WEBVTT

NOTE duration: ”00:12:29.098”

NOTE Confidence: 0.94266075

00:00:00.160 --> 00:00:01.939 Alright, everyone. We're gonna resume

NOTE Confidence: 0.94266075

00:00:02.159 --> 00:00:03.460 our second part,

NOTE Confidence: 0.96977735

00:00:04.080 --> 00:00:04.720 of this,

NOTE Confidence: 0.6685064

00:00:06.160 --> 00:00:06.899 Dean workshop.

NOTE Confidence: 0.98935676

00:00:07.440 --> 00:00:08.800 We have the next session

NOTE Confidence: 0.98935676

00:00:08.800 --> 00:00:10.080 is two talks by,

NOTE Confidence: 0.97903496

00:00:10.800 --> 00:00:11.539 we entitled

NOTE Confidence: 0.74571276

00:00:11.840 --> 00:00:13.139 Imaging Success Stories,

NOTE Confidence: 0.96091706

00:00:14.425 --> 00:00:16.025 of two heavy users who

NOTE Confidence: 0.96091706

00:00:16.025 --> 00:00:16.585 really have,

NOTE Confidence: 0.9680084

00:00:17.225 --> 00:00:18.685 made a career using imaging.

NOTE Confidence: 0.9251048

00:00:19.545 --> 00:00:21.305 And I'm delighted to introduce

NOTE Confidence: 0.9251048

00:00:21.305 --> 00:00:22.744 them. I'll start with doctor

NOTE Confidence: 0.9251048

00:00:22.744 --> 00:00:24.265 Kelly Cosgrove who received her

NOTE Confidence: 0.9251048

00:00:24.265 --> 00:00:24.765 PhD

NOTE Confidence: 0.94520473

00:00:25.224 --> 00:00:27.085 in clinical psychology from Minnesota,

NOTE Confidence: 0.97382665

00:00:27.680 --> 00:00:29.280 Complete her internship at South

NOTE Confidence: 0.97382665

00:00:29.280 --> 00:00:29.780 Carolina,

NOTE Confidence: 0.9959206

00:00:30.560 --> 00:00:31.940 before coming to psychiatry

NOTE Confidence: 0.9423761

00:00:32.320 --> 00:00:33.760 here, for a post doc

NOTE Confidence: 0.9423761

00:00:33.760 --> 00:00:34.420 at Yale.

NOTE Confidence: 0.90942454

00:00:34.720 --> 00:00:36.100 She's a professor of psychiatry,

NOTE Confidence: 0.90942454

00:00:36.239 --> 00:00:38.180 neuroscience, and radiology and biomedical

NOTE Confidence: 0.90942454

00:00:38.239 --> 00:00:38.739 imaging.

NOTE Confidence: 0.98373944

00:00:39.120 --> 00:00:40.479 And her research focuses on

NOTE Confidence: 0.98373944

00:00:40.479 --> 00:00:42.020 using neuroimaging techniques

NOTE Confidence: 0.8953353

00:00:42.485 --> 00:00:44.245 to understand and inform treatment

NOTE Confidence: 0.8953353

00:00:44.245 --> 00:00:46.104 of psychiatric disorders. Kenny?

NOTE Confidence: 0.9932633

00:00:52.964 --> 00:00:54.085 Hi. Can you guys hear

NOTE Confidence: 0.9932633

00:00:54.085 --> 00:00:55.925 me? Okay. So I'm gonna

NOTE Confidence: 0.9932633

00:00:55.925 --> 00:00:57.305 talk about two studies

NOTE Confidence: 0.97838557

00:00:57.830 --> 00:00:59.350 that we've done using PET

NOTE Confidence: 0.97838557

00:00:59.350 --> 00:01:00.950 to image the neuroimmune system

NOTE Confidence: 0.97838557

00:01:00.950 --> 00:01:02.410 that I think really highlight

NOTE Confidence: 0.97838557

00:01:02.470 --> 00:01:04.410 how important brain PET is.

NOTE Confidence: 0.97838557

00:01:04.709 --> 00:01:06.810 I'm gonna specifically talk about

NOTE Confidence: 0.97838557

00:01:06.950 --> 00:01:07.850 measuring microglia

NOTE Confidence: 0.99469453

00:01:08.470 --> 00:01:09.670 and how that has helped

NOTE Confidence: 0.99469453

00:01:09.670 --> 00:01:10.729 inform our understanding

NOTE Confidence: 0.97016746

00:01:11.110 --> 00:01:12.470 of the neurobiology of post

NOTE Confidence: 0.97016746

00:01:12.470 --> 00:01:14.935 traumatic stress disorder or PTSD.

NOTE Confidence: 0.99273497

00:01:15.795 --> 00:01:16.935 So for some background,

NOTE Confidence: 0.99977666

00:01:17.315 --> 00:01:17.815 microglia

NOTE Confidence: 0.97687984

00:01:18.194 --> 00:01:19.795 are the immune cells of

NOTE Confidence: 0.97687984

00:01:19.795 --> 00:01:21.795 the brain, sometimes referred to

NOTE Confidence: 0.97687984

00:01:21.795 --> 00:01:23.575 as the brain's resonant macrophages.

NOTE Confidence: 0.9693311

00:01:24.435 --> 00:01:26.194 And they're important for healthy

NOTE Confidence: 0.9693311

00:01:26.194 --> 00:01:28.150 brain function, in particular for

NOTE Confidence: 0.9693311

00:01:28.150 --> 00:01:30.330 synaptic function and synaptic plasticity.

NOTE Confidence: 0.98689806

00:01:31.030 --> 00:01:31.909 And when they're in their

NOTE Confidence: 0.98689806

00:01:31.909 --> 00:01:33.750 so called resting state, they

NOTE Confidence: 0.98689806

00:01:33.750 --> 00:01:34.630 have a cell body, and

NOTE Confidence: 0.98689806

00:01:34.630 --> 00:01:35.770 they have all these processes

NOTE Confidence: 0.98906976

00:01:36.069 --> 00:01:36.729 that protrude.

