WEBVTT

NOTE duration:"01:09:51.2640000"

NOTE language:en-us

NOTE Confidence: 0.85609347

00:00:00.000 --> 00:00:03.320 For the annual Flynn Lecture an it's my

NOTE Confidence: 0.85609347

00:00:03.320 --> 00:00:06.275 pleasure to be able to introduce both

NOTE Confidence: 0.85609347

00:00:06.275 --> 00:00:09.540 the lecture and also our speaker today,

NOTE Confidence: 0.85609347

00:00:09.540 --> 00:00:12.604 so the Flint Lecture is in honor of

NOTE Confidence: 0.85609347

00:00:12.604 --> 00:00:15.588 a faculty member in our department.

NOTE Confidence: 0.85609347

00:00:15.590 --> 00:00:16.954 Doctor John P. Flynn,

NOTE Confidence: 0.85609347

00:00:16.954 --> 00:00:19.630 who was a pioneer in the understanding

NOTE Confidence: 0.85609347

00:00:19.630 --> 00:00:22.936 how the brain contributes to behavior,

NOTE Confidence: 0.85609347

00:00:22.940 --> 00:00:25.971 and it's hard to think now of

NOTE Confidence: 0.85609347

00:00:25.971 --> 00:00:28.120 how revolutionary his work was,

NOTE Confidence: 0.85609347

00:00:28.120 --> 00:00:29.584 but in particular.

NOTE Confidence: 0.85609347

00:00:29.584 --> 00:00:33.600 I look back to this paper from 1964,

NOTE Confidence: 0.85609347

00:00:33.600 --> 00:00:36.564 which Full disclosure I was already

NOTE Confidence: 0.85609347

00:00:36.564 --> 00:00:40.424 born but just barely and what he and

NOTE Confidence: 0.85609347

00:00:40.424 --> 00:00:43.118 his colleagues did was to stimulate

NOTE Confidence: 0.85609347

00:00:43.215 --> 00:00:46.545 part of the cat brain and to find that

NOTE Confidence: 0.85609347

00:00:46.545 --> 00:00:51.204 the cat would attack a rat or another.

NOTE Confidence: 0.85609347

00:00:51.210 --> 00:00:54.346 Other rat sorry a cat would attacker at

NOTE Confidence: 0.85609347

00:00:54.346 --> 00:00:57.891 yes and that this would be completely

NOTE Confidence: 0.85609347

00:00:57.891 --> 00:01:00.561 independent of any other stimulus.

NOTE Confidence: 0.85609347

00:01:00.570 --> 00:01:03.846 Any other thing happening in the environment?

NOTE Confidence: 0.85609347

00:01:03.850 --> 00:01:05.718 Just this electrical stimulation

NOTE Confidence: 0.85609347

00:01:05.718 --> 00:01:07.586 could result in attack,

NOTE Confidence: 0.85609347

00:01:07.590 --> 00:01:10.824 and it began to form our concept

NOTE Confidence: 0.85609347

00:01:10.824 --> 00:01:13.694 that aggression had a brain basis

NOTE Confidence: 0.85609347

00:01:13.694 --> 00:01:16.478 and this work is still inspiring.

NOTE Confidence: 0.85609347

00:01:16.480 --> 00:01:17.755 Today in 2011,

NOTE Confidence: 0.85609347

00:01:17.755 --> 00:01:20.305 a paper in which the hypothalamus

NOTE Confidence: 0.85609347

00:01:20.305 --> 00:01:22.619 was stimulated with light.

NOTE Confidence: 0.85609347

00:01:22.620 --> 00:01:25.115 In using novel molecular genetic

NOTE Confidence: 0.85609347

00:01:25.115 --> 00:01:28.107 tools was really based very much

NOTE Confidence: 0.85609347

00:01:28.107 --> 00:01:30.949 on this 1964 paper and Alan Lewis,

NOTE Confidence: 0.85609347

00:01:30.950 --> 00:01:34.359 who was a resident in our department

NOTE Confidence: 0.85609347

00:01:34.359 --> 00:01:36.969 and who worked in our lab,

NOTE Confidence: 0.85609347

00:01:36.970 --> 00:01:39.748 also followed up on this work

NOTE Confidence: 0.85609347

00:01:39.748 --> 00:01:40.674 using molecular,

NOTE Confidence: 0.85609347

00:01:40.680 --> 00:01:42.800 genetic and pharmacological tools.

NOTE Confidence: 0.85609347

00:01:42.800 --> 00:01:45.980 Looking at Astro choline and its

NOTE Confidence: 0.85609347

00:01:46.061 --> 00:01:48.053 receptors so seriously influential

NOTE Confidence: 0.85609347

00:01:48.053 --> 00:01:51.041 from the time that this work

NOTE Confidence: 0.85609347

00:01:51.125 --> 00:01:53.339 was done to the present day.

NOTE Confidence: 0.85609347

00:01:53.340 --> 00:01:56.140 I also want to note that we have

NOTE Confidence: 0.85609347

00:01:56.140 --> 00:01:58.489 Doctor Flynn's daughter Sarah Flynn.

NOTE Confidence: 0.85609347

00:01:58.490 --> 00:02:00.716 Joining us today and it's always

NOTE Confidence: 0.85609347

00:02:00.716 --> 00:02:03.393 been one of the real pleasures of

NOTE Confidence: 0.85609347

00:02:03.393 --> 00:02:05.990 this of this lecture for me to

NOTE Confidence: 0.85609347

00:02:06.070 --> 00:02:08.390 meet Doctor Flynn's late life,

NOTE Confidence: 0.85609347

00:02:08.390 --> 00:02:10.370 Holda and his daughter Sarah.

NOTE Confidence: 0.85609347

00:02:10.370 --> 00:02:13.925 I wish that we could be meeting in person,

NOTE Confidence: 0.85609347

00:02:13.930 --> 00:02:16.306 but certainly in the coming years.

NOTE Confidence: 0.85609347

00:02:16.310 --> 00:02:18.686 As as we move beyond this

NOTE Confidence: 0.85609347

00:02:18.686 --> 00:02:20.270 pandemic will move back,

NOTE Confidence: 0.85609347

00:02:20.270 --> 00:02:22.274 hopefully to to having

NOTE Confidence: 0.85609347

00:02:22.274 --> 00:02:24.278 this lecture in person.

NOTE Confidence: 0.85609347

00:02:24.280 --> 00:02:27.298 The winners of or the winners.

NOTE Confidence: 0.85609347

00:02:27.300 --> 00:02:30.499 The presenters of this lecture have been

NOTE Confidence: 0.85609347

00:02:30.499 --> 00:02:33.350 luminaries and our current presenter,

NOTE Confidence: 0.85609347

00:02:33.350 --> 00:02:37.206 Doctor Campti is is no less of a

NOTE Confidence: 0.85609347

00:02:37.206 --> 00:02:40.290 luminary than any of our previous

NOTE Confidence: 0.85609347

00:02:40.290 --> 00:02:43.940 presenters Ann Dr Ty did her work.

NOTE Confidence: 0.85609347

00:02:43.940 --> 00:02:47.454 Her undergraduate training at the at MIT,

NOTE Confidence: 0.85609347

00:02:47.460 --> 00:02:51.219 where she graduated with a major in

NOTE Confidence: 0.85609347

00:02:51.219 --> 00:02:54.599 brain and cognitive sciences in 2003.

NOTE Confidence: 0.85609347

00:02:54.600 --> 00:02:57.967 After taking a year off to travel,

NOTE Confidence: 0.85609347

00:02:57.970 --> 00:03:00.693 she joined Patricia Genics lab at UCSF

NOTE Confidence: 0.85609347

00:03:00.693 --> 00:03:03.740 and began her work in electrophysiological

NOTE Confidence: 0.85609347

00:03:03.740 --> 00:03:06.136 recording from brain areas.

NOTE Confidence: 0.85609347

00:03:06.140 --> 00:03:08.064 Important for emotional behavior

NOTE Confidence: 0.85609347

00:03:08.064 --> 00:03:10.469 and connecting those circuits too.

NOTE Confidence: 0.85609347

00:03:10.470 --> 00:03:11.928 Important behavioral outputs.

NOTE Confidence: 0.85609347

00:03:11.928 --> 00:03:14.844 She then moved to Carl Daesrath

NOTE Confidence: 0.85609347

00:03:14.844 --> 00:03:16.794 Laboratory at Stanford University

NOTE Confidence: 0.85609347

00:03:16.794 --> 00:03:18.646 as a postdoctoral fellow,

NOTE Confidence: 0.85609347

00:03:18.650 --> 00:03:21.536 where she began to use the

NOTE Confidence: 0.85609347

00:03:21.536 --> 00:03:22.979 molecular genetic approaches.

NOTE Confidence: 0.85609347

00:03:22.980 --> 00:03:25.560 The labeling approaches to identify

NOTE Confidence: 0.85609347

00:03:25.560 --> 00:03:27.108 specific neuronal subtypes.

NOTE Confidence: 0.85609347

00:03:27.110 --> 00:03:29.228 These stimulate stimula Tori approaches that

NOTE Confidence: 0.85609347

00:03:29.228 --> 00:03:31.860 allowed her to isolate specific sub circuits,

NOTE Confidence: 0.85609347

00:03:31.860 --> 00:03:33.680 and these tools allowed her

NOTE Confidence: 0.85609347

00:03:33.680 --> 00:03:35.136 to unleash your creativity.

NOTE Confidence: 0.85609347

00:03:35.140 --> 00:03:37.464 Ann became the basis of the work

NOTE Confidence: 0.85609347

00:03:37.464 --> 00:03:39.715 that her lab members she and

NOTE Confidence: 0.85609347

00:03:39.715 --> 00:03:42.073 her lab members have been doing.

NOTE Confidence: 0.85609347

00:03:42.080 --> 00:03:43.202 To this day,

NOTE Confidence: 0.85609347

00:03:43.202 --> 00:03:45.072 she became an assistant professor

NOTE Confidence: 0.85609347

00:03:45.072 --> 00:03:46.459 at MIT in 2012,

NOTE Confidence: 0.84423935

00:03:46.460 --> 00:03:47.920 was rapidly promoted to

NOTE Confidence: 0.84423935

00:03:47.920 --> 00:03:49.380 associate professor with tenure,

NOTE Confidence: 0.84423935

00:03:49.380 --> 00:03:51.200 and then moved her laboratory

NOTE Confidence: 0.84423935

00:03:51.200 --> 00:03:52.656 to the Salk Institute,

NOTE Confidence: 0.84423935

00:03:52.660 --> 00:03:55.876 where she was promoted to professor.

NOTE Confidence: 0.84423935

00:03:55.880 --> 00:03:57.800 Doctor Ty is currently professor

NOTE Confidence: 0.84423935

00:03:57.800 --> 00:04:00.240 and the Wiley Veiled Chair of

NOTE Confidence: 0.84423935

00:04:00.240 --> 00:04:02.515 Systems Neuroscience at the Salk

NOTE Confidence: 0.84423935

00:04:02.515 --> 00:04:04.335 Institute for Biological Sciences.

NOTE Confidence: 0.84423935

00:04:04.340 --> 00:04:07.700 She's also an adjunct faculty member at the

NOTE Confidence: 0.84423935

00:04:07.700 --> 00:04:10.688 University of California at San Diego and,

NOTE Confidence: 0.84423935

00:04:10.690 --> 00:04:11.854 as I mentioned,

NOTE Confidence: 0.84423935

00:04:11.854 --> 00:04:14.182 her research broadly is focused on

NOTE Confidence: 0.84423935

00:04:14.182 --> 00:04:16.074 understanding the neurobiological mechanisms

NOTE Confidence: 0.84423935

00:04:16.074 --> 00:04:18.469 underlying social and emotional processes

NOTE Confidence: 0.84423935

00:04:18.469 --> 00:04:21.678 at the circuit level at the cellular level,

NOTE Confidence: 0.84423935

00:04:21.680 --> 00:04:23.632 at the synaptic level,

NOTE Confidence: 0.84423935

00:04:23.632 --> 00:04:25.584 and particularly those relevant

NOTE Confidence: 0.84423935

00:04:25.584 --> 00:04:27.200 to psychiatric illness.

NOTE Confidence: 0.84423935

00:04:27.200 --> 00:04:29.582 Professor ties been recognized with a

NOTE Confidence: 0.84423935

00:04:29.582 --> 00:04:31.640 number of prestigious research awards.

NOTE Confidence: 0.84423935

00:04:31.640 --> 00:04:32.412 In fact,

NOTE Confidence: 0.84423935

00:04:32.412 --> 00:04:36.004 it's hard to find out an award that has

NOTE Confidence: 0.84423935

00:04:36.004 --> 00:04:39.712 not really pulled out her work to to honor.

NOTE Confidence: 0.84423935

00:04:39.720 --> 00:04:41.745 She received the NIH Director's

NOTE Confidence: 0.84423935

00:04:41.745 --> 00:04:42.960 New Innovator Award,

NOTE Confidence: 0.84423935

00:04:42.960 --> 00:04:44.980 the presidential early Career award.

NOTE Confidence: 0.84423935

00:04:44.980 --> 00:04:45.786 For scientists,

NOTE Confidence: 0.84423935

00:04:45.786 --> 00:04:46.995 scientists and engineering

NOTE Confidence: 0.84423935

00:04:46.995 --> 00:04:48.607 from the White House,

NOTE Confidence: 0.84423935

00:04:48.610 --> 00:04:50.222 the Society for Neuroscience

NOTE Confidence: 0.84423935

00:04:50.222 --> 00:04:51.834 is Young Investigator award.

NOTE Confidence: 0.84423935

00:04:51.840 --> 00:04:54.190 She was listed as technology

NOTE Confidence: 0.84423935

00:04:54.190 --> 00:04:56.540 reviews Top 35 in among.

NOTE Confidence: 0.84423935

00:04:56.540 --> 00:04:59.634 The reviews top 35 innovators under 35.

NOTE Confidence: 0.84423935

00:04:59.640 --> 00:05:01.408 She received the NIH

NOTE Confidence: 0.84423935

00:05:01.408 --> 00:05:02.734 Director's Pioneer Award,

NOTE Confidence: 0.84423935

00:05:02.740 --> 00:05:04.955 and she's also been recognized

NOTE Confidence: 0.84423935

00:05:04.955 --> 00:05:07.170 with a number of awards.

NOTE Confidence: 0.84423935

00:05:07.170 --> 00:05:09.390 From mentoring at the undergraduate,

NOTE Confidence: 0.84423935

00:05:09.390 --> 00:05:11.278 graduate and postdoctoral level,

NOTE Confidence: 0.84423935

00:05:11.278 --> 00:05:15.080 and this is a place where I know

NOTE Confidence: 0.84423935

00:05:15.080 --> 00:05:17.720 that she really has made incredible

NOTE Confidence: 0.84423935

00:05:17.720 --> 00:05:20.680 efforts and I want to highlight her

NOTE Confidence: 0.84423935

00:05:20.680 --> 00:05:23.646 trainees who have been at the forefront

NOTE Confidence: 0.84423935

00:05:23.646 --> 00:05:26.544 of the wiki project to recognize.

NOTE Confidence: 0.84423935

00:05:26.550 --> 00:05:28.202 Scientists who are generally

NOTE Confidence: 0.84423935

00:05:28.202 --> 00:05:29.028 under represented,

NOTE Confidence: 0.84423935

00:05:29.030 --> 00:05:31.210 both women and members of

NOTE Confidence: 0.84423935

00:05:31.210 --> 00:05:32.954 underrepresented groups in Wikipedia

NOTE Confidence: 0.84423935

00:05:32.954 --> 00:05:35.236 for the work that they've done,

NOTE Confidence: 0.84423935

00:05:35.240 --> 00:05:36.896 and it's no short.

NOTE Confidence: 0.84423935

00:05:36.896 --> 00:05:38.966 Nothing short of a revolution.

NOTE Confidence: 0.84423935

00:05:38.970 --> 00:05:41.616 What she and her trainees have done

NOTE Confidence: 0.84423935

00:05:41.616 --> 00:05:44.350 to further the efforts of outreach,

NOTE Confidence: 0.84423935

00:05:44.350 --> 00:05:47.490 diversity and inclusion in science.

NOTE Confidence: 0.84423935

00:05:47.490 --> 00:05:49.800 So without any further ado,

NOTE Confidence: 0.84423935

00:05:49.800 --> 00:05:52.720 I'm going to now.

NOTE Confidence: 0.84423935

00:05:52.720 --> 00:05:55.222 Turn the podium over to doctor

NOTE Confidence: 0.84423935

00:05:55.222 --> 00:05:56.056 ties presentation.

NOTE Confidence: 0.84423935

00:05:56.060 --> 00:05:58.145 She will be joining us

NOTE Confidence: 0.84423935

00:05:58.145 --> 00:06:00.230 for questions at the end,

NOTE Confidence: 0.84423935

00:06:00.230 --> 00:06:03.558 so please do put them in the chat.

