WEBVTT

NOTE duration:"00:44:38.2800000"

NOTE recognizability:0.554

NOTE language:en-us

NOTE Confidence: 0.58605236

00:00:00.000 --> 00:00:03.555 Be here and share my work with you guys.

NOTE Confidence: 0.58605236

00:00:03.560 --> 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 --> 00:00:20.893 with some problems and hurdles and

NOTE Confidence: 0.58605236

00:00:20.893 --> 00:00:23.358 the neuroimaging field in psychiatry,

NOTE Confidence: 0.58605236

00:00:23.360 --> 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 --> 00:00:32.247 deciding whether there's ever going

NOTE Confidence: 0.58605236

00:00:32.247 --> 00:00:35.488 to be any horizon in which imaging is

NOTE Confidence: 0.58605236

00:00:35.488 --> 00:00:37.840 actually useful in their clinical practice.

NOTE Confidence: 0.58605236

00:00:37.840 --> 00:00:41.074 I would argue that it isn't typically.

NOTE Confidence: 0.58605236

00:00:41.080 --> 00:00:45.320 And so some of the hurdles and

NOTE Confidence: 0.58605236

00:00:45.320 --> 00:00:48.840 and problems in the field include

NOTE Confidence: 0.58605236

00:00:48.840 --> 00:00:51.884 a lot of various issues, right.

NOTE Confidence: 0.58605236

00:00:51.884 --> 00:00:55.880 Some of them have to do with really finding

NOTE Confidence: 0.58605236

00:00:55.978 --> 00:00:59.358 no clear neurobiological evidence that

NOTE Confidence: 0.58605236

00:00:59.360 --> 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 --> 00:01:07.340 and other behavioral scales tend

NOTE Confidence: 0.58605236

00:01:07.340 --> 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 --> 00:01:16.370 decision making on the the reliability

NOTE Confidence: 0.58605236

00:01:16.370 --> 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 --> 00:01:25.052 So we have all these recent publications

NOTE Confidence: 0.58605236

00:01:25.052 --> 00:01:27.422 right in the last few years that

NOTE Confidence: 0.58605236

00:01:27.422 --> 00:01:29.644 that are really causing us to re

NOTE Confidence: 0.58605236

00:01:29.644 --> 00:01:31.974 evaluate what we're doing and and what

NOTE Confidence: 0.58605236

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 --> 00:01:41.370 Even though as we are able to share more

NOTE Confidence: 0.4773955

00:01:41.370 --> 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 --> 00:01:49.896 and studies when you combine them this way.

NOTE Confidence: 0.4773955

00:01:49.896 --> 00:01:53.452 There have been some hits to finding

NOTE Confidence: 0.4773955

00:01:53.452 --> 00:01:56.638 biomarkers and biotypes in recent years,

NOTE Confidence: 0.4773955

00:01:56.640 --> 00:01:59.310 including this paper and many hundreds

NOTE Confidence: 0.4773955

00:01:59.310 --> 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 --> 00:02:11.491 not being able to find a clear signature

NOTE Confidence: 0.4773955

00:02:11.491 --> 00:02:15.280 that hears our depression imaging marker.

NOTE Confidence: 0.4773955

00:02:15.280 --> 00:02:18.280 All right, so that's that's problematic.

NOTE Confidence: 0.4773955

00:02:18.280 --> 00:02:20.696 But this may be more familiar with the

NOTE Confidence: 0.4773955

00:02:20.696 --> 00:02:22.736 clinician for the clinicians who don't

NOTE Confidence: 0.4773955

00:02:22.736 --> 00:02:25.320 typically pay as much attention to imaging,

NOTE Confidence: 0.4773955

00:02:25.320 --> 00:02:27.588 which is that the diagnosis itself

NOTE Confidence: 0.4773955

00:02:27.588 --> 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 --> 00:02:35.945 kind of nebulous and not very precise

NOTE Confidence: 0.4773955

00:02:35.945 --> 00:02:39.004 and then you try to create a precise

NOTE Confidence: 0.4773955

00:02:39.004 --> 00:02:41.951 measurement of that with an imaging marker,

NOTE Confidence: 0.4773955

00:02:41.960 --> 00:02:43.820 of course you know there's there's

NOTE Confidence: 0.4773955

00:02:43.820 --> 00:02:46.680 going to be a a real difficulty there.

NOTE Confidence: 0.4773955

00:02:46.680 --> 00:02:50.124 We can't even agree amongst one another

NOTE Confidence: 0.4773955

00:02:50.124 --> 00:02:53.240 from clinician to clinician what the

NOTE Confidence: 0.4773955

00:02:53.240 --> 00:02:56.036 right diagnosis is for a patient.

NOTE Confidence: 0.4773955

00:02:56.040 --> 00:02:56.964 So these are hurdles.

NOTE Confidence: 0.4773955

00:02:56.964 --> 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

NOTE Confidence: 0.4773955

00:03:01.656 --> 00:03:04.701 to bring up some of the struggles

NOTE Confidence: 0.4773955

00:03:04.701 --> 00:03:06.033 and the challenges.

NOTE Confidence: 0.4773955

00:03:06.040 --> 00:03:07.665 I'll say on the neuroscience

NOTE Confidence: 0.4773955

00:03:07.665 --> 00:03:08.640 side with imaging.

NOTE Confidence: 0.4773955

00:03:08.640 --> 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 --> 00:03:16.248 centered decision making.

NOTE Confidence: 0.4773955

00:03:16.248 --> 00:03:19.640 One of them is that you can have.

NOTE Confidence: 0.4773955

00:03:19.640 --> 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 --> 00:03:25.660 who was saying that as neuroscientists,

NOTE Confidence: 0.4773955

00:03:25.660 --> 00:03:28.579 we have these average brains and we've

NOTE Confidence: 0.4773955

00:03:28.579 --> 00:03:31.078 all seen pictures of these and they

NOTE Confidence: 0.4773955

00:03:31.078 --> 00:03:33.272 have features that in aggregate have

NOTE Confidence: 0.4773955

00:03:33.272 --> 00:03:35.960 never been observed in any single patient.

NOTE Confidence: 0.4773955

00:03:35.960 --> 00:03:38.090 And and so that's problematic if

NOTE Confidence: 0.4773955

00:03:38.090 --> 00:03:40.090 you're looking at an average brain

NOTE Confidence: 0.4773955

00:03:40.090 --> 00:03:41.640 image and you're thinking about,

NOTE Confidence: 0.4773955

00:03:41.640 --> 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 --> 00:03:44.720 how can I make the use of this for applying

NOTE Confidence: 0.4773955

00:03:44.720 --> 00:03:46.800 to this patient who's in front of me?

NOTE Confidence: 0.4773955

00:03:46.800 --> 00:03:48.474 This is problematic.

NOTE Confidence: 0.4773955

00:03:48.474 --> 00:03:52.380 Reinforcing this idea is a paper by

NOTE Confidence: 0.4773955

00:03:52.483 --> 00:03:54.940 Deanna Barch from many years ago,

NOTE Confidence: 0.4773955

00:03:54.940 --> 00:03:56.515 more than 10 years ago,

NOTE Confidence: 0.4773955

00:03:56.520 --> 00:03:58.840 and there have been other instances of this.

NOTE Confidence: 0.4773955

00:03:58.840 --> 00:04:01.514 On the left side you see something

NOTE Confidence: 0.4773955

00:04:01.514 --> 00:04:03.682 that's used very widely in

NOTE Confidence: 0.4773955

00:04:03.682 --> 00:04:06.037 cognitive neuroscience which is in

NOTE Confidence: 0.4773955

00:04:06.040 --> 00:04:08.120 designed to capture working memory,

NOTE Confidence: 0.4773955

00:04:08.120 --> 00:04:09.680 other attentional kind of factors.

NOTE Confidence: 0.4773955

00:04:09.680 --> 00:04:12.720 So this is an N back task where you have

NOTE Confidence: 0.4773955

00:04:12.802 --> 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 --> 00:04:19.918 which ones are strongly active And

NOTE Confidence: 0.4773955

00:04:19.918 --> 00:04:22.740 on the left, the left set of images

NOTE Confidence: 0.4773955

00:04:22.740 --> 00:04:24.875 are the average brain maps, right?

NOTE Confidence: 0.4773955

00:04:24.875 --> 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 --> 00:04:29.942 This is what we usually show

NOTE Confidence: 0.4773955

00:04:29.942 --> 00:04:30.960 in an imaging experiment.

NOTE Confidence: 0.4773955

00:04:30.960 --> 00:04:32.096 This is the output.

NOTE Confidence: 0.4773955

00:04:32.096 --> 00:04:33.516 If on the other hand,

NOTE Confidence: 0.4773955

00:04:33.520 --> 00:04:35.030 instead of taking the average

NOTE Confidence: 0.4773955

00:04:35.030 --> 00:04:36.238 from the same contrast,

NOTE Confidence: 0.4773955

00:04:36.240 --> 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 --> 00:04:43.756 are showing strong activation,

NOTE Confidence: 0.4773955

00:04:43.760 --> 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 --> 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 --> 00:04:51.360 it's it's much more sparse.

NOTE Confidence: 0.59921736

00:04:51.360 --> 00:04:52.650 There's some areas that look

NOTE Confidence: 0.59921736

00:04:52.650 --> 00:04:54.477 like they have a lot more going

NOTE Confidence: 0.59921736

00:04:54.477 --> 00:04:56.157 on than on the left side maps.

NOTE Confidence: 0.59921736

00:04:56.160 --> 00:04:57.960 And I would argue something on

NOTE Confidence: 0.59921736

00:04:57.960 --> 00:05:00.087 the right side is more relevant

NOTE Confidence: 0.59921736

00:05:00.087 --> 00:05:01.799 to the individual patients.

NOTE Confidence: 0.59921736

00:05:01.800 --> 00:05:02.872 On the left side,

NOTE Confidence: 0.59921736

00:05:02.872 --> 00:05:04.212 especially with small end studies

NOTE Confidence: 0.59921736

00:05:04.212 --> 00:05:05.684 which are typical in imaging

NOTE Confidence: 0.59921736

00:05:05.684 --> 00:05:06.836 because it's so expensive.

NOTE Confidence: 0.59921736

00:05:06.840 --> 00:05:10.252 You can you can throw off the average

NOTE Confidence: 0.59921736

00:05:10.252 --> 00:05:12.004 map by having a few individuals

NOTE Confidence: 0.59921736

00:05:12.004 --> 00:05:13.520 showing lots of activation.

NOTE Confidence: 0.59921736

00:05:13.520 --> 00:05:15.464 Whereas on the right side we're

NOTE Confidence: 0.59921736

00:05:15.464 --> 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 --> 00:05:20.759 group and we want to know like is

NOTE Confidence: 0.59921736

00:05:20.759 --> 00:05:22.620 the typical patient going to show a

NOTE Confidence: 0.59921736

00:05:22.620 --> 00:05:24.360 bunch of activation in this spot.

NOTE Confidence: 0.59921736

00:05:24.360 --> 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 --> 00:05:32.036 in imaging and thinking about how

NOTE Confidence: 0.59921736

00:05:32.036 --> 00:05:36.960 imaging can be applied more to individuals.

NOTE Confidence: 0.59921736

00:05:36.960 --> 00:05:39.984 Another thing to bring up since I'm

NOTE Confidence: 0.59921736

00:05:39.984 --> 00:05:43.246 doing TMS depression is there's a lot

NOTE Confidence: 0.59921736

00:05:43.246 --> 00:05:45.130 of excitement building especially

NOTE Confidence: 0.59921736

00:05:45.130 --> 00:05:48.077 from Nolan Williams work at Stanford

NOTE Confidence: 0.59921736

00:05:48.080 --> 00:05:51.020 that left led to an FDA approval

NOTE Confidence: 0.59921736

00:05:51.020 --> 00:05:54.212 for a new way of doing TMS for

NOTE Confidence: 0.59921736

00:05:54.212 --> 00:05:55.400 treatment resistant depression.