NOTE Confidence: 0.998776

00:01:37.190 --> 00:01:39.130 And those processes are constantly

NOTE Confidence: 0.998776

00:01:39.350 --> 00:01:41.350 surveying and maintaining the brain's

NOTE Confidence: 0.998776

00:01:41.350 --> 00:01:41.850 environment.

NOTE Confidence: 0.9870818

00:01:42.405 --> 00:01:44.505 When there's an immune stimulus,

NOTE Confidence: 0.96455383

00:01:44.965 --> 00:01:46.885 the microglia become activated, they

NOTE Confidence: 0.96455383

00:01:46.885 --> 00:01:48.665 increase in number or proliferate,

NOTE Confidence: 0.9826992

00:01:49.765 --> 00:01:51.365 and they can change shape,

NOTE Confidence: 0.9826992

00:01:51.365 --> 00:01:53.445 ultimately becoming more amoeboid, which

NOTE Confidence: 0.9826992

00:01:53.445 --> 00:01:55.225 helps them engulf debris.

NOTE Confidence: 0.98496825

00:01:55.860 --> 00:01:56.980 And then that in a

NOTE Confidence: 0.98496825

00:01:56.980 --> 00:01:58.980 healthy system, that would reset.

NOTE Confidence: 0.98496825

00:01:58.980 --> 00:02:00.660 And so healthy microglia are

NOTE Confidence: 0.98496825

00:02:00.660 --> 00:02:02.820 associated with healthy neurons. But

NOTE Confidence: 0.98496825

00:02:02.820 --> 00:02:04.820 if there's chronic activation, there's

NOTE Confidence: 0.98496825

00:02:04.820 --> 00:02:06.660 dysfunction in the system, and

NOTE Confidence: 0.98496825

00:02:06.660 --> 00:02:08.340 then that's associated with poor

NOTE Confidence: 0.98496825

00:02:08.340 --> 00:02:09.480 neuronal outcomes,

NOTE Confidence: 0.99456203

00:02:10.035 --> 00:02:11.014 including neurodegeneration.

NOTE Confidence: 0.9973886

00:02:12.915 --> 00:02:14.275 And we can measure a

NOTE Confidence: 0.9973886

00:02:14.275 --> 00:02:15.715 marker of microglia in the

NOTE Confidence: 0.9973886

00:02:15.715 --> 00:02:16.215 brain.

NOTE Confidence: 0.999643

00:02:16.675 --> 00:02:18.275 The protein that we measure

NOTE Confidence: 0.999643

00:02:18.275 --> 00:02:19.175 is translocator

NOTE Confidence: 0.97536755

00:02:19.555 --> 00:02:20.775 protein or TSPO.

NOTE Confidence: 0.99370563

00:02:21.875 --> 00:02:23.635 It's found on mitochondria, and

NOTE Confidence: 0.99370563

00:02:23.635 --> 00:02:25.930 it's present predominantly in microglia.

NOTE Confidence: 0.9411775

00:02:26.470 --> 00:02:28.070 The radio tracer that binds

NOTE Confidence: 0.9411775

00:02:28.070 --> 00:02:29.830 to TSPO is carbon eleven

NOTE Confidence: 0.9411775

00:02:29.830 --> 00:02:31.910 labeled PBR twenty eight. And

NOTE Confidence: 0.9411775

00:02:31.910 --> 00:02:33.110 the radio tracer has been

NOTE Confidence: 0.9411775

00:02:33.110 --> 00:02:33.590 used,

NOTE Confidence: 0.99909055

00:02:33.910 --> 00:02:35.270 to study a variety of

NOTE Confidence: 0.99909055

00:02:35.270 --> 00:02:36.169 immune related

NOTE Confidence: 0.9829492

00:02:36.470 --> 00:02:38.550 disorders, including Alzheimer's. So you

NOTE Confidence: 0.9829492

00:02:38.550 --> 00:02:39.690 can see in the picture,

NOTE Confidence: 0.9829492

00:02:39.965 --> 00:02:41.405 these are axial slices of

NOTE Confidence: 0.9829492

00:02:41.405 --> 00:02:43.084 a human brain, and there's

NOTE Confidence: 0.9829492

00:02:43.084 --> 00:02:44.385 low levels of the radiotracer

NOTE Confidence: 0.98356265

00:02:44.685 --> 00:02:46.444 in the healthy control, but

NOTE Confidence: 0.98356265

00:02:46.444 --> 00:02:47.965 much higher concentration of the

NOTE Confidence: 0.98356265

00:02:47.965 --> 00:02:48.465 radiotracer

NOTE Confidence: 0.9683286

00:02:48.845 --> 00:02:49.805 throughout the brain in the

NOTE Confidence: 0.9683286

00:02:49.805 --> 00:02:52.224 person with Alzheimer's disease, indicating

NOTE Confidence: 0.9683286

00:02:52.284 --> 00:02:54.010 higher levels of microglia or

NOTE Confidence: 0.9683286

00:02:54.010 --> 00:02:55.389 what we might call neuroinflammation.

NOTE Confidence: 0.95785356

00:02:56.889 --> 00:02:58.810 And so we use these

NOTE Confidence: 0.95785356

00:02:58.810 --> 00:03:00.750 techniques to study the neuroimmune

NOTE Confidence: 0.95785356

00:03:00.889 --> 00:03:02.990 system in people with PTSD,

NOTE Confidence: 0.99801993

00:03:03.530 --> 00:03:04.730 and we were interested in

NOTE Confidence: 0.99801993

00:03:04.730 --> 00:03:05.610 that because there was a

NOTE Confidence: 0.99801993

00:03:05.610 --> 00:03:07.070 large literature suggesting

NOTE Confidence: 0.99954706

00:03:07.745 --> 00:03:08.965 a heightened inflammatory

NOTE Confidence: 0.9999137

00:03:09.264 --> 00:03:09.764 profile

NOTE Confidence: 0.99971926

00:03:10.224 --> 00:03:11.364 in people with PTSD.