NOTE Confidence: 0.84423935

00:06:03.560 --> 00:06:06.738 I will moderate the chat as after

NOTE Confidence: 0.84423935

00:06:06.738 --> 00:06:08.961 the presentation is finished and

NOTE Confidence: 0.84423935

00:06:08.961 --> 00:06:11.656 I hope that you will all join

NOTE Confidence: 0.84423935

00:06:11.656 --> 00:06:14.280 me in welcoming doctor Thai.

NOTE Confidence: 0.84423935

00:06:14.280 --> 00:06:18.160 And I will now. Share her presentation.

NOTE Confidence: 0.83259946

00:06:25.790 --> 00:06:28.382 Hi, it's such a pleasure to be here

NOTE Confidence: 0.83259946

00:06:28.382 --> 00:06:30.770 for the Flynn lecture at Yale,

NOTE Confidence: 0.83259946

00:06:30.770 --> 00:06:32.842 where I'm going to tell you about

NOTE Confidence: 0.83259946

00:06:32.842 --> 00:06:34.682 the neural circuits of motivational

NOTE Confidence: 0.83259946

00:06:34.682 --> 00:06:36.470 processing focusing on violence.

NOTE Confidence: 0.68969816

00:06:40.450 --> 00:06:44.626 Some stimuli carry innate emotional valence.

NOTE Confidence: 0.68969816

00:06:44.630 --> 00:06:47.480 No training or learning is required

NOTE Confidence: 0.68969816

00:06:47.480 --> 00:06:50.059 to have emotional responses to them.

NOTE Confidence: 0.68969816

00:06:50.060 --> 00:06:51.940 Other stimuli are initially neutral,

NOTE Confidence: 0.68969816

00:06:51.940 --> 00:06:53.810 unless paired with an emotionally

NOTE Confidence: 0.68969816

00:06:53.810 --> 00:06:54.558 significant stimulus.

NOTE Confidence: 0.68969816

00:06:54.560 --> 00:06:57.560 So to have an emotional response to this,

NOTE Confidence: 0.68969816

00:06:57.560 --> 00:07:01.344 we need to learn the associations between the

NOTE Confidence: 0.68969816

00:07:01.344 --> 00:07:04.956 Twin Towers and the horrific events of 911.

NOTE Confidence: 0.68969816

00:07:04.960 --> 00:07:08.434 There's been quite a bit of controversy in my

NOTE Confidence: 0.68969816

00:07:08.434 --> 00:07:11.201 field about whether emotion is experienced

NOTE Confidence: 0.68969816

00:07:11.201 --> 00:07:14.797 by humans and by animals in the same way.

NOTE Confidence: 0.68969816

00:07:14.800 --> 00:07:16.960 There is no way to ever really know

NOTE Confidence: 0.68969816

00:07:16.960 --> 00:07:19.298 how an animal experiences emotion.

NOTE Confidence: 0.68969816

00:07:19.300 --> 00:07:21.700 There is no way to say whether it

NOTE Confidence: 0.68969816

00:07:21.700 --> 00:07:24.489 is the same as a humans experience.

NOTE Confidence: 0.68969816

00:07:24.490 --> 00:07:27.138 There's also no way for me to ever

NOTE Confidence: 0.68969816

00:07:27.138 --> 00:07:29.428 truly know whether my subjectively

NOTE Confidence: 0.68969816

00:07:29.428 --> 00:07:32.008 experienced emotions are the same

NOTE Confidence: 0.68969816

00:07:32.008 --> 00:07:34.439 or different as another humans.

NOTE Confidence: 0.68969816

00:07:34.440 --> 00:07:36.282 So you know what I'm interested

NOTE Confidence: 0.68969816

00:07:36.282 --> 00:07:37.203 in is emotion.

NOTE Confidence: 0.68969816

00:07:37.210 --> 00:07:39.366 What I actually study is motivated behavior.

NOTE Confidence: 0.8249697

00:07:41.570 --> 00:07:43.310 I've always been interested in how

NOTE Confidence: 0.8249697

00:07:43.310 --> 00:07:44.867 we assign positive negative balance

NOTE Confidence: 0.8249697

00:07:44.867 --> 00:07:46.584 to environmental cues. For example,

NOTE Confidence: 0.8249697

00:07:46.584 --> 00:07:49.930 think of a track star and a war veteran.

NOTE Confidence: 0.8249697

00:07:49.930 --> 00:07:52.695 They both had the same auditory stimulus,

NOTE Confidence: 0.8249697

00:07:52.700 --> 00:07:53.756 bang a gunshot.

NOTE Confidence: 0.8249697

00:07:53.756 --> 00:07:56.740 The track star might have a rush of

NOTE Confidence: 0.8249697

00:07:56.740 --> 00:07:58.940 excitement while the war veteran

NOTE Confidence: 0.8249697

00:07:58.940 --> 00:08:01.810 might have sensations of panic or fear,

NOTE Confidence: 0.8249697

00:08:01.810 --> 00:08:04.078 someone presented with these stimuli many

NOTE Confidence: 0.8249697

00:08:04.078 --> 00:08:06.170 times without consequences may habituate.

NOTE Confidence: 0.8249697

00:08:06.170 --> 00:08:07.355 An experienced neutral

NOTE Confidence: 0.8249697

00:08:07.355 --> 00:08:08.935 valence and low arousal.

NOTE Confidence: 0.8249697

00:08:08.940 --> 00:08:11.306 So why would the same sound produce

NOTE Confidence: 0.8249697

00:08:11.306 --> 00:08:13.690 opposing reactions in different individuals?

NOTE Confidence: 0.8249697

00:08:13.690 --> 00:08:15.638 Sure, they've had different

NOTE Confidence: 0.8249697

00:08:15.638 --> 00:08:17.586 experiences in the past.

NOTE Confidence: 0.8249697

00:08:17.590 --> 00:08:19.613 That have changed the way they experience

NOTE Confidence: 0.8249697

00:08:19.613 --> 00:08:21.084 their environment now, but how?

NOTE Confidence: 0.8249697

00:08:21.084 --> 00:08:23.198 How do our brains tell us if

NOTE Confidence: 0.8249697

00:08:23.198 --> 00:08:24.530 something is good or bad?

NOTE Confidence: 0.8249697

00:08:24.530 --> 00:08:27.266 What actually makes our brains different?

NOTE Confidence: 0.8249697

00:08:27.270 --> 00:08:29.881 Solving this mystery would shed light on

NOTE Confidence: 0.8249697

00:08:29.881 --> 00:08:31.729 the fundamental principles of survival,

NOTE Confidence: 0.8249697

00:08:31.730 --> 00:08:34.334 as well as really help us understanding.

NOTE Confidence: 0.8249697

00:08:34.340 --> 00:08:37.106 The key hallmark features of many

NOTE Confidence: 0.8249697

00:08:37.106 --> 00:08:38.950 different psychiatric disease states.

NOTE Confidence: 0.8249697

00:08:38.950 --> 00:08:40.936 So by plotting things here in

NOTE Confidence: 0.8249697

00:08:40.936 --> 00:08:43.123 a simplified version of the two

NOTE Confidence: 0.8249697

00:08:43.123 --> 00:08:44.707 dimensional theory of emotion,

NOTE Confidence: 0.8249697

00:08:44.710 --> 00:08:47.027 where on one axis we have the

NOTE Confidence: 0.8249697

00:08:47.027 --> 00:08:48.670 intensity or the arousal,

NOTE Confidence: 0.8249697

00:08:48.670 --> 00:08:51.190 and on the other axis we have

NOTE Confidence: 0.8249697

00:08:51.190 --> 00:08:52.270 balance orthodontic value.

NOTE Confidence: 0.8249697

00:08:52.270 --> 00:08:53.778 This is the implication,

NOTE Confidence: 0.8249697

00:08:53.778 --> 00:08:57.149 and this is we can also compare this.

NOTE Confidence: 0.8249697

00:08:57.150 --> 00:08:59.230 Framework with another framework called

NOTE Confidence: 0.8249697

00:08:59.230 --> 00:09:02.217 the two factor theory of emotion that

NOTE Confidence: 0.8249697

00:09:02.217 --> 00:09:04.307 suggests an order of operations.

NOTE Confidence: 0.8249697

00:09:04.310 --> 00:09:06.830 And then she got back to theory of motion.

NOTE Confidence: 0.8249697

00:09:06.830 --> 00:09:08.462 We think about stimuli that coming

NOTE Confidence: 0.8249697

00:09:08.462 --> 00:09:10.739 in and the first question we have to

NOTE Confidence: 0.8249697

00:09:10.739 --> 00:09:12.622 ask ourselves is, is this stimulus important?

NOTE Confidence: 0.8249697

00:09:12.622 --> 00:09:14.535 You can think of that as absolute

NOTE Confidence: 0.8249697

00:09:14.535 --> 00:09:16.070 value if it's not important,

NOTE Confidence: 0.8249697

00:09:16.070 --> 00:09:16.910 we ignore it.

NOTE Confidence: 0.8249697

00:09:16.910 --> 00:09:18.030 If it is important,

NOTE Confidence: 0.8249697

00:09:18.030 --> 00:09:19.920 the next question we need to ask

NOTE Confidence: 0.8249697

00:09:19.920 --> 00:09:21.670 ourselves is how is it important?

NOTE Confidence: 0.8249697

00:09:21.670 --> 00:09:23.910 Is it something that is good or bad?

NOTE Confidence: 0.8249697

00:09:23.910 --> 00:09:27.366 Do we want to avoid this Daniels or

NOTE Confidence: 0.8249697

00:09:27.366 --> 00:09:28.230 approach it?

NOTE Confidence: 0.8249697

00:09:28.230 --> 00:09:31.070 And so this is what I want to focus on today.

NOTE Confidence: 0.8249697

00:09:31.070 --> 00:09:32.790 Where is the fork in the road and

NOTE Confidence: 0.8249697

00:09:32.790 --> 00:09:34.749 how do we determine what gets routed

NOTE Confidence: 0.8249697

00:09:34.749 --> 00:09:36.224 down one path or another?

NOTE Confidence: 0.8573632

00:09:39.350 --> 00:09:41.429 So if we think why am I so obsessed

NOTE Confidence: 0.8573632

00:09:41.429 --> 00:09:42.852 with understanding the perturbations

NOTE Confidence: 0.8573632

00:09:42.852 --> 00:09:45.108 that could occur with you know

NOTE Confidence: 0.8573632

00:09:45.108 --> 00:09:47.085 of motivational valence, really?

NOTE Confidence: 0.8573632

00:09:47.085 --> 00:09:49.360 Because I think this could be a

NOTE Confidence: 0.8573632

00:09:49.360 --> 00:09:51.606 common thread between many different

NOTE Confidence: 0.8573632

00:09:51.606 --> 00:09:53.139 psychiatric disease states.

NOTE Confidence: 0.8573632

00:09:53.140 --> 00:09:55.534 For example, in the case of anxiety,

NOTE Confidence: 0.8573632

00:09:55.540 --> 00:09:57.738 perhaps there is a shift to too

NOTE Confidence: 0.8573632

00:09:57.738 --> 00:09:59.709 much motivation to avoid potential

NOTE Confidence: 0.8573632

00:09:59.709 --> 00:10:01.158 negative consequences relative

NOTE Confidence: 0.8573632

00:10:01.158 --> 00:10:03.573 to motivation to seek rewards.

NOTE Confidence: 0.8573632

00:10:03.580 --> 00:10:05.746 The converse can also be true.

NOTE Confidence: 0.8573632

00:10:05.750 --> 00:10:07.586 Too much motivation to seek potential

NOTE Confidence: 0.8573632

00:10:07.586 --> 00:10:09.749 rewards and not enough motivation to

NOTE Confidence: 0.8573632

00:10:09.749 --> 00:10:11.517 avoid potential negative consequences.

NOTE Confidence: 0.8573632

00:10:11.520 --> 00:10:13.364 And you know, admittedly,

NOTE Confidence: 0.8573632

00:10:13.364 --> 00:10:16.130 this is a very simplified perspective.

NOTE Confidence: 0.8573632

00:10:16.130 --> 00:10:18.167 And then in the case of depression,

NOTE Confidence: 0.8573632

00:10:18.170 --> 00:10:20.420 perhaps we just have reduced

NOTE Confidence: 0.8573632

00:10:20.420 --> 00:10:21.770 motivation over all.

NOTE Confidence: 0.8573632

00:10:21.770 --> 00:10:24.255 So how do we implement this process?

NOTE Confidence: 0.8573632

00:10:24.260 --> 00:10:27.100 How does the brain carry out this very,

NOTE Confidence: 0.8573632

00:10:27.100 --> 00:10:28.880 very simple process of asking

NOTE Confidence: 0.8573632

00:10:28.880 --> 00:10:31.000 if something is good or bad?

NOTE Confidence: 0.8573632

00:10:31.000 --> 00:10:33.443 So there are a few different neural

NOTE Confidence: 0.8573632

00:10:33.443 --> 00:10:35.259 circuit motifs that we've seen,

NOTE Confidence: 0.8573632

00:10:35.260 --> 00:10:35.950 you know,

NOTE Confidence: 0.8573632

00:10:35.950 --> 00:10:38.020 recur and appear over and over

NOTE Confidence: 0.8573632

00:10:38.020 --> 00:10:40.667 again as the field of circuit

NOTE Confidence: 0.8573632

00:10:40.667 --> 00:10:43.017 neuroscience has developed and matured.

NOTE Confidence: 0.8573632

00:10:43.020 --> 00:10:45.036 And I'm not going to really talk

NOTE Confidence: 0.8573632

00:10:45.036 --> 00:10:46.823 about the labeled lines model just

NOTE Confidence: 0.8573632

00:10:46.823 --> 00:10:48.839 because it's sort of a straw man.

NOTE Confidence: 0.8573632

00:10:48.840 --> 00:10:50.616 When we think about balance processing

NOTE Confidence: 0.8573632

00:10:50.616 --> 00:10:52.410 because it doesn't really allow for

NOTE Confidence: 0.8573632

00:10:52.410 --> 00:10:54.078 learning to happen reversals to occur.

NOTE Confidence: 0.8573632

00:10:54.080 --> 00:10:54.664 You know,

NOTE Confidence: 0.8573632

00:10:54.664 --> 00:10:56.124 aside from just strengthening or

NOTE Confidence: 0.8573632

00:10:56.124 --> 00:10:57.614 weakening the lines of information

NOTE Confidence: 0.8573632

00:10:57.614 --> 00:10:59.024 flow as they already exist,

NOTE Confidence: 0.8573632

00:10:59.030 --> 00:11:00.194 you know it doesn't.

NOTE Confidence: 0.8573632

00:11:00.194 --> 00:11:02.568 It doesn't explain how we can learn to

NOTE Confidence: 0.8573632

00:11:02.568 --> 00:11:04.848 like a bitter taste like coffee or beer,

NOTE Confidence: 0.8573632

00:11:04.850 --> 00:11:06.614 or how we can adapt to changing

NOTE Confidence: 0.8573632

00:11:06.614 --> 00:11:08.050 conditions in the environment.

NOTE Confidence: 0.78140694

00:11:10.300 --> 00:11:13.030 So what we want other machines that

NOTE Confidence: 0.78140694

00:11:13.030 --> 00:11:15.523 we have explored include divergent has

NOTE Confidence: 0.78140694

00:11:15.523 --> 00:11:18.720 where a common scene is is coming on.

NOTE Confidence: 0.78140694

00:11:18.720 --> 00:11:21.024 To posit that send information to

NOTE Confidence: 0.78140694

00:11:21.024 --> 00:11:22.560 different downstream targets were

NOTE Confidence: 0.78140694

00:11:22.620 --> 00:11:24.340 different processes may occur,

NOTE Confidence: 0.78140694

00:11:24.340 --> 00:11:26.430 and pretty Danbury and Anabella

NOTE Confidence: 0.78140694

00:11:26.430 --> 00:11:29.149 have worked on this in my lab.

NOTE Confidence: 0.78140694

00:11:29.150 --> 00:11:31.150 Will talk about that momentarily.

NOTE Confidence: 0.78140694

00:11:31.150 --> 00:11:33.970 Another possible motif is that opposing

NOTE Confidence: 0.78140694

00:11:33.970 --> 00:11:36.570 components where the anatomical origin and

NOTE Confidence: 0.78140694

00:11:36.570 --> 00:11:39.162 and target the point A&B are the same,

NOTE Confidence: 0.78140694

00:11:39.170 --> 00:11:40.334 but the lines of.

NOTE Confidence: 0.78140694

00:11:40.334 --> 00:11:42.080 But the circuits that are are

NOTE Confidence: 0.78140694

00:11:42.149 --> 00:11:44.159 sending messages from point A to

NOTE Confidence: 0.78140694

00:11:44.159 --> 00:11:46.370 point B are different functionally.

NOTE Confidence: 0.78140694

00:11:46.370 --> 00:11:47.090 For example,

NOTE Confidence: 0.78140694

00:11:47.090 --> 00:11:48.890 if there glutamate and GABA

NOTE Confidence: 0.78140694

00:11:48.890 --> 00:11:50.858 going from point A to point B,

NOTE Confidence: 0.78140694

00:11:50.860 --> 00:11:53.446 what really matters is is the

NOTE Confidence: 0.78140694

00:11:53.446 --> 00:11:55.170 neurons integrate that information

NOTE Confidence: 0.78140694

00:11:55.245 --> 00:11:56.965 of those opponent components to

NOTE Confidence: 0.78140694

00:11:56.965 --> 00:11:59.359 sort of do a winner take all?