NOTE Confidence: 0.59921736

00:05:55.400 --> 00:05:57.892 And so we have the distressed patient

NOTE Confidence: 0.59921736

00:05:57.892 --> 00:06:02.264 or a we apply even a really amazing

NOTE Confidence: 0.59921736

00:06:02.264 --> 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 --> 00:06:10.720 remission in treatment resistant depression.

NOTE Confidence: 0.59921736

00:06:10.720 --> 00:06:12.380 Obviously a really important tool

NOTE Confidence: 0.59921736

00:06:12.380 --> 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

NOTE Confidence: 0.59921736

00:06:16.632 --> 00:06:17.715 respond to medication.

NOTE Confidence: 0.59921736

00:06:17.720 --> 00:06:21.560 So you do the stimulation protocol,

NOTE Confidence: 0.59921736

00:06:21.560 --> 00:06:23.360 you measure the treatment response.

NOTE Confidence: 0.59921736

00:06:23.360 --> 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 --> 00:06:29.198 some of the patients do worse.

NOTE Confidence: 0.59921736

00:06:29.200 --> 00:06:31.080 And you're left struggling saying,

NOTE Confidence: 0.59921736

00:06:31.080 --> 00:06:33.236 well, what do we do about that?

NOTE Confidence: 0.59921736

00:06:33.240 --> 00:06:34.872 What do we do about the patients who

NOTE Confidence: 0.59921736

00:06:34.872 --> 00:06:37.280 don't do well, The ones that do great,

NOTE Confidence: 0.59921736

00:06:37.280 --> 00:06:38.452 like, OK, problem solved,

NOTE Confidence: 0.59921736

00:06:38.452 --> 00:06:40.643 but what about for all the patients

NOTE Confidence: 0.59921736

00:06:40.643 --> 00:06:42.478 that don't do especially well?

NOTE Confidence: 0.59921736

00:06:42.480 --> 00:06:45.678 I would argue that you stimulated

NOTE Confidence: 0.59921736

00:06:45.680 --> 00:06:48.880 based on an imaging marker.

NOTE Confidence: 0.59921736

00:06:48.880 --> 00:06:51.582 You don't know what TMS actually did

NOTE Confidence: 0.59921736

00:06:51.582 --> 00:06:54.338 to that imaging marker and that may

NOTE Confidence: 0.59921736

00:06:54.338 --> 00:06:57.360 be critical in figuring out why patients,

NOTE Confidence: 0.59921736

00:06:57.360 --> 00:06:58.452 some patients don't respond.

NOTE Confidence: 0.59921736

00:06:58.452 --> 00:07:00.560 But if we don't do brain imaging,

NOTE Confidence: 0.59921736

00:07:00.560 --> 00:07:02.996 we don't do any brain based measurement,

NOTE Confidence: 0.59921736

00:07:03.000 --> 00:07:05.401 then it's gonna be really hard to

NOTE Confidence: 0.59921736

00:07:05.401 --> 00:07:07.480 unpack that and further refine

NOTE Confidence: 0.59921736

00:07:07.480 --> 00:07:09.472 the treatment and optimize it at

NOTE Confidence: 0.59921736

00:07:09.472 --> 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 --> 00:07:20.420 where I think it's especially

NOTE Confidence: 0.6194585

00:07:20.420 --> 00:07:22.960 relevant and appropriate to think

NOTE Confidence: 0.6194585

00:07:23.041 --> 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 --> 00:07:31.100 We have this very straightforward

NOTE Confidence: 0.6194585

00:07:31.100 --> 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 --> 00:07:36.680 all of our interventions are brain based,

NOTE Confidence: 0.6194585

00:07:36.680 --> 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 --> 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 --> 00:07:49.680 alleviation of symptoms with TMS,

NOTE Confidence: 0.6194585

00:07:49.680 --> 00:07:51.725 you have to choose something, right?

NOTE Confidence: 0.6194585

00:07:51.725 --> 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 --> 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 --> 00:08:03.585 understanding or that background

NOTE Confidence: 0.6194585

00:08:03.585 --> 00:08:06.571 and the relevance of of the brain

NOTE Confidence: 0.6194585

00:08:06.571 --> 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 --> 00:08:20.919 psychiatry and showing that there is

NOTE Confidence: 0.6194585

00:08:20.920 --> 00:08:24.900 some utility of the imaging for for

NOTE Confidence: 0.6194585

00:08:24.900 --> 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 --> 00:08:35.168 response takes a little while to

NOTE Confidence: 0.6194585

00:08:35.168 --> 00:08:37.330 really show a strong signal when

NOTE Confidence: 0.6194585

00:08:37.330 --> 00:08:39.605 you have some kind of psychological

NOTE Confidence: 0.6194585

00:08:39.605 --> 00:08:42.326 event which you know is is one of

NOTE Confidence: 0.6194585

00:08:42.326 --> 00:08:44.455 its shortcomings if you want to

NOTE Confidence: 0.6194585

00:08:44.455 --> 00:08:46.400 capture things moving really quickly.

NOTE Confidence: 0.6194585

00:08:46.400 --> 00:08:49.472 But it has a major advantage for me

NOTE Confidence: 0.6194585

00:08:49.472 --> 00:08:51.917 delivering pulses of TMS in the scanner,

NOTE Confidence: 0.6194585

00:08:51.920 --> 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 --> 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 --> 00:09:04.568 evokes response in the rest of the

NOTE Confidence: 0.6194585

00:09:04.568 --> 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 --> 00:09:13.112 in a way that traditional imaging

NOTE Confidence: 0.6194585

00:09:13.112 --> 00:09:15.684 doesn't have within its toolbox.

NOTE Confidence: 0.6194585

00:09:15.684 --> 00:09:17.716 So we do that.

NOTE Confidence: 0.6194585

00:09:17.720 --> 00:09:20.368 We started this was work that I did

NOTE Confidence: 0.6194585

00:09:20.368 --> 00:09:23.516 with the media and back at Stanford said,

NOTE Confidence: 0.6194585

00:09:23.520 --> 00:09:24.384 all right, well,

NOTE Confidence: 0.6194585

00:09:24.384 --> 00:09:25.824 we have these canonical resting

NOTE Confidence: 0.6194585

00:09:25.824 --> 00:09:26.400 state networks.

NOTE Confidence: 0.6194585

00:09:26.400 --> 00:09:27.880 They're all based on correlations.

NOTE Confidence: 0.6194585

00:09:27.880 --> 00:09:30.142 Let's throw some little like causal

NOTE Confidence: 0.6194585

00:09:30.142 --> 00:09:33.044 pings into this situation by stimulating

NOTE Confidence: 0.6194585

00:09:33.044 --> 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 --> 00:09:38.753 different things.

NOTE Confidence: 0.6194585

00:09:38.760 --> 00:09:39.480 We want to say, well,

NOTE Confidence: 0.6194585

00:09:39.480 --> 00:09:42.350 if you hit one node of a

NOTE Confidence: 0.6194585

00:09:42.350 --> 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 --> 00:09:47.560 So if we ping that with a pulse of TMS,

NOTE Confidence: 0.6194585

00:09:47.560 --> 00:09:49.360 can we actually engage the network,

NOTE Confidence: 0.6194585

00:09:49.360 --> 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

NOTE Confidence: 0.6194585

00:09:54.531 --> 00:09:56.554 evidence that we could in a couple

NOTE Confidence: 0.6194585

00:09:56.554 --> 00:09:58.479 of different task positive networks.

NOTE Confidence: 0.6194585

00:09:58.480 --> 00:09:59.720 So that's really reassuring.

NOTE Confidence: 0.6194585

00:09:59.720 --> 00:10:02.029 I suggest they we we are engaging

NOTE Confidence: 0.6194585

00:10:02.029 --> 00:10:03.984 networks even though we're stimulating

NOTE Confidence: 0.6194585

00:10:03.984 --> 00:10:06.200 a single brain area at a time.

NOTE Confidence: 0.6194585

00:10:06.200 --> 00:10:07.682 The other thing that we wanted

NOTE Confidence: 0.6194585

00:10:07.682 --> 00:10:09.820 to do had more to do with turning

NOTE Confidence: 0.6194585

00:10:09.820 --> 00:10:11.980 the correlations from resting

NOTE Confidence: 0.6194585

00:10:11.980 --> 00:10:14.680 state into more causal maps.

NOTE Confidence: 0.6194585

00:10:14.680 --> 00:10:17.281 And so we we sought to ping the task

NOTE Confidence: 0.6194585

00:10:17.281 --> 00:10:19.470 positive networks and based on the

NOTE Confidence: 0.6194585

00:10:19.470 --> 00:10:22.080 correlations in the past people thought OK,

NOTE Confidence: 0.6194585

00:10:22.080 --> 00:10:24.160 well there's this antagonistic

NOTE Confidence: 0.6194585

00:10:24.160 --> 00:10:25.706 relationship between the test

NOTE Confidence: 0.6194585

00:10:25.706 --> 00:10:27.758 positive networks and the DMN but

NOTE Confidence: 0.6194585

00:10:27.758 --> 00:10:29.724 it's not easy to causally test

NOTE Confidence: 0.6194585

00:10:29.724 --> 00:10:31.720 that non invasively in a human.

NOTE Confidence: 0.6194585

00:10:31.720 --> 00:10:33.550 So we pinned some of these

NOTE Confidence: 0.6194585

00:10:33.550 --> 00:10:34.770 test positive networks and

NOTE Confidence: 0.7076512

00:10:34.829 --> 00:10:37.083 looked at the evoke response in the

NOTE Confidence: 0.7076512

00:10:37.083 --> 00:10:39.319 default mode network and we supported the,

NOTE Confidence: 0.7076512

00:10:39.320 --> 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 --> 00:10:45.160 relationships between these networks.

NOTE Confidence: 0.7076512

00:10:45.160 --> 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 --> 00:10:52.165 So we're adding this causal argument to

NOTE Confidence: 0.7076512

00:10:52.165 --> 00:10:54.265 what's traditional been traditionally

NOTE Confidence: 0.7076512

00:10:54.265 --> 00:10:56.799 been just time series correlations.

NOTE Confidence: 0.5931011

00:10:59.000 --> 00:11:01.744 When I arrived at Penn about eight years

NOTE Confidence: 0.5931011

00:11:01.744 --> 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 --> 00:11:11.000 most relevant for anxiety and depression,

NOTE Confidence: 0.5931011

00:11:11.000 --> 00:11:12.665 starting with the subtennial cingular

NOTE Confidence: 0.5931011

00:11:12.665 --> 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 --> 00:11:21.318 but through those these network approaches,

NOTE Confidence: 0.5931011

00:11:21.320 --> 00:11:24.074 can you stimulate one of the nodes in the

NOTE Confidence: 0.5931011

00:11:24.074 --> 00:11:26.221 cortical surface and show evidence that

NOTE Confidence: 0.5931011

00:11:26.221 --> 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 --> 00:11:36.888 that this happens at the circuit level?

NOTE Confidence: 0.5931011

00:11:36.888 --> 00:11:38.760 How do you kind of prioritize

NOTE Confidence: 0.5931011

00:11:38.823 --> 00:11:40.718 which brain areas to stimulate?