NOTE Confidence: 0.9770134

00:03:12.305 --> 00:03:14.064 So PTSD is diagnosed when

NOTE Confidence: 0.9770134

00:03:14.064 --> 00:03:15.444 somebody has a life threatening

NOTE Confidence: 0.9770134

00:03:15.504 --> 00:03:17.344 traumatic event, and then they

NOTE Confidence: 0.9770134

00:03:17.344 --> 00:03:19.424 develop symptoms that cluster around

NOTE Confidence: 0.9770134

00:03:19.424 --> 00:03:21.044 threat and loss, like,

NOTE Confidence: 0.966767

00:03:21.519 --> 00:03:23.940 flashbacks, nightmares. There's increased arousal

NOTE Confidence: 0.8788929

00:03:24.319 --> 00:03:25.860 and, typically, mood symptoms.

NOTE Confidence: 0.9772628

00:03:26.239 --> 00:03:28.019 And these symptoms are significantly

NOTE Confidence: 0.9772628

00:03:28.239 --> 00:03:29.940 interfering with their life. So

NOTE Confidence: 0.9772628

00:03:30.080 --> 00:03:31.620 a person under chronic stress

NOTE Confidence: 0.9772628

00:03:31.680 --> 00:03:33.200 with higher levels of immune

NOTE Confidence: 0.9772628

00:03:33.200 --> 00:03:33.700 markers

NOTE Confidence: 0.7271634

00:03:34.159 --> 00:03:35.060 in blood,

NOTE Confidence: 0.9857832

00:03:35.965 --> 00:03:37.405 For example, there's a lot

NOTE Confidence: 0.9857832

00:03:37.405 --> 00:03:38.685 of studies that have shown

NOTE Confidence: 0.9857832

00:03:38.685 --> 00:03:40.365 higher levels of peripheral c

NOTE Confidence: 0.9857832

00:03:40.365 --> 00:03:42.305 reactive protein or CRP,

NOTE Confidence: 0.98604506

00:03:42.685 --> 00:03:44.445 which is a nonspecific immune

NOTE Confidence: 0.98604506

00:03:44.445 --> 00:03:46.125 marker. And the higher the

NOTE Confidence: 0.98604506

00:03:46.125 --> 00:03:47.805 levels of CRP, the worse

NOTE Confidence: 0.98604506

00:03:47.805 --> 00:03:48.465 the PTSD.

NOTE Confidence: 0.97462004

00:03:50.260 --> 00:03:51.300 A lot of studies have

NOTE Confidence: 0.97462004

00:03:51.300 --> 00:03:53.060 also shown higher levels of

NOTE Confidence: 0.97462004

00:03:53.060 --> 00:03:54.740 pro inflammatory cytokines, and these

NOTE Confidence: 0.97462004

00:03:54.740 --> 00:03:56.340 are the signaling proteins that

NOTE Confidence: 0.97462004

00:03:56.340 --> 00:03:58.040 regulate the immune response.

NOTE Confidence: 0.97338283

00:03:58.580 --> 00:04:00.260 And this is supported by

NOTE Confidence: 0.97338283

00:04:00.260 --> 00:04:02.020 preclinical studies. So in rodents

NOTE Confidence: 0.97338283

00:04:02.020 --> 00:04:03.720 with PTSD like behaviors,

NOTE Confidence: 0.92487305

00:04:04.395 --> 00:04:06.715 there's elevated pro inflammatory markers

NOTE Confidence: 0.92487305

00:04:06.715 --> 00:04:07.455 in brain.

NOTE Confidence: 0.9540217

00:04:07.834 --> 00:04:08.875 And so, all this was

NOTE Confidence: 0.9540217

00:04:08.875 --> 00:04:10.235 the basis, served as the

NOTE Confidence: 0.9540217

00:04:10.235 --> 00:04:12.315 basis for advocating testing of

NOTE Confidence: 0.9540217

00:04:12.315 --> 00:04:13.935 anti inflammatory medications,

NOTE Confidence: 0.9827855

00:04:14.475 --> 00:04:15.275 but we didn't know if

NOTE Confidence: 0.9827855

00:04:15.275 --> 00:04:16.635 there was no inflammation in

NOTE Confidence: 0.9827855

00:04:16.635 --> 00:04:18.235 PTSD. And it's important to

NOTE Confidence: 0.9827855

00:04:18.235 --> 00:04:19.514 understand what's happening in the

NOTE Confidence: 0.9827855

00:04:19.514 --> 00:04:21.330 brain to inform treatment of

NOTE Confidence: 0.9827855

00:04:21.330 --> 00:04:22.550 psychiatric disorders.

NOTE Confidence: 0.99776715

00:04:23.730 --> 00:04:24.690 And I think this is

NOTE Confidence: 0.99776715

00:04:24.690 --> 00:04:26.550 where PET is really helpful.

NOTE Confidence: 0.9615574

00:04:27.170 --> 00:04:28.930 So we used the radio

NOTE Confidence: 0.9615574

00:04:28.930 --> 00:04:30.210 tracer in PET to image

NOTE Confidence: 0.9615574

00:04:30.210 --> 00:04:31.670 people with and without PTSD.

NOTE Confidence: 0.9615574

00:04:31.970 --> 00:04:33.010 And based on all the

NOTE Confidence: 0.9615574

00:04:33.010 --> 00:04:33.990 existing literature,

NOTE Confidence: 0.9992629

00:04:34.464 --> 00:04:35.205 we confidently

NOTE Confidence: 0.9944018

00:04:35.505 --> 00:04:36.705 hypothesized that we were gonna

NOTE Confidence: 0.9944018

00:04:36.705 --> 00:04:38.485 find elevated levels of microglia

NOTE Confidence: 0.9778317

00:04:38.945 --> 00:04:39.685 and neuroinflammation,

NOTE Confidence: 0.995008

00:04:41.104 --> 00:04:42.485 and we found the opposite.

NOTE Confidence: 0.995008

00:04:42.705 --> 00:04:44.565 So we found that microglia

NOTE Confidence: 0.995008

00:04:44.705 --> 00:04:46.384 levels were lower in people

NOTE Confidence: 0.995008

00:04:46.384 --> 00:04:47.044 with PTSD.