NOTE Confidence: 0.78140694

00:11:59.360 --> 00:12:01.580 And for that, my graduate student,

NOTE Confidence: 0.78140694

00:12:01.580 --> 00:12:02.690 former graduate student,

NOTE Confidence: 0.78140694

00:12:02.690 --> 00:12:04.910 Edward now who's now at Princeton,

NOTE Confidence: 0.78140694

00:12:04.910 --> 00:12:07.130 explored this in his thesis work,

NOTE Confidence: 0.78140694

00:12:07.130 --> 00:12:09.350 and then the 4th would be

NOTE Confidence: 0.78140694

00:12:09.350 --> 00:12:10.830 that of Neuromodulatory gain.

NOTE Confidence: 0.78140694

00:12:10.830 --> 00:12:13.050 And so we've looked at this

NOTE Confidence: 0.78140694

00:12:13.050 --> 00:12:14.530 in the prefrontal cortex,

NOTE Confidence: 0.78140694

00:12:14.530 --> 00:12:16.010 Caitlin Vanderweel and Cody

NOTE Confidence: 0.78140694

00:12:16.010 --> 00:12:18.230 Siciliano have explored this in and

NOTE Confidence: 0.78140694

00:12:18.289 --> 00:12:20.221 today I'm going to tell you about

NOTE Confidence: 0.78140694

00:12:20.221 --> 00:12:22.012 a new venture of understanding

NOTE Confidence: 0.78140694

00:12:22.012 --> 00:12:23.820 how neuropeptides can influence

NOTE Confidence: 0.78140694

00:12:23.820 --> 00:12:26.078 the divergent circuit motifs that

NOTE Confidence: 0.78140694

00:12:26.078 --> 00:12:28.766 we already know about within the

NOTE Confidence: 0.78140694

00:12:28.766 --> 00:12:31.338 basil lateral and make the left.

NOTE Confidence: 0.78140694

00:12:31.340 --> 00:12:33.265 For today I'm going to be focusing

NOTE Confidence: 0.78140694

00:12:33.265 --> 00:12:35.767 on these two motifs and how they're

NOTE Confidence: 0.78140694

00:12:35.767 --> 00:12:37.379 relevant for balance processing.

NOTE Confidence: 0.78140694

00:12:37.380 --> 00:12:40.926 So the road map for today are just three.

NOTE Confidence: 0.78140694

00:12:40.930 --> 00:12:42.900 Sort of big general questions.

NOTE Confidence: 0.78140694

00:12:42.900 --> 00:12:45.126 One is a little bit of review

NOTE Confidence: 0.78140694

00:12:45.126 --> 00:12:47.168 where to circuits encoding positive

NOTE Confidence: 0.78140694

00:12:47.168 --> 00:12:49.200 and negative bills diverge.

NOTE Confidence: 0.78140694

00:12:49.200 --> 00:12:51.958 There's many places where they could diverge,

NOTE Confidence: 0.78140694

00:12:51.960 --> 00:12:55.104 but will will go through one case study.

NOTE Confidence: 0.78140694

00:12:55.110 --> 00:12:57.474 What are the local interactions between

NOTE Confidence: 0.78140694

00:12:57.474 --> 00:12:59.050 these functionally distinct circuits?

NOTE Confidence: 0.78140694

00:12:59.050 --> 00:13:01.264 Just form give rise to function

NOTE Confidence: 0.78140694

00:13:01.264 --> 00:13:03.864 and then third how can narrow

NOTE Confidence: 0.78140694

00:13:03.864 --> 00:13:05.960 modulation participate in the

NOTE Confidence: 0.78140694

00:13:05.960 --> 00:13:08.056 process of valence assignment?

NOTE Confidence: 0.78140694

00:13:08.060 --> 00:13:09.434 And then well.

NOTE Confidence: 0.78140694

00:13:09.434 --> 00:13:10.350 Rabbit up,

NOTE Confidence: 0.78140694

00:13:10.350 --> 00:13:13.647 so the first hints of the Amygdala's

NOTE Confidence: 0.78140694

00:13:13.647 --> 00:13:15.635 involvement in emotional processing

NOTE Confidence: 0.78140694

00:13:15.635 --> 00:13:18.105 came from temporal lobe activities

NOTE Confidence: 0.78140694

00:13:18.105 --> 00:13:21.089 in primates over a century ago.

NOTE Confidence: 0.78140694

00:13:21.090 --> 00:13:22.900 Following Brown and cheaper work,

NOTE Confidence: 0.78140694

00:13:22.900 --> 00:13:24.670 Kluver Bucy coined the term

NOTE Confidence: 0.78140694

00:13:24.670 --> 00:13:26.861 psychic blindness to refer to what

NOTE Confidence: 0.78140694

00:13:26.861 --> 00:13:28.985 happens to these animals when they

NOTE Confidence: 0.78140694

00:13:28.985 --> 00:13:30.860 lose their innate fear snakes,

NOTE Confidence: 0.78140694

00:13:30.860 --> 00:13:31.175 or,

NOTE Confidence: 0.78140694

00:13:31.175 --> 00:13:31.805 you know,

NOTE Confidence: 0.78140694

00:13:31.805 --> 00:13:34.497 sort of lose interest in food and treat

NOTE Confidence: 0.78140694

00:13:34.497 --> 00:13:37.374 sort of inanimate objects like light bulbs,

NOTE Confidence: 0.78140694

00:13:37.380 --> 00:13:39.624 similarly to what would have been

NOTE Confidence: 0.78140694

00:13:39.624 --> 00:13:41.513 previously fearful rewarding stimuli or

NOTE Confidence: 0.78140694

00:13:41.513 --> 00:13:43.529 Larry Weiss grants then identified these.

NOTE Confidence: 0.78140694

00:13:43.530 --> 00:13:45.766 These phenotypes were actually

NOTE Confidence: 0.78140694

00:13:45.766 --> 00:13:47.443 specifically attributable to

NOTE Confidence: 0.78140694

00:13:47.443 --> 00:13:49.780 selective amygdala lesions later on.

NOTE Confidence: 0.78140694

00:13:49.780 --> 00:13:51.424 There's also the important

NOTE Confidence: 0.78140694

00:13:51.424 --> 00:13:53.480 case study patient ** who,

NOTE Confidence: 0.78140694

00:13:53.480 --> 00:13:55.120 following bilateral amygdala damage,

NOTE Confidence: 0.78140694

00:13:55.120 --> 00:13:57.586 lost fear to snakes and spiders.

NOTE Confidence: 0.78140694

00:13:57.590 --> 00:13:59.234 The ability to recognize

NOTE Confidence: 0.78140694

00:13:59.234 --> 00:14:01.289 emotion in other peoples faces,

NOTE Confidence: 0.78140694

00:14:01.290 --> 00:14:03.340 and even lost the fear.

NOTE Confidence: 0.78140694

00:14:03.340 --> 00:14:05.400 Fear responses to being mugged,

NOTE Confidence: 0.78140694

00:14:05.400 --> 00:14:07.044 which actually happened several

NOTE Confidence: 0.78140694

00:14:07.044 --> 00:14:09.254 times in her life, however.

NOTE Confidence: 0.78140694

00:14:09.254 --> 00:14:12.638 When she was at suffocation when

NOTE Confidence: 0.78140694

00:14:12.638 --> 00:14:14.330 she's experiencing suffocation,

NOTE Confidence: 0.78140694

00:14:14.330 --> 00:14:17.078 she still could have the autonomic

NOTE Confidence: 0.78140694

00:14:17.078 --> 00:14:19.540 responses increase in autonomic arousal,

NOTE Confidence: 0.78140694

00:14:19.540 --> 00:14:20.406 heart rate,

NOTE Confidence: 0.78140694

00:14:20.406 --> 00:14:21.272 sweating, etc.

NOTE Confidence: 0.78140694

00:14:21.272 --> 00:14:23.437 Suggesting the amygdala is important

NOTE Confidence: 0.78140694

00:14:23.437 --> 00:14:26.002 for the assignment of environmental

NOTE Confidence: 0.78140694

00:14:26.002 --> 00:14:28.070 significance to sensory stimuli,

NOTE Confidence: 0.78140694

00:14:28.070 --> 00:14:30.630 but not necessarily the production

NOTE Confidence: 0.78140694

00:14:30.630 --> 00:14:33.190 of the autonomic or arousal

NOTE Confidence: 0.81227297

00:14:33.276 --> 00:14:35.589 and physiological responses.

NOTE Confidence: 0.81227297

00:14:35.590 --> 00:14:38.690 So in my in my lab, we work in mice and

NOTE Confidence: 0.81227297

00:14:38.690 --> 00:14:41.447 if you take a look at the mouse brain,

NOTE Confidence: 0.81227297

00:14:41.450 --> 00:14:43.494 take a little section and look here,

NOTE Confidence: 0.81227297

00:14:43.500 --> 00:14:45.844 there are 13 sub nuclei of the amygdala,

NOTE Confidence: 0.81227297

00:14:45.850 --> 00:14:47.761 actually, but I'll just be focusing on

NOTE Confidence: 0.81227297

00:14:47.761 --> 00:14:49.950 two of them for simplicity of today.

NOTE Confidence: 0.7513969

00:14:54.490 --> 00:14:56.035 So where does circuits encoding

NOTE Confidence: 0.7513969

00:14:56.035 --> 00:14:57.580 positive and negative balance diverge?

NOTE Confidence: 0.7513969

00:14:57.580 --> 00:14:59.314 Well, I've already sort of hinted

NOTE Confidence: 0.7513969

00:14:59.314 --> 00:15:01.598 to you that the bill is important.

NOTE Confidence: 0.7513969

00:15:01.600 --> 00:15:03.092 Why you know what?

NOTE Confidence: 0.7513969

00:15:03.092 --> 00:15:04.957 What else about the amygdala?

NOTE Confidence: 0.7513969

00:15:04.960 --> 00:15:07.840 Do you make alot is kind of this

NOTE Confidence: 0.7513969

00:15:07.840 --> 00:15:10.338 primitive analog of of the cortical

NOTE Confidence: 0.7513969

00:15:10.338 --> 00:15:12.468 striatal circuit and some have

NOTE Confidence: 0.7513969

00:15:12.468 --> 00:15:15.099 referred to it as the alligator brain.

NOTE Confidence: 0.7513969

00:15:15.100 --> 00:15:17.698 It's it's primitive brain within the

NOTE Confidence: 0.7513969

00:15:17.698 --> 00:15:20.083 brain because the amygdala days auto

NOTE Confidence: 0.7513969

00:15:20.083 --> 00:15:21.790 mgla is 90% glutamatergic neurons

NOTE Confidence: 0.7513969

00:15:21.790 --> 00:15:23.890 and described the cortical cortical

NOTE Confidence: 0.7513969

00:15:23.890 --> 00:15:26.272 like in that it forms associations

NOTE Confidence: 0.7513969

00:15:26.272 --> 00:15:28.396 is not a laminated structure like

NOTE Confidence: 0.7513969

00:15:28.396 --> 00:15:30.310 the cortical like the cortex,

NOTE Confidence: 0.7513969

00:15:30.310 --> 00:15:32.260 but other than that there

NOTE Confidence: 0.7513969

00:15:32.260 --> 00:15:33.430 are some similarities.

NOTE Confidence: 0.7513969

00:15:33.430 --> 00:15:35.058 The central amygdala is

NOTE Confidence: 0.7513969

00:15:35.058 --> 00:15:36.279 striatal like because.

NOTE Confidence: 0.7513969

00:15:36.280 --> 00:15:38.275 It's 95% Gabaergic medium spiny

NOTE Confidence: 0.7513969

00:15:38.275 --> 00:15:40.270 neurons in a similar manner.

NOTE Confidence: 0.7513969

00:15:40.270 --> 00:15:43.286 So there is a very rich body of

NOTE Confidence: 0.7513969

00:15:43.286 --> 00:15:44.837 literature suggesting that the

NOTE Confidence: 0.7513969

00:15:44.837 --> 00:15:47.371 PLA is well positioned to be where

NOTE Confidence: 0.7513969

00:15:47.371 --> 00:15:49.448 valence encoding neurons exist.

NOTE Confidence: 0.7513969

00:15:49.450 --> 00:15:51.760 So we know that neurons in the

NOTE Confidence: 0.7513969

00:15:51.760 --> 00:15:53.787 PLA encode positive and negative

NOTE Confidence: 0.7513969

00:15:53.787 --> 00:15:56.197 balance that all modalities of

NOTE Confidence: 0.7513969

00:15:56.197 --> 00:15:58.087 sensory information converges in

NOTE Confidence: 0.7513969

00:15:58.087 --> 00:16:00.677 the basal lateral make the love that

NOTE Confidence: 0.7513969

00:16:00.677 --> 00:16:03.470 learning induces synaptic plasticity.

NOTE Confidence: 0.7513969

00:16:03.470 --> 00:16:06.235 And just a brief didactic direction here,

NOTE Confidence: 0.7513969

00:16:06.240 --> 00:16:08.370 so so.

NOTE Confidence: 0.7513969

00:16:08.370 --> 00:16:10.240 We believe plasticity occurs in

NOTE Confidence: 0.7513969

00:16:10.240 --> 00:16:12.110 synapses that were previously weak

NOTE Confidence: 0.7513969

00:16:12.170 --> 00:16:14.280 synapses that might carry information

NOTE Confidence: 0.7513969

00:16:14.280 --> 00:16:15.968 about the condition stimulus,

NOTE Confidence: 0.7513969

00:16:15.970 --> 00:16:17.970 such as an auditory tone,

NOTE Confidence: 0.7513969

00:16:17.970 --> 00:16:20.370 but once is paired with either

NOTE Confidence: 0.7513969

00:16:20.370 --> 00:16:21.970 a reward or punishment,

NOTE Confidence: 0.7513969

00:16:21.970 --> 00:16:23.173 will be strengthened,

NOTE Confidence: 0.7513969

00:16:23.173 --> 00:16:27.168 and so just to I'll come back to this later,

NOTE Confidence: 0.7513969

00:16:27.170 --> 00:16:28.582 but just very quickly.

NOTE Confidence: 0.7513969

00:16:28.582 --> 00:16:31.686 We are using ampata NMJ ratio as a

NOTE Confidence: 0.7513969

00:16:31.686 --> 00:16:33.966 proxy for glutamatergic synaptic strength,

NOTE Confidence: 0.7513969

00:16:33.970 --> 00:16:36.770 because after your garden variety LTP occurs,

NOTE Confidence: 0.7513969

00:16:36.770 --> 00:16:38.394 you will see an.

NOTE Confidence: 0.7513969

00:16:38.394 --> 00:16:40.018 Increase in Emperor Scepter

NOTE Confidence: 0.7513969

00:16:40.018 --> 00:16:40.830 mediated currents.

NOTE Confidence: 0.6712021

00:16:46.560 --> 00:16:50.322 We have already seen that fear

NOTE Confidence: 0.6712021

00:16:50.322 --> 00:16:53.630 conditioning increases Amp'd MD ratio

NOTE Confidence: 0.6712021

00:16:53.630 --> 00:16:57.085 in putative flammable DLA synapses.

NOTE Confidence: 0.6712021

00:16:57.090 --> 00:16:59.060 In this particular putative synapse

NOTE Confidence: 0.6712021

00:16:59.060 --> 00:17:02.512 I've also found when I was a graduate

NOTE Confidence: 0.6712021

00:17:02.512 --> 00:17:04.388 student that reward conditioning

NOTE Confidence: 0.6712021

00:17:04.388 --> 00:17:06.888 also increased ampata MDA ratio in

NOTE Confidence: 0.6712021

00:17:06.888 --> 00:17:08.928 putative clam Omega Listen apps is

NOTE Confidence: 0.6712021

00:17:08.928 --> 00:17:11.300 in the same computer the senses,

NOTE Confidence: 0.6712021

00:17:11.300 --> 00:17:15.284 and so when I was a grad student.

NOTE Confidence: 0.6712021

00:17:15.290 --> 00:17:16.498 I presented these data.

NOTE Confidence: 0.6712021

00:17:16.498 --> 00:17:18.651 This is my first time meeting and

NOTE Confidence: 0.6712021

00:17:18.651 --> 00:17:20.604 one of my colleagues came up to

NOTE Confidence: 0.6712021

00:17:20.604 --> 00:17:22.260 me afterwards and just, you know,

NOTE Confidence: 0.6712021

00:17:22.260 --> 00:17:24.733 gave me gave me a lot of Flack about

NOTE Confidence: 0.6712021

00:17:24.733 --> 00:17:27.008 you know how does this make sense?

NOTE Confidence: 0.6712021

00:17:27.010 --> 00:17:28.768 How can the same mechanism underlying

NOTE Confidence: 0.6712021

00:17:28.768 --> 00:17:29.940 fear and reward conditioning?

NOTE Confidence: 0.89172715

00:17:32.960 --> 00:17:35.858 Well, there's a few different possibilities.

