer term follow up you see on

NOTE Confidence: 0.94476616

 $00:32:53.567 \rightarrow 00:32:55.706$ the top left the PTSD checklist.

NOTE Confidence: 0.94476616

00:32:55.706 --> 00:32:58.238 So in terms of PTSD symptoms,

NOTE Confidence: 0.94476616

 $00{:}32{:}58{.}240 \dashrightarrow 00{:}33{:}00{.}865$ the scalp target and the FBI guided

NOTE Confidence: 0.94476616

 $00{:}33{:}00{.}865 \dashrightarrow 00{:}33{:}02{.}984$ targets seem to work decently well.

NOTE Confidence: 0.94476616

 $00{:}33{:}02{.}984$ --> $00{:}33{:}05{.}168$ Both of them look pretty similar even NOTE Confidence: 0.94476616

 $00:33:05.168 \dashrightarrow 00:33:07.640$ in the longer term follow up that they NOTE Confidence: 0.94476616

 $00:33:07.640 \rightarrow 00:33:09.680$ held pretty tight with one another.

NOTE Confidence: 0.94476616

 $00{:}33{:}09{.}680 \dashrightarrow 00{:}33{:}13{.}290$ There was one subscale of PCL that

NOTE Confidence: 0.94476616

 $00:33:13.290 \longrightarrow 00:33:15.215$ showed a slight difference which

 $00:33:15.215 \longrightarrow 00:33:18.022$ is the bottom left and that was

NOTE Confidence: 0.94476616

 $00{:}33{:}18.022 \dashrightarrow 00{:}33{:}19.598$ the hyper arous al subscale.

NOTE Confidence: 0.94476616

 $00{:}33{:}19.600 \dashrightarrow 00{:}33{:}22.894$ So we showed some clear evidence

NOTE Confidence: 0.94476616

00:33:22.894 --> 00:33:25.541 like immediately post treatment out

NOTE Confidence: 0.94476616

 $00{:}33{:}25{.}541 \dashrightarrow 00{:}33{:}28{.}075$ to week 10 where the fMRI guided

NOTE Confidence: 0.94476616

 $00:33:28.075 \dashrightarrow 00:33:31.080$ 1 tended to be more efficacious.

NOTE Confidence: 0.94476616

 $00{:}33{:}31{.}080 \dashrightarrow 00{:}33{:}33{.}400$ Some of that kind of slipped back in

NOTE Confidence: 0.94476616

 $00:33:33.400 \dashrightarrow 00:33:35.557$ longer term follow up where they they

NOTE Confidence: 0.94476616

00:33:35.557 --> 00:33:37.948 looked a little bit more similar where

NOTE Confidence: 0.94476616

 $00{:}33{:}37{.}948 \dashrightarrow 00{:}33{:}40{.}664$ we saw the the best more striking

NOTE Confidence: 0.94476616

 $00{:}33{:}40.664 \dashrightarrow 00{:}33{:}42.978$ group differences is in the PHQ 9

NOTE Confidence: 0.94476616

 $00{:}33{:}42.978 \dashrightarrow 00{:}33{:}44.920$ depression scale on the top right.

NOTE Confidence: 0.94476616

 $00{:}33{:}44{.}920 \dashrightarrow 00{:}33{:}48{.}632$ You can see that kind of from early

NOTE Confidence: 0.94476616

 $00{:}33{:}48.632 \dashrightarrow 00{:}33{:}52.332$ on those two kind of profiles

NOTE Confidence: 0.94476616

 $00:33:52.332 \rightarrow 00:33:53.398$ look different.

 $00:33:53.400 \rightarrow 00:33:55.320$ The fMRI guided continues to beat

NOTE Confidence: 0.94476616

 $00:33:55.320 \longrightarrow 00:33:57.181$ the scalp based target and even

NOTE Confidence: 0.94476616

 $00{:}33{:}57{.}181 \dashrightarrow 00{:}33{:}59{.}015$ in the longer term follow up it

NOTE Confidence: 0.94476616

 $00:33:59.015 \dashrightarrow 00:34:00.999$ could becomes even more pronounced.

NOTE Confidence: 0.94476616

00:34:01.000 --> 00:34:02.376 Like the scalp target,

NOTE Confidence: 0.94476616

 $00{:}34{:}02{.}376 \dashrightarrow 00{:}34{:}04{.}888$ the symptoms start to kind of push

NOTE Confidence: 0.94476616

 $00{:}34{:}04.888 \dashrightarrow 00{:}34{:}06.952$ back towards the baseline a lot

NOTE Confidence: 0.94476616

 $00{:}34{:}06{.}952 \dashrightarrow 00{:}34{:}09{.}362$ more than the fMRI guided one that

NOTE Confidence: 0.94476616

 $00{:}34{:}09{.}362 \dashrightarrow 00{:}34{:}10{.}838$ tends to stick around.

NOTE Confidence: 0.94476616

 $00:34:10.840 \rightarrow 00:34:13.065$ So these these are significantly

NOTE Confidence: 0.94476616

00:34:13.065 --> 00:34:16.780 different even accounting for the baseline

NOTE Confidence: 0.94476616

 $00:34:16.780 \rightarrow 00:34:19.600$ symptom differences and measures.

NOTE Confidence: 0.94476616

 $00{:}34{:}19.600 \dashrightarrow 00{:}34{:}20.150$ OK.