NOTE Confidence: 0.5931011

00:11:40.720 --> 00:11:43.812 And so we we collect baseline resting

NOTE Confidence: 0.5931011

00:11:43.812 --> 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 --> 00:11:52.190 cortex and try stimulating them and

NOTE Confidence: 0.5931011

00:11:52.190 --> 00:11:54.599 evoking responses deeper in the brain

NOTE Confidence: 0.5931011

00:11:54.600 --> 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 --> 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 --> 00:12:04.760 and this is not neuromodulation,

NOTE Confidence: 0.5931011

00:12:04.760 --> 00:12:06.440 this is not repetitive TMS.

NOTE Confidence: 0.5931011

00:12:06.440 --> 00:12:08.858 This is just sending individual pings

NOTE Confidence: 0.5931011

00:12:08.858 --> 00:12:11.847 through that circuit a bunch of times just

NOTE Confidence: 0.5931011

00:12:11.847 --> 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 --> 00:12:19.440 to motor evoke potential.

NOTE Confidence: 0.5931011

00:12:19.440 --> 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 --> 00:12:24.196 of the circuit is measured.

NOTE Confidence: 0.5931011

00:12:24.200 --> 00:12:25.556 Instead of in a finger twitch,

NOTE Confidence: 0.5931011

00:12:25.560 --> 00:12:28.437 it's measured in an fMRI BOLD response.

NOTE Confidence: 0.5931011

00:12:28.440 --> 00:12:30.654 But conceptually we see them very

NOTE Confidence: 0.5931011

00:12:30.654 --> 00:12:33.391 similarly that if the circuit is really

NOTE Confidence: 0.5931011

00:12:33.391 --> 00:12:36.163 intact for an individual through the this

NOTE Confidence: 0.5931011

00:12:36.234 --> 00:12:38.719 cortical node that we're stimulating,

NOTE Confidence: 0.5931011

00:12:38.720 --> 00:12:40.628 then your evoked response deeper in

NOTE Confidence: 0.5931011

00:12:40.628 --> 00:12:42.999 the brain should be especially strong.

NOTE Confidence: 0.5931011

00:12:43.000 --> 00:12:45.624 So that's how we measure it and what we

NOTE Confidence: 0.5931011

00:12:45.624 --> 00:12:47.592 capture is the whole brain response.

NOTE Confidence: 0.5931011

00:12:47.600 --> 00:12:51.758 So this this is not only like

NOTE Confidence: 0.5931011

00:12:51.760 --> 00:12:52.560 direct pathways,

NOTE Confidence: 0.5931011

00:12:52.560 --> 00:12:55.360 we're getting a bunch of these like

NOTE Confidence: 0.5931011

00:12:55.360 --> 00:12:58.136 downstream multi synaptic kind of responses

NOTE Confidence: 0.5931011

00:12:58.136 --> 00:13:01.440 that are downstream of where we stimulate.

NOTE Confidence: 0.5931011

00:13:01.440 --> 00:13:03.771 But you can still make a causal

NOTE Confidence: 0.5931011

00:13:03.771 --> 00:13:05.694 argument because we stimulated at

NOTE Confidence: 0.5931011

00:13:05.694 --> 00:13:07.839 a particular node cortically and

NOTE Confidence: 0.5931011

00:13:07.840 --> 00:13:10.120 generated these whole brain responses.

NOTE Confidence: 0.5931011

00:13:10.120 --> 00:13:12.960 I think we could learn a lot about

NOTE Confidence: 0.5931011

00:13:12.960 --> 00:13:16.164 how the signal kind of propagates and

NOTE Confidence: 0.5931011

00:13:16.164 --> 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 --> 00:13:23.264 Also,

NOTE Confidence: 0.5931011

00:13:23.264 --> 00:13:26.044 just to say that imaging right

NOTE Confidence: 0.5931011

00:13:26.044 --> 00:13:27.554 has come a long way.

NOTE Confidence: 0.5931011

00:13:27.560 --> 00:13:30.280 There's a lot of different methods and tools,

NOTE Confidence: 0.5931011

00:13:30.280 --> 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,

NOTE Confidence: 0.5931011

00:13:35.228 --> 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 --> 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 --> 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 --> 00:13:55.800 atlases and how the brain is organized

NOTE Confidence: 0.5931011

00:13:55.800 --> 00:13:58.685 into networks and you can test them

NOTE Confidence: 0.5931011

00:13:58.685 --> 00:14:01.080 like causally by picking these spots.

NOTE Confidence: 0.5931011

00:14:01.080 --> 00:14:03.229 So we will collect a a baseline

NOTE Confidence: 0.5931011

00:14:03.229 --> 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 --> 00:14:09.303 camera and we mark some fiducial

NOTE Confidence: 0.5931011

00:14:09.303 --> 00:14:11.749 points on their scalp and then we can
NOTE Confidence: 0.5931011
00:14:11.749 --> 00:14:13.890 line up and find out exactly where
NOTE Confidence: 0.5931011
00:14:13.890 --> 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 --> 00:14:19.840 to your target really well by
NOTE Confidence: 0.47924274
00:14:19.840 --> 00:14:21.982 holding your TMS coil and getting
NOTE Confidence: 0.47924274
00:14:21.982 --> 00:14:24.191 this feedback from the camera on
NOTE Confidence: 0.47924274
00:14:24.191 --> 00:14:25.976 which brain area you're overlying
NOTE Confidence: 0.47924274
00:14:25.976 --> 00:14:27.880 while you do stimulation.
NOTE Confidence: 0.47924274
00:14:27.880 --> 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 --> 00:14:38.158 But we did a smaller pilot study
NOTE Confidence: 0.4464437
00:14:38.158 --> 00:14:40.776 in 14 subjects where we looked at
NOTE Confidence: 0.4464437
00:14:40.776 --> 00:14:42.340 resting connectivity based pings
NOTE Confidence: 0.4464437
00:14:42.340 --> 00:14:44.288 and found subtennial and amygdala

NOTE Confidence: 0.4464437

00:14:44.288 --> 00:14:46.080 engagement through those pathways.

NOTE Confidence: 0.4464437

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

NOTE Confidence: 0.4464437

00:14:48.234 --> 00:14:50.275 they're in bigger cohorts and we

NOTE Confidence: 0.4464437

00:14:50.275 --> 00:14:52.920 explored a little bit more kind of

NOTE Confidence: 0.4464437

00:14:52.920 --> 00:14:55.880 evidence for which target is doing what.

NOTE Confidence: 0.4464437

00:14:55.880 --> 00:14:58.519 So this is in 32 healthy subjects.

NOTE Confidence: 0.4464437

00:14:58.520 --> 00:15:00.650 We did the resting fMRI

NOTE Confidence: 0.4464437

00:15:00.650 --> 00:15:01.848 guided stimulation right,

NOTE Confidence: 0.4464437

00:15:01.848 --> 00:15:04.152 based on the subgenual connectivity and

NOTE Confidence: 0.4464437

00:15:04.152 --> 00:15:06.200 we stimulated through those pathways.

NOTE Confidence: 0.4464437

00:15:06.200 --> 00:15:08.084 We had a control region and

NOTE Confidence: 0.4464437

00:15:08.084 --> 00:15:10.078 motor cortex and we say, hey,

NOTE Confidence: 0.4464437

00:15:10.078 --> 00:15:12.466 can we reliably ping this target

NOTE Confidence: 0.4464437

00:15:12.466 --> 00:15:14.919 in in through these circuits?

NOTE Confidence: 0.4464437

00:15:14.920 --> 00:15:17.097 And we found that there was evidence

NOTE Confidence: 0.4464437

00:15:17.097 --> 00:15:19.548 we could engage the subgenual singlet

NOTE Confidence: 0.4464437

00:15:19.548 --> 00:15:21.833 better than the control region,

NOTE Confidence: 0.4464437

00:15:21.840 --> 00:15:23.692 suggesting that there's some

NOTE Confidence: 0.4464437

00:15:23.692 --> 00:15:25.544 pathway specificity in choosing

NOTE Confidence: 0.4464437

00:15:25.544 --> 00:15:27.172 these individualized resting guided

NOTE Confidence: 0.4464437

00:15:27.172 --> 00:15:29.398 targets and that when we ping them,

NOTE Confidence: 0.4464437

00:15:29.400 --> 00:15:31.475 we can reliably engage that

NOTE Confidence: 0.4464437

00:15:31.475 --> 00:15:32.720 deeper brain region.

NOTE Confidence: 0.516610831538462

00:15:35.440 --> 00:15:39.016 All right. So another replication and

NOTE Confidence: 0.516610831538462

00:15:39.016 --> 00:15:42.480 extension that we tried is to say,

NOTE Confidence: 0.516610831538462

00:15:42.480 --> 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 --> 00:15:49.754 correlated brain stimulation targets.

NOTE Confidence: 0.516610831538462

00:15:49.760 --> 00:15:51.296 That's including the same

NOTE Confidence: 0.516610831538462

00:15:51.296 --> 00:15:52.980 protocol and there's pretty nice

NOTE Confidence: 0.516610831538462

00:15:52.980 --> 00:15:54.280 clinical evidence for that.

NOTE Confidence: 0.516610831538462

00:15:54.280 --> 00:15:56.666 You look for the subgenual negative

NOTE Confidence: 0.516610831538462

00:15:56.666 --> 00:15:58.690 functional connectivity partner on

NOTE Confidence: 0.516610831538462

00:15:58.690 --> 00:16:01.398 the brain service and you stimulate

NOTE Confidence: 0.516610831538462

00:16:01.398 --> 00:16:03.093 that clinically and show that

NOTE Confidence: 0.516610831538462

00:16:03.093 --> 00:16:04.469 there's a relationship between

NOTE Confidence: 0.516610831538462

00:16:04.469 --> 00:16:06.287 how patients do and the strength

NOTE Confidence: 0.516610831538462

00:16:06.287 --> 00:16:07.919 of connectivity to that pathway.

NOTE Confidence: 0.516610831538462

00:16:07.920 --> 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 --> 00:16:16.840 important that you get the anti correlated

NOTE Confidence: 0.516610831538462

00:16:16.840 --> 00:16:19.130 spot or what actually happens if you

NOTE Confidence: 0.516610831538462

00:16:19.130 --> 00:16:20.920 look at a positively correlated spot.

NOTE Confidence: 0.516610831538462

00:16:20.920 --> 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 --> 00:16:27.815 stimulation and trying to map

NOTE Confidence: 0.516610831538462

00:16:27.815 --> 00:16:30.160 those networks from Reston State.

NOTE Confidence: 0.516610831538462

00:16:30.160 --> 00:16:33.275 And it looks like the positively correlated

NOTE Confidence: 0.516610831538462

00:16:33.275 --> 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 --> 00:16:39.160 related effects in the brain sort of thought,

NOTE Confidence: 0.516610831538462

00:16:39.160 --> 00:16:39.432 hey,

NOTE Confidence: 0.516610831538462

00:16:39.432 --> 00:16:41.336 what we should we should at least

NOTE Confidence: 0.516610831538462

00:16:41.336 --> 00:16:42.861 look into the positive connectivity

NOTE Confidence: 0.516610831538462

00:16:42.861 --> 00:16:45.719 spots and see what we get in terms of

NOTE Confidence: 0.516610831538462

00:16:45.719 --> 00:16:47.675 the evoked response in the subgenual.