NOTE Confidence: 0.9991874

00:04:47.345 --> 00:04:47.845 So

NOTE Confidence: 0.9637448

00:04:48.160 --> 00:04:50.100 the green circles are controls.

NOTE Confidence: 0.9637448

00:04:50.240 --> 00:04:51.600 The pink triangles are people

NOTE Confidence: 0.9637448

00:04:51.600 --> 00:04:52.420 with PTSD.

NOTE Confidence: 0.9916965

00:04:53.520 --> 00:04:55.440 Lower levels across these brain

NOTE Confidence: 0.9916965

00:04:55.440 --> 00:04:56.480 regions that are known to

NOTE Confidence: 0.9916965

00:04:56.480 --> 00:04:57.860 be important in PTSD,

NOTE Confidence: 0.9778587

00:04:58.640 --> 00:04:59.140 specifically

NOTE Confidence: 0.93947554

00:04:59.600 --> 00:05:02.180 insula and ventromedial prefrontal cortex.

NOTE Confidence: 0.92904085

00:05:02.714 --> 00:05:03.455 And importantly,

NOTE Confidence: 0.9984694

00:05:04.315 --> 00:05:05.835 this was correlated with clinical

NOTE Confidence: 0.9984694

00:05:05.835 --> 00:05:06.335 outcomes

NOTE Confidence: 0.94305265

00:05:07.035 --> 00:05:08.315 so that the lower the

NOTE Confidence: 0.94305265

00:05:08.315 --> 00:05:10.315 TSPO or microglial levels, the

NOTE Confidence: 0.94305265

00:05:10.315 --> 00:05:11.935 worse the PTSD symptoms.

NOTE Confidence: 0.9480599

00:05:13.915 --> 00:05:15.915 We confirmed in our sample

NOTE Confidence: 0.9480599

00:05:15.915 --> 00:05:17.675 the previous finding about c

NOTE Confidence: 0.9480599

00:05:17.675 --> 00:05:19.260 reactive reactive protein. So in

NOTE Confidence: 0.9480599

00:05:19.260 --> 00:05:20.860 our sample, the people with

NOTE Confidence: 0.9480599

00:05:20.860 --> 00:05:21.360 PTSD

NOTE Confidence: 0.99745685

00:05:21.660 --> 00:05:23.120 did have higher levels of,

NOTE Confidence: 0.98907244

00:05:24.139 --> 00:05:25.279 peripheral CRP,

NOTE Confidence: 0.9785472

00:05:25.660 --> 00:05:27.260 and that was associated with

NOTE Confidence: 0.9785472

00:05:27.260 --> 00:05:28.080 worse symptoms.

NOTE Confidence: 0.9856533

00:05:29.180 --> 00:05:30.700 But then the higher levels

NOTE Confidence: 0.9856533

00:05:30.700 --> 00:05:32.000 of CRP in the periphery

NOTE Confidence: 0.9856533

00:05:32.220 --> 00:05:33.740 were associated with lower levels

NOTE Confidence: 0.9856533

00:05:33.740 --> 00:05:34.615 of TSPO,

NOTE Confidence: 0.9340898

00:05:34.995 --> 00:05:35.735 so high

NOTE Confidence: 0.998591

00:05:36.115 --> 00:05:36.615 peripheral

NOTE Confidence: 0.98064315

00:05:37.235 --> 00:05:39.315 inflammatory markers being associated with

NOTE Confidence: 0.98064315

00:05:39.315 --> 00:05:40.615 a microglial deficit.

NOTE Confidence: 0.9756743

00:05:42.515 --> 00:05:43.735 And this was unexpected,

NOTE Confidence: 0.9919552

00:05:44.195 --> 00:05:45.495 suggesting a dysregulated

NOTE Confidence: 0.87568444

00:05:45.955 --> 00:05:47.895 or a disconnected immune system,

NOTE Confidence: 0.986354

00:05:48.229 --> 00:05:49.509 but this is also just

NOTE Confidence: 0.986354

00:05:49.509 --> 00:05:50.870 one scan, one point in

NOTE Confidence: 0.986354

00:05:50.870 --> 00:05:52.650 time. And we're also interested

NOTE Confidence: 0.9786734

00:05:53.029 --> 00:05:55.210 in learning about neuroimmune function.

NOTE Confidence: 0.9786734

00:05:55.270 --> 00:05:57.190 So what's the response to

NOTE Confidence: 0.9786734

00:05:57.190 --> 00:05:58.330 an immune stressor?

NOTE Confidence: 0.9989915

00:05:58.870 --> 00:06:00.310 And we had previously developed

NOTE Confidence: 0.9989915

00:06:00.310 --> 00:06:00.970 a paradigm

NOTE Confidence: 0.99310905

00:06:01.755 --> 00:06:03.835 to measure neuroimmune function in

NOTE Confidence: 0.99310905

00:06:03.835 --> 00:06:05.375 response to a lipopolysaccharide

NOTE Confidence: 0.9798126

00:06:06.555 --> 00:06:08.815 or LPS injection. So LPS

NOTE Confidence: 0.9798126

00:06:08.955 --> 00:06:10.475 is a bacteria that when

NOTE Confidence: 0.9798126

00:06:10.475 --> 00:06:11.675 given to a person or

NOTE Confidence: 0.9798126

00:06:11.675 --> 00:06:12.175 animal,

NOTE Confidence: 0.9800391

00:06:12.715 --> 00:06:14.895 elicits a very robust, reliable

NOTE Confidence: 0.9800391

00:06:14.955 --> 00:06:15.855 immune response.