NOTE Confidence: 0.94476616

 $00:34:20.150 \longrightarrow 00:34:21.800$ So this is,

NOTE Confidence: 0.94476616

 $00{:}34{:}21{.}800 \dashrightarrow 00{:}34{:}24{.}945$ this is something of you know hope

NOTE Confidence: 0.94476616

 $00:34:24.945 \longrightarrow 00:34:27.150$ for the future which is that to

- NOTE Confidence: 0.94476616
- $00{:}34{:}27{.}223 \dashrightarrow 00{:}34{:}29{.}379$ mess up MRI might guide us more

 $00:34:29.379 \rightarrow 00:34:31.876$ quickly to a more efficacious target

NOTE Confidence: 0.94476616

 $00:34:31.876 \longrightarrow 00:34:33.876$ for an individual patient.

NOTE Confidence: 0.94476616

 $00:34:33.880 \longrightarrow 00:34:36.015$ So you have a couple of different

NOTE Confidence: 0.94476616

00:34:36.015 -> 00:34:37.440 imaging based market markers,

NOTE Confidence: 0.94476616

 $00:34:37.440 \longrightarrow 00:34:39.264$ right and you say well there's

NOTE Confidence: 0.94476616

 $00:34:39.264 \rightarrow 00:34:40.480$ a connectivity peak here,

NOTE Confidence: 0.94476616

 $00{:}34{:}40{.}480 \dashrightarrow 00{:}34{:}43{.}000$ there's a DTI based target down here.

NOTE Confidence: 0.94476616

00:34:43.000 --> 00:34:43.640 I don't,

NOTE Confidence: 0.94476616

00:34:43.640 --> 00:34:45.880 I'm not sure which one is better,

NOTE Confidence: 0.94476616

 $00:34:45.880 \rightarrow 00:34:48.080$ but I do feel like engaging the subgenual,

NOTE Confidence: 0.94476616

 $00:34:48.080 \longrightarrow 00:34:49.400$ there's good evidence for that.

NOTE Confidence: 0.94476616

 $00{:}34{:}49{.}400 \dashrightarrow 00{:}34{:}51{.}320$ So put them in the scanner,

NOTE Confidence: 0.94476616

 $00:34:51.320 \longrightarrow 00:34:53.360$ you ping a couple of different

NOTE Confidence: 0.94476616

 $00:34:53.360 \rightarrow 00:34:54.040$ potential pathways,

 $00:34:54.040 \rightarrow 00:34:56.120$ you measure the evoked response,

NOTE Confidence: 0.94476616

 $00:34:56.120 \longrightarrow 00:34:57.535$ right for that individual patient

NOTE Confidence: 0.94476616

 $00:34:57.535 \rightarrow 00:34:59.320$ through that pathway and you say ah,

NOTE Confidence: 0.94476616

 $00{:}34{:}59{.}320 \dashrightarrow 00{:}35{:}01{.}960$ it looks much stronger at this red site.

NOTE Confidence: 0.94476616

 $00:35:01.960 \longrightarrow 00:35:04.144$ And so you carry that forward

NOTE Confidence: 0.94476616

 $00{:}35{:}04{.}144 \dashrightarrow 00{:}35{:}05{.}600$ as your treatment target.

NOTE Confidence: 0.94476616

00:35:05.600 --> 00:35:06.130 You know,

NOTE Confidence: 0.94476616

00:35:06.130 --> 00:35:06.660 if this,

NOTE Confidence: 0.94476616

 $00{:}35{:}06.660 \dashrightarrow 00{:}35{:}08.250$ if this evidence continues to build

NOTE Confidence: 0.8656689

 $00:35:08.306 \rightarrow 00:35:09.878$ the way we're starting out here,

NOTE Confidence: 0.8656689

 $00{:}35{:}09{.}880 \dashrightarrow 00{:}35{:}12{.}010$ that engaging the circuits is really

NOTE Confidence: 0.8656689

 $00:35:12.010 \rightarrow 00:35:13.920$ critical and tells you something

NOTE Confidence: 0.8656689

 $00{:}35{:}13{.}920 \dashrightarrow 00{:}35{:}16{.}030$ about how effective the brain

NOTE Confidence: 0.8656689

00:35:16.030 --> 00:35:17.718 stimulation treatment will be,

NOTE Confidence: 0.8656689

 $00:35:17.720 \longrightarrow 00:35:20.070$ an approach like this might

NOTE Confidence: 0.8656689

00:35:20.070 - 00:35:21.480 be particularly valuable.

- NOTE Confidence: 0.8656689
- $00:35:21.480 \longrightarrow 00:35:24.080$ Save us a lot of time make the

 $00:35:24.080 \dashrightarrow 00:35:25.480$ treatment protocols work better.

NOTE Confidence: 0.3334847

 $00{:}35{:}30{.}400 \dashrightarrow 00{:}35{:}34{.}010$ All right. So in conclusion, fMRI guided

NOTE Confidence: 0.3334847

 $00:35:34.010 \rightarrow 00:35:36.920$ TMS seems to engage intended targets,

NOTE Confidence: 0.3334847

 $00{:}35{:}36{.}920 \dashrightarrow 00{:}35{:}38{.}999$ at least these ones that we tried so far,

NOTE Confidence: 0.3334847

 $00:35:39.000 \dashrightarrow 00:35:41.280$ the subennial singular and the amygdala.

NOTE Confidence: 0.3334847

00:35:41.280 --> 00:35:42.715 So I've seen people in talk say,

NOTE Confidence: 0.3334847

 $00:35:42.720 \dashrightarrow 00:35:45.024$ oh maybe we need ultrasound a lot less

NOTE Confidence: 0.3334847

 $00{:}35{:}45.024 \dashrightarrow 00{:}35{:}46.676$ developed as some other treatment

NOTE Confidence: 0.3334847

00:35:46.676 --> 00:35:49.049 because TMS can't reach the amygdala or

NOTE Confidence: 0.3334847

00:35:49.107 --> 00:35:51.513 the subennial simulant And so showing

NOTE Confidence: 0.3334847

 $00{:}35{:}51{.}513$ --> $00{:}35{:}53{.}798$ evidence that actually indirectly it can.