NOTE Confidence: 0.89172715

00:17:35.860 --> 00:17:38.660 Maybe the amygdala just encode salients and

NOTE Confidence: 0.89172715

00:17:38.660 --> 00:17:42.289 it it you know anything that's important,

NOTE Confidence: 0.89172715

00:17:42.290 --> 00:17:45.608 good or bad, will induce plasticity.

NOTE Confidence: 0.89172715

00:17:45.610 --> 00:17:47.098 Or maybe the amygdala is actually

NOTE Confidence: 0.89172715

00:17:47.098 --> 00:17:48.660 the site of valence assignment,

NOTE Confidence: 0.89172715

00:17:48.660 --> 00:17:50.522 but it occurs by a distinct projections

NOTE Confidence: 0.89172715

00:17:50.522 --> 00:17:52.485 that we just didn't discriminate between

NOTE Confidence: 0.89172715

00:17:52.485 --> 00:17:56.940 when we were patching blindly. So dumb.

NOTE Confidence: 0.89172715

00:17:56.940 --> 00:17:59.831 We know that the essential medial nucleus

NOTE Confidence: 0.89172715

00:17:59.831 --> 00:18:02.818 is critical for the expression of fear.

NOTE Confidence: 0.89172715

00:18:02.820 --> 00:18:05.286 We know that up genetically stimulating,

NOTE Confidence: 0.89172715

00:18:05.290 --> 00:18:07.494 central medial nucleus neurons

NOTE Confidence: 0.89172715

00:18:07.494 --> 00:18:09.147 evokes freezing responses.

NOTE Confidence: 0.89172715

00:18:09.150 --> 00:18:12.027 We also know that disconnecting the basal

NOTE Confidence: 0.89172715

00:18:12.027 --> 00:18:14.750 lateral amygdala from the central medial

NOTE Confidence: 0.89172715

00:18:14.750 --> 00:18:17.115 nucleus will abolished fear expression.

NOTE Confidence: 0.89172715

00:18:17.120 --> 00:18:18.119 But of course,

NOTE Confidence: 0.89172715

00:18:18.119 --> 00:18:20.450 the central amygdala does many other things,

NOTE Confidence: 0.89172715

00:18:20.450 --> 00:18:22.790 and there are a number of

NOTE Confidence: 0.89172715

00:18:22.790 --> 00:18:24.800 fantastic studies that show this.

NOTE Confidence: 0.89172715

00:18:24.800 --> 00:18:26.460 So it's not this simple.

NOTE Confidence: 0.89172715

00:18:26.460 --> 00:18:28.440 Same thing for the nucleus incumbents.

NOTE Confidence: 0.89172715

00:18:28.440 --> 00:18:30.880 Of course we know that the nucleus income

NOTE Confidence: 0.89172715

00:18:30.880 --> 00:18:33.080 is important for diversity of functions,

NOTE Confidence: 0.89172715

00:18:33.080 --> 00:18:36.321 but it's best known for its importance

NOTE Confidence: 0.89172715

00:18:36.321 --> 00:18:38.620 in reward related processes.

NOTE Confidence: 0.89172715

00:18:38.620 --> 00:18:40.315 We know that Papa genetically

NOTE Confidence: 0.89172715

00:18:40.315 --> 00:18:41.671 stimulating VLA terminals and

NOTE Confidence: 0.89172715

00:18:41.671 --> 00:18:43.264 nuclear comments supports self

NOTE Confidence: 0.89172715

00:18:43.264 --> 00:18:44.856 stimulation in place preference.

NOTE Confidence: 0.788228

00:18:47.550 --> 00:18:49.435 When Praneeth Embery Annabelle or

NOTE Confidence: 0.788228

00:18:49.435 --> 00:18:52.262 came to my lab, they came ready to

NOTE Confidence: 0.788228

00:18:52.262 --> 00:18:54.230 tackle this question about what the

NOTE Confidence: 0.788228

00:18:54.297 --> 00:18:56.422 circuit mechanism is for signing

NOTE Confidence: 0.788228

00:18:56.422 --> 00:18:58.122 positive and negative balance.

NOTE Confidence: 0.788228

00:18:58.130 --> 00:19:00.020 So the hypothesis is simple,

NOTE Confidence: 0.788228

00:19:00.020 --> 00:19:01.910 just that the specific downstream

NOTE Confidence: 0.788228

00:19:01.910 --> 00:19:03.044 projection neuron matters.

NOTE Confidence: 0.788228

00:19:03.050 --> 00:19:05.437 So if you pair a tone with

NOTE Confidence: 0.788228

00:19:05.437 --> 00:19:07.210 foot shock for example,

NOTE Confidence: 0.788228

00:19:07.210 --> 00:19:10.840 you'll see a strengthening of synapses.

NOTE Confidence: 0.788228

00:19:10.840 --> 00:19:13.288 Coming on to see M projectors.

NOTE Confidence: 0.788228

00:19:13.290 --> 00:19:16.190 Whereas if we are.

NOTE Confidence: 0.788228

00:19:16.190 --> 00:19:17.960 I'm going to pair the tone

NOTE Confidence: 0.788228

00:19:17.960 --> 00:19:19.740 with a reward like sucrose.

NOTE Confidence: 0.788228

00:19:19.740 --> 00:19:21.280 We would see strengthening of

NOTE Confidence: 0.788228

00:19:21.280 --> 00:19:23.300 synapses coming on to feeling neurons,

NOTE Confidence: 0.788228

00:19:23.300 --> 00:19:24.588 projecting the nucleus of

NOTE Confidence: 0.788228

00:19:24.588 --> 00:19:25.876 Commons so very simply,

NOTE Confidence: 0.788228

00:19:25.880 --> 00:19:28.134 we just used retrogradely traveling for us.

NOTE Confidence: 0.788228

00:19:28.140 --> 00:19:30.240 It feeds and check into them into

NOTE Confidence: 0.788228

00:19:30.240 --> 00:19:31.895 either the nucleus of comments

NOTE Confidence: 0.788228

00:19:31.895 --> 00:19:33.625 or the central medial nucleus,

NOTE Confidence: 0.788228

00:19:33.630 --> 00:19:35.295 then train animals and either

NOTE Confidence: 0.788228

00:19:35.295 --> 00:19:36.960 a fear conditioning task or

NOTE Confidence: 0.788228

00:19:37.019 --> 00:19:38.480 reward conditioning task.

NOTE Confidence: 0.788228

00:19:38.480 --> 00:19:39.952 Simulated putative built Alanic

NOTE Confidence: 0.788228

00:19:39.952 --> 00:19:41.792 inputs to the amygdala and

NOTE Confidence: 0.788228

00:19:41.792 --> 00:19:43.618 then recorded just as before.

NOTE Confidence: 0.788228

00:19:43.620 --> 00:19:46.734 Except now we just know where

NOTE Confidence: 0.788228

00:19:46.734 --> 00:19:49.650 the targets are very simple.

NOTE Confidence: 0.788228

00:19:49.650 --> 00:19:52.762 And what we found was that after fear

NOTE Confidence: 0.788228

00:19:52.762 --> 00:19:55.147 conditioning we see a button increase

NOTE Confidence: 0.788228

00:19:55.147 --> 00:19:58.249 in synaptic strength on to see M neurons,

NOTE Confidence: 0.788228

00:19:58.250 --> 00:20:00.542 CN projectors excuse me and decrease

NOTE Confidence: 0.788228

00:20:00.542 --> 00:20:04.107 in amber ratio on to PLA to see M

NOTE Confidence: 0.788228

00:20:04.107 --> 00:20:05.679 neurons after reward conditioning.

NOTE Confidence: 0.71817434

00:20:07.870 --> 00:20:08.938 Conversely, for being

NOTE Confidence: 0.71817434

00:20:08.938 --> 00:20:10.718 late to a Commons neurons,

NOTE Confidence: 0.71817434

00:20:10.720 --> 00:20:12.724 we saw synaptic strengthening on to

NOTE Confidence: 0.71817434

00:20:12.724 --> 00:20:15.612 them or some Excuse me Ltd a reduction

NOTE Confidence: 0.71817434

00:20:15.612 --> 00:20:17.838 and Anthony ratio after fear conditioning,

NOTE Confidence: 0.71817434

00:20:17.840 --> 00:20:19.970 but an increase in synaptic strength

NOTE Confidence: 0.71817434

00:20:19.970 --> 00:20:21.035 after reward conditioning.

NOTE Confidence: 0.71817434

00:20:21.040 --> 00:20:24.148 So just the opposite.

NOTE Confidence: 0.71817434

00:20:24.150 --> 00:20:24.924 And importantly,

NOTE Confidence: 0.71817434

00:20:24.924 --> 00:20:28.604 what I want to point out is that even

NOTE Confidence: 0.71817434

00:20:28.604 --> 00:20:31.129 conditions like food restriction can

NOTE Confidence: 0.71817434

00:20:31.129 --> 00:20:34.180 change the basil amput empty ratio.

NOTE Confidence: 0.71817434

00:20:34.180 --> 00:20:36.132 So if the visa lottery legal is truly

NOTE Confidence: 0.71817434

00:20:36.132 --> 00:20:38.621 the site at which we translate sensory

NOTE Confidence: 0.71817434

00:20:38.621 --> 00:20:40.177 information into motivated behavior,

NOTE Confidence: 0.71817434

00:20:40.180 --> 00:20:42.516 then be light inputs should be able to

NOTE Confidence: 0.71817434

00:20:42.516 --> 00:20:44.919 drive motor behaviors in the naive animal.

NOTE Confidence: 0.8699819

00:20:47.810 --> 00:20:50.554 OK, but is there a causal relationship

NOTE Confidence: 0.8699819

00:20:50.554 --> 00:20:52.910 and we show that there is.

NOTE Confidence: 0.8699819

00:20:52.910 --> 00:20:54.870 If we fail to stimulate

NOTE Confidence: 0.8699819

00:20:54.870 --> 00:20:56.046 village Commons animals,

NOTE Confidence: 0.8699819

00:20:56.050 --> 00:20:58.010 we get intracranial self stimulation.

NOTE Confidence: 0.8699819

00:20:58.010 --> 00:21:01.142 Just replicating work that gets tuber

NOTE Confidence: 0.8699819

00:21:01.142 --> 00:21:04.559 and John Britton have already shown.

NOTE Confidence: 0.8699819

00:21:04.560 --> 00:21:07.035 And we also show that if we simulate dealing

NOTE Confidence: 0.8699819

00:21:07.035 --> 00:21:09.497 arms protecting the central medial nucleus,

NOTE Confidence: 0.8699819

00:21:09.500 --> 00:21:11.300 we actually get punishment

NOTE Confidence: 0.8699819

00:21:11.300 --> 00:21:12.650 avoidance place avoidance.

NOTE Confidence: 0.8699819

00:21:12.650 --> 00:21:15.980 So OK, if it's true that if this whole

NOTE Confidence: 0.8699819

00:21:15.980 --> 00:21:18.510 hypothesis is true and this is relying

NOTE Confidence: 0.8699819

00:21:18.510 --> 00:21:21.489 on an MDA receptor dependent mechanism,

NOTE Confidence: 0.8699819

00:21:21.490 --> 00:21:25.108 what happens with with an MD or soldier LDP?

NOTE Confidence: 0.8699819

00:21:25.110 --> 00:21:26.642 I'm sure you know,

NOTE Confidence: 0.8699819

00:21:26.642 --> 00:21:29.940 but if you don't know glutamate is released,

NOTE Confidence: 0.8699819

00:21:29.940 --> 00:21:32.346 it will bind to gloomy receptors,

NOTE Confidence: 0.8699819

00:21:32.350 --> 00:21:33.553 including an perceptors.

NOTE Confidence: 0.8699819

00:21:33.553 --> 00:21:34.756 An MDA receptors,

NOTE Confidence: 0.8699819

00:21:34.760 --> 00:21:37.539 however NMD a receptors are have a

NOTE Confidence: 0.8699819

00:21:37.539 --> 00:21:40.450 magnesium blockade that sits in the poor

NOTE Confidence: 0.8699819

00:21:40.450 --> 00:21:42.916 of energy receptors and the depolarization.

NOTE Confidence: 0.8699819

00:21:42.920 --> 00:21:44.368 Caused by glutamate binding

NOTE Confidence: 0.8699819

00:21:44.368 --> 00:21:45.454 and amp receptors.

NOTE Confidence: 0.8699819

00:21:45.460 --> 00:21:47.280 Allows the influx of sodium.

NOTE Confidence: 0.8699819

00:21:47.280 --> 00:21:48.892 Then it becomes depolarized.

NOTE Confidence: 0.8699819

00:21:48.892 --> 00:21:51.310 This allows the magnesium blockade to

NOTE Confidence: 0.8699819

00:21:51.373 --> 00:21:53.445 come out of the NBA receptor poor,

NOTE Confidence: 0.8699819

00:21:53.450 --> 00:21:56.140 allowing calcium influx to occur.

NOTE Confidence: 0.8699819

00:21:56.140 --> 00:21:57.724 So if this is,

NOTE Confidence: 0.8699819

00:21:57.724 --> 00:21:58.516 you know,

NOTE Confidence: 0.8699819

00:21:58.520 --> 00:22:01.292 this is all true that this is

NOTE Confidence: 0.8699819

00:22:01.292 --> 00:22:02.480 how energy receptors.

NOTE Confidence: 0.8699819

00:22:02.480 --> 00:22:05.640 This is how NBA receptor dependent LTP works.

NOTE Confidence: 0.8699819

00:22:05.640 --> 00:22:07.240 Then hyperpolarizing the postsynaptic

NOTE Confidence: 0.8699819

00:22:07.240 --> 00:22:10.466 neuron at a critical time point here would

NOTE Confidence: 0.8699819

00:22:10.466 --> 00:22:12.770 then prevent learning because we couldn't,

NOTE Confidence: 0.8699819

00:22:12.770 --> 00:22:16.124 you wouldn't be able to remove

NOTE Confidence: 0.8699819

00:22:16.124 --> 00:22:18.360 that that magnesium blockade.

NOTE Confidence: 0.8699819

00:22:18.360 --> 00:22:20.320 So we did this experiment.

NOTE Confidence: 0.8699819

00:22:20.320 --> 00:22:23.158 This is bilateral Weezer dual virus

NOTE Confidence: 0.8699819

00:22:23.158 --> 00:22:25.050 approach to express halorhodopsin

NOTE Confidence: 0.8699819

00:22:25.122 --> 00:22:27.216 in either Bealach na Si Productions

NOTE Confidence: 0.8699819

00:22:27.216 --> 00:22:29.361 or belay to see M Productions

NOTE Confidence: 0.8699819

00:22:29.361 --> 00:22:31.713 and then train them again on a

NOTE Confidence: 0.8699819

00:22:31.713 --> 00:22:33.718 fear or reward conditioning task.

NOTE Confidence: 0.8699819

00:22:33.718 --> 00:22:35.803 Photo inhibiting only when the

NOTE Confidence: 0.8699819

00:22:35.803 --> 00:22:38.144 US the unconditioned stimulus was

NOTE Confidence: 0.8699819

00:22:38.144 --> 00:22:40.928 presented either for shock or sucrose.

NOTE Confidence: 0.8699819

00:22:40.930 --> 00:22:43.558 And what we found.

NOTE Confidence: 0.8699819

00:22:43.560 --> 00:22:45.896 I've sort of what I said for the

NOTE Confidence: 0.8699819

00:22:45.896 --> 00:22:47.599 fear conditioning and that when we

NOTE Confidence: 0.8699819

00:22:47.599 --> 00:22:49.710 photo inhibited be late to a comment,

NOTE Confidence: 0.8699819

00:22:49.710 --> 00:22:50.254 something happened.

NOTE Confidence: 0.8699819

00:22:50.254 --> 00:22:51.614 But if we silenced Beladice

NOTE Confidence: 0.8699819

00:22:51.614 --> 00:22:52.940 central medial nucleus projections,

NOTE Confidence: 0.8699819

00:22:52.940 --> 00:22:54.984 we saw an impairment in fear conditioning.

NOTE Confidence: 0.7586047

00:22:57.280 --> 00:22:59.446 When we looked at reward conditioning,

NOTE Confidence: 0.7586047

00:22:59.450 --> 00:23:00.530 however, something sort

NOTE Confidence: 0.7586047

00:23:00.530 --> 00:23:01.610 of unexpected happened.

NOTE Confidence: 0.7586047

00:23:01.610 --> 00:23:03.415 It was surprising because we

NOTE Confidence: 0.7586047

00:23:03.415 --> 00:23:05.220 actually didn't see an impairment

NOTE Confidence: 0.7586047

00:23:05.282 --> 00:23:07.027 to belay and astie inhibition,

NOTE Confidence: 0.7586047

00:23:07.030 --> 00:23:08.830 as I would have expected,

NOTE Confidence: 0.7586047

00:23:08.830 --> 00:23:10.820 we actually saw in enhancement

NOTE Confidence: 0.7586047

00:23:10.820 --> 00:23:13.720 when feeling to see an innovation.

NOTE Confidence: 0.7586047

00:23:13.720 --> 00:23:16.457 OK, so that was a little confusing,

NOTE Confidence: 0.7586047

00:23:16.460 --> 00:23:18.410 but it'll make sense later.

NOTE Confidence: 0.7586047

00:23:18.410 --> 00:23:20.566 So so just an interim summary is

NOTE Confidence: 0.7586047

00:23:20.566 --> 00:23:22.961 that I've told you that opposite

NOTE Confidence: 0.7586047

00:23:22.961 --> 00:23:24.825 synaptic changes map onto

NOTE Confidence: 0.7586047

00:23:24.825 --> 00:23:26.620 production following either fear,

NOTE Confidence: 0.7586047

00:23:26.620 --> 00:23:28.692 conditioning or reward conditioning.

NOTE Confidence: 0.7586047

00:23:28.692 --> 00:23:30.992 If we just, you know,

NOTE Confidence: 0.7586047

00:23:30.992 --> 00:23:32.847 circumvent all of this upstream

NOTE Confidence: 0.7586047

00:23:32.847 --> 00:23:34.832 plasticity and just cut right

NOTE Confidence: 0.7586047

00:23:34.832 --> 00:23:36.842 to the chase and manipulate

NOTE Confidence: 0.7586047

00:23:36.842 --> 00:23:38.048 these projector populations,

NOTE Confidence: 0.7586047

00:23:38.050 --> 00:23:40.250 activation of projections will

NOTE Confidence: 0.7586047

00:23:40.250 --> 00:23:43.000 either cause avoidance or approach.

NOTE Confidence: 0.7586047

00:23:43.000 --> 00:23:45.260 If we then bilaterally inhibit

NOTE Confidence: 0.7586047

00:23:45.260 --> 00:23:47.068 either of these productions,

NOTE Confidence: 0.7586047

00:23:47.070 --> 00:23:50.442 will see that inhibition of central

NOTE Confidence: 0.7586047

00:23:50.442 --> 00:23:52.690 medial projectors impairs fear

NOTE Confidence: 0.7586047

00:23:52.782 --> 00:23:55.507 but enhances reward learning OK?

NOTE Confidence: 0.7586047

00:23:55.510 --> 00:23:57.568 But is it really that simple?

NOTE Confidence: 0.7586047

00:23:57.570 --> 00:23:59.978 And of course the answer is no.

NOTE Confidence: 0.7586047

00:23:59.980 --> 00:24:01.700 There's a lot of heterogeneity.

NOTE Confidence: 0.7586047

00:24:01.700 --> 00:24:03.016 It's it's, you know,

NOTE Confidence: 0.7586047

00:24:03.016 --> 00:24:04.661 all these neurons that are

NOTE Confidence: 0.7586047

00:24:04.661 --> 00:24:05.490 anatomically defined,

NOTE Confidence: 0.7586047

00:24:05.490 --> 00:24:07.548 have a lot of functional heterogeneity.

NOTE Confidence: 0.7586047

00:24:07.550 --> 00:24:09.832 We do address this that even though

NOTE Confidence: 0.7586047

00:24:09.832 --> 00:24:12.293 it's really exciting that we can target

NOTE Confidence: 0.7586047

00:24:12.293 --> 00:24:14.423 things more specifically than ever before,

NOTE Confidence: 0.7586047

00:24:14.430 --> 00:24:15.802 we're still possibly only

NOTE Confidence: 0.7586047

00:24:15.802 --> 00:24:17.174 observing a majority vote.

NOTE Confidence: 0.7586047

00:24:17.180 --> 00:24:18.227 There you know,

NOTE Confidence: 0.7586047

00:24:18.227 --> 00:24:19.972 just because an offer genetic

NOTE Confidence: 0.7586047

00:24:19.972 --> 00:24:21.728 manipulation can produce only one

NOTE Confidence: 0.7586047

00:24:21.728 --> 00:24:23.720 measurable behavior in a given task,

NOTE Confidence: 0.7586047

00:24:23.720 --> 00:24:25.868 this does not in any way

NOTE Confidence: 0.7586047

00:24:25.868 --> 00:24:26.942 suggest functional homogeneity.

NOTE Confidence: 0.7586047

00:24:26.950 --> 00:24:29.645 Of neurons anymore than having you know,

NOTE Confidence: 0.7586047

00:24:29.650 --> 00:24:32.890 one president of the country suggest

NOTE Confidence: 0.7586047

00:24:32.890 --> 00:24:36.288 that everyone agrees who it should be.

NOTE Confidence: 0.7586047

00:24:36.290 --> 00:24:37.286 So Eve Marder,

NOTE Confidence: 0.7586047

00:24:37.286 --> 00:24:38.614 once said very wisely,

NOTE Confidence: 0.7586047

00:24:38.620 --> 00:24:40.285 you know very artistic I

NOTE Confidence: 0.7586047

00:24:40.285 --> 00:24:41.950 love I love this club,

NOTE Confidence: 0.7586047

00:24:41.950 --> 00:24:44.947 that optic tools tell us what neurons can do,

NOTE Confidence: 0.7586047

00:24:44.950 --> 00:24:46.610 not what neurons do do.

NOTE Confidence: 0.7586047

00:24:46.610 --> 00:24:48.332 So it's very important we need to

NOTE Confidence: 0.7586047

00:24:48.332 --> 00:24:50.476 be able to explore the endogenous

NOTE Confidence: 0.7586047

00:24:50.476 --> 00:24:52.268 functional properties of neurons.

NOTE Confidence: 0.7586047

00:24:52.270 --> 00:24:53.494 Really understand them.

NOTE Confidence: 0.7586047

00:24:53.494 --> 00:24:55.942 So the minimal the absolute minimal

NOTE Confidence: 0.7586047

00:24:55.942 --> 00:24:57.658 criteria for violence in coding

NOTE Confidence: 0.7586047

00:24:57.658 --> 00:24:59.770 a single cells is that number 10,

NOTE Confidence: 0.7586047

00:24:59.770 --> 00:25:02.010 and I should say before I get

NOTE Confidence: 0.7586047

00:25:02.010 --> 00:25:03.940 into this set on one axis,

NOTE Confidence: 0.7586047

00:25:03.940 --> 00:25:06.817 there's the response to rewarding CS is.

NOTE Confidence: 0.7586047

00:25:06.820 --> 00:25:08.064 On the other access,

NOTE Confidence: 0.7586047

00:25:08.064 --> 00:25:09.619 there's a response to aversive

NOTE Confidence: 0.7586047

00:25:09.619 --> 00:25:11.028 CS is in either case,

NOTE Confidence: 0.7586047

00:25:11.030 --> 00:25:13.438 and in both cases we can either have

NOTE Confidence: 0.7586047

00:25:13.438 --> 00:25:16.160 innovation, no response or an excitation.

NOTE Confidence: 0.7586047

00:25:16.160 --> 00:25:18.700 Uhm?

NOTE Confidence: 0.7586047

00:25:18.700 --> 00:25:19.876 So the so,

NOTE Confidence: 0.7586047

00:25:19.876 --> 00:25:21.836 given these combinations of responses.

NOTE Confidence: 0.7586047

00:25:21.840 --> 00:25:24.540 Of course, if.

NOTE Confidence: 0.7586047

00:25:24.540 --> 00:25:25.030 Just.

NOTE Confidence: 0.78889453

00:25:27.560 --> 00:25:29.264 They conclude that it fails in

NOTE Confidence: 0.78889453

00:25:29.264 --> 00:25:31.908 coding a little bit harder is to say

NOTE Confidence: 0.78889453

00:25:31.908 --> 00:25:33.356 that it's differential responding.

NOTE Confidence: 0.78889453

00:25:33.360 --> 00:25:35.292 You want to say if it's

NOTE Confidence: 0.78889453

00:25:35.292 --> 00:25:36.580 responding in a similar,

NOTE Confidence: 0.78889453

00:25:36.580 --> 00:25:37.960 indistinguishable manner to to

NOTE Confidence: 0.78889453

00:25:37.960 --> 00:25:39.685 both positive and negative stimuli

NOTE Confidence: 0.78889453

00:25:39.685 --> 00:25:41.409 that it is not encoding balance.

NOTE Confidence: 0.78889453

00:25:41.410 --> 00:25:42.794 This is pretty important.

NOTE Confidence: 0.78889453

00:25:42.794 --> 00:25:44.870 Oftentimes studies will only show or

NOTE Confidence: 0.78889453

00:25:44.928 --> 00:25:46.804 response to one or the other within

NOTE Confidence: 0.78889453

00:25:46.804 --> 00:25:49.024 a given cell an you really need

NOTE Confidence: 0.78889453

00:25:49.024 --> 00:25:50.724 responses to both without seeing

NOTE Confidence: 0.78889453

00:25:50.724 --> 00:25:53.110 responses to both in the same cell

NOTE Confidence: 0.78889453

00:25:53.110 --> 00:25:55.075 you you can't differentiate between

NOTE Confidence: 0.78889453

00:25:55.075 --> 00:25:57.745 salience responses and balance responses.

NOTE Confidence: 0.78889453

00:25:57.750 --> 00:25:59.885 And then finally it needs to be

NOTE Confidence: 0.78889453

00:25:59.885 --> 00:26:01.370 independent of sensory features.

NOTE Confidence: 0.78889453

00:26:01.370 --> 00:26:04.238 It's not just tracking the modality

NOTE Confidence: 0.78889453

00:26:04.238 --> 00:26:06.605 or the specific frequency of

NOTE Confidence: 0.78889453

00:26:06.605 --> 00:26:08.109 the tone or whatever.

NOTE Confidence: 0.78889453

00:26:08.110 --> 00:26:10.528 OK, so this just underscores the

NOTE Confidence: 0.78889453

00:26:10.528 --> 00:26:12.900 importance of seller resolution recordings.

NOTE Confidence: 0.78889453

00:26:12.900 --> 00:26:15.510 So on a baler performed this

NOTE Confidence: 0.78889453

00:26:15.510 --> 00:26:18.119 and it had fixed task an.

NOTE Confidence: 0.78889453

00:26:18.120 --> 00:26:19.878 In this task,

NOTE Confidence: 0.78889453

00:26:19.878 --> 00:26:22.808 one tone predicts sucrose delivery.

NOTE Confidence: 0.78889453

00:26:22.810 --> 00:26:25.465 As you can see here and then in another,

NOTE Confidence: 0.78889453

00:26:25.470 --> 00:26:27.240 another town predicts quiet time delivery,

NOTE Confidence: 0.78889453

00:26:27.240 --> 00:26:29.010 which is a no go trial.

NOTE Confidence: 0.7276678

00:26:32.140 --> 00:26:35.080 So we did a match modality,

NOTE Confidence: 0.7276678

00:26:35.080 --> 00:26:38.265 build task where both the CSS and

NOTE Confidence: 0.7276678

00:26:38.265 --> 00:26:42.428 both US is were of the same modality.

NOTE Confidence: 0.7276678

00:26:42.430 --> 00:26:46.366 Auditory stimuli and gusta Tori outcomes.

NOTE Confidence: 0.7276678

00:26:46.370 --> 00:26:47.486 And generally speaking,

NOTE Confidence: 0.7276678

00:26:47.486 --> 00:26:49.718 for the non specific PLA recordings,

NOTE Confidence: 0.7276678

00:26:49.720 --> 00:26:51.970 we just reproduced publications that already

NOTE Confidence: 0.7276678

00:26:51.970 --> 00:26:54.550 existed from Dan Saltzman and Trajanic slabs,

NOTE Confidence: 0.7276678

00:26:54.550 --> 00:26:56.410 but we didn't, you know,

NOTE Confidence: 0.7276678

00:26:56.410 --> 00:26:58.270 go through all this trouble.

NOTE Confidence: 0.7276678

00:26:58.270 --> 00:27:00.130 We did record 1600 neurons,

NOTE Confidence: 0.7276678

00:27:00.130 --> 00:27:01.246 just we producers,

NOTE Confidence: 0.7276678

00:27:01.246 --> 00:27:02.734 although it's always nice,

NOTE Confidence: 0.7276678

00:27:02.740 --> 00:27:05.434 we wanted to know what neurons

NOTE Confidence: 0.7276678

00:27:05.434 --> 00:27:07.640 of Goan production target did.

NOTE Confidence: 0.7276678

00:27:07.640 --> 00:27:09.902 And so we used an approach

NOTE Confidence: 0.7276678

00:27:09.902 --> 00:27:11.780 developed in Tony Zeiders lab,

NOTE Confidence: 0.7276678

00:27:11.780 --> 00:27:13.965 which he termed Photostimulation assisted

NOTE Confidence: 0.7276678

00:27:13.965 --> 00:27:15.713 identification of neuronal populations

NOTE Confidence: 0.7276678

00:27:15.713 --> 00:27:18.009 which many people would refer to as

NOTE Confidence: 0.7276678

00:27:18.009 --> 00:27:19.670 photo identification or photo tagging.

NOTE Confidence: 0.7276678

00:27:19.670 --> 00:27:21.550 And basically the idea is

NOTE Confidence: 0.7276678

00:27:21.550 --> 00:27:23.054 you've got an electrode.

NOTE Confidence: 0.7276678

00:27:23.060 --> 00:27:24.940 You've got an optical fiber,

NOTE Confidence: 0.7276678

00:27:24.940 --> 00:27:27.060 and you've got some specific

NOTE Confidence: 0.7276678

00:27:27.060 --> 00:27:29.739 cell population that you have are

NOTE Confidence: 0.7276678

00:27:29.739 --> 00:27:32.119 expressing opposition and so first.

NOTE Confidence: 0.7276678

00:27:32.120 --> 00:27:34.556 You know it's near on a spikes.

NOTE Confidence: 0.7276678

00:27:34.560 --> 00:27:37.360 We can record that if neuron B spikes,

NOTE Confidence: 0.7276678

00:27:37.360 --> 00:27:39.496 we can record that too and we just

NOTE Confidence: 0.7276678

00:27:39.496 --> 00:27:41.877 want to record all the endogenous

NOTE Confidence: 0.7276678

00:27:41.877 --> 00:27:43.657 naturally occurring activity during

NOTE Confidence: 0.7276678

00:27:43.657 --> 00:27:46.076 the task after the task is over,

NOTE Confidence: 0.7276678

00:27:46.080 --> 00:27:48.024 we can shine light and get

NOTE Confidence: 0.7276678

00:27:48.024 --> 00:27:49.920 spikes out of the neuron.

NOTE Confidence: 0.7276678

00:27:49.920 --> 00:27:53.100 That is expressing option.

NOTE Confidence: 0.7276678

00:27:53.100 --> 00:27:55.028 Then we can look at that and determine

NOTE Confidence: 0.7276678

00:27:55.028 --> 00:27:56.808 whether there was a photoresponse or not.

NOTE Confidence: 0.7276678

00:27:56.810 --> 00:27:57.592 Importantly, very,

NOTE Confidence: 0.7276678

00:27:57.592 --> 00:27:58.374 very importantly,

NOTE Confidence: 0.7276678

00:27:58.374 --> 00:28:01.400 we need to control for recurrent excitation,

NOTE Confidence: 0.7276678

00:28:01.400 --> 00:28:04.088 particularly if you're doing photo tagging

NOTE Confidence: 0.7276678

00:28:04.088 --> 00:28:07.649 in any place known to have it like cortex,

NOTE Confidence: 0.7276678

00:28:07.650 --> 00:28:09.810 hippocampus, amygdala.

NOTE Confidence: 0.7276678

00:28:09.810 --> 00:28:10.946 What does this mean?

NOTE Confidence: 0.7276678

00:28:10.946 --> 00:28:11.230 Well,

NOTE Confidence: 0.7276678

00:28:11.230 --> 00:28:12.838 it's just referring to this compound

NOTE Confidence: 0.7276678

00:28:12.838 --> 00:28:15.129 that can occur if you have secret to

NOTE Confidence: 0.7276678

00:28:15.129 --> 00:28:16.881 expressing ones that are protected from,

NOTE Confidence: 0.7276678

00:28:16.890 --> 00:28:18.300 for example, BL A2 incumbents.

NOTE Confidence: 0.7276678

00:28:18.300 --> 00:28:19.432 Let's say that's great.

NOTE Confidence: 0.7276678

00:28:19.432 --> 00:28:21.130 Where were expressing in those cells?

NOTE Confidence: 0.7276678

00:28:21.130 --> 00:28:23.104 We can verify that anatomically post hoc,

NOTE Confidence: 0.7276678

00:28:23.110 --> 00:28:25.462 and it's easy in vivo to tell the

NOTE Confidence: 0.7276678

00:28:25.462 --> 00:28:27.419 difference between a teacher to expressing

NOTE Confidence: 0.7276678

00:28:27.419 --> 00:28:29.387 cell and a non expressing neighbor

NOTE Confidence: 0.7276678

00:28:29.444 --> 00:28:31.644 that is not responsive to light at all.

NOTE Confidence: 0.7276678

00:28:31.650 --> 00:28:32.133 However,

NOTE Confidence: 0.7276678

00:28:32.133 --> 00:28:35.514 there may also be non expressing neighbors

NOTE Confidence: 0.7276678

00:28:35.514 --> 00:28:37.725 that receive recurrent excitation

NOTE Confidence: 0.7276678

00:28:37.725 --> 00:28:40.635 from the opsin expressing neuron.

NOTE Confidence: 0.7276678

00:28:40.640 --> 00:28:42.360 And so when we pass,

NOTE Confidence: 0.7276678

00:28:42.360 --> 00:28:43.560 we can validate this.

NOTE Confidence: 0.7276678

00:28:43.560 --> 00:28:46.140 That doesn't help us in vivo necessarily,

NOTE Confidence: 0.7276678

00:28:46.140 --> 00:28:46.828 you'd think.

NOTE Confidence: 0.7276678

00:28:46.828 --> 00:28:49.580 But let's look at this and we can.

NOTE Confidence: 0.7276678

00:28:49.580 --> 00:28:50.450 We can patch.

NOTE Confidence: 0.7276678

00:28:50.450 --> 00:28:52.190 We can look at different light

NOTE Confidence: 0.7276678

00:28:52.190 --> 00:28:54.158 powers and determine a distribution

NOTE Confidence: 0.7276678

00:28:54.158 --> 00:28:55.778 of photo response latency's,

NOTE Confidence: 0.7276678

00:28:55.780 --> 00:28:57.490 because if it is through

NOTE Confidence: 0.7276678

00:28:57.490 --> 00:28:58.174 recurrent excitation,

NOTE Confidence: 0.7276678

00:28:58.180 --> 00:29:00.848 there's this added synapse.

NOTE Confidence: 0.7276678

00:29:00.850 --> 00:29:03.010 So sometimes the response to non

NOTE Confidence: 0.7276678

00:29:03.010 --> 00:29:04.908 expressing neighbors that are receiving

NOTE Confidence: 0.7276678

00:29:04.908 --> 00:29:07.278 input which you can determine and

NOTE Confidence: 0.7276678

00:29:07.278 --> 00:29:08.989 know about unequivocally ex vivo,

NOTE Confidence: 0.7276678

00:29:08.990 --> 00:29:10.598 you get the distribution.

NOTE Confidence: 0.7276678

00:29:10.598 --> 00:29:12.206 This distribution is completely

NOTE Confidence: 0.7276678

00:29:12.206 --> 00:29:13.995 non overlapping with those cells

NOTE Confidence: 0.7276678

00:29:13.995 --> 00:29:15.843 are actually trying to record from

NOTE Confidence: 0.7276678

00:29:15.843 --> 00:29:17.867 this feature to expressing neurons.

NOTE Confidence: 0.7276678

00:29:17.870 --> 00:29:20.966 That's great. That's often the case.

NOTE Confidence: 0.7276678

00:29:20.970 --> 00:29:21.582 Sometimes, though,

NOTE Confidence: 0.7276678

00:29:21.582 --> 00:29:23.724 the case is that there's some partial

NOTE Confidence: 0.7276678

00:29:23.724 --> 00:29:25.130 overlap where you for wrestle with

NOTE Confidence: 0.7276678

00:29:25.130 --> 00:29:26.950 once a pot with a false positive,

NOTE Confidence: 0.7276678

00:29:26.950 --> 00:29:27.962 once a false negative,

NOTE Confidence: 0.7276678

00:29:27.962 --> 00:29:29.227 and then some cases there's

NOTE Confidence: 0.7276678

00:29:29.227 --> 00:29:30.490 so much overlap issues.

NOTE Confidence: 0.7276678

00:29:30.490 --> 00:29:31.216 Different approach,

NOTE Confidence: 0.7276678

00:29:31.216 --> 00:29:33.394 like maybe you know genetically incredible

NOTE Confidence: 0.7276678

00:29:33.394 --> 00:29:34.749 calcium indicators or something.

NOTE Confidence: 0.7276678

00:29:34.750 --> 00:29:35.754 So we did this.

NOTE Confidence: 0.7276678

00:29:35.754 --> 00:29:36.758 I'm going to skip.

NOTE Confidence: 0.7276678

00:29:36.760 --> 00:29:38.284 I'm going to skip to the

NOTE Confidence: 0.7276678

00:29:38.284 --> 00:29:39.300 punchline of this story

NOTE Confidence: 0.81243426

00:29:39.355 --> 00:29:40.520 to tell you about new,

NOTE Confidence: 0.81243426

00:29:40.520 --> 00:29:41.651 unpublished data, but.

NOTE Confidence: 0.81243426

00:29:41.651 --> 00:29:43.536 We use multiple different types

NOTE Confidence: 0.81243426

00:29:43.536 --> 00:29:45.599 of analysis and found that in

NOTE Confidence: 0.81243426

00:29:45.599 --> 00:29:47.154 general it's true that village,

NOTE Confidence: 0.81243426

00:29:47.160 --> 00:29:49.128 an AC predominantly encodes positive balance.

NOTE Confidence: 0.81243426

00:29:49.130 --> 00:29:50.765 Be latest central amygdala predominantly

NOTE Confidence: 0.81243426

00:29:50.765 --> 00:29:52.718 encodes negative balance, and we've

NOTE Confidence: 0.81243426

00:29:52.718 --> 00:29:56.590 shown this in a bunch of different ways.

NOTE Confidence: 0.81243426

00:29:56.590 --> 00:29:58.090 So it is heterogeneous genius.

NOTE Confidence: 0.81243426

00:29:58.090 --> 00:29:59.878 There is a lot of heterogeneity,

NOTE Confidence: 0.81243426

00:29:59.880 --> 00:30:01.668 but the general trend is history.

NOTE Confidence: 0.81243426

00:30:01.670 --> 00:30:03.686 So what about the local interactions between

NOTE Confidence: 0.81243426

00:30:03.686 --> 00:30:04.960 these functionally distinct circuits?

NOTE Confidence: 0.81243426

00:30:04.960 --> 00:30:06.968 Why do we have them all like salt

NOTE Confidence: 0.81243426

00:30:06.968 --> 00:30:08.586 and pepper mingled together in

NOTE Confidence: 0.81243426

00:30:08.586 --> 00:30:10.336 the basal lateral make alone?

NOTE Confidence: 0.73263353

00:30:12.800 --> 00:30:15.960 What is the microcircuit architecture,

NOTE Confidence: 0.73263353

00:30:15.960 --> 00:30:19.648 so to speak well?

NOTE Confidence: 0.73263353

00:30:19.650 --> 00:30:22.386 If I have here in green reward encoding you

NOTE Confidence: 0.73263353

00:30:22.386 --> 00:30:25.048 know principle drones or production runs,

NOTE Confidence: 0.73263353

00:30:25.050 --> 00:30:29.334 fear encoding principles and then of course.

NOTE Confidence: 0.73263353

00:30:29.340 --> 00:30:31.645 Some interneurons that are that

NOTE Confidence: 0.73263353

00:30:31.645 --> 00:30:33.028 are Gabaergic interneurons,

NOTE Confidence: 0.73263353

00:30:33.030 --> 00:30:36.257 you might have one motif where there's

NOTE Confidence: 0.73263353

00:30:36.257 --> 00:30:38.100 mutual inhibition, where reward

NOTE Confidence: 0.73263353

00:30:38.100 --> 00:30:40.400 encoding neurons can silence fear,

NOTE Confidence: 0.73263353

00:30:40.400 --> 00:30:43.400 encoding neurons, and vice versa.

NOTE Confidence: 0.73263353

00:30:43.400 --> 00:30:45.563 You might actually also have a uni

NOTE Confidence: 0.73263353

00:30:45.563 --> 00:30:47.110 directional or asymmetric inhibition,

NOTE Confidence: 0.73263353

00:30:47.110 --> 00:30:48.790 where fear encoding neurons would

NOTE Confidence: 0.73263353

00:30:48.790 --> 00:30:50.134 silence reward encoding runs,

NOTE Confidence: 0.73263353

00:30:50.140 --> 00:30:51.484 but not vice versa.

NOTE Confidence: 0.73263353

00:30:51.484 --> 00:30:54.176 And honestly, when I first drew this picture,

NOTE Confidence: 0.73263353

00:30:54.180 --> 00:30:56.500 I just drew it 'cause I thought like

NOTE Confidence: 0.73263353

00:30:56.500 --> 00:30:58.229 technically it's another possibility.

NOTE Confidence: 0.73263353

00:30:58.230 --> 00:31:00.534 I didn't actually think it was

NOTE Confidence: 0.73263353

00:31:00.534 --> 00:31:02.740 going to be the answer.

NOTE Confidence: 0.73263353

00:31:02.740 --> 00:31:03.984 And then of course,

NOTE Confidence: 0.73263353

00:31:03.984 --> 00:31:05.228 like the third possibility,

NOTE Confidence: 0.73263353

00:31:05.230 --> 00:31:07.420 being that there's a neutral

NOTE Confidence: 0.73263353

00:31:07.420 --> 00:31:08.296 excitatory response.

NOTE Confidence: 0.73263353

00:31:08.300 --> 00:31:10.220 Felt thanks to Klong Hoon Chung.

NOTE Confidence: 0.73263353

00:31:10.220 --> 00:31:12.443 We were able to look at this and you

NOTE Confidence: 0.73263353

00:31:12.443 --> 00:31:14.494 can see here some bling NEC ability

NOTE Confidence: 0.73263353

00:31:14.494 --> 00:31:17.016 to see an cells within the lateral

NOTE Confidence: 0.73263353

00:31:17.016 --> 00:31:19.176 nebula intermingled so much together,

NOTE Confidence: 0.73263353

00:31:19.180 --> 00:31:22.477 but also you know there's a gradient.

NOTE Confidence: 0.73263353

00:31:22.480 --> 00:31:24.920 So indeed there are gradients.

NOTE Confidence: 0.73263353

00:31:24.920 --> 00:31:27.188 We can quantify them,

NOTE Confidence: 0.73263353

00:31:27.188 --> 00:31:29.456 and they are intermingled.

NOTE Confidence: 0.73263353

00:31:29.460 --> 00:31:31.574 So this sort of underscores the need

NOTE Confidence: 0.73263353

00:31:31.574 --> 00:31:33.974 to think about the relationship between

NOTE Confidence: 0.73263353

00:31:33.974 --> 00:31:36.349 these different populations of neurons,

NOTE Confidence: 0.73263353

00:31:36.350 --> 00:31:39.797 so I'll just show you one little tidbit here.

NOTE Confidence: 0.73263353

00:31:39.800 --> 00:31:42.348 But when we looked at the latest

NOTE Confidence: 0.73263353

00:31:42.348 --> 00:31:43.914 central amygdala neurons that

NOTE Confidence: 0.73263353

00:31:43.914 --> 00:31:45.546 were photo identified here,

NOTE Confidence: 0.73263353

00:31:45.550 --> 00:31:46.974 we've got 33 units.

NOTE Confidence: 0.73263353

00:31:46.974 --> 00:31:49.110 We can also see neurons that

NOTE Confidence: 0.73263353

00:31:49.192 --> 00:31:50.530 are photo excited,

NOTE Confidence: 0.73263353

00:31:50.530 --> 00:31:52.440 meaning they have slower latency,

NOTE Confidence: 0.73263353

00:31:52.440 --> 00:31:55.470 excitation, and response to light.

NOTE Confidence: 0.73263353

00:31:55.470 --> 00:31:57.636 Order on that were photo inhibited,

NOTE Confidence: 0.73263353

00:31:57.640 --> 00:31:59.908 meaning they were silenced by the activation

NOTE Confidence: 0.73263353

00:31:59.908 --> 00:32:02.329 of the late Essential Omega neurons.

NOTE Confidence: 0.73263353

00:32:02.330 --> 00:32:04.857 So if you look at these numbers,

NOTE Confidence: 0.73263353

00:32:04.860 --> 00:32:07.556 you can see that the the the amount

NOTE Confidence: 0.73263353

00:32:07.556 --> 00:32:09.549 of neurons that it's silent.

NOTE Confidence: 0.73263353

00:32:09.550 --> 00:32:11.518 These bileta CN neurons or silencing

NOTE Confidence: 0.73263353

00:32:11.518 --> 00:32:13.520 is greater than them themselves,

NOTE Confidence: 0.73263353

00:32:13.520 --> 00:32:16.608 and so there's this huge ability for them

NOTE Confidence: 0.73263353

00:32:16.608 --> 00:32:19.719 to suppress the responses of other neurons.

NOTE Confidence: 0.73263353

00:32:19.720 --> 00:32:21.360 So.

NOTE Confidence: 0.73263353

00:32:21.360 --> 00:32:22.080 You know,

NOTE Confidence: 0.73263353

00:32:22.080 --> 00:32:23.160 perhaps it's true,

NOTE Confidence: 0.73263353

00:32:23.160 --> 00:32:25.288 like if we compare these numbers that

NOTE Confidence: 0.73263353

00:32:25.288 --> 00:32:27.739 I just showed you for the normalizing

NOTE Confidence: 0.73263353

00:32:27.739 --> 00:32:29.953 to the neurons that actually expressed

NOTE Confidence: 0.73263353

00:32:30.022 --> 00:32:31.987 channelrhodopsin and then looking at

NOTE Confidence: 0.73263353

00:32:31.987 --> 00:32:34.320 the proportion of neurons are excited

NOTE Confidence: 0.73263353

00:32:34.320 --> 00:32:36.120 or inhibited by those projectors.

NOTE Confidence: 0.73263353

00:32:36.120 --> 00:32:38.598 You can see that the latest Central

NOTE Confidence: 0.73263353

00:32:38.598 --> 00:32:40.441 McDonald's inhibit far more neurons

NOTE Confidence: 0.73263353

00:32:40.441 --> 00:32:42.954 than do either of the other productions.

NOTE Confidence: 0.73263353

00:32:42.960 --> 00:32:45.480 So maybe when it comes down to

NOTE Confidence: 0.73263353

00:32:45.480 --> 00:32:47.896 a majority vote, so so to speak,

NOTE Confidence: 0.73263353

00:32:47.896 --> 00:32:49.900 at the Bellator CN population is

NOTE Confidence: 0.73263353

00:32:49.973 --> 00:32:52.478 more influential than local network.

NOTE Confidence: 0.73263353

00:32:52.480 --> 00:32:54.846 And maybe their votes count more similar,

NOTE Confidence: 0.73263353

00:32:54.850 --> 00:32:55.492 you know,

NOTE Confidence: 0.73263353

00:32:55.492 --> 00:32:57.418 so that might be like something

NOTE Confidence: 0.73263353

00:32:57.418 --> 00:32:59.239 that we want to consider.

NOTE Confidence: 0.73263353

00:32:59.240 --> 00:33:00.925 It's not necessarily that all

NOTE Confidence: 0.73263353

00:33:00.925 --> 00:33:01.936 votes are equal,

NOTE Confidence: 0.73263353

00:33:01.940 --> 00:33:03.968 not necessarily just a majority vote.

NOTE Confidence: 0.73263353

00:33:03.970 --> 00:33:05.764 Some neurons are positioned to be

NOTE Confidence: 0.73263353

00:33:05.764 --> 00:33:07.436 able to exert greater influence

NOTE Confidence: 0.73263353

00:33:07.436 --> 00:33:10.401 over their neighbors, like be late,

NOTE Confidence: 0.73263353

00:33:10.401 --> 00:33:12.669 essential in Glen Rose.

NOTE Confidence: 0.73263353

00:33:12.670 --> 00:33:15.934 Now, why won't the brain work this way?

NOTE Confidence: 0.73263353

00:33:15.940 --> 00:33:18.439 If we record from this is published

NOTE Confidence: 0.73263353

00:33:18.439 --> 00:33:20.849 in in Gwendolyn Calhouns preprint.

NOTE Confidence: 0.73263353

00:33:20.850 --> 00:33:23.678 But when we record from from NEC

NOTE Confidence: 0.73263353

00:33:23.678 --> 00:33:25.350 Projectors and green Eyes,

NOTE Confidence: 0.73263353

00:33:25.350 --> 00:33:27.612 just abbreviated it end and patch

NOTE Confidence: 0.73263353

00:33:27.612 --> 00:33:30.504 a record from from any project and

NOTE Confidence: 0.73263353

00:33:30.504 --> 00:33:33.114 stimulate CN protectors or vice versa.

NOTE Confidence: 0.7511034

00:33:33.120 --> 00:33:34.752 You know, recording stimulate

NOTE Confidence: 0.7511034

00:33:34.752 --> 00:33:36.792 from the opposite pairing you.

NOTE Confidence: 0.7511034

00:33:36.800 --> 00:33:39.386 We actually see that they have

NOTE Confidence: 0.7511034

00:33:39.386 --> 00:33:41.110 different asymmetric impact on

NOTE Confidence: 0.7511034

00:33:41.187 --> 00:33:43.307 each other when you stimulate.

NOTE Confidence: 0.7511034

00:33:43.310 --> 00:33:46.280 Uhm? A common projectors recording

NOTE Confidence: 0.7511034

00:33:46.280 --> 00:33:48.656 from central appraisal of

NOTE Confidence: 0.7511034

00:33:48.656 --> 00:33:51.350 projectors you actually facilitate.

NOTE Confidence: 0.7511034

00:33:51.350 --> 00:33:52.985 Excitation, whereas in the other

NOTE Confidence: 0.7511034

00:33:52.985 --> 00:33:55.284 direction you suppress it, so why would?

NOTE Confidence: 0.7511034

00:33:55.284 --> 00:33:57.580 Why would the brain work this way?

NOTE Confidence: 0.7511034

00:33:57.580 --> 00:34:00.204 I did not expect to see an asymmetric

NOTE Confidence: 0.7511034

00:34:00.204 --> 00:34:00.860 unidirectional relationship,

NOTE Confidence: 0.7511034

00:34:00.860 --> 00:34:03.226 but maybe that makes sense because you

NOTE Confidence: 0.7511034

00:34:03.226 --> 00:34:06.110 know you can mate or eat or drink later.

NOTE Confidence: 0.7511034

00:34:06.110 --> 00:34:08.336 You need to escape from that predator

NOTE Confidence: 0.7511034

00:34:08.336 --> 00:34:10.698 right now that is the most immediate,

NOTE Confidence: 0.7511034

00:34:10.700 --> 00:34:12.340 most urgent demand or threat

NOTE Confidence: 0.7511034

00:34:12.340 --> 00:34:13.324 on your survival.

NOTE Confidence: 0.7511034

00:34:13.330 --> 00:34:15.286 So you have to address that.

NOTE Confidence: 0.8124424

00:34:17.850 --> 00:34:19.362 Further, maybe it makes sense 'cause

NOTE Confidence: 0.8124424

00:34:19.362 --> 00:34:21.149 reward seeking is just inherently risky.

NOTE Confidence: 0.8124424

00:34:21.150 --> 00:34:23.697 If I'm a mouse that lives in in my

NOTE Confidence: 0.8124424

00:34:23.697 --> 00:34:25.768 borough and I need to, I need to.

NOTE Confidence: 0.8124424

00:34:25.768 --> 00:34:28.030 I want to forage for food or water.

NOTE Confidence: 0.8124424

00:34:28.030 --> 00:34:29.986 Then you know, providing a skip

NOTE Confidence: 0.8124424

00:34:29.986 --> 00:34:32.540 could be a good insurance policy.

NOTE Confidence: 0.8124424

00:34:32.540 --> 00:34:34.280 OK, so that's some speculation

NOTE Confidence: 0.8124424

00:34:34.280 --> 00:34:36.374 and just contacts, but how does

NOTE Confidence: 0.8124424

00:34:36.374 --> 00:34:38.462 neuromodulation play a role in here?

NOTE Confidence: 0.8124424

00:34:38.470 --> 00:34:40.920 So this is the third final questions.

NOTE Confidence: 0.8124424

00:34:40.920 --> 00:34:44.637 Main big question or focus on today.

NOTE Confidence: 0.8124424

00:34:44.640 --> 00:34:46.992 And for that meeting that I want to

NOTE Confidence: 0.8124424

00:34:46.992 --> 00:34:48.840 actually show you the the questions

NOTE Confidence: 0.8124424

00:34:48.840 --> 00:34:51.240 that that make me lose sleep at night.

NOTE Confidence: 0.8124424

00:34:51.240 --> 00:34:52.920 So it's great that we found that

NOTE Confidence: 0.8124424

00:34:52.920 --> 00:34:54.360 you know after fear conditioning

NOTE Confidence: 0.8124424

00:34:54.360 --> 00:34:56.020 we see strengthening of synapses

NOTE Confidence: 0.8124424

00:34:56.020 --> 00:34:57.839 going down one path afterward,

NOTE Confidence: 0.8124424

00:34:57.840 --> 00:34:59.640 conditioning with the strengthening of steps,

NOTE Confidence: 0.8124424

00:34:59.640 --> 00:35:02.350 going down another path, but.

NOTE Confidence: 0.8124424

00:35:02.350 --> 00:35:05.017 When this is happening in real life,

NOTE Confidence: 0.8124424

00:35:05.020 --> 00:35:08.450 you know animals are capable of 1

NOTE Confidence: 0.8124424

00:35:08.450 --> 00:35:10.762 trial learning. How is this possible?

NOTE Confidence: 0.8124424

00:35:10.762 --> 00:35:11.428 You know?

NOTE Confidence: 0.8124424

00:35:11.430 --> 00:35:13.418 So I think the timescales how do

NOTE Confidence: 0.8124424

00:35:13.418 --> 00:35:15.176 the synapses know which postsynaptic

NOTE Confidence: 0.8124424

00:35:15.176 --> 00:35:16.439 neurons are which,

NOTE Confidence: 0.8124424

00:35:16.440 --> 00:35:18.450 and what you're supposed to do,

NOTE Confidence: 0.8124424

00:35:18.450 --> 00:35:20.543 so you know if you think about

NOTE Confidence: 0.8124424

00:35:20.543 --> 00:35:22.120 spike timing dependent plasticity,

NOTE Confidence: 0.8124424

00:35:22.120 --> 00:35:24.240 you know shifting things from

NOTE Confidence: 0.8124424

00:35:24.240 --> 00:35:26.360 just 50 or 100 milliseconds.

NOTE Confidence: 0.8124424

00:35:26.360 --> 00:35:27.744 Can dramatically impact whether

NOTE Confidence: 0.8124424

00:35:27.744 --> 00:35:29.128 it's LTP or Ltd.

NOTE Confidence: 0.8124424

00:35:29.130 --> 00:35:30.860 If we record in vivo,

NOTE Confidence: 0.8124424

00:35:30.860 --> 00:35:33.148 you can see that after the onset of

NOTE Confidence: 0.8124424

00:35:33.148 --> 00:35:35.707 the Q this the the auditory tone

NOTE Confidence: 0.8124424

00:35:35.707 --> 00:35:38.120 just 100 or 200 milliseconds later,

NOTE Confidence: 0.8124424

00:35:38.120 --> 00:35:39.850 we're back down to baseline.

NOTE Confidence: 0.8124424

00:35:39.850 --> 00:35:40.879 We don't have.

NOTE Confidence: 0.8124424

00:35:40.879 --> 00:35:43.280 You know the neurons are no longer

NOTE Confidence: 0.8124424

00:35:43.350 --> 00:35:46.078 active even as the Q continues to play.

NOTE Confidence: 0.8124424

00:35:46.080 --> 00:35:48.222 And then let's think about the

NOTE Confidence: 0.8124424

00:35:48.222 --> 00:35:50.391 most common paradigms used in the

NOTE Confidence: 0.8124424

00:35:50.391 --> 00:35:51.743 field where condition stimulus

NOTE Confidence: 0.8124424

00:35:51.743 --> 00:35:54.039 will play for 10 or 20 seconds,

NOTE Confidence: 0.8124424

00:35:54.040 --> 00:35:56.265 the beeline neurons that are

NOTE Confidence: 0.8124424

00:35:56.265 --> 00:35:58.045 critical for the plasticity.

NOTE Confidence: 0.8124424

00:35:58.050 --> 00:35:59.952 Please tell a very transient activation

NOTE Confidence: 0.8124424

00:35:59.952 --> 00:36:02.608 at the onset of the condition stimulus,

NOTE Confidence: 0.8124424

00:36:02.610 --> 00:36:05.458 then then go back down to baseline and

NOTE Confidence: 0.8124424

00:36:05.458 --> 00:36:08.229 you know could be 10 or 20 seconds.

NOTE Confidence: 0.8124424

00:36:08.230 --> 00:36:09.980 The unconditioned stimulus is presented.

NOTE Confidence: 0.8124424

00:36:09.980 --> 00:36:12.086 So how does the brain solve

NOTE Confidence: 0.8124424

00:36:12.086 --> 00:36:13.490 the valence assignment problem?

NOTE Confidence: 0.8124424

00:36:13.490 --> 00:36:15.695 How does the brain attach these things

NOTE Confidence: 0.8124424

00:36:15.695 --> 00:36:18.407 that are so desperate in time together?

NOTE Confidence: 0.8124424

00:36:18.410 --> 00:36:21.569 So first there's the question of how do they?

NOTE Confidence: 0.8124424

00:36:21.570 --> 00:36:23.670 How does the brain know which

NOTE Confidence: 0.8124424

00:36:23.670 --> 00:36:25.430 synapses route information to wear?

NOTE Confidence: 0.8124424

00:36:25.430 --> 00:36:28.294 So there's a few different options here so.

NOTE Confidence: 0.8124424

00:36:28.300 --> 00:36:29.488 In terms of knowing,

NOTE Confidence: 0.8124424

00:36:29.488 --> 00:36:30.973 knowing who's who in terms

NOTE Confidence: 0.8124424

00:36:30.973 --> 00:36:32.758 of the postsynaptic neuron,

NOTE Confidence: 0.8124424

00:36:32.760 --> 00:36:35.736 we wanted to explore this and so we

NOTE Confidence: 0.8124424

00:36:35.736 --> 00:36:38.310 sequenced violate any simulated CM neurons.

NOTE Confidence: 0.8124424

00:36:38.310 --> 00:36:40.716 And look for surface receptor specifically.

NOTE Confidence: 0.8124424

00:36:40.720 --> 00:36:41.093 Indeed,

NOTE Confidence: 0.8124424

00:36:41.093 --> 00:36:43.704 one service provider that we identified as

NOTE Confidence: 0.8124424

00:36:43.704 --> 00:36:45.950 interesting is the Neurotensin receptor,

NOTE Confidence: 0.8124424

00:36:45.950 --> 00:36:48.982 one which we see to be enriched have

NOTE Confidence: 0.8124424

00:36:48.982 --> 00:36:51.170 enriched expression and Sian projectors.

NOTE Confidence: 0.8124424

00:36:51.170 --> 00:36:54.455 Now why am I going to focus in on

NOTE Confidence: 0.8124424

00:36:54.455 --> 00:36:57.790 the nearest ends in one receptor?

NOTE Confidence: 0.8124424

00:36:57.790 --> 00:36:58.144 Well,

NOTE Confidence: 0.8124424

00:36:58.144 --> 00:37:00.976 we know that there is a one receptor

NOTE Confidence: 0.8124424

00:37:00.976 --> 00:37:03.829 controls a G protein coupled receptor GP CR.

NOTE Confidence: 0.8124424

00:37:03.830 --> 00:37:05.828 The function of this receptor has

NOTE Confidence: 0.8124424

00:37:05.828 --> 00:37:09.086 been linked to both LDP in the PLA and

NOTE Confidence: 0.8124424

00:37:09.086 --> 00:37:10.570 also contextual fear conditioning.

NOTE Confidence: 0.8124424

00:37:10.570 --> 00:37:13.330 And the thing that really got me was

NOTE Confidence: 0.8124424

00:37:13.330 --> 00:37:16.997 done by Kimberly Kempadoo and she found that.

NOTE Confidence: 0.7342665

00:37:17.000 --> 00:37:19.280 Different concentrations of narrow tense,

NOTE Confidence: 0.7342665

00:37:19.280 --> 00:37:22.458 and this is a different cell population,

NOTE Confidence: 0.7342665

00:37:22.460 --> 00:37:24.180 but different concentrations are

NOTE Confidence: 0.7342665

00:37:24.180 --> 00:37:26.330 intense and could actually either

NOTE Confidence: 0.7342665

00:37:26.330 --> 00:37:28.050 facilitate glutamatergic transmission

NOTE Confidence: 0.7342665

00:37:28.050 --> 00:37:30.510 or suppress glutamatergic transmission.

NOTE Confidence: 0.7342665

00:37:30.510 --> 00:37:34.808 So if this is possible, you know then?

NOTE Confidence: 0.7342665

00:37:34.808 --> 00:37:37.724 We hypothesize that but the same

NOTE Confidence: 0.7342665

00:37:37.724 --> 00:37:40.680 concentration of their attention could then,

NOTE Confidence: 0.7342665

00:37:40.680 --> 00:37:42.960 you know, drive effects differently on

NOTE Confidence: 0.7342665

00:37:42.960 --> 00:37:45.005 these projector populations that have

NOTE Confidence: 0.7342665

00:37:45.005 --> 00:37:46.889 different receptor expression profiles.

NOTE Confidence: 0.7342665

00:37:46.890 --> 00:37:48.855 OK, so if different concentrations

NOTE Confidence: 0.7342665

00:37:48.855 --> 00:37:51.440 are neurons at the same profile,

NOTE Confidence: 0.7342665

00:37:51.440 --> 00:37:53.510 can can make glutamatergic transmission

NOTE Confidence: 0.7342665

00:37:53.510 --> 00:37:55.580 either be facilitated or suppressed,

NOTE Confidence: 0.7342665

00:37:55.580 --> 00:37:57.854 then maybe one concentration of their

NOTE Confidence: 0.7342665

00:37:57.854 --> 00:38:00.196 attention can shift the balance from

NOTE Confidence: 0.7342665

00:38:00.196 --> 00:38:02.849 one population to another if they have

NOTE Confidence: 0.7342665

00:38:02.849 --> 00:38:05.099 different receptor expression profiles.

NOTE Confidence: 0.7793689

00:38:07.530 --> 00:38:09.918 So first we want to explore

NOTE Confidence: 0.7793689

00:38:09.918 --> 00:38:11.510 this an we performed.

NOTE Confidence: 0.7793689

00:38:11.510 --> 00:38:14.205 We did some pharmacological manipulations

NOTE Confidence: 0.7793689

00:38:14.205 --> 00:38:16.900 where we administered the audience

NOTE Confidence: 0.7793689

00:38:16.976 --> 00:38:19.148 or want agonist in today's letter

NOTE Confidence: 0.7793689

00:38:19.148 --> 00:38:22.367 will make the lab and we actually saw

NOTE Confidence: 0.7793689

00:38:22.367 --> 00:38:24.492 an enhancement of reward learning.

NOTE Confidence: 0.7793689

00:38:24.500 --> 00:38:26.840 We saw a nonsignificant trend towards

NOTE Confidence: 0.7793689

00:38:26.840 --> 00:38:29.330 an impairment of fear conditioning.

NOTE Confidence: 0.7793689

00:38:29.330 --> 00:38:31.640 OK, so that's potentially, you know,

NOTE Confidence: 0.7793689

00:38:31.640 --> 00:38:33.180 suggested that narrative could

NOTE Confidence: 0.7793689

00:38:33.180 --> 00:38:35.490 play a role in balance processing,

NOTE Confidence: 0.7793689

00:38:35.490 --> 00:38:38.017 and we also see that indeed there

NOTE Confidence: 0.7793689

00:38:38.017 --> 00:38:39.915 are different effects you know

NOTE Confidence: 0.7793689

00:38:39.915 --> 00:38:41.785 match for credit concentration of

NOTE Confidence: 0.7793689

00:38:41.785 --> 00:38:43.959 Billy and Acnb licien neurons.

NOTE Confidence: 0.7793689

00:38:43.960 --> 00:38:46.860 We do indeed see different

NOTE Confidence: 0.7793689

00:38:46.860 --> 00:38:48.600 dose response curves.

NOTE Confidence: 0.7793689

00:38:48.600 --> 00:38:51.162 These differences at a given concentration

NOTE Confidence: 0.7793689

00:38:51.162 --> 00:38:54.268 of tendon, animal or near attention,

NOTE Confidence: 0.7793689

00:38:54.268 --> 00:38:59.298 we can see an increase of billet and AC.

NOTE Confidence: 0.7793689

00:38:59.300 --> 00:39:01.502 Amplitudes EPS evoked from Billy the

NOTE Confidence: 0.7793689

00:39:01.502 --> 00:39:04.070 NACS neurons, and a suppression of EPS,

NOTE Confidence: 0.7793689

00:39:04.070 --> 00:39:07.006 sees a bug from the legacy M neurons,

NOTE Confidence: 0.7793689

00:39:07.010 --> 00:39:10.069 and this is blocked by the NPS

NOTE Confidence: 0.7793689

00:39:10.069 --> 00:39:11.380 are one antagonist.

NOTE Confidence: 0.7793689

00:39:11.380 --> 00:39:14.140 OK, great, but where do we get near?

NOTE Confidence: 0.7793689

00:39:14.140 --> 00:39:15.520 It ends in front.

NOTE Confidence: 0.7793689

00:39:15.520 --> 00:39:17.245 Where does it come from?

NOTE Confidence: 0.7793689

00:39:17.250 --> 00:39:19.994 So we we trace upstream and looked for

NOTE Confidence: 0.7793689

00:39:19.994 --> 00:39:21.451 colocalization of Tracer suggesting

NOTE Confidence: 0.7793689

00:39:21.451 --> 00:39:23.936 that you were protecting the leg as

NOTE Confidence: 0.7793689

00:39:23.936 --> 00:39:25.974 well as expression of neural tension

NOTE Confidence: 0.7793689

00:39:25.974 --> 00:39:29.979 in the New York Times and cream mask.

NOTE Confidence: 0.7793689

00:39:29.980 --> 00:39:32.725 And so we found that the PDT was a

NOTE Confidence: 0.7793689

00:39:32.725 --> 00:39:35.119 prime target and photo stimulating

NOTE Confidence: 0.7793689

00:39:35.119 --> 00:39:38.137 PDT to belay neurons produces valence

NOTE Confidence: 0.7793689

00:39:38.217 --> 00:39:40.807 specific effects that we actually.

NOTE Confidence: 0.7793689

00:39:40.810 --> 00:39:44.698 If we stimulate this PT input to be alive,

NOTE Confidence: 0.7793689

00:39:44.700 --> 00:39:46.844 which includes neurotensin neurons,

NOTE Confidence: 0.7793689

00:39:46.844 --> 00:39:50.631 we see a facilitation of reward learning

NOTE Confidence: 0.7793689

00:39:50.631 --> 00:39:53.577 and an impairment of fear looming.

NOTE Confidence: 0.7793689

00:39:53.580 --> 00:39:55.897 Next to this huge body of work

NOTE Confidence: 0.7793689

00:39:55.897 --> 00:39:58.327 that I'm about to tell you about to

NOTE Confidence: 0.7793689

00:39:58.327 --> 00:40:00.746 get into is a by Hailee a postdoc

NOTE Confidence: 0.7793689

00:40:00.746 --> 00:40:02.708 in my lab here at salt.

NOTE Confidence: 0.7793689

00:40:02.710 --> 00:40:03.340 And what,

NOTE Confidence: 0.7793689

00:40:03.340 --> 00:40:06.448 how found was that the PDT to bill a

NOTE Confidence: 0.7793689

00:40:06.448 --> 00:40:09.023 nuro 10 synergic projection contributes

NOTE Confidence: 0.7793689

00:40:09.023 --> 00:40:11.083 heavily to Billy computations,

NOTE Confidence: 0.7793689

00:40:11.090 --> 00:40:14.177 and so he said to look at this and

NOTE Confidence: 0.7793689

00:40:14.177 --> 00:40:16.443 interrogate the contribution of Neuro

NOTE Confidence: 0.7793689

00:40:16.443 --> 00:40:19.890 10 synergic input from this specific pathway,

NOTE Confidence: 0.7793689

00:40:19.890 --> 00:40:21.506 we first Chris Byrd.

NOTE Confidence: 0.7793689

00:40:21.506 --> 00:40:23.930 We used CRISPR to knock down

NOTE Confidence: 0.7793689

00:40:24.022 --> 00:40:26.167 that near attend and Gene.

NOTE Confidence: 0.7793689

00:40:26.170 --> 00:40:29.482 And so the PDT input would either have

NOTE Confidence: 0.7793689

00:40:29.482 --> 00:40:32.756 knocked down or control of your attention.

NOTE Confidence: 0.7793689

00:40:32.760 --> 00:40:35.712 Then we wanted to be able to perform

NOTE Confidence: 0.7793689

00:40:35.712 --> 00:40:38.529 recordings in the basil lateral amygdala,

NOTE Confidence: 0.7793689

00:40:38.530 --> 00:40:40.522 in both control an crisper animals

NOTE Confidence: 0.7793689

00:40:40.522 --> 00:40:43.038 and be able to photo identify

NOTE Confidence: 0.7793689

00:40:43.038 --> 00:40:44.706 the different populations.

NOTE Confidence: 0.7793689

00:40:44.710 --> 00:40:47.806 So first I'm just showing you that the

NOTE Confidence: 0.7793689

00:40:47.806 --> 00:40:50.210 crisper works we can inactivate the

NOTE Confidence: 0.7793689

00:40:50.210 --> 00:40:53.360 near 10s and gene and preserve glutamate.

NOTE Confidence: 0.5319372

00:40:55.460 --> 00:40:57.480 Narrative the neurons coberly's glutamate.

NOTE Confidence: 0.738340900000001

00:40:59.610 --> 00:41:02.130 And we found that the crisper animals

NOTE Confidence: 0.738340900000001

00:41:02.130 --> 00:41:04.282 will be knocked down the narrow

NOTE Confidence: 0.738340900000001

00:41:04.282 --> 00:41:06.613 Tenzin gene within the PD gbla we

NOTE Confidence: 0.738340900000001

00:41:06.683 --> 00:41:09.197 see an impairment of reward learning,

NOTE Confidence: 0.738340900000001

00:41:09.200 --> 00:41:11.050 and this also promotes fear.

NOTE Confidence: 0.738340900000001

00:41:11.050 --> 00:41:13.969 Learning this is again suggesting this role

NOTE Confidence: 0.738340900000001

00:41:13.969 --> 00:41:16.828 for near Tencent in Valence processing.

NOTE Confidence: 0.738340900000001

00:41:16.830 --> 00:41:19.926 OK, but how is this role actually like?

NOTE Confidence: 0.738340900000001

00:41:19.930 --> 00:41:21.860 What does this look like?

NOTE Confidence: 0.738340900000001

00:41:21.860 --> 00:41:23.015 What? How does?

NOTE Confidence: 0.738340900000001

00:41:23.015 --> 00:41:24.940 How do the computations that

NOTE Confidence: 0.738340900000001

00:41:24.940 --> 00:41:27.278 are being performed in the PLA?

NOTE Confidence: 0.738340900000001

00:41:27.280 --> 00:41:29.245 How are the computations being

NOTE Confidence: 0.738340900000001

00:41:29.245 --> 00:41:31.210 modified when you know there's

NOTE Confidence: 0.738340900000001

00:41:31.280 --> 00:41:32.700 more attention or not?

NOTE Confidence: 0.766144792857143

00:41:34.850 --> 00:41:38.130 And so dumb. How recorded from hundreds of

NOTE Confidence: 0.766144792857143

00:41:38.130 --> 00:41:41.038 neurons from the basal lateral amygdala,

NOTE Confidence: 0.766144792857143

00:41:41.040 --> 00:41:44.048 in a task where animals had to just

NOTE Confidence: 0.766144792857143

00:41:44.048 --> 00:41:46.030 differentiate between a reward and

NOTE Confidence: 0.766144792857143

00:41:46.030 --> 00:41:48.726 shock predictive cues, as well as a

NOTE Confidence: 0.766144792857143

00:41:48.726 --> 00:41:51.030 neutral Q that didn't predict anything,

NOTE Confidence: 0.766144792857143

00:41:51.030 --> 00:41:52.945 and we perform functional agglomerative

NOTE Confidence: 0.766144792857143

00:41:52.945 --> 00:41:55.250 clustering, and we can see that

NOTE Confidence: 0.766144792857143

00:41:55.250 --> 00:41:57.170 across different types of clusters.

NOTE Confidence: 0.766144792857143

00:41:57.170 --> 00:41:59.858 Here, Gray is controlled and blue is

NOTE Confidence: 0.766144792857143

00:41:59.858 --> 00:42:03.355 crisper and across the board. But you know,

NOTE Confidence: 0.766144792857143

00:42:03.355 --> 00:42:05.980 there's a diversity of responses.

NOTE Confidence: 0.766144792857143

00:42:05.980 --> 00:42:08.290 But what you can see across the

NOTE Confidence: 0.766144792857143

00:42:08.290 --> 00:42:10.582 board in each of these clusters

NOTE Confidence: 0.766144792857143

00:42:10.582 --> 00:42:13.030 is that the response is blunted.

NOTE Confidence: 0.766144792857143

00:42:13.030 --> 00:42:14.885 When we Chris Brown your

NOTE Confidence: 0.766144792857143

00:42:14.885 --> 00:42:16.369 attention on both directions,

NOTE Confidence: 0.766144792857143

00:42:16.370 --> 00:42:18.220 both for excitations an ambitions,

NOTE Confidence: 0.766144792857143

00:42:18.220 --> 00:42:20.075 the absolute value of the

NOTE Confidence: 0.766144792857143

00:42:20.075 --> 00:42:21.559 amplitude of the response,

NOTE Confidence: 0.766144792857143

00:42:21.560 --> 00:42:23.465 the change in physical activity

NOTE Confidence: 0.766144792857143

00:42:23.465 --> 00:42:25.370 in either direction to reward

NOTE Confidence: 0.766144792857143

00:42:25.440 --> 00:42:27.130 or Punish Inc uses reduced,

NOTE Confidence: 0.766144792857143

00:42:27.130 --> 00:42:29.190 so every all the valence

NOTE Confidence: 0.766144792857143

00:42:29.190 --> 00:42:31.250 processing just looks blunted by

NOTE Confidence: 0.766144792857143

00:42:31.324 --> 00:42:33.709 the knockdown of their attention.

NOTE Confidence: 0.766144792857143

00:42:33.710 --> 00:42:37.060 OK, So what about specifically

NOTE Confidence: 0.766144792857143

00:42:37.060 --> 00:42:39.740 to BLAN AC projectors?

NOTE Confidence: 0.766144792857143

00:42:39.740 --> 00:42:43.708 We see that indeed.

NOTE Confidence: 0.766144792857143

00:42:43.710 --> 00:42:46.356 Control animals we replicate this general

NOTE Confidence: 0.766144792857143

00:42:46.356 --> 00:42:49.370 effect of having a reward you know,

NOTE Confidence: 0.766144792857143

00:42:49.370 --> 00:42:51.560 a positive balance biased encoding

NOTE Confidence: 0.766144792857143

00:42:51.560 --> 00:42:54.590 property which drops sort of to neutral.

NOTE Confidence: 0.766144792857143

00:42:54.590 --> 00:42:57.306 When we Chris Brown are tense and

NOTE Confidence: 0.766144792857143

00:42:57.306 --> 00:42:59.370 same thing central projectors.

NOTE Confidence: 0.766144792857143

00:42:59.370 --> 00:43:01.455 We reproduced our initial response

NOTE Confidence: 0.766144792857143

00:43:01.455 --> 00:43:04.065 of having a negative balance biased

NOTE Confidence: 0.766144792857143

00:43:04.065 --> 00:43:06.330 response of this whole population,

NOTE Confidence: 0.766144792857143

00:43:06.330 --> 00:43:08.670 which again is sort of neutralized

NOTE Confidence: 0.766144792857143

00:43:08.670 --> 00:43:10.829 or attenuated with the knockdown

NOTE Confidence: 0.766144792857143

00:43:10.829 --> 00:43:12.419 of crisper injustice.

NOTE Confidence: 0.766144792857143

00:43:12.420 --> 00:43:15.276 Pacific PDT to be late input.

NOTE Confidence: 0.766144792857143

00:43:15.280 --> 00:43:16.726 Neurotensin everywhere else

NOTE Confidence: 0.766144792857143

00:43:16.726 --> 00:43:19.136 in the brain is intact.

NOTE Confidence: 0.766144792857143

00:43:19.140 --> 00:43:19.473 OK,

NOTE Confidence: 0.766144792857143

00:43:19.473 --> 00:43:22.137 so this is just showing the opposite effects

NOTE Confidence: 0.766144792857143

00:43:22.137 --> 00:43:24.890 of the different projector populations.

NOTE Confidence: 0.766144792857143

00:43:24.890 --> 00:43:28.250 And then what I want to show you here is,

NOTE Confidence: 0.766144792857143

00:43:28.250 --> 00:43:29.590 this is what normally

NOTE Confidence: 0.766144792857143

00:43:29.590 --> 00:43:31.265 happens for each trial type.

NOTE Confidence: 0.766144792857143

00:43:31.270 --> 00:43:32.614 We've got sucrose neutral,

NOTE Confidence: 0.766144792857143

00:43:32.614 --> 00:43:33.958 an shock condition stimuli,

NOTE Confidence: 0.766144792857143

00:43:33.960 --> 00:43:36.305 and each trajectory begins here in time.

NOTE Confidence: 0.766144792857143

00:43:36.310 --> 00:43:38.558 Then the Q will be on set and

NOTE Confidence: 0.766144792857143

00:43:38.558 --> 00:43:40.678 then the response will occur.

NOTE Confidence: 0.766144792857143

00:43:40.680 --> 00:43:43.025 And what am I showing you here?

NOTE Confidence: 0.766144792857143

00:43:43.030 --> 00:43:45.242 This is looking at the neural ensemble

NOTE Confidence: 0.766144792857143

00:43:45.242 --> 00:43:47.399 as visualized as a neural trajectory.

NOTE Confidence: 0.766144792857143

00:43:47.400 --> 00:43:49.980 So what does that mean?

NOTE Confidence: 0.766144792857143

00:43:49.980 --> 00:43:50.571 How do you?

NOTE Confidence: 0.766144792857143

00:43:50.571 --> 00:43:52.480 How do we think about an ensemble of neurons?

NOTE Confidence: 0.766144792857143

00:43:52.480 --> 00:43:54.136 So if you if you had 100 neurons,

NOTE Confidence: 0.766144792857143

00:43:54.140 --> 00:43:56.080 I mean here we have.

NOTE Confidence: 0.766144792857143

00:43:56.080 --> 00:43:57.252 Sam called 700 rounds,

NOTE Confidence: 0.766144792857143

00:43:57.252 --> 00:43:59.931 but if you have 100 rounds and you want

NOTE Confidence: 0.766144792857143

00:43:59.931 --> 00:44:02.360 to see what the whole population is doing,

NOTE Confidence: 0.766144792857143

00:44:02.360 --> 00:44:04.397 you could plot that in 100 dimensional

NOTE Confidence: 0.766144792857143

00:44:04.397 --> 00:44:06.872 space and then just look at each neuron

NOTE Confidence: 0.766144792857143

00:44:06.872 --> 00:44:08.754 as representing a dimension and then

NOTE Confidence: 0.766144792857143

00:44:08.754 --> 00:44:10.756 just look at the trajectory of that

NOTE Confidence: 0.766144792857143

00:44:10.756 --> 00:44:12.990 ensemble in activity space across time.

NOTE Confidence: 0.766144792857143

00:44:12.990 --> 00:44:14.650 It's an aerial trajectory.

NOTE Confidence: 0.766144792857143

00:44:14.650 --> 00:44:17.254 It's hard to plot 100 dimensional space,

NOTE Confidence: 0.766144792857143

00:44:17.260 --> 00:44:20.329 so of course what we can do is perform

NOTE Confidence: 0.766144792857143

00:44:20.329 --> 00:44:21.734 dimensionality reduction principle

NOTE Confidence: 0.766144792857143

00:44:21.734 --> 00:44:24.214 components analysis and then reduce

NOTE Confidence: 0.766144792857143

00:44:24.214 --> 00:44:26.824 reduce the dimensions down to those

NOTE Confidence: 0.766144792857143

00:44:26.824 --> 00:44:28.930 that can offer the most covariance.

NOTE Confidence: 0.766144792857143

00:44:28.930 --> 00:44:31.018 So that's what we're doing here.

NOTE Confidence: 0.766144792857143

00:44:31.020 --> 00:44:32.424 Principal component one principal

NOTE Confidence: 0.766144792857143

00:44:32.424 --> 00:44:34.179 component to it that you

NOTE Confidence: 0.766144792857143

00:44:34.179 --> 00:44:35.594 components that offer contributed

NOTE Confidence: 0.766144792857143

00:44:35.594 --> 00:44:37.279 most covariance here and then.

NOTE Confidence: 0.766144792857143

00:44:37.280 --> 00:44:39.786 You can see that the sucrose trajectory's

NOTE Confidence: 0.766144792857143

00:44:39.786 --> 00:44:42.560 once the the tone comes on you can

NOTE Confidence: 0.766144792857143

00:44:42.560 --> 00:44:44.590 see the animals are showing this.

NOTE Confidence: 0.766144792857143

00:44:44.590 --> 00:44:47.610 This divergent of the trajectory's.

NOTE Confidence: 0.766144792857143

00:44:47.610 --> 00:44:49.210 These are the control animals,

NOTE Confidence: 0.8035762

00:44:49.210 --> 00:44:51.754 though. What happens when you put Chris Rock,

NOTE Confidence: 0.8035762

00:44:51.760 --> 00:44:53.040 Chris Brown? You say?

NOTE Confidence: 0.8035762

00:44:53.040 --> 00:44:55.333 Well actually it's this little blob right

NOTE Confidence: 0.8035762

00:44:55.333 --> 00:44:57.496 here that you can't even see anything.

NOTE Confidence: 0.8035762

00:44:57.500 --> 00:44:59.621 It's so small, so I'm going to

NOTE Confidence: 0.8035762

00:44:59.621 --> 00:45:01.650 blow it up in this inset,

NOTE Confidence: 0.8035762

00:45:01.650 --> 00:45:03.883 but here the arbitrary units were on

NOTE Confidence: 0.8035762

00:45:03.883 --> 00:45:05.821 a different scale. It's so small.

NOTE Confidence: 0.8035762

00:45:05.821 --> 00:45:07.783 So basically all of these trajectories

NOTE Confidence: 0.8035762

00:45:07.783 --> 00:45:10.260 shrivel up into into nothing, so when when,

NOTE Confidence: 0.8035762

00:45:10.260 --> 00:45:11.540 when trajectory length shrink,

NOTE Confidence: 0.8035762

00:45:11.540 --> 00:45:13.130 that suggests that the ensemble

NOTE Confidence: 0.8035762

00:45:13.130 --> 00:45:14.402 is either less dynamic,

NOTE Confidence: 0.8035762

00:45:14.410 --> 00:45:16.936 changing less or changing less quickly.

NOTE Confidence: 0.8035762

00:45:16.940 --> 00:45:19.856 So. The dynamics of the of

NOTE Confidence: 0.8035762

00:45:19.856 --> 00:45:21.800 amygdala neurons are blunted

NOTE Confidence