NOTE Confidence: 0.96986073

00:06:16.220 --> 00:06:17.100 It's kind of like a

NOTE Confidence: 0.96986073

00:06:17.180 --> 00:06:17.900 you can think of it

NOTE Confidence: 0.96986073

00:06:17.900 --> 00:06:18.860 kind of like a vaccine

NOTE Confidence: 0.96986073

00:06:18.860 --> 00:06:20.380 response in that people get

NOTE Confidence: 0.96986073

00:06:20.540 --> 00:06:21.580 they get a little bit

NOTE Confidence: 0.96986073

00:06:21.580 --> 00:06:22.700 sick. They get flu like

NOTE Confidence: 0.96986073

00:06:22.700 --> 00:06:24.540 symptoms, but it's transient. So

NOTE Confidence: 0.96986073

00:06:24.540 --> 00:06:26.460 it dissipates, and it, they're

NOTE Confidence: 0.96986073

00:06:26.460 --> 00:06:27.420 back to normal by the

NOTE Confidence: 0.96986073

00:06:27.420 --> 00:06:28.880 end of our study day.

NOTE Confidence: 0.96986073

00:06:29.164 --> 00:06:30.525 And our study day is

NOTE Confidence: 0.96986073

00:06:30.525 --> 00:06:31.404 people come in, they get

NOTE Confidence: 0.96986073

00:06:31.404 --> 00:06:33.085 the baseline PET scan, we

NOTE Confidence: 0.96986073

00:06:33.085 --> 00:06:33.904 give LPS,

NOTE Confidence: 0.9935453

00:06:34.365 --> 00:06:35.164 and then we do a

NOTE Confidence: 0.9935453

00:06:35.164 --> 00:06:36.604 second PET scan. And so

NOTE Confidence: 0.9935453

00:06:36.604 --> 00:06:37.904 we can measure the microglial

NOTE Confidence: 0.99778533

00:06:38.685 --> 00:06:39.904 increase or activation

NOTE Confidence: 0.9891786

00:06:40.685 --> 00:06:42.125 by measuring the increase in

NOTE Confidence: 0.9891786

00:06:42.125 --> 00:06:43.645 TSPO from scan one to

NOTE Confidence: 0.9891786

00:06:43.645 --> 00:06:44.910 scan two. And so that's

NOTE Confidence: 0.9891786

00:06:44.910 --> 00:06:46.190 what you see in the

NOTE Confidence: 0.9891786

00:06:46.190 --> 00:06:46.690 black,

NOTE Confidence: 0.9982091

00:06:47.229 --> 00:06:48.690 bar graph. It's a percent

NOTE Confidence: 0.978129

00:06:49.310 --> 00:06:51.470 increase in TSPO levels from

NOTE Confidence: 0.978129

00:06:51.470 --> 00:06:52.750 scan one to scan two.

NOTE Confidence: 0.978129

00:06:52.750 --> 00:06:54.029 And it's across the brain.

NOTE Confidence: 0.978129

00:06:54.029 --> 00:06:55.389 We see this increase of

NOTE Confidence: 0.978129

00:06:55.389 --> 00:06:56.750 an average of almost fifty

NOTE Confidence: 0.978129

00:06:56.750 --> 00:06:57.250 percent

NOTE Confidence: 0.9843748

00:06:57.565 --> 00:06:58.685 across regions, which is a

NOTE Confidence: 0.9843748

00:06:58.685 --> 00:06:59.885 really big signal for a

NOTE Confidence: 0.9843748

00:06:59.885 --> 00:07:01.645 PET study. You can clearly

NOTE Confidence: 0.9843748

00:07:01.645 --> 00:07:02.785 see that in the picture

NOTE Confidence: 0.9629471

00:07:03.404 --> 00:07:04.065 as well.

NOTE Confidence: 0.9754559

00:07:04.605 --> 00:07:06.685 And we measure cytokines and

NOTE Confidence: 0.9754559

00:07:06.685 --> 00:07:08.205 sickness symptoms over the course

NOTE Confidence: 0.9754559

00:07:08.205 --> 00:07:09.745 of the day. So

NOTE Confidence: 0.9791696

00:07:10.490 --> 00:07:12.350 the cytokines listed there increase

NOTE Confidence: 0.9791696

00:07:12.410 --> 00:07:14.030 after the LPS injection.

NOTE Confidence: 0.98163474

00:07:14.490 --> 00:07:15.610 They peak around two to

NOTE Confidence: 0.98163474

00:07:15.610 --> 00:07:16.729 three hours, which is when

NOTE Confidence: 0.98163474

00:07:16.729 --> 00:07:17.850 we do our second PET

NOTE Confidence: 0.98163474

00:07:17.850 --> 00:07:18.350 scan.

NOTE Confidence: 0.9984782

00:07:18.810 --> 00:07:19.789 And there's increases

NOTE Confidence: 0.97140354

00:07:20.090 --> 00:07:21.449 in things like fatigue and

NOTE Confidence: 0.97140354

00:07:21.449 --> 00:07:23.050 sickness and then reductions in

NOTE Confidence: 0.97140354

00:07:23.050 --> 00:07:24.030 things like energy

NOTE Confidence: 0.9723175

00:07:24.475 --> 00:07:26.235 and desire to socialize. And

NOTE Confidence: 0.9723175

00:07:26.235 --> 00:07:27.035 you can see that those

NOTE Confidence: 0.9723175

00:07:27.035 --> 00:07:28.395 are back to baseline by

NOTE Confidence: 0.9723175

00:07:28.395 --> 00:07:29.455 the end of the study.

NOTE Confidence: 0.9723175

00:07:29.675 --> 00:07:31.355 And this is good. This

NOTE Confidence: 0.9723175

00:07:31.355 --> 00:07:32.795 is a healthy response if

NOTE Confidence: 0.9723175

00:07:32.795 --> 00:07:34.395 you are exposed to something

NOTE Confidence: 0.9723175

00:07:34.395 --> 00:07:35.775 like LPS. You want,

NOTE Confidence: 0.9490714

00:07:36.075 --> 00:07:37.115 to have a really nice

NOTE Confidence: 0.9490714

00:07:37.115 --> 00:07:38.575 robust immune response.