NOTE Confidence: 0.3334847

 $00{:}35{:}53.798 \dashrightarrow 00{:}35{:}55.493$ We're we're not arguing TMS

NOTE Confidence: 0.3334847

 $00{:}35{:}55{.}493 \dashrightarrow 00{:}35{:}57{.}279$ directly engages these brain areas.

NOTE Confidence: 0.3334847

00:35:57.280 --> 00:35:58.840 TMS doesn't go very deep.

00:35:58.840 --> 00:36:00.440 But building on all this,

NOTE Confidence: 0.3334847

 $00:36:00.440 \longrightarrow 00:36:02.615$ it's really great neuroscience and

NOTE Confidence: 0.3334847

 $00:36:02.615 \rightarrow 00:36:05.480$ imaging data related to brain networks.

NOTE Confidence: 0.3334847

 $00:36:05.480 \longrightarrow 00:36:07.195$ There's a cortical representation of

NOTE Confidence: 0.3334847

 $00:36:07.195 \rightarrow 00:36:09.559$ almost any network that you would want.

NOTE Confidence: 0.3334847

00:36:09.560 $\operatorname{-->}$ 00:36:12.296 And so if we can show that we can

NOTE Confidence: 0.3334847

00:36:12.296 --> 00:36:14.626 effectively engage even these deep sub

NOTE Confidence: 0.3334847

 $00:36:14.626 \rightarrow 00:36:16.956$ critical downstream regions with TMS

NOTE Confidence: 0.3334847

 $00{:}36{:}16{.}960 \dashrightarrow 00{:}36{:}19{.}156$ then that may be a a great piece of

NOTE Confidence: 0.3334847

 $00:36:19.156 \rightarrow 00:36:21.396$ evidence to encourage more people to use it.

NOTE Confidence: 0.8860244

 $00{:}36{:}23.600 \dashrightarrow 00{:}36{:}26.239$ We also showed that there's a clinical

NOTE Confidence: 0.8860244

 $00:36:26.239 \rightarrow 00:36:28.093$ relevance that engagement at this

NOTE Confidence: 0.8860244

 $00:36:28.093 \rightarrow 00:36:30.073$ target that how strong does this

NOTE Confidence: 0.8860244

 $00{:}36{:}30.073 \dashrightarrow 00{:}36{:}32.355$ circuit respond to a pulse of TMS

NOTE Confidence: 0.8860244

 $00:36:32.355 \longrightarrow 00:36:33.915$ actually tells you something useful

NOTE Confidence: 0.8860244

 $00:36:33.920 \rightarrow 00:36:36.755$ about how well the TMS is going

- NOTE Confidence: 0.8860244
- $00:36:36.755 \rightarrow 00:36:38.988$ to treat that person's symptoms.

 $00:36:38.988 \rightarrow 00:36:42.400$ So I'd love to continue building on that.

NOTE Confidence: 0.8860244

 $00:36:42.400 \longrightarrow 00:36:44.500$ And then in this first initial

NOTE Confidence: 0.8860244

 $00:36:44.500 \rightarrow 00:36:46.360$ stab with this clinical trial,

NOTE Confidence: 0.8860244

 $00{:}36{:}46{.}360 \dashrightarrow 00{:}36{:}48{.}502$ we found that there's at least

NOTE Confidence: 0.8860244

 $00{:}36{:}48.502 \dashrightarrow 00{:}36{:}50.796$ some evidence that the fMRI guided

NOTE Confidence: 0.8860244

 $00:36:50.796 \longrightarrow 00:36:52.781$ is more clinically effective than

NOTE Confidence: 0.8860244

 $00{:}36{:}52{.}781 \dashrightarrow 00{:}36{:}54{.}520$ a stout based target.

NOTE Confidence: 0.8860244

 $00{:}36{:}54{.}520 \dashrightarrow 00{:}36{:}55{.}396$ I'm not sure if I mentioned,

NOTE Confidence: 0.8860244

 $00{:}36{:}55{.}400 \dashrightarrow 00{:}36{:}59{.}704$ but the fMRI guided is like moving the

NOTE Confidence: 0.8860244

00:36:59.704 --> 00:37:03.196 PHQ like 60% improvement on average and

NOTE Confidence: 0.8860244

 $00:37:03.196 \rightarrow 00:37:07.160$ the scale based target is like 52 percent,

NOTE Confidence: 0.8860244

 $00{:}37{:}07{.}160 \dashrightarrow 00{:}37{:}09{.}352$ 51% something like that.

NOTE Confidence: 0.8860244

00:37:09.352 --> 00:37:10.996 So significant difference,

NOTE Confidence: 0.8860244

 $00:37:11.000 \rightarrow 00:37:13.261$ is it worth the time trouble expertise

00:37:13.261 --> 00:37:15.272 of doing the fMRI guided target

NOTE Confidence: 0.8860244

 $00{:}37{:}15{.}272 \dashrightarrow 00{:}37{:}17{.}533$ like that would still be an open

NOTE Confidence: 0.8860244

 $00{:}37{:}17.605 \dashrightarrow 00{:}37{:}19.837$ question I I'd say and is this the

NOTE Confidence: 0.8860244

 $00:37:19.837 \longrightarrow 00:37:21.875$ best fMRI guided target that we can

NOTE Confidence: 0.8860244

 $00:37:21.875 \rightarrow 00:37:23.999$ come up with more PTSD impression,

NOTE Confidence: 0.8860244

00:37:23.999 --> 00:37:25.238 I'd say no,

NOTE Confidence: 0.8860244

 $00:37:25.240 \longrightarrow 00:37:26.365$ but probably not.