NOTE Confidence: 0.516610831538462

00:16:47.680 --> 00:16:50.040 So we did that with our typical interleave,

NOTE Confidence: 0.516610831538462

00:16:50.040 --> 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 --> 00:16:55.230 just pinging the circuit and we found

NOTE Confidence: 0.516610831538462

00:16:55.230 --> 00:16:57.260 that for healthy controls this is a

NOTE Confidence: 0.516610831538462

00:16:57.326 --> 00:16:59.566 replication again that the positive

NOTE Confidence: 0.516610831538462

00:16:59.566 --> 00:17:01.358 and negative connectivity spots

NOTE Confidence: 0.516610831538462

00:17:01.358 --> 00:17:03.319 engage the circuit pretty well.

NOTE Confidence: 0.516610831538462

00:17:03.320 --> 00:17:06.400 They they do pretty similarly to one another.

NOTE Confidence: 0.516610831538462

00:17:06.400 --> 00:17:08.528 So both of them are effective as long

NOTE Confidence: 0.516610831538462

00:17:08.528 --> 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 --> 00:17:14.480 correlated or positively correlated.

NOTE Confidence: 0.516610831538462

00:17:14.480 --> 00:17:17.630 They both seem to do pretty similar

NOTE Confidence: 0.516610831538462

00:17:17.630 --> 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 --> 00:17:25.280 we found that there was a difference.

NOTE Confidence: 0.516610831538462

00:17:25.280 --> 00:17:27.765 The anti correlated spots still

NOTE Confidence: 0.516610831538462

00:17:27.765 --> 00:17:29.753 engaged the subgenual cingulant.

NOTE Confidence: 0.516610831538462

00:17:29.760 --> 00:17:33.000 So if the subgenual engagement is

NOTE Confidence: 0.516610831538462

00:17:33.000 --> 00:17:35.531 really critical for the antidepressant

NOTE Confidence: 0.516610831538462

00:17:35.531 --> 00:17:37.757 effects of TMS through that pathway,

NOTE Confidence: 0.516610831538462

00:17:37.760 --> 00:17:39.398 then this is consistent with that right.

NOTE Confidence: 0.516610831538462

00:17:39.400 --> 00:17:41.880 It it suggests that there is a real

NOTE Confidence: 0.516610831538462

00:17:41.880 --> 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 --> 00:17:47.560 work through those pathways.

NOTE Confidence: 0.516610831538462

00:17:47.560 --> 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 --> 00:17:52.003 there's like a significant difference

NOTE Confidence: 0.516610831538462

00:17:52.003 --> 00:17:53.930 in the strength of the evoked response

NOTE Confidence: 0.516610831538462

00:17:53.930 --> 00:17:55.275 depending on whether it's anti

NOTE Confidence: 0.516610831538462

00:17:55.275 --> 00:17:56.638 correlated or positively correlated.

NOTE Confidence: 0.516610831538462

00:17:56.640 --> 00:17:58.080 The positively correlated ones

NOTE Confidence: 0.516610831538462

00:17:58.080 --> 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 --> 00:18:03.360 that mechanistically,

NOTE Confidence: 0.516610831538462

00:18:03.360 --> 00:18:04.972 engagement of that subgenual

NOTE Confidence: 0.516610831538462

00:18:04.972 --> 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 --> 00:18:11.086 Why not start testing out the positively

NOTE Confidence: 0.516610831538462

00:18:11.086 --> 00:18:13.074 correlated spots and see if our

NOTE Confidence: 0.516610831538462

00:18:13.074 --> 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 --> 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 --> 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 --> 00:18:39.598 propagates from our stimulation site,

NOTE Confidence: 0.6126814

00:18:39.600 --> 00:18:41.553 which tended to which tended to be

NOTE Confidence: 0.6126814

00:18:41.553 --> 00:18:42.817 in the ventrilateral prefrontal

NOTE Confidence: 0.6126814

00:18:42.817 --> 00:18:44.677 cortex and engaging the amygdala.

NOTE Confidence: 0.6126814

00:18:44.680 --> 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 --> 00:18:54.040 fMRI connectivity based targeting again.

NOTE Confidence: 0.6126814

00:18:54.040 --> 00:18:56.443 But we also did some DTI at the baseline

NOTE Confidence: 0.6126814

00:18:56.443 --> 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 --> 00:19:04.316 the amygdala and the DTI measure.

NOTE Confidence: 0.6126814

00:19:04.320 --> 00:19:06.174 We found some evidence that there

NOTE Confidence: 0.6126814

00:19:06.174 --> 00:19:08.080 there seems to be a pathway,

NOTE Confidence: 0.6126814

00:19:08.080 --> 00:19:10.312 a direct pathway between where we

NOTE Confidence: 0.6126814

00:19:10.312 --> 00:19:12.755 were stimulating in VLPFC and the

NOTE Confidence: 0.6126814

00:19:12.755 --> 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 --> 00:19:21.980 evoked response to TMS was associated

NOTE Confidence: 0.6126814

00:19:21.980 --> 00:19:25.678 with the fiber density of that pathway

NOTE Confidence: 0.6126814

00:19:25.680 --> 00:19:28.120 at the individual subject level.

NOTE Confidence: 0.6126814

00:19:28.120 --> 00:19:31.352 This supports the idea that TMS likes to

NOTE Confidence: 0.6126814

00:19:31.352 --> 00:19:34.147 flow around along white matter and that

NOTE Confidence: 0.6126814

00:19:34.147 --> 00:19:37.025 this pathway may be a direct pathway

NOTE Confidence: 0.6126814

00:19:37.025 --> 00:19:40.096 and that this may partially explain

NOTE Confidence: 0.6126814

00:19:40.096 --> 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 --> 00:19:48.600 well, these are nice tricks.

NOTE Confidence: 0.48297837

00:19:48.600 --> 00:19:50.238 You're doing these pings of these circuits.

NOTE Confidence: 0.48297837

00:19:50.240 --> 00:19:51.900 You're showing evoked responses.

NOTE Confidence: 0.48297837

00:19:51.900 --> 00:19:53.560 That's kind of neat,

NOTE Confidence: 0.48297837

00:19:53.560 --> 00:19:55.948 but is there any like clinical

NOTE Confidence: 0.48297837

00:19:55.948 --> 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 --> 00:20:01.782 don't know anything happening in

NOTE Confidence: 0.48297837

00:20:01.782 --> 00:20:03.888 the brain and how's that relevant

NOTE Confidence: 0.48297837

00:20:03.888 --> 00:20:06.608 for the any clinical effects.

NOTE Confidence: 0.48297837

00:20:06.608 --> 00:20:10.147 The first we're looking at TMSF MRI in

NOTE Confidence: 0.48297837

00:20:10.147 --> 00:20:12.800 this more clinically relevant context,

NOTE Confidence: 0.48297837

00:20:12.800 --> 00:20:14.906 but it's this requires a little

NOTE Confidence: 0.48297837

00:20:14.906 --> 00:20:15.959 bit of explanation.

NOTE Confidence: 0.48297837

00:20:15.960 --> 00:20:18.120 We didn't do this full clinical

NOTE Confidence: 0.48297837

00:20:18.120 --> 00:20:20.599 trial with the pings along the way.

NOTE Confidence: 0.48297837

00:20:20.600 --> 00:20:23.957 We tried to take some bit of a shortcut,

NOTE Confidence: 0.48297837

00:20:23.960 --> 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 --> 00:20:32.680 like design. Yeah.

NOTE Confidence: 0.76734865

00:20:32.680 --> 00:20:36.836 So one of the difficulties of doing

NOTE Confidence: 0.76734865

00:20:36.840 --> 00:20:39.269 a treatment with TMS is that they

NOTE Confidence: 0.76734865

00:20:39.269 --> 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 --> 00:20:46.048 you have to do 10 sessions per day

NOTE Confidence: 0.76734865

00:20:46.048 --> 00:20:48.618 and then we have the four to six week

NOTE Confidence: 0.76734865

00:20:48.618 --> 00:20:50.175 traditional clinical TMS for depression

NOTE Confidence: 0.76734865

00:20:50.175 --> 00:20:52.352 protocol and that takes a long time.

NOTE Confidence: 0.76734865

00:20:52.360 --> 00:20:53.032 So we thought, OK,

NOTE Confidence: 0.76734865

00:20:53.032 --> 00:20:54.240 can we speed this up at all?

NOTE Confidence: 0.76734865

00:20:54.240 --> 00:20:56.400 Let's let's try to pack in a fair

NOTE Confidence: 0.76734865

00:20:56.400 --> 00:20:58.638 amount of stimulation in three days.

NOTE Confidence: 0.76734865

00:20:58.640 --> 00:21:00.824 And we thought that that's probably

NOTE Confidence: 0.76734865

00:21:00.824 --> 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,

NOTE Confidence: 0.76734865

00:21:04.760 --> 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 in the other TMS studies,

NOTE Confidence: 0.48220587

00:21:10.960 --> 00:21:12.955 imaging has been sort of an afterthought.

NOTE Confidence: 0.48220587

00:21:12.960 --> 00:21:15.030 And the case here, we're really

NOTE Confidence: 0.48220587

00:21:15.030 --> 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 --> 00:21:24.563 MRI can be useful here to show that

NOTE Confidence: 0.48220587

00:21:24.563 --> 00:21:26.520 there's a change in the pathway.

NOTE Confidence: 0.48220587

00:21:26.520 --> 00:21:28.795 And then usually the imaging in other

NOTE Confidence: 0.48220587

00:21:28.795 --> 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 --> 00:21:35.066 of MRI and see if if there's any

NOTE Confidence: 0.48220587

00:21:35.066 --> 00:21:36.984 utility in looking at it there.

NOTE Confidence: 0.48220587

00:21:36.984 --> 00:21:39.060 There's of course the patient provider

NOTE Confidence: 0.48220587

00:21:39.125 --> 00:21:41.240 burden of the traditional protocols.

NOTE Confidence: 0.48220587

00:21:41.240 --> 00:21:43.680 We wanna do this in a very short,

NOTE Confidence: 0.48220587

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

NOTE Confidence: 0.48220587

00:21:45.510 --> 00:21:48.560 with only a single protocol.

NOTE Confidence: 0.48220587

00:21:48.560 --> 00:21:50.680 Also throw in this little bit about sham.

NOTE Confidence: 0.48220587

00:21:50.680 --> 00:21:52.800 You can't do sham stimulation in the scanner.

NOTE Confidence: 0.48220587

00:21:52.800 --> 00:21:55.232 There isn't a commercially

NOTE Confidence: 0.48220587

00:21:55.232 --> 00:21:58.280 available stimulator for doing that.

NOTE Confidence: 0.48220587

00:21:58.280 --> 00:22:00.728 And I'll also say clinically there's

NOTE Confidence: 0.48220587

00:22:00.728 --> 00:22:02.730 at least some considerations with

NOTE Confidence: 0.48220587

00:22:02.730 --> 00:22:04.536 doing sham that you know does

NOTE Confidence: 0.48220587

00:22:04.536 --> 00:22:06.639 not reach the brain effectively.

NOTE Confidence: 0.48220587

00:22:06.640 --> 00:22:09.076 And so asking the patients to

NOTE Confidence: 0.48220587

00:22:09.076 --> 00:22:12.451 wait that out and like have these

NOTE Confidence: 0.48220587

00:22:12.451 --> 00:22:13.979 extended symptom assessments,

NOTE Confidence: 0.48220587

00:22:13.979 --> 00:22:16.912 you know that they're not getting an

NOTE Confidence: 0.48220587

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

NOTE Confidence: 0.48220587

00:22:18.589 --> 00:22:21.826 just another hurdle to considering

NOTE Confidence: 0.48220587

00:22:21.826 --> 00:22:23.956 adding sham to TMS studies.