NOTE Confidence: 0.9986226

00:07:39.060 --> 00:07:40.180 So we had a subset

NOTE Confidence: 0.9986226

00:07:40.180 --> 00:07:41.300 of people from our first

NOTE Confidence: 0.9986226

00:07:41.300 --> 00:07:42.360 study with PTSD,

NOTE Confidence: 0.96455014

00:07:43.300 --> 00:07:44.900 participate in this paradigm. So

NOTE Confidence: 0.96455014

00:07:44.900 --> 00:07:46.660 have their baseline scan and

NOTE Confidence: 0.96455014

00:07:46.660 --> 00:07:48.500 then stay for LPS in

NOTE Confidence: 0.96455014

00:07:48.500 --> 00:07:49.720 a second PET scan.

NOTE Confidence: 0.97978973

00:07:51.525 --> 00:07:52.805 And we were not as

NOTE Confidence: 0.97978973

00:07:52.805 --> 00:07:54.725 surprised with this finding that

NOTE Confidence: 0.97978973

00:07:54.725 --> 00:07:56.265 there was a suppressed neuroimmune

NOTE Confidence: 0.97978973

00:07:56.325 --> 00:07:57.545 response in PTSD,

NOTE Confidence: 0.98605424

00:07:59.365 --> 00:07:59.865 significantly

NOTE Confidence: 0.9997255

00:08:00.245 --> 00:08:00.745 lower

NOTE Confidence: 0.9992131

00:08:01.765 --> 00:08:02.265 magnitude

NOTE Confidence: 0.9838027

00:08:02.645 --> 00:08:04.725 of neuroimmune response to the

NOTE Confidence: 0.9838027

00:08:04.725 --> 00:08:05.705 LPS injection.

NOTE Confidence: 0.9662772

00:08:06.310 --> 00:08:07.669 So the healthy controls are

NOTE Confidence: 0.9662772

00:08:07.669 --> 00:08:09.449 in blue. People with PTSD

NOTE Confidence: 0.9662772

00:08:09.509 --> 00:08:10.410 are in red,

NOTE Confidence: 0.98360133

00:08:11.509 --> 00:08:13.830 significantly suppressed response across these

NOTE Confidence: 0.98360133

00:08:13.830 --> 00:08:15.050 different brain regions.

NOTE Confidence: 0.9673477

00:08:15.669 --> 00:08:17.289 And this also was correlated

NOTE Confidence: 0.9673477

00:08:17.350 --> 00:08:18.570 with clinical outcomes

NOTE Confidence: 0.9809353

00:08:19.955 --> 00:08:21.235 so that the people that

NOTE Confidence: 0.9809353

00:08:21.235 --> 00:08:23.075 had the most suppressed or

NOTE Confidence: 0.9809353

00:08:23.075 --> 00:08:25.175 the most blunted neuroimmune response,

NOTE Confidence: 0.8758911

00:08:25.875 --> 00:08:28.135 had reported the worst anhedonia,

NOTE Confidence: 0.992749

00:08:28.515 --> 00:08:29.815 anhedonic symptoms.

NOTE Confidence: 0.99917424

00:08:31.169 --> 00:08:31.910 We measured

NOTE Confidence: 0.9984795

00:08:32.450 --> 00:08:34.550 cytokine responses to the LPS.

NOTE Confidence: 0.99773026

00:08:35.570 --> 00:08:37.890 Interestingly, there weren't really very

NOTE Confidence: 0.99773026

00:08:37.890 --> 00:08:39.029 many group differences,

NOTE Confidence: 0.9206145

00:08:40.529 --> 00:08:41.830 except with one exception.

NOTE Confidence: 0.96690977

00:08:42.210 --> 00:08:44.210 And the exception is a

NOTE Confidence: 0.96690977

00:08:44.210 --> 00:08:46.154 g c GM CSF, which

NOTE Confidence: 0.96690977

00:08:46.154 --> 00:08:47.375 is spelled out there.

NOTE Confidence: 0.9679735

00:08:47.755 --> 00:08:49.035 And you can see the

NOTE Confidence: 0.9679735

00:08:49.035 --> 00:08:51.514 blue, control, red, PTSD. There's

NOTE Confidence: 0.9679735

00:08:51.514 --> 00:08:53.195 a much more blunted response

NOTE Confidence: 0.9679735

00:08:53.195 --> 00:08:54.714 in the PTSD group than

NOTE Confidence: 0.9679735

00:08:54.714 --> 00:08:55.774 the control group.

NOTE Confidence: 0.9963939

00:08:56.154 --> 00:08:57.595 And it made sense because

NOTE Confidence: 0.9963939

00:08:57.595 --> 00:08:59.115 this is a cytokine that's

NOTE Confidence: 0.9963939

00:08:59.115 --> 00:09:00.554 important for the initiation of

NOTE Confidence: 0.9963939

00:09:00.554 --> 00:09:01.535 the immune response.

NOTE Confidence: 0.9977056

00:09:01.860 --> 00:09:02.820 So you have sort of

NOTE Confidence: 0.9977056

00:09:02.820 --> 00:09:03.559 a blunted,

NOTE Confidence: 0.9931285

00:09:04.740 --> 00:09:06.200 immune response in the periphery

NOTE Confidence: 0.9931285

00:09:06.339 --> 00:09:07.720 associated with the blunted,

NOTE Confidence: 0.99926674

00:09:08.500 --> 00:09:10.420 response in the brain. And

NOTE Confidence: 0.99926674

00:09:10.420 --> 00:09:11.880 because these were originally

NOTE Confidence: 0.973185

00:09:12.260 --> 00:09:13.940 unexpected findings, we did a

NOTE Confidence: 0.973185

00:09:13.940 --> 00:09:15.160 little bit of,

NOTE Confidence: 0.9355466

00:09:16.245 --> 00:09:18.084 digging, and we collaborated with

NOTE Confidence: 0.9355466

00:09:18.084 --> 00:09:20.105 doctor Matt Jurginty, who has

NOTE Confidence: 0.9314995

00:09:20.565 --> 00:09:22.105 post mortem brain tissue,

NOTE Confidence: 0.9763798

00:09:22.964 --> 00:09:24.644 from people with PTSD, from

NOTE Confidence: 0.9763798

00:09:24.644 --> 00:09:26.324 a PTSD brain bank. And

NOTE Confidence: 0.9763798

00:09:26.324 --> 00:09:27.125 so then he can look

NOTE Confidence: 0.9763798

00:09:27.125 --> 00:09:28.004 at some of these same

NOTE Confidence: 0.9763798

00:09:28.004 --> 00:09:29.605 markers that we look at

NOTE Confidence: 0.9763798

00:09:29.605 --> 00:09:30.425 with PEP.