NOTE Confidence: 0.8860244

 $00:37:26.365 \longrightarrow 00:37:28.240$ But let's continue building on

NOTE Confidence: 0.8860244

 $00{:}37{:}28{.}240 \dashrightarrow 00{:}37{:}30{.}892$ that and see if we can do the

NOTE Confidence: 0.8860244

 $00{:}37{:}30.892 \dashrightarrow 00{:}37{:}32.836$ circuit based specific symptom

NOTE Confidence: 0.8860244

00:37:32.836 --> 00:37:35.834 kind of mappings and continue to

NOTE Confidence: 0.8860244

 $00:37:35.834 \rightarrow 00:37:37.799$ improve our targeting and dosing

NOTE Confidence: 0.7644311

 $00{:}37{:}40{.}280 \dashrightarrow 00{:}37{:}43{.}574$ and hopefully more of these fantastic

NOTE Confidence: 0.7644311

00:37:43.574 --> 00:37:46.363 clinical studies will add on imaging

NOTE Confidence: 0.7644311

 $00{:}37{:}46{.}363 \dashrightarrow 00{:}37{:}48{.}301$ of any kind Functional imaging

NOTE Confidence: 0.7644311

 $00{:}37{:}48{.}301 \dashrightarrow 00{:}37{:}50{.}131$ would be better than just holding

 $00:37:50.131 \rightarrow 00:37:52.409$ on to this black box where we don't

NOTE Confidence: 0.7644311

 $00:37:52.409 \rightarrow 00:37:54.159$ know why some patients respond,

NOTE Confidence: 0.7644311

 $00{:}37{:}54.160 \dashrightarrow 00{:}37{:}56.365$ We don't know what happened to the

NOTE Confidence: 0.7644311

 $00:37:56.365 \dashrightarrow 00:37:58.892$ circuits in response to TMS which I think NOTE Confidence: 0.7644311

 $00:37:58.892 \rightarrow 00:38:01.136$ is really critical for pushing the field

NOTE Confidence: 0.7644311

 $00{:}38{:}01{.}136 \dashrightarrow 00{:}38{:}02{.}756$ forward and treating patients better.

NOTE Confidence: 0.43447363

00:38:06.600 --> 00:38:09.302 All right. So this this works really

NOTE Confidence: 0.43447363

 $00:38:09.302 \rightarrow 00:38:12.278$ well with some NIH funding priorities.

NOTE Confidence: 0.43447363

00:38:12.280 --> 00:38:14.818 We have a pending R61R33 that I think if

NOTE Confidence: 0.43447363

00:38:14.818 --> 00:38:17.080 you're talking about target engagement.

NOTE Confidence: 0.43447363

 $00{:}38{:}17.080 \dashrightarrow 00{:}38{:}19.240$ However this is a very straightforward

NOTE Confidence: 0.43447363

 $00{:}38{:}19{.}240$ --> $00{:}38{:}22{.}107$ way of showing that you can engage with NOTE Confidence: 0.43447363

 $00:38:22.107 \dashrightarrow 00:38:24.426$ particular target and then build on that NOTE Confidence: 0.43447363

 $00:38:24.426 \rightarrow 00:38:26.800$ to do a more definitive clinical trial.

NOTE Confidence: 0.43447363

 $00:38:26.800 \longrightarrow 00:38:28.784$ So it's a very good fit I think

 $00:38:28.784 \rightarrow 00:38:31.216$ with some objectives of of some

NOTE Confidence: 0.43447363

 $00:38:31.216 \longrightarrow 00:38:33.636$ of the funders out there.

NOTE Confidence: 0.43447363

 $00:38:33.640 \rightarrow 00:38:36.400$ So these are my team, the,

NOTE Confidence: 0.43447363

 $00:38:36.400 \rightarrow 00:38:40.560$ the people in my center and my closest

NOTE Confidence: 0.43447363

 $00{:}38{:}40{.}560 \dashrightarrow 00{:}38{:}42{.}557$ collaborators see that we have a little time.

NOTE Confidence: 0.43447363

00:38:42.560 --> 00:38:47.113 So I have some extra slides that are

NOTE Confidence: 0.43447363

 $00{:}38{:}47{.}113 \dashrightarrow 00{:}38{:}51{.}217$ based on questions that I be asked in

NOTE Confidence: 0.43447363

 $00:38:51.217 \rightarrow 00:38:53.921$ manuscripts and in talks as just giving

NOTE Confidence: 0.43447363

 $00{:}38{:}53{.}921 \dashrightarrow 00{:}38{:}56{.}759$ you a a brief response to some of these.

NOTE Confidence: 0.43447363

00:38:56.760 --> 00:38:59.153 So you'll say all right well you

NOTE Confidence: 0.43447363

 $00{:}38{:}59{.}153 \dashrightarrow 00{:}39{:}00{.}918$ you take these unmedicated patients,

NOTE Confidence: 0.43447363

 $00{:}39{:}00{.}920 \dashrightarrow 00{:}39{:}02{.}552$ those are not really a typical

NOTE Confidence: 0.43447363

 $00{:}39{:}02{.}552 \dashrightarrow 00{:}39{:}04{.}377$ So what happens in the medicated

NOTE Confidence: 0.43447363

 $00:39:04.377 \longrightarrow 00:39:06.750$ patients and totally agree we want to

NOTE Confidence: 0.43447363

 $00:39:06.750 \dashrightarrow 00:39:08.478$ replicate in a medicated patients.