NOTE Confidence: 0.48220587

00:22:23.960 --> 00:22:26.696 And I'll say in this case we can

NOTE Confidence: 0.48220587

00:22:26.696 --> 00:22:28.773 still show some control conditions

NOTE Confidence: 0.48220587

00:22:28.773 --> 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 --> 00:22:35.480 We also have a specific symptom

NOTE Confidence: 0.48220587

00:22:35.546 --> 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 --> 00:22:41.016 some evidence of how well we did with

NOTE Confidence: 0.48220587

00:22:41.016 --> 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 --> 00:22:50.040 So we collect a baseline scan,

NOTE Confidence: 0.48220587

00:22:50.040 --> 00:22:52.440 we use that to determine the

NOTE Confidence: 0.48220587

00:22:52.440 --> 00:22:53.240 connectivity targets.

NOTE Confidence: 0.48220587

00:22:53.240 --> 00:22:55.240 So they're personalized high

NOTE Confidence: 0.48220587

00:22:55.240 --> 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 --> 00:23:02.750 We also collect an amygdala seated

NOTE Confidence: 0.48220587

00:23:02.750 --> 00:23:05.380 connectivity profile for a second

NOTE Confidence: 0.48220587

00:23:05.380 --> 00:23:08.980 stimulation site and then before the

NOTE Confidence: 0.48220587

00:23:08.980 --> 00:23:12.900 intervention we pin the circuit in

NOTE Confidence: 0.48220587

00:23:12.900 --> 00:23:15.288 both kind of connectivity targets

NOTE Confidence: 0.48220587

00:23:15.288 --> 00:23:17.460 and then we do our intervention

NOTE Confidence: 0.48220587

00:23:17.521 --> 00:23:19.544 over the three days and then we

NOTE Confidence: 0.48220587

00:23:19.544 --> 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 --> 00:23:25.152 We do a pre and post measure and we're

NOTE Confidence: 0.48220587

00:23:25.152 --> 00:23:26.922 focusing on this subgeneral pathway

NOTE Confidence: 0.48220587

00:23:26.922 --> 00:23:29.305 to see if we can link the TMS up

NOTE Confidence: 0.48220587

00:23:29.305 --> 00:23:31.236 from Rye with some clinical change.

NOTE Confidence: 0.48220587

00:23:31.236 --> 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 --> 00:23:37.107 I call it an intervention because I

NOTE Confidence: 0.48220587

00:23:37.107 --> 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 --> 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 --> 00:23:51.399 it enough that we can capture this

NOTE Confidence: 0.48220587

00:23:51.400 --> 00:23:54.676 more acute response and link the TMS,

NOTE Confidence: 0.48220587

00:23:54.680 --> 00:23:57.116 HEP, MRI to a clinical change.

NOTE Confidence: 0.48220587

00:23:57.120 --> 00:23:58.767 So that's what we set out to do when

NOTE Confidence: 0.48220587

00:23:58.767 --> 00:24:00.597 we actually deliver the intervention.

NOTE Confidence: 0.48220587

00:24:00.600 --> 00:24:02.235 They're not in the scanner, right?

NOTE Confidence: 0.48220587

00:24:02.235 --> 00:24:04.115 We just do the pings before and after.

NOTE Confidence: 0.48220587

00:24:04.120 --> 00:24:04.906 So the intervention,

NOTE Confidence: 0.48220587

00:24:04.906 --> 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 --> 00:24:11.950 intermittent date of births per

NOTE Confidence: 0.48220587

00:24:12.024 --> 00:24:13.475 day for three consecutive days and

NOTE Confidence: 0.48220587

00:24:13.475 --> 00:24:15.276 then we ping them in the scanner

NOTE Confidence: 0.48220587

00:24:15.276 --> 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 --> 00:24:24.923 association between the strength of

NOTE Confidence: 0.5028308

00:24:24.923 --> 00:24:27.401 the ping the evoked response before

NOTE Confidence: 0.5028308

00:24:27.401 --> 00:24:30.740 the intervention and how well they do

NOTE Confidence: 0.5028308

00:24:30.740 --> 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 --> 00:24:41.240 hypothesis that engaging the subgenual is

NOTE Confidence: 0.5028308

00:24:41.240 --> 00:24:43.864 really relevant for depression improvement.

NOTE Confidence: 0.5028308

00:24:43.864 --> 00:24:47.640 And so we found some evidence of that.

NOTE Confidence: 0.5028308

00:24:47.640 --> 00:24:49.732 We also did the ping after all, right.

NOTE Confidence: 0.5028308

00:24:49.732 --> 00:24:50.764 So we did the pre and

NOTE Confidence: 0.5028308

00:24:50.764 --> 00:24:51.679 post change and the ping,

NOTE Confidence: 0.5028308

00:24:51.680 --> 00:24:55.220 the evoked response change was also

NOTE Confidence: 0.5028308

00:24:55.220 --> 00:24:57.692 associated with depression improvement.

NOTE Confidence: 0.5028308

00:24:57.692 --> 00:25:01.146 So showing evidence that TMS fMRI

NOTE Confidence: 0.5028308

00:25:01.146 --> 00:25:03.744 not only tells you something about

NOTE Confidence: 0.5028308

00:25:03.744 --> 00:25:05.534 circuit integrity that's relevant

NOTE Confidence: 0.5028308

00:25:05.534 --> 00:25:06.872 to improvement clinically,

NOTE Confidence: 0.5028308

00:25:06.872 --> 00:25:09.824 but it also measures a change in

NOTE Confidence: 0.5028308

00:25:09.824 --> 00:25:11.804 the communication in that pathway

NOTE Confidence: 0.5028308

00:25:11.804 --> 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 --> 00:25:22.360 the circuit specificities.

NOTE Confidence: 0.35288116

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

NOTE Confidence: 0.35288116

00:25:23.385 --> 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 --> 00:25:27.576 We didn't even have another active site

NOTE Confidence: 0.35288116

00:25:27.576 --> 00:25:29.717 that we delivered the intervention to.

NOTE Confidence: 0.35288116

00:25:29.720 --> 00:25:33.208 But what we did have is two different

NOTE Confidence: 0.35288116

00:25:33.208 --> 00:25:35.013 stimulation pathways and two

NOTE Confidence: 0.35288116

00:25:35.013 --> 00:25:36.691 different downstream targets that

NOTE Confidence: 0.35288116

00:25:36.691 --> 00:25:39.193 we can measure evoked responses in.

NOTE Confidence: 0.35288116

00:25:39.200 --> 00:25:41.006 So we looked at the amygdala evoked

NOTE Confidence: 0.35288116

00:25:41.006 --> 00:25:42.647 response and the subgenual evoked

NOTE Confidence: 0.35288116

00:25:42.647 --> 00:25:44.682 response through the amygdala functional

NOTE Confidence: 0.35288116

00:25:44.682 --> 00:25:46.869 connectivity pathway and the subgenual

NOTE Confidence: 0.35288116

00:25:46.869 --> 00:25:48.240 functional connectivity pathway.

NOTE Confidence: 0.35288116

00:25:48.240 --> 00:25:50.382 And so our hypothesis was only the

NOTE Confidence: 0.35288116

00:25:50.382 --> 00:25:52.391 solid blue line that's the place

NOTE Confidence: 0.35288116

00:25:52.391 --> 00:25:54.226 where we delivered the intervention

NOTE Confidence: 0.35288116

00:25:54.226 --> 00:25:56.556 and that's our downstream target.

NOTE Confidence: 0.35288116

00:25:56.560 --> 00:25:58.904 We we thought that if if if our

NOTE Confidence: 0.35288116

00:25:58.904 --> 00:26:00.759 hypothesis is right that engaging

NOTE Confidence: 0.35288116

00:26:00.759 --> 00:26:02.749 that target and modulating that

NOTE Confidence: 0.35288116

00:26:02.749 --> 00:26:05.424 target is the is the one most

NOTE Confidence: 0.35288116

00:26:05.424 --> 00:26:06.872 relevant to depression change,

NOTE Confidence: 0.35288116

00:26:06.880 --> 00:26:08.620 then that's the only evoked response

NOTE Confidence: 0.35288116

00:26:08.620 --> 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 --> 00:26:13.399 that's indeed what we found.

NOTE Confidence: 0.35288116

00:26:13.400 --> 00:26:15.518 So we found some circuit specificity

NOTE Confidence: 0.35288116

00:26:15.518 --> 00:26:17.640 some region of interest specificity

NOTE Confidence: 0.33387774

00:26:20.680 --> 00:26:23.680 also say that anxiety improved

NOTE Confidence: 0.33387774

00:26:23.680 --> 00:26:25.534 even though we were aiming at

NOTE Confidence: 0.33387774

00:26:25.534 --> 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 --> 00:26:32.941 with change in subgenual evoked response

NOTE Confidence: 0.33387774

00:26:32.941 --> 00:26:35.317 only depression improvement loss.

NOTE Confidence: 0.33387774

00:26:35.320 --> 00:26:38.287 Now let's show some degree of symptom

NOTE Confidence: 0.33387774

00:26:38.287 --> 00:26:40.522 specificity and relevance to that

NOTE Confidence: 0.33387774

00:26:40.522 --> 00:26:43.040 pathway with the subgenual stimulant.

NOTE Confidence: 0.31938392

00:26:45.680 --> 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 --> 00:26:53.640 our medicated patients,

NOTE Confidence: 0.31938392

00:26:53.640 --> 00:26:55.488 which are not the difficult patients

NOTE Confidence: 0.31938392

00:26:55.488 --> 00:26:57.352 in the TMS clinical studies because

NOTE Confidence: 0.31938392

00:26:57.352 --> 00:26:59.640 we wanted to kind of clean our brain

NOTE Confidence: 0.31938392

00:26:59.700 --> 00:27:01.590 response as our first stab at linking

NOTE Confidence: 0.31938392

00:27:01.590 --> 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 --> 00:27:07.918 patients that have not responded to

NOTE Confidence: 0.31938392

00:27:07.920 --> 00:27:09.772 multiple rounds of antidepressant

NOTE Confidence: 0.31938392

00:27:09.772 --> 00:27:12.550 medication and they tended to have

NOTE Confidence: 0.31938392

00:27:12.626 --> 00:27:14.601 stronger higher levels of depression

NOTE Confidence: 0.31938392

00:27:14.601 --> 00:27:17.400 which is the blue bar on the left

NOTE Confidence: 0.31938392

00:27:17.400 --> 00:27:19.716 compared to the non treatment resistant.

NOTE Confidence: 0.31938392

00:27:19.720 --> 00:27:22.456 But their clinical response to the

NOTE Confidence: 0.31938392

00:27:22.456 --> 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 --> 00:27:30.420 they respond equally well

NOTE Confidence: 0.31938392

00:27:30.420 --> 00:27:32.520 to this brief intervention.

NOTE Confidence: 0.34967873

00:27:35.800 --> 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?

NOTE Confidence: 0.34967873

00:27:39.710 --> 00:27:42.050 And so I'm talking all about

NOTE Confidence: 0.34967873

00:27:42.050 --> 00:27:43.648 the subgenual cingulate and a

NOTE Confidence: 0.34967873

00:27:43.648 --> 00:27:45.158 little bit about the amygdala.

NOTE Confidence: 0.34967873

00:27:45.160 --> 00:27:46.740 Maybe the subgenual cingulate

NOTE Confidence: 0.34967873

00:27:46.740 --> 00:27:48.715 is not even a hotspot,

NOTE Confidence: 0.34967873

00:27:48.720 --> 00:27:50.596 you're aiming for it, you engaged it,

NOTE Confidence: 0.34967873

00:27:50.600 --> 00:27:51.856 you showed these relationships.