NOTE Confidence: 0.99978155

00:09:30.870 --> 00:09:31.910 And if you look at

NOTE Confidence: 0.99978155

00:09:31.910 --> 00:09:32.809 the pink

NOTE Confidence: 0.99840903

00:09:33.270 --> 00:09:34.630 bar graph, what this is

NOTE Confidence: 0.99840903

00:09:34.630 --> 00:09:36.250 showing is that in

NOTE Confidence: 0.9211447

00:09:36.710 --> 00:09:38.550 people with PTSD, there's a

NOTE Confidence: 0.9211447

00:09:38.550 --> 00:09:39.050 significantly

NOTE Confidence: 0.9945015

00:09:39.990 --> 00:09:41.610 lower expression of TSPO,

NOTE Confidence: 0.91481876

00:09:42.950 --> 00:09:43.610 in PTSD

NOTE Confidence: 0.96763295

00:09:43.910 --> 00:09:45.585 relative to the control group.

NOTE Confidence: 0.96763295

00:09:45.825 --> 00:09:47.425 And this was more apparent

NOTE Confidence: 0.96763295

00:09:47.425 --> 00:09:48.785 in the females in this

NOTE Confidence: 0.96763295

00:09:48.785 --> 00:09:49.285 sample.

NOTE Confidence: 0.94469833

00:09:49.905 --> 00:09:51.905 And the other side shows

NOTE Confidence: 0.94469833

00:09:51.905 --> 00:09:53.985 that he looked at numbers

NOTE Confidence: 0.94469833

00:09:53.985 --> 00:09:55.265 of microglia, and this is

NOTE Confidence: 0.94469833

00:09:55.265 --> 00:09:57.125 dorsal lateral prefrontal cortex,

NOTE Confidence: 0.98195904

00:09:57.585 --> 00:09:58.705 and found that in the

NOTE Confidence: 0.98195904

00:09:58.705 --> 00:10:00.485 PTSD group, there was significantly

NOTE Confidence: 0.98195904

00:10:00.705 --> 00:10:02.740 fewer micro glia, compared to

NOTE Confidence: 0.98195904

00:10:02.740 --> 00:10:04.100 the control group. And so

NOTE Confidence: 0.98195904

00:10:04.100 --> 00:10:05.059 this was just sort of

NOTE Confidence: 0.98195904

00:10:05.059 --> 00:10:06.980 a nice extra confirmation of

NOTE Confidence: 0.98195904

00:10:06.980 --> 00:10:08.580 our finding that what we

NOTE Confidence: 0.98195904

00:10:08.580 --> 00:10:09.860 think we have found is

NOTE Confidence: 0.98195904

00:10:09.860 --> 00:10:10.440 a microglial

NOTE Confidence: 0.97886294

00:10:11.140 --> 00:10:12.120 or a neuroimmune

NOTE Confidence: 0.9997687

00:10:12.580 --> 00:10:13.080 deficit

NOTE Confidence: 0.93778884

00:10:13.540 --> 00:10:14.280 in this,

NOTE Confidence: 0.9961968

00:10:15.059 --> 00:10:15.559 disorder.

NOTE Confidence: 0.8953152

00:10:17.235 --> 00:10:18.755 And and so we think

NOTE Confidence: 0.8953152

00:10:18.755 --> 00:10:20.035 that instead of having this

NOTE Confidence: 0.8953152

00:10:20.035 --> 00:10:22.455 sort of overly activated microglia

NOTE Confidence: 0.8953152

00:10:22.515 --> 00:10:23.095 and neuroinflammation,

NOTE Confidence: 0.9529374

00:10:24.195 --> 00:10:25.735 that over time, the microglia

NOTE Confidence: 0.9529374

00:10:25.955 --> 00:10:27.155 are sort of burning out

NOTE Confidence: 0.9529374

00:10:27.155 --> 00:10:29.495 or becoming dystrophic or senescent.

NOTE Confidence: 0.9886386

00:10:30.100 --> 00:10:30.980 And then when they're in

NOTE Confidence: 0.9886386

00:10:30.980 --> 00:10:32.660 this state, they can't they

NOTE Confidence: 0.9886386

00:10:32.660 --> 00:10:34.440 can't support healthy brain function.

NOTE Confidence: 0.9749365

00:10:34.820 --> 00:10:36.500 They can't support healthy synaptic

NOTE Confidence: 0.9749365

00:10:36.500 --> 00:10:38.120 function or synaptic plasticity,

NOTE Confidence: 0.97654873

00:10:38.660 --> 00:10:39.780 and that this may be

NOTE Confidence: 0.97654873

00:10:39.780 --> 00:10:41.780 contributing to symptom severity or

NOTE Confidence: 0.97654873

00:10:41.780 --> 00:10:43.220 sort of contributing to the

NOTE Confidence: 0.97654873

00:10:43.220 --> 00:10:44.360 maintenance of PTSD.

NOTE Confidence: 0.9738129

00:10:45.215 --> 00:10:46.335 And that changes how we

NOTE Confidence: 0.9738129

00:10:46.335 --> 00:10:47.455 think about treating it because

NOTE Confidence: 0.9738129

00:10:47.455 --> 00:10:48.575 instead of sort of trying

NOTE Confidence: 0.9738129

00:10:48.575 --> 00:10:50.275 to tamp down the inflammation,

NOTE Confidence: 0.9738129

00:10:50.495 --> 00:10:51.535 we wanna think about how

NOTE Confidence: 0.9738129

00:10:51.535 --> 00:10:53.075 can we rescue the deficit.