NOTE Confidence: 0.43447363

 $00:39:08.480 \rightarrow 00:39:10.430$ So the pending new grant starting

- NOTE Confidence: 0.43447363
- $00:39:10.430 \longrightarrow 00:39:11.620$ in December, we're gonna,

 $00{:}39{:}11{.}620 \dashrightarrow 00{:}39{:}14{.}040$ we're gonna allow for that and check it out.

NOTE Confidence: 0.43447363

 $00:39:14.040 \longrightarrow 00:39:14.536$ I'll say,

NOTE Confidence: 0.43447363

 $00:39:14.536 \rightarrow 00:39:16.520$ well you did this brief 3 day intervention,

NOTE Confidence: 0.43447363

 $00:39:16.520 \rightarrow 00:39:19.268$ maybe that's not exactly what happens

NOTE Confidence: 0.43447363

 $00{:}39{:}19{.}268 \dashrightarrow 00{:}39{:}22{.}519$ in the brain with a higher dose of

NOTE Confidence: 0.43447363

 $00:39:22.520 \dashrightarrow 00:39:24.764$ of more stimulation in the sync

NOTE Confidence: 0.43447363

 $00:39:24.764 \rightarrow 00:39:27.200$ protocol or even the old original

NOTE Confidence: 0.43447363

 $00{:}39{:}27{.}200 \dashrightarrow 00{:}39{:}28{.}408$ 10 minutes for depression.

NOTE Confidence: 0.43447363

 $00:39:28.408 \longrightarrow 00:39:29.314$ I totally agree.

NOTE Confidence: 0.43447363

 $00:39:29.320 \longrightarrow 00:39:31.120$ Let's check it out with a higher dose.

NOTE Confidence: 0.43447363

 $00:39:31.120 \longrightarrow 00:39:32.896$ Now that we have the evidence

NOTE Confidence: 0.43447363

 $00:39:32.896 \rightarrow 00:39:34.080$ linking these measurements together,

NOTE Confidence: 0.43447363

00:39:34.080 --> 00:39:35.920 I mean it's worthwhile

NOTE Confidence: 0.43447363

 $00:39:35.920 \longrightarrow 00:39:38.680$ exploring that in a higher dose.

 $00:39:38.680 \rightarrow 00:39:40.815$ The imaging aficionados you may say that's

NOTE Confidence: 0.43447363

 $00{:}39{:}40.815 \dashrightarrow 00{:}39{:}43.039$ a region with low signal noise ratio.

NOTE Confidence: 0.43447363

 $00:39:43.040 \longrightarrow 00:39:45.040$ So you shouldn't use it.

NOTE Confidence: 0.43447363

 $00{:}39{:}45.040 \dashrightarrow 00{:}39{:}47.792$ And I would say well we have this

NOTE Confidence: 0.43447363

 $00{:}39{:}47.792 \dashrightarrow 00{:}39{:}49.489$ evidence nevertheless that we're

NOTE Confidence: 0.43447363

 $00{:}39{:}49{.}489{\:}{\dashrightarrow}{>}00{:}39{:}51{.}369$ getting significant about responses

NOTE Confidence: 0.43447363

 $00{:}39{:}51{.}369 \dashrightarrow 00{:}39{:}53{.}249$ and differences and clinical

NOTE Confidence: 0.43447363

 $00:39:53.312 \dashrightarrow 00:39:56.000$ relevance with our TMS, FM, RI data.

NOTE Confidence: 0.43447363

 $00{:}39{:}56{.}000 \dashrightarrow 00{:}39{:}58{.}560$ But that being said, I think we can do,

NOTE Confidence: 0.43447363

 $00:39:58.560 \rightarrow 00:40:01.940$ we can collect higher fidelity images

NOTE Confidence: 0.43447363

 $00{:}40{:}01{.}940 \dashrightarrow 00{:}40{:}04{.}724$ for example we have an 8 channel volume NOTE Confidence: 0.43447363

 $00:40:04.724 \rightarrow 00:40:06.728$ coil coming that we're gonna start

NOTE Confidence: 0.43447363

 $00{:}40{:}06.728 \dashrightarrow 00{:}40{:}08.972$ using in our new studies say well

NOTE Confidence: 0.43447363

 $00{:}40{:}08{.}972 \dashrightarrow 00{:}40{:}10{.}694$ depression is a network it's not just

NOTE Confidence: 0.43447363

 $00:40:10.694 \rightarrow 00:40:12.588$ a subgenual you shouldn't be focusing

NOTE Confidence: 0.43447363

 $00:40:12.588 \rightarrow 00:40:14.912$ on single brain areas like that and.

- NOTE Confidence: 0.43447363
- $00{:}40{:}14.912 \dashrightarrow 00{:}40{:}15.856$ I agree.
- NOTE Confidence: 0.43447363
- $00:40:15.856 \rightarrow 00:40:19.120$ I'd say if you have a network that you feel
- NOTE Confidence: 0.43447363
- $00{:}40{:}19{.}120 \dashrightarrow 00{:}40{:}22{.}599$ is a better fit for TMS depression outcomes,
- NOTE Confidence: 0.43447363
- 00:40:22.600 --> 00:40:23.680 like happy to consider pulling
- NOTE Confidence: 0.43447363
- $00{:}40{:}23.680 \dashrightarrow 00{:}40{:}24.760$ it out of our data.
- NOTE Confidence: 0.43447363
- $00:40:24.760 \longrightarrow 00:40:25.840$ Having a look at it,
- NOTE Confidence: 0.43447363
- 00:40:25.840 00:40:28.200 we did another grad student in my lab,
- NOTE Confidence: 0.43447363
- 00:40:28.200 --> 00:40:29.616 I did an amygdala,
- NOTE Confidence: 0.43447363
- $00:40:29.616 \rightarrow 00:40:32.746$ found an amygdala change in fMRI and its
- NOTE Confidence: 0.43447363
- $00:40:32.746 \longrightarrow 00:40:35.076$ meta analysis for depression treatment.
- NOTE Confidence: 0.43447363
- $00{:}40{:}35{.}080 \dashrightarrow 00{:}40{:}37{.}299$ We pulled that out of our data
- NOTE Confidence: 0.43447363
- $00{:}40{:}37{.}299 \dashrightarrow 00{:}40{:}39{.}201$ and didn't find an association
- NOTE Confidence: 0.43447363
- $00{:}40{:}39{.}201 \dashrightarrow 00{:}40{.}40{.}900$ with the interventions outcome,
- NOTE Confidence: 0.43447363
- $00{:}40{:}40{.}900 \dashrightarrow 00{:}40{:}43{.}420$ but there there are probably other
- NOTE Confidence: 0.43447363
- $00{:}40{:}43{.}420 \dashrightarrow 00{:}40{:}45{.}715$ ones that that are better in
- NOTE Confidence: 0.43447363

- $00{:}40{:}45.715 \dashrightarrow 00{:}40{:}47.159$ terms of network responses.
- NOTE Confidence: 0.43447363
- 00:40:47.160 --> 00:40:48.632 So yeah,
- NOTE Confidence: 0.43447363
- $00:40:48.632 \rightarrow 00:40:51.416$ even improving the imaging we
- NOTE Confidence: 0.43447363
- $00:40:51.416 \longrightarrow 00:40:53.432$ do at baseline to make a better,
- NOTE Confidence: 0.43447363
- $00:40:53.440 \longrightarrow 00:40:54.480$ more precise,
- NOTE Confidence: 0.43447363
- $00{:}40{:}54{.}480 \dashrightarrow 00{:}40{:}56{.}560$ more personalized target for
- NOTE Confidence: 0.43447363
- 00:40:56.560 --> 00:40:57.600 doing stimulation,
- NOTE Confidence: 0.43447363
- $00:40:57.600 \longrightarrow 00:40:59.680$ absolutely you can do better.
- NOTE Confidence: 0.43447363
- $00{:}40{:}59{.}680 \dashrightarrow 00{:}41{:}01{.}192$ We try to keep up with the imaging field.
- NOTE Confidence: 0.43447363
- 00:41:01.200 --> 00:41:03.168 We're gonna do some multi echo
- NOTE Confidence: 0.43447363
- $00{:}41{:}03.168 \dashrightarrow 00{:}41{:}05.161$ collect more fMRI data to make
- NOTE Confidence: 0.43447363
- $00:41:05.161 \rightarrow 00:41:06.397$ a more reliable target
- NOTE Confidence: 0.60579586
- $00:41:06.400 \longrightarrow 00:41:07.800$ for the individual patients.
- NOTE Confidence: 0.60579586
- 00:41:07.800 --> 00:41:10.820 So definitely up for you know further
- NOTE Confidence: 0.60579586
- $00:41:10.820 \rightarrow 00:41:13.520$ improvements in the imaging protocol.
- NOTE Confidence: 0.60579586
- $00:41:13.520 \longrightarrow 00:41:16.128$ All right. Then there's the a lot of

 $00{:}41{:}16.128 \dashrightarrow 00{:}41{:}18.519$ papers that are showing this anti

NOTE Confidence: 0.60579586

 $00{:}41{:}18.519 \dashrightarrow 00{:}41{:}21.440$ correlated like spots really seem to

NOTE Confidence: 0.60579586

 $00:41:21.440 \longrightarrow 00:41:23.891$ be relevant to depression outcome.

NOTE Confidence: 0.60579586

 $00{:}41{:}23{.}891 \dashrightarrow 00{:}41{:}27{.}080$ But that there is a a recent paper from

NOTE Confidence: 0.60579586

 $00{:}41{:}27.080 \dashrightarrow 00{:}41{:}28.680$ Connor Liston suggesting that there's

NOTE Confidence: 0.60579586

 $00{:}41{:}28.680 \dashrightarrow 00{:}41{:}30.998$ a a subgroup of patients that are

NOTE Confidence: 0.60579586

 $00{:}41{:}30{.}998 \dashrightarrow 00{:}41{:}33{.}080$ anomalous that are driving that but it.

NOTE Confidence: 0.60579586

00:41:33.080 --> 00:41:35.186 But I'll also just say that once the field

NOTE Confidence: 0.60579586

 $00{:}41{:}35{.}186 \dashrightarrow 00{:}41{:}36{.}769$ sort of focuses on something they're

NOTE Confidence: 0.60579586

 $00{:}41{:}36.769 \dashrightarrow 00{:}41{:}38.827$ like oh look at that there's evidence

NOTE Confidence: 0.60579586

 $00:41:38.827 \rightarrow 00:41:40.957$ everywhere for the anti correlated spot.

NOTE Confidence: 0.60579586

00:41:40.960 --> 00:41:42.910 They some sometimes we might get

NOTE Confidence: 0.60579586

00:41:42.910 --> 00:41:45.112 a like we might have a propensity

NOTE Confidence: 0.60579586

 $00{:}41{:}45{.}112 \dashrightarrow 00{:}41{:}47{.}523$ to put blinders on and chase the

NOTE Confidence: 0.60579586

 $00{:}41{:}47{.}523 \dashrightarrow 00{:}41{:}49{.}353$ same targets in every body's labs.

 $00{:}41{:}49{.}360 \dashrightarrow 00{:}41{:}50{.}520$ But at least for me,

NOTE Confidence: 0.60579586

 $00{:}41{:}50{.}520 \dashrightarrow 00{:}41{:}53{.}236$ I feel like this basic brain measurement

NOTE Confidence: 0.60579586

 $00:41:53.240 \rightarrow 00:41:56.240$ data of the positive connectivity

NOTE Confidence: 0.60579586

 $00:41:56.240 \rightarrow 00:41:59.000$ sites makes it worth considering.

NOTE Confidence: 0.60579586

00:41:59.000 --> 00:42:01.394 Like if if people are wearing blinders,

NOTE Confidence: 0.60579586

 $00{:}42{:}01{.}400 \dashrightarrow 00{:}42{:}03{.}352$ maybe we can like open up the field NOTE Confidence: 0.60579586

00:42:03.352 --> 00:42:05.434 a little bit more and and look

NOTE Confidence: 0.60579586

 $00:42:05.434 \rightarrow 00:42:06.964$ for the possibility of positively

NOTE Confidence: 0.60579586

 $00{:}42{:}07{.}020 \dashrightarrow 00{:}42{:}08{.}800$ correlated spots being relevant.

NOTE Confidence: 0.40430865

 $00:42:11.840 \longrightarrow 00:42:12.347$ And then again,

NOTE Confidence: 0.40430865

 $00:42:12.347 \longrightarrow 00:42:13.760$ since we have a little bit of time,

NOTE Confidence: 0.40430865

 $00:42:13.760 \longrightarrow 00:42:15.482$ I just want to mention some other

NOTE Confidence: 0.40430865

 $00:42:15.482 \longrightarrow 00:42:16.799$ things that we're working on.

NOTE Confidence: 0.40430865

00:42:16.800 --> 00:42:19.320 So we're doing a lot of TMS up MRI,

NOTE Confidence: 0.40430865

 $00:42:19.320 \rightarrow 00:42:21.132$ closed loop things where we're doing

NOTE Confidence: 0.40430865

 $00:42:21.132 \rightarrow 00:42:22.038$ different stimulation frequencies,
NOTE Confidence: 0.40430865

00:42:22.040 --> 00:42:23.720 trying them out on working memories,

NOTE Confidence: 0.40430865

 $00{:}42{:}23.720 \dashrightarrow 00{:}42{:}25.862$ so personalizing not just the target

NOTE Confidence: 0.40430865

 $00{:}42{:}25.862 \dashrightarrow 00{:}42{:}28.000$ but also the stimulation parameters.

NOTE Confidence: 0.40430865

 $00:42:28.000 \rightarrow 00:42:30.828$ So testing this out and worry and

NOTE Confidence: 0.40430865

00:42:30.828 --> 00:42:32.452 rumination Also different targeting

NOTE Confidence: 0.40430865

 $00{:}42{:}32{.}452 \dashrightarrow 00{:}42{:}35{.}294$ methods based on DTI or resting some

NOTE Confidence: 0.40430865

 $00{:}42{:}35{.}294 \dashrightarrow 00{:}42{:}38{.}026$ different ways of splitting up the brain

NOTE Confidence: 0.40430865

 $00{:}42{:}38.026 \dashrightarrow 00{:}42{:}40.050$ and personalizing target with network

NOTE Confidence: 0.40430865

 $00{:}42{:}40.050 \dashrightarrow 00{:}42{:}42.275$ control theory and deep learning.

NOTE Confidence: 0.40430865

 $00{:}42{:}42{.}280 \dashrightarrow 00{:}42{:}44{.}476$ We're doing some basic methods things

NOTE Confidence: 0.40430865

 $00{:}42{:}44{.}476 \dashrightarrow 00{:}42{:}47{.}395$ like single pulse TMS with stereo EEG and

NOTE Confidence: 0.40430865

 $00{:}42{:}47{.}395 \dashrightarrow 00{:}42{:}49{.}920$ epilepsy patients trying to get that going,

NOTE Confidence: 0.40430865

 $00{:}42{:}49{.}920 \dashrightarrow 00{:}42{:}52{.}494$ some really cool stuff with KC

NOTE Confidence: 0.40430865

 $00{:}42{:}52{.}494 \dashrightarrow 00{:}42{:}54{.}210$ help partners and neurosurgeon

NOTE Confidence: 0.40430865

 $00:42:54.282 \rightarrow 00:42:58.958$ here on personalizing DBS for OCD.

NOTE Confidence: 0.40430865

 $00:42:58.960 \rightarrow 00:43:00.442$ Things that I'm looking for collaborators

NOTE Confidence: 0.40430865

 $00{:}43{:}00{.}442 \dashrightarrow 00{:}43{:}02{.}237$ on these will be new things that I,

NOTE Confidence: 0.40430865

00:43:02.240 --> 00:43:04.400 I, I do start to pilot.

NOTE Confidence: 0.40430865

 $00:43:04.400 \longrightarrow 00:43:06.456$ There's a controllable TMS

NOTE Confidence: 0.40430865

 $00:43:06.456 \rightarrow 00:43:07.998$ system commercially available.

NOTE Confidence: 0.40430865

00:43:08.000 - 00:43:09.560 I'm showing it down there on the left.

NOTE Confidence: 0.40430865

 $00:43:09.560 \rightarrow 00:43:11.680$ We want to play with that pulse

NOTE Confidence: 0.40430865

00:43:11.680 - 00:43:14.877 width and shape can be potentially

NOTE Confidence: 0.40430865

00:43:14.877 --> 00:43:16.862 even more efficacious and changing

NOTE Confidence: 0.40430865

 $00{:}43{:}16.862 \dashrightarrow 00{:}43{:}19.080$ some of the stimulation protocols.

NOTE Confidence: 0.40430865

 $00{:}43{:}19{.}080 \dashrightarrow 00{:}43{:}21{.}312$ Also if you if you have a clinic

NOTE Confidence: 0.40430865

 $00:43:21.312 \rightarrow 00:43:22.559$ where you're doing TMS,

NOTE Confidence: 0.40430865

 $00:43:22.560 \rightarrow 00:43:24.436$ we should take every single patient that

NOTE Confidence: 0.40430865

 $00:43:24.436 \longrightarrow 00:43:26.915$ comes in and do some kind of study with them.

NOTE Confidence: 0.40430865

 $00:43:26.920 \longrightarrow 00:43:28.385$ Like it doesn't actually cost

NOTE Confidence: 0.40430865

00:43:28.385 --> 00:43:30.624 anything to just try a brain state

- NOTE Confidence: 0.40430865
- $00:43:30.624 \rightarrow 00:43:32.399$ manipulation and seeing how that

NOTE Confidence: 0.40430865

 $00{:}43{:}32{.}400 \dashrightarrow 00{:}43{:}34{.}324$ contributes to patient outcomes.

NOTE Confidence: 0.40430865

 $00:43:34.324 \rightarrow 00:43:36.248$ So that's pretty straightforward

NOTE Confidence: 0.40430865

 $00:43:36.248 \longrightarrow 00:43:38.568$ one that we're starting with

NOTE Confidence: 0.40430865

 $00:43:38.568 \longrightarrow 00:43:40.280$ a couple of collaborators,

NOTE Confidence: 0.40430865

 $00{:}43{:}40{.}280 \dashrightarrow 00{:}43{:}41{.}200$ I'll say we're not the,

NOTE Confidence: 0.40430865

 $00:43:41.200 \longrightarrow 00:43:43.643$ we're not the only ones that think

NOTE Confidence: 0.40430865

 $00:43:43.643 \longrightarrow 00:43:45.154$ circuit engagement with brain

NOTE Confidence: 0.40430865

00:43:45.154 --> 00:43:47.139 stimulation using an imaging marker

NOTE Confidence: 0.40430865

 $00:43:47.139 \longrightarrow 00:43:49.520$ may be clinically really interesting.

NOTE Confidence: 0.40430865

 $00{:}43{:}49{.}520 \dashrightarrow 00{:}43{:}51{.}586$ So this is from Andres Lozano's

NOTE Confidence: 0.40430865

00:43:51.586 --> 00:43:53.716 group in Toronto and showing

NOTE Confidence: 0.40430865

 $00{:}43{:}53.716$ --> $00{:}43{:}55.924$ an association that DBS FM RI.

NOTE Confidence: 0.40430865

 $00{:}43{:}55{.}924 \dashrightarrow 00{:}43{:}57{.}464$ It also tells you something

NOTE Confidence: 0.40430865

 $00{:}43{:}57{.}464 \dashrightarrow 00{:}43{:}59{.}186$ about circuit engagement that's

NOTE Confidence: 0.40430865

 $00:43:59.186 \longrightarrow 00:44:01.278$ relevant to depression improvement.

NOTE Confidence: 0.40430865

 $00:44:01.280 \longrightarrow 00:44:03.080$ So we definitely agree with this.

NOTE Confidence: 0.40430865

 $00{:}44{:}03{.}080 \dashrightarrow 00{:}44{:}05{.}120$ We want to build on this ourselves in NOTE Confidence: 0.40430865

00:44:05.120 --> 00:44:07.039 a variety of ways that I described.

NOTE Confidence: 0.40430865

00:44:07.040 --> 00:44:09.713 I think we can learn a lot about causal

NOTE Confidence: 0.40430865

 $00:44:09.713 \rightarrow 00:44:11.478$ connections in the brain writ large,

NOTE Confidence: 0.40430865

00:44:11.480 --> 00:44:13.960 but also specifically with these

NOTE Confidence: 0.40430865

 $00{:}44{:}13.960 \dashrightarrow 00{:}44{:}15.965$ intervention tools that I think

NOTE Confidence: 0.40430865

 $00{:}44{:}15{.}965 \dashrightarrow 00{:}44{:}17{.}970$ is really important for building

NOTE Confidence: 0.40430865

 $00:44:18.042 \rightarrow 00:44:19.798$ this bridge between imaging,

NOTE Confidence: 0.40430865

00:44:19.800 --> 00:44:24.504 making it clinically useful and you know,

NOTE Confidence: 0.40430865

 $00:44:24.504 \rightarrow 00:44:28.164$ optimizing the the stimulation parameters

NOTE Confidence: 0.40430865

 $00{:}44{:}28{.}164 \dashrightarrow 00{:}44{:}32{.}119$ and locations going into the future.

NOTE Confidence: 0.40430865

 $00:44:32.120 \longrightarrow 00:44:33.040$ So look at that.

NOTE Confidence: 0.40430865

 $00:44:33.040 \rightarrow 00:44:33.960$ Thanks for your attention.

NOTE Confidence: 0.29934937

 $00:44:37.680 \longrightarrow 00:44:38.280$ Yes, thank you, Des.