NOTE Confidence: 0.34967873

00:27:51.856 --> 00:27:54.478 But if you looked at the evoked response

NOTE Confidence: 0.34967873

00:27:54.478 --> 00:27:56.837 changes through the rest of the brain,

NOTE Confidence: 0.34967873

00:27:56.840 --> 00:27:58.320 probably some other parts

NOTE Confidence: 0.34967873

00:27:58.320 --> 00:28:00.066 of the network are yes,

NOTE Confidence: 0.34967873

00:28:00.066 --> 00:28:01.396 is relevant, maybe more relevant.

NOTE Confidence: 0.34967873

00:28:01.400 --> 00:28:03.434 So we looked at the rest of the brain,

NOTE Confidence: 0.34967873

00:28:03.440 --> 00:28:05.120 we looked at the evoked response

NOTE Confidence: 0.34967873

00:28:05.120 --> 00:28:07.400 change map and the symptom improvement.

NOTE Confidence: 0.34967873

00:28:07.400 --> 00:28:08.972 So this is different from other

NOTE Confidence: 0.34967873

00:28:08.972 --> 00:28:10.672 brain images that you may have

NOTE Confidence: 0.34967873

00:28:10.672 --> 00:28:12.157 seen that are just correlational.

NOTE Confidence: 0.34967873

00:28:12.160 --> 00:28:15.368 These are the evoked response changes, right?

NOTE Confidence: 0.34967873

00:28:15.368 --> 00:28:19.653 So a very unique measurement and I

NOTE Confidence: 0.34967873

00:28:19.653 --> 00:28:21.759 will say for a depression change,

NOTE Confidence: 0.34967873

00:28:21.760 --> 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 --> 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 --> 00:28:29.062 other brain areas are also changing

NOTE Confidence: 0.34967873

00:28:29.062 --> 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 --> 00:28:33.750 posterior singlet.

NOTE Confidence: 0.34967873

00:28:33.750 --> 00:28:35.880 A bunch of these other brain

NOTE Confidence: 0.34967873

00:28:35.880 --> 00:28:37.503 areas also come along.

NOTE Confidence: 0.34967873

00:28:37.503 --> 00:28:40.450 And then we we recognized that the

NOTE Confidence: 0.34967873

00:28:40.536 --> 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 --> 00:28:49.520 So we looked at the other parts of the brain.

NOTE Confidence: 0.34967873

00:28:49.520 --> 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 --> 00:28:57.200 that changed in response to stimulation,

NOTE Confidence: 0.34967873

00:28:57.200 --> 00:29:00.130 some other regions and posterior

NOTE Confidence: 0.34967873

00:29:00.130 --> 00:29:01.878 cingulate orbital frontal cortex.

NOTE Confidence: 0.34967873

00:29:01.878 --> 00:29:04.194 So there are other regions that

NOTE Confidence: 0.34967873

00:29:04.194 --> 00:29:06.637 seem to have been modulated and that

NOTE Confidence: 0.34967873

00:29:06.640 --> 00:29:09.160 are relevant to anxiety change.

NOTE Confidence: 0.34967873

00:29:09.160 --> 00:29:11.470 I would say these maps could be

NOTE Confidence: 0.34967873

00:29:11.470 --> 00:29:13.369 really useful because these can

NOTE Confidence: 0.34967873

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 --> 00:29:17.368 well we want to,

NOTE Confidence: 0.34967873

00:29:17.368 --> 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 --> 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 --> 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 --> 00:29:27.505 or we can try to capture something

NOTE Confidence: 0.34967873

00:29:27.547 --> 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 --> 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 --> 00:29:33.568 that gives us some evidence that this

NOTE Confidence: 0.34967873

00:29:33.568 --> 00:29:35.959 is a pathway we want to modulate.

NOTE Confidence: 0.34967873

00:29:35.960 --> 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 --> 00:29:43.812 other cortical targets and see if

NOTE Confidence: 0.34967873

00:29:43.812 --> 00:29:45.588 that actually is more effective

NOTE Confidence: 0.34967873

00:29:45.588 --> 00:29:48.080 as a as a treatment for anxiety.

NOTE Confidence: 0.42380634

00:29:50.800 --> 00:29:53.880 All right. So I tried to demonstrate

NOTE Confidence: 0.42380634

00:29:53.880 --> 00:29:56.452 some evidence that our our positive

NOTE Confidence: 0.42380634

00:29:56.452 --> 00:29:58.782 connectivity targets for the subgenual

NOTE Confidence: 0.42380634

00:29:58.782 --> 00:30:02.264 may be especially clinically relevant,

NOTE Confidence: 0.42380634

00:30:02.264 --> 00:30:05.664 but there's the brief intervention

NOTE Confidence: 0.42380634

00:30:05.664 --> 00:30:10.476 study that may not be as similar to

NOTE Confidence: 0.42380634

00:30:10.476 --> 00:30:12.361 traditional RTMS clinical trials.

NOTE Confidence: 0.42380634

00:30:12.361 --> 00:30:14.296 So what about purely based

NOTE Confidence: 0.42380634

00:30:14.296 --> 00:30:15.720 on clinical evidence,

NOTE Confidence: 0.42380634

00:30:15.720 --> 00:30:18.400 what can we show maybe it's

NOTE Confidence: 0.42380634

00:30:18.400 --> 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 --> 00:30:22.954 are questions or people want

NOTE Confidence: 0.42380634

00:30:22.954 --> 00:30:25.173 to get into more of the sham

NOTE Confidence: 0.42380634

00:30:25.173 --> 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 --> 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 --> 00:30:36.761 and get a clinical difference

NOTE Confidence: 0.62573975

00:30:36.761 --> 00:30:39.361 than it is to deliver sham where

NOTE Confidence: 0.62573975

00:30:39.361 --> 00:30:41.972 we know it's not engaging the the

NOTE Confidence: 0.62573975

00:30:41.972 --> 00:30:43.623 brain networks or modulating them.

NOTE Confidence: 0.62573975

00:30:43.623 --> 00:30:46.094 So let's say it's it's sort of a

NOTE Confidence: 0.62573975

00:30:46.094 --> 00:30:47.864 higher bar to have another active

NOTE Confidence: 0.62573975

00:30:47.864 --> 00:30:49.806 site that you think may actually

NOTE Confidence: 0.62573975

00:30:49.806 --> 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 --> 00:30:56.316 that you hope is even better.

NOTE Confidence: 0.62573975

00:30:56.320 --> 00:30:59.800 So we tried this out in a cohort

NOTE Confidence: 0.62573975

00:30:59.800 --> 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 --> 00:31:14.521 that to a six centimeter anterior

NOTE Confidence: 0.62573975

00:31:14.521 --> 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 --> 00:31:20.040 and seems to work decently well.

NOTE Confidence: 0.62573975

00:31:20.040 --> 00:31:22.469 So we have these two active site

NOTE Confidence: 0.62573975

00:31:22.469 --> 00:31:24.538 targets we did between subjects

NOTE Confidence: 0.62573975

00:31:24.538 --> 00:31:27.478 design on those we have two

NOTE Confidence: 0.62573975

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

NOTE Confidence: 0.62573975

00:31:30.290 --> 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 --> 00:31:38.953 through some psychological tasks

NOTE Confidence: 0.62573975

00:31:38.953 --> 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 --> 00:31:45.680 interactions were not significant.

NOTE Confidence: 0.62573975

00:31:45.680 --> 00:31:47.944 We expected them to be with the target

NOTE Confidence: 0.62573975

00:31:47.944 --> 00:31:50.035 and what tasks they were doing there.

NOTE Confidence: 0.62573975

00:31:50.035 --> 00:31:51.595 There's maybe a little bit of signal there.

NOTE Confidence: 0.62573975

00:31:51.600 --> 00:31:53.112 We want to try to follow up on it.

NOTE Confidence: 0.62573975

00:31:53.120 --> 00:31:54.848 But the the basic design here

NOTE Confidence: 0.62573975

00:31:54.848 --> 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 --> 00:32:00.320 versus the six centimeter target

NOTE Confidence: 0.94476616

00:32:02.440 --> 00:32:04.420 and this is what the cortical

NOTE Confidence: 0.94476616

00:32:04.420 --> 00:32:06.839 sites look like in standard space.

NOTE Confidence: 0.94476616

00:32:06.840 --> 00:32:08.359 So you can see the blue ones,

NOTE Confidence: 0.94476616

00:32:08.360 --> 00:32:09.638 those are the 6 centimeter ones,

NOTE Confidence: 0.94476616

00:32:09.640 --> 00:32:11.677 they tend to cluster fairly well together.

NOTE Confidence: 0.94476616

00:32:11.680 --> 00:32:13.906 Some people's heads are longer or shorter

NOTE Confidence: 0.94476616

00:32:13.906 --> 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 --> 00:32:20.200 whereas the fMRI guided ones,

NOTE Confidence: 0.94476616

00:32:20.200 --> 00:32:22.294 those have a little bit more

NOTE Confidence: 0.94476616

00:32:22.294 --> 00:32:24.080 variability in where they land.

NOTE Confidence: 0.94476616

00:32:24.080 --> 00:32:26.327 So we're looking at a nice consistent

NOTE Confidence: 0.94476616

00:32:26.327 --> 00:32:28.663 cluster that has high positive connectivity

NOTE Confidence: 0.94476616

00:32:28.663 --> 00:32:30.838 individually guided for that subgenual

NOTE Confidence: 0.94476616

00:32:30.838 --> 00:32:33.197 and you can see there's overlap,

NOTE Confidence: 0.94476616

00:32:33.200 --> 00:32:36.518 There's definitely overlap in standard space.

NOTE Confidence: 0.94476616

00:32:36.520 --> 00:32:40.187 But we still anticipated that the

NOTE Confidence: 0.94476616

00:32:40.187 --> 00:32:42.432 personalization was going to make

NOTE Confidence: 0.94476616

00:32:42.432 --> 00:32:45.208 a difference and help the symptoms

NOTE Confidence: 0.94476616

00:32:45.208 --> 00:32:47.480 even more and this is the clinical

NOTE Confidence: 0.94476616

00:32:47.480 --> 00:32:48.680 evidence that that we found.

NOTE Confidence: 0.94476616

00:32:48.680 --> 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 --> 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 --> 00:33:00.865 the scalp target and the FBI guided

NOTE Confidence: 0.94476616

00:33:00.865 --> 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 --> 00:33:07.640 in the longer term follow up that they

NOTE Confidence: 0.94476616

00:33:07.640 --> 00:33:09.680 held pretty tight with one another.

NOTE Confidence: 0.94476616

00:33:09.680 --> 00:33:13.290 There was one subscale of PCL that

NOTE Confidence: 0.94476616

00:33:13.290 --> 00:33:15.215 showed a slight difference which

NOTE Confidence: 0.94476616

00:33:15.215 --> 00:33:18.022 is the bottom left and that was

NOTE Confidence: 0.94476616

00:33:18.022 --> 00:33:19.598 the hyper arousal subscale.

NOTE Confidence: 0.94476616

00:33:19.600 --> 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 --> 00:33:28.075 to week 10 where the fMRI guided

NOTE Confidence: 0.94476616

00:33:28.075 --> 00:33:31.080 1 tended to be more efficacious.

NOTE Confidence: 0.94476616

00:33:31.080 --> 00:33:33.400 Some of that kind of slipped back in

NOTE Confidence: 0.94476616

00:33:33.400 --> 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 --> 00:33:40.664 we saw the the best more striking

NOTE Confidence: 0.94476616

00:33:40.664 --> 00:33:42.978 group differences is in the PHQ 9

NOTE Confidence: 0.94476616

00:33:42.978 --> 00:33:44.920 depression scale on the top right.

NOTE Confidence: 0.94476616

00:33:44.920 --> 00:33:48.632 You can see that kind of from early

NOTE Confidence: 0.94476616

00:33:48.632 --> 00:33:52.332 on those those two kind of profiles

NOTE Confidence: 0.94476616

00:33:52.332 --> 00:33:53.398 look different.

NOTE Confidence: 0.94476616

00:33:53.400 --> 00:33:55.320 The fMRI guided continues to beat

NOTE Confidence: 0.94476616

00:33:55.320 --> 00:33:57.181 the scalp based target and even

NOTE Confidence: 0.94476616

00:33:57.181 --> 00:33:59.015 in the longer term follow up it

NOTE Confidence: 0.94476616

00:33:59.015 --> 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 --> 00:34:04.888 the symptoms start to kind of push

NOTE Confidence: 0.94476616

00:34:04.888 --> 00:34:06.952 back towards the baseline a lot

NOTE Confidence: 0.94476616

00:34:06.952 --> 00:34:09.362 more than the fMRI guided one that

NOTE Confidence: 0.94476616

00:34:09.362 --> 00:34:10.838 tends to stick around.

NOTE Confidence: 0.94476616

00:34:10.840 --> 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 --> 00:34:19.600 symptom differences and measures.

NOTE Confidence: 0.94476616

00:34:19.600 --> 00:34:20.150 OK.

NOTE Confidence: 0.94476616

00:34:20.150 --> 00:34:21.800 So this is,

NOTE Confidence: 0.94476616

00:34:21.800 --> 00:34:24.945 this is something of you know hope

NOTE Confidence: 0.94476616

00:34:24.945 --> 00:34:27.150 for the future which is that to

NOTE Confidence: 0.94476616

00:34:27.223 --> 00:34:29.379 mess up MRI might guide us more

NOTE Confidence: 0.94476616

00:34:29.379 --> 00:34:31.876 quickly to a more efficacious target

NOTE Confidence: 0.94476616

00:34:31.876 --> 00:34:33.876 for an individual patient.

NOTE Confidence: 0.94476616

00:34:33.880 --> 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 --> 00:34:39.264 right and you say well there's

NOTE Confidence: 0.94476616

00:34:39.264 --> 00:34:40.480 a connectivity peak here,

NOTE Confidence: 0.94476616

00:34:40.480 --> 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 --> 00:34:48.080 but I do feel like engaging the subgenual,

NOTE Confidence: 0.94476616

00:34:48.080 --> 00:34:49.400 there's good evidence for that.

NOTE Confidence: 0.94476616

00:34:49.400 --> 00:34:51.320 So put them in the scanner,

NOTE Confidence: 0.94476616

00:34:51.320 --> 00:34:53.360 you ping a couple of different

NOTE Confidence: 0.94476616

00:34:53.360 --> 00:34:54.040 potential pathways,

NOTE Confidence: 0.94476616

00:34:54.040 --> 00:34:56.120 you measure the evoked response,

NOTE Confidence: 0.94476616

00:34:56.120 --> 00:34:57.535 right for that individual patient

NOTE Confidence: 0.94476616

00:34:57.535 --> 00:34:59.320 through that pathway and you say ah,

NOTE Confidence: 0.94476616

00:34:59.320 --> 00:35:01.960 it looks much stronger at this red site.

NOTE Confidence: 0.94476616

00:35:01.960 --> 00:35:04.144 And so you carry that forward

NOTE Confidence: 0.94476616

00:35:04.144 --> 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 --> 00:35:08.250 if this evidence continues to build

NOTE Confidence: 0.8656689

00:35:08.306 --> 00:35:09.878 the way we're starting out here,

NOTE Confidence: 0.8656689

00:35:09.880 --> 00:35:12.010 that engaging the circuits is really

NOTE Confidence: 0.8656689

00:35:12.010 --> 00:35:13.920 critical and tells you something

NOTE Confidence: 0.8656689

00:35:13.920 --> 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 --> 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 --> 00:35:24.080 Save us a lot of time make the

NOTE Confidence: 0.8656689

00:35:24.080 --> 00:35:25.480 treatment protocols work better.

NOTE Confidence: 0.3334847

00:35:30.400 --> 00:35:34.010 All right. So in conclusion, fMRI guided

NOTE Confidence: 0.3334847

00:35:34.010 --> 00:35:36.920 TMS seems to engage intended targets,

NOTE Confidence: 0.3334847

00:35:36.920 --> 00:35:38.999 at least these ones that we tried so far,

NOTE Confidence: 0.3334847

00:35:39.000 --> 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 --> 00:35:45.024 oh maybe we need ultrasound a lot less

NOTE Confidence: 0.3334847

00:35:45.024 --> 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 --> 00:35:55.493 We're we're not arguing TMS

NOTE Confidence: 0.3334847

00:35:55.493 --> 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.

NOTE Confidence: 0.3334847

00:35:58.840 --> 00:36:00.440 But building on all this,

NOTE Confidence: 0.3334847

00:36:00.440 --> 00:36:02.615 it's really great neuroscience and

NOTE Confidence: 0.3334847

00:36:02.615 --> 00:36:05.480 imaging data related to brain networks.

NOTE Confidence: 0.3334847

00:36:05.480 --> 00:36:07.195 There's a cortical representation of

NOTE Confidence: 0.3334847

00:36:07.195 --> 00:36:09.559 almost any network that you would want.

NOTE Confidence: 0.3334847

00:36:09.560 --> 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 --> 00:36:16.956 critical downstream regions with TMS

NOTE Confidence: 0.3334847

00:36:16.960 --> 00:36:19.156 then that may be a a great piece of

NOTE Confidence: 0.3334847

00:36:19.156 --> 00:36:21.396 evidence to encourage more people to use it.

NOTE Confidence: 0.8860244

00:36:23.600 --> 00:36:26.239 We also showed that there's a clinical

NOTE Confidence: 0.8860244

00:36:26.239 --> 00:36:28.093 relevance that engagement at this

NOTE Confidence: 0.8860244

00:36:28.093 --> 00:36:30.073 target that how strong does this

NOTE Confidence: 0.8860244

00:36:30.073 --> 00:36:32.355 circuit respond to a pulse of TMS

NOTE Confidence: 0.8860244

00:36:32.355 --> 00:36:33.915 actually tells you something useful

NOTE Confidence: 0.8860244

00:36:33.920 --> 00:36:36.755 about how well the TMS is going

NOTE Confidence: 0.8860244

00:36:36.755 --> 00:36:38.988 to treat that person's symptoms.

NOTE Confidence: 0.8860244

00:36:38.988 --> 00:36:42.400 So I'd love to continue building on that.

NOTE Confidence: 0.8860244

00:36:42.400 --> 00:36:44.500 And then in this first initial

NOTE Confidence: 0.8860244

00:36:44.500 --> 00:36:46.360 stab with this clinical trial,

NOTE Confidence: 0.8860244

00:36:46.360 --> 00:36:48.502 we found that there's at least

NOTE Confidence: 0.8860244

00:36:48.502 --> 00:36:50.796 some evidence that the fMRI guided

NOTE Confidence: 0.8860244

00:36:50.796 --> 00:36:52.781 is more clinically effective than

NOTE Confidence: 0.8860244

00:36:52.781 --> 00:36:54.520 a stout based target.

NOTE Confidence: 0.8860244

00:36:54.520 --> 00:36:55.396 I'm not sure if I mentioned,

NOTE Confidence: 0.8860244

00:36:55.400 --> 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 --> 00:37:07.160 the scale based target is like 52 percent,

NOTE Confidence: 0.8860244

00:37:07.160 --> 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 --> 00:37:13.261 is it worth the time trouble expertise

NOTE Confidence: 0.8860244

00:37:13.261 --> 00:37:15.272 of doing the fMRI guided target

NOTE Confidence: 0.8860244

00:37:15.272 --> 00:37:17.533 like that would still be an open

NOTE Confidence: 0.8860244

00:37:17.605 --> 00:37:19.837 question I I'd say and is this the

NOTE Confidence: 0.8860244

00:37:19.837 --> 00:37:21.875 best fMRI guided target that we can

NOTE Confidence: 0.8860244

00:37:21.875 --> 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 --> 00:37:26.365 but probably not.

NOTE Confidence: 0.8860244

00:37:26.365 --> 00:37:28.240 But let's continue building on

NOTE Confidence: 0.8860244

00:37:28.240 --> 00:37:30.892 that and see if we can do the

NOTE Confidence: 0.8860244

00:37:30.892 --> 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 --> 00:37:37.799 improve our targeting and dosing

NOTE Confidence: 0.7644311

00:37:40.280 --> 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 --> 00:37:48.301 of of any kind Functional imaging

NOTE Confidence: 0.7644311

00:37:48.301 --> 00:37:50.131 would be better than just holding

NOTE Confidence: 0.7644311

00:37:50.131 --> 00:37:52.409 on to this black box where we don't

NOTE Confidence: 0.7644311

00:37:52.409 --> 00:37:54.159 know why some patients respond,

NOTE Confidence: 0.7644311

00:37:54.160 --> 00:37:56.365 We don't know what happened to the

NOTE Confidence: 0.7644311

00:37:56.365 --> 00:37:58.892 circuits in response to TMS which I think

NOTE Confidence: 0.7644311

00:37:58.892 --> 00:38:01.136 is really critical for pushing the field

NOTE Confidence: 0.7644311

00:38:01.136 --> 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 --> 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 --> 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 --> 00:38:24.426 particular target and then build on that

NOTE Confidence: 0.43447363

00:38:24.426 --> 00:38:26.800 to do a more definitive clinical trial.

NOTE Confidence: 0.43447363

00:38:26.800 --> 00:38:28.784 So it's a very good fit I think

NOTE Confidence: 0.43447363

00:38:28.784 --> 00:38:31.216 with some objectives of of some

NOTE Confidence: 0.43447363

00:38:31.216 --> 00:38:33.636 of the funders out there.

NOTE Confidence: 0.43447363

00:38:33.640 --> 00:38:36.400 So these are my team, the,

NOTE Confidence: 0.43447363

00:38:36.400 --> 00:38:40.560 the people in my center and my closest

NOTE Confidence: 0.43447363

00:38:40.560 --> 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 --> 00:38:51.217 based on questions that I be asked in

NOTE Confidence: 0.43447363

00:38:51.217 --> 00:38:53.921 manuscripts and in talks as just giving

NOTE Confidence: 0.43447363

00:38:53.921 --> 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 --> 00:39:00.918 you take these unmedicated patients,

NOTE Confidence: 0.43447363

00:39:00.920 --> 00:39:02.552 those are not really a typical

NOTE Confidence: 0.43447363

00:39:02.552 --> 00:39:04.377 So what happens in the medicated

NOTE Confidence: 0.43447363

00:39:04.377 --> 00:39:06.750 patients and totally agree we want to

NOTE Confidence: 0.43447363

00:39:06.750 --> 00:39:08.478 replicate in a medicated patients.

NOTE Confidence: 0.43447363

00:39:08.480 --> 00:39:10.430 So the pending new grant starting

NOTE Confidence: 0.43447363

00:39:10.430 --> 00:39:11.620 in December, we're gonna,

NOTE Confidence: 0.43447363

00:39:11.620 --> 00:39:14.040 we're gonna allow for that and check it out.

NOTE Confidence: 0.43447363

00:39:14.040 --> 00:39:14.536 I'll say,

NOTE Confidence: 0.43447363

00:39:14.536 --> 00:39:16.520 well you did this brief 3 day intervention,

NOTE Confidence: 0.43447363

00:39:16.520 --> 00:39:19.268 maybe that's not exactly what happens

NOTE Confidence: 0.43447363

00:39:19.268 --> 00:39:22.519 in the brain with a higher dose of

NOTE Confidence: 0.43447363

00:39:22.520 --> 00:39:24.764 of more stimulation in the sync

NOTE Confidence: 0.43447363

00:39:24.764 --> 00:39:27.200 protocol or even the old original

NOTE Confidence: 0.43447363

00:39:27.200 --> 00:39:28.408 10 minutes for depression.

NOTE Confidence: 0.43447363

00:39:28.408 --> 00:39:29.314 I totally agree.

NOTE Confidence: 0.43447363

00:39:29.320 --> 00:39:31.120 Let's check it out with a higher dose.

NOTE Confidence: 0.43447363

00:39:31.120 --> 00:39:32.896 Now that we have the evidence

NOTE Confidence: 0.43447363

00:39:32.896 --> 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 --> 00:39:38.680 exploring that in a higher dose.

NOTE Confidence: 0.43447363

00:39:38.680 --> 00:39:40.815 The imaging aficionados you may say that's

NOTE Confidence: 0.43447363

00:39:40.815 --> 00:39:43.039 a region with low signal noise ratio.

NOTE Confidence: 0.43447363

00:39:43.040 --> 00:39:45.040 So you shouldn't use it.

NOTE Confidence: 0.43447363

00:39:45.040 --> 00:39:47.792 And I would say well we have this

NOTE Confidence: 0.43447363

00:39:47.792 --> 00:39:49.489 evidence nevertheless that we're

NOTE Confidence: 0.43447363

00:39:49.489 --> 00:39:51.369 getting significant about responses

NOTE Confidence: 0.43447363

00:39:51.369 --> 00:39:53.249 and differences and clinical

NOTE Confidence: 0.43447363

00:39:53.312 --> 00:39:56.000 relevance with our TMS, FM, RI data.

NOTE Confidence: 0.43447363

00:39:56.000 --> 00:39:58.560 But that being said, I think we can do,

NOTE Confidence: 0.43447363

00:39:58.560 --> 00:40:01.940 we can collect higher fidelity images

NOTE Confidence: 0.43447363

00:40:01.940 --> 00:40:04.724 for example we have an 8 channel volume

NOTE Confidence: 0.43447363

00:40:04.724 --> 00:40:06.728 coil coming that we're gonna start

NOTE Confidence: 0.43447363

00:40:06.728 --> 00:40:08.972 using in our new studies say well

NOTE Confidence: 0.43447363

00:40:08.972 --> 00:40:10.694 depression is a network it's not just

NOTE Confidence: 0.43447363

00:40:10.694 --> 00:40:12.588 a subgenual you shouldn't be focusing

NOTE Confidence: 0.43447363

00:40:12.588 --> 00:40:14.912 on single brain areas like that and.

NOTE Confidence: 0.43447363

00:40:14.912 --> 00:40:15.856 I agree.

NOTE Confidence: 0.43447363

00:40:15.856 --> 00:40:19.120 I'd say if you have a network that you feel

NOTE Confidence: 0.43447363

00:40:19.120 --> 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 --> 00:40:24.760 it out of our data.

NOTE Confidence: 0.43447363

00:40:24.760 --> 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 --> 00:40:32.746 found an amygdala change in fMRI and its

NOTE Confidence: 0.43447363

00:40:32.746 --> 00:40:35.076 meta analysis for depression treatment.

NOTE Confidence: 0.43447363

00:40:35.080 --> 00:40:37.299 We pulled that out of our data

NOTE Confidence: 0.43447363

00:40:37.299 --> 00:40:39.201 and didn't find an association

NOTE Confidence: 0.43447363

00:40:39.201 --> 00:40:40.900 with the interventions outcome,

NOTE Confidence: 0.43447363

00:40:40.900 --> 00:40:43.420 but there there are probably other

NOTE Confidence: 0.43447363

00:40:43.420 --> 00:40:45.715 ones that that are better in

NOTE Confidence: 0.43447363

00:40:45.715 --> 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 --> 00:40:51.416 even improving the imaging we

NOTE Confidence: 0.43447363

00:40:51.416 --> 00:40:53.432 do at baseline to make a better,

NOTE Confidence: 0.43447363

00:40:53.440 --> 00:40:54.480 more precise,

NOTE Confidence: 0.43447363

00:40:54.480 --> 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 --> 00:40:59.680 absolutely you can do better.

NOTE Confidence: 0.43447363

00:40:59.680 --> 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 --> 00:41:05.161 collect more fMRI data to make

NOTE Confidence: 0.43447363

00:41:05.161 --> 00:41:06.397 a more reliable target

NOTE Confidence: 0.60579586

00:41:06.400 --> 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 --> 00:41:13.520 improvements in the imaging protocol.

NOTE Confidence: 0.60579586

00:41:13.520 --> 00:41:16.128 All right. Then there's the a lot of

NOTE Confidence: 0.60579586

00:41:16.128 --> 00:41:18.519 papers that are showing this anti

NOTE Confidence: 0.60579586

00:41:18.519 --> 00:41:21.440 correlated like spots really seem to

NOTE Confidence: 0.60579586

00:41:21.440 --> 00:41:23.891 be relevant to depression outcome.

NOTE Confidence: 0.60579586

00:41:23.891 --> 00:41:27.080 But that there is a a recent paper from

NOTE Confidence: 0.60579586

00:41:27.080 --> 00:41:28.680 Connor Liston suggesting that there's

NOTE Confidence: 0.60579586

00:41:28.680 --> 00:41:30.998 a a subgroup of patients that are

NOTE Confidence: 0.60579586

00:41:30.998 --> 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 --> 00:41:36.769 sort of focuses on something they're

NOTE Confidence: 0.60579586

00:41:36.769 --> 00:41:38.827 like oh look at that there's evidence

NOTE Confidence: 0.60579586

00:41:38.827 --> 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 --> 00:41:47.523 to put blinders on and chase the

NOTE Confidence: 0.60579586

00:41:47.523 --> 00:41:49.353 same targets in everybody's labs.

NOTE Confidence: 0.60579586

00:41:49.360 --> 00:41:50.520 But at least for me,

NOTE Confidence: 0.60579586

00:41:50.520 --> 00:41:53.236 I feel like this basic brain measurement

NOTE Confidence: 0.60579586

00:41:53.240 --> 00:41:56.240 data of of the positive connectivity

NOTE Confidence: 0.60579586

00:41:56.240 --> 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 --> 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 --> 00:42:06.964 for the possibility of positively

NOTE Confidence: 0.60579586

00:42:07.020 --> 00:42:08.800 correlated spots being relevant.

NOTE Confidence: 0.40430865

00:42:11.840 --> 00:42:12.347 And then again,

NOTE Confidence: 0.40430865

00:42:12.347 --> 00:42:13.760 since we have a little bit of time,

NOTE Confidence: 0.40430865

00:42:13.760 --> 00:42:15.482 I just want to mention some other

NOTE Confidence: 0.40430865

00:42:15.482 --> 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 --> 00:42:21.132 closed loop things where we're doing

NOTE Confidence: 0.40430865

00:42:21.132 --> 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 --> 00:42:25.862 so personalizing not just the target

NOTE Confidence: 0.40430865

00:42:25.862 --> 00:42:28.000 but also the stimulation parameters.

NOTE Confidence: 0.40430865

00:42:28.000 --> 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 --> 00:42:35.294 methods based on DTI or resting some

NOTE Confidence: 0.40430865

00:42:35.294 --> 00:42:38.026 different ways of splitting up the brain

NOTE Confidence: 0.40430865

00:42:38.026 --> 00:42:40.050 and personalizing target with network

NOTE Confidence: 0.40430865

00:42:40.050 --> 00:42:42.275 control theory and deep learning.

NOTE Confidence: 0.40430865

00:42:42.280 --> 00:42:44.476 We're doing some basic methods things

NOTE Confidence: 0.40430865

00:42:44.476 --> 00:42:47.395 like single pulse TMS with stereo EEG and

NOTE Confidence: 0.40430865

00:42:47.395 --> 00:42:49.920 epilepsy patients trying to get that going,

NOTE Confidence: 0.40430865

00:42:49.920 --> 00:42:52.494 some really cool stuff with KC

NOTE Confidence: 0.40430865

00:42:52.494 --> 00:42:54.210 help partners and neurosurgeon

NOTE Confidence: 0.40430865

00:42:54.282 --> 00:42:58.958 here on personalizing DBS for OCD.

NOTE Confidence: 0.40430865

00:42:58.960 --> 00:43:00.442 Things that I'm looking for collaborators

NOTE Confidence: 0.40430865

00:43:00.442 --> 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 --> 00:43:06.456 There's a controllable TMS

NOTE Confidence: 0.40430865

00:43:06.456 --> 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 --> 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 --> 00:43:19.080 some of the stimulation protocols.

NOTE Confidence: 0.40430865

00:43:19.080 --> 00:43:21.312 Also if you if you have a clinic

NOTE Confidence: 0.40430865

00:43:21.312 --> 00:43:22.559 where you're doing TMS,

NOTE Confidence: 0.40430865

00:43:22.560 --> 00:43:24.436 we should take every single patient that

NOTE Confidence: 0.40430865

00:43:24.436 --> 00:43:26.915 comes in and do some kind of study with them.

NOTE Confidence: 0.40430865

00:43:26.920 --> 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 --> 00:43:32.399 manipulation and seeing how that

NOTE Confidence: 0.40430865

00:43:32.400 --> 00:43:34.324 contributes to patient outcomes.

NOTE Confidence: 0.40430865

00:43:34.324 --> 00:43:36.248 So that's pretty straightforward

NOTE Confidence: 0.40430865

00:43:36.248 --> 00:43:38.568 one that we're starting with

NOTE Confidence: 0.40430865

00:43:38.568 --> 00:43:40.280 a couple of collaborators,

NOTE Confidence: 0.40430865

00:43:40.280 --> 00:43:41.200 I'll say we're not the,

NOTE Confidence: 0.40430865

00:43:41.200 --> 00:43:43.643 we're not the only ones that think

NOTE Confidence: 0.40430865

00:43:43.643 --> 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 --> 00:43:49.520 may be clinically really interesting.

NOTE Confidence: 0.40430865

00:43:49.520 --> 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 --> 00:43:57.464 It also tells you something

NOTE Confidence: 0.40430865

00:43:57.464 --> 00:43:59.186 about circuit engagement that's

NOTE Confidence: 0.40430865

00:43:59.186 --> 00:44:01.278 relevant to depression improvement.

NOTE Confidence: 0.40430865

00:44:01.280 --> 00:44:03.080 So we definitely agree with this.

NOTE Confidence: 0.40430865

00:44:03.080 --> 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 --> 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 --> 00:44:15.965 intervention tools that I think

NOTE Confidence: 0.40430865

00:44:15.965 --> 00:44:17.970 is really important for building

NOTE Confidence: 0.40430865

00:44:18.042 --> 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 --> 00:44:28.164 optimizing the the stimulation parameters

NOTE Confidence: 0.40430865

00:44:28.164 --> 00:44:32.119 and locations going into the future.

NOTE Confidence: 0.40430865

00:44:32.120 --> 00:44:33.040 So look at that.

NOTE Confidence: 0.40430865

00:44:33.040 --> 00:44:33.960 Thanks for your attention.

NOTE Confidence: 0.29934937

00:44:37.680 --> 00:44:38.280 Yes, thank you, Des.