NOTE Confidence: 0.9977254

00:10:54.095 --> 00:10:55.535 And we're working on some

NOTE Confidence: 0.9977254

00:10:55.535 --> 00:10:56.815 ideas about that. I would

NOTE Confidence: 0.9977254

00:10:56.815 --> 00:10:57.695 be happy to hear if

NOTE Confidence: 0.9977254

00:10:57.695 --> 00:10:59.695 anybody has any ideas as

NOTE Confidence: 0.9977254

00:10:59.695 --> 00:11:00.195 well.

NOTE Confidence: 0.96197355

00:11:00.959 --> 00:11:02.160 And I just wanna highlight

NOTE Confidence: 0.96197355

00:11:02.160 --> 00:11:03.600 the importance of pet, right?

NOTE Confidence: 0.96197355

00:11:03.600 --> 00:11:05.279 Because our hypothesis was based

NOTE Confidence: 0.96197355

00:11:05.279 --> 00:11:07.220 on peripheral findings in people

NOTE Confidence: 0.97115886

00:11:07.920 --> 00:11:10.019 and in from the preclinical

NOTE Confidence: 0.97115886

00:11:10.160 --> 00:11:11.920 literature, and we assumed that

NOTE Confidence: 0.97115886

00:11:11.920 --> 00:11:12.899 that would hold.

NOTE Confidence: 0.992536

00:11:13.425 --> 00:11:14.545 And I think there's lots

NOTE Confidence: 0.992536

00:11:14.545 --> 00:11:15.265 of areas,

NOTE Confidence: 0.9739391

00:11:15.585 --> 00:11:17.184 particularly in neuroscience, where a

NOTE Confidence: 0.9739391

00:11:17.184 --> 00:11:18.465 lot of our understanding comes

NOTE Confidence: 0.9739391

00:11:18.465 --> 00:11:19.925 from the preclinical literature.

NOTE Confidence: 0.94924396

00:11:20.625 --> 00:11:22.225 And it's very important to

NOTE Confidence: 0.94924396

00:11:22.225 --> 00:11:23.825 have techniques such as PET

NOTE Confidence: 0.94924396

00:11:23.825 --> 00:11:25.184 where we can translate those

NOTE Confidence: 0.94924396

00:11:25.184 --> 00:11:25.684 findings

NOTE Confidence: 0.96657705

00:11:26.059 --> 00:11:27.420 and measure brain chemistry in

NOTE Confidence: 0.96657705

00:11:27.420 --> 00:11:28.459 people who are living with

NOTE Confidence: 0.96657705

00:11:28.459 --> 00:11:29.980 the disorder that we're interested

NOTE Confidence: 0.96657705

00:11:29.980 --> 00:11:30.720 in treating.

NOTE Confidence: 0.9538516

00:11:32.300 --> 00:11:33.740 There are limitations of the

NOTE Confidence: 0.9538516

00:11:33.740 --> 00:11:35.600 radio tracer that we used.

NOTE Confidence: 0.9538516

00:11:35.820 --> 00:11:36.779 We are working with the

NOTE Confidence: 0.9538516

00:11:36.779 --> 00:11:37.820 Pet Center and lots of

NOTE Confidence: 0.9538516

00:11:37.820 --> 00:11:38.940 other people in the field

NOTE Confidence: 0.9538516

00:11:38.940 --> 00:11:40.540 are working on developing radio

NOTE Confidence: 0.9538516

00:11:40.540 --> 00:11:41.040 tracers,

NOTE Confidence: 0.9665838

00:11:42.325 --> 00:11:44.565 that label different proteins in

NOTE Confidence: 0.9665838

00:11:44.565 --> 00:11:46.485 the neuroimmune system. And so

NOTE Confidence: 0.9665838

00:11:46.485 --> 00:11:47.705 these are just some examples

NOTE Confidence: 0.9665838

00:11:47.765 --> 00:11:50.025 from a review paper of

NOTE Confidence: 0.9665838

00:11:50.245 --> 00:11:52.085 targets that we have tracers

NOTE Confidence: 0.9665838

00:11:52.085 --> 00:11:54.165 for or that we are

NOTE Confidence: 0.9665838

00:11:54.165 --> 00:11:56.665 in develop developing tracers for.

NOTE Confidence: 0.9435641

00:11:58.820 --> 00:12:00.820 We have used these techniques

NOTE Confidence: 0.9435641

00:12:00.820 --> 00:12:01.940 and apply them to other

NOTE Confidence: 0.9435641

00:12:01.940 --> 00:12:03.080 psychiatric disorders,

NOTE Confidence: 0.966049

00:12:03.940 --> 00:12:05.140 and many other people have

NOTE Confidence: 0.966049

00:12:05.140 --> 00:12:06.420 used these techniques and apply

NOTE Confidence: 0.966049

00:12:06.420 --> 00:12:07.940 them to other psychiatric disorders

NOTE Confidence: 0.966049

00:12:07.940 --> 00:12:08.440 in

NOTE Confidence: 0.7703383

00:12:08.900 --> 00:12:09.559 the department.

NOTE Confidence: 0.9582233

00:12:09.985 --> 00:12:11.425 We have really interesting findings

NOTE Confidence: 0.9582233

00:12:11.425 --> 00:12:12.705 in people with alcohol use

NOTE Confidence: 0.9582233

00:12:12.705 --> 00:12:13.505 disorder, and we have a

NOTE Confidence: 0.9582233

00:12:13.505 --> 00:12:15.105 poster later if you are

NOTE Confidence: 0.9582233

00:12:15.105 --> 00:12:16.965 interested in hearing about that.

NOTE Confidence: 0.9858508

00:12:18.073 --> 00:12:19.193 And then I would just

NOTE Confidence: 0.9858508

00:12:19.193 --> 00:12:21.193 like to thank our funding

NOTE Confidence: 0.9858508

00:12:21.193 --> 00:12:22.333 sources, participants,

NOTE Confidence: 0.9946996

00:12:23.113 --> 00:12:24.313 and these are some of

NOTE Confidence: 0.9946996

00:12:24.313 --> 00:12:26.393 the individuals who really helped

NOTE Confidence: 0.9946996

00:12:26.393 --> 00:12:27.913 lead, the studies that I

NOTE Confidence: 0.9946996

00:12:27.913 --> 00:12:28.973 talked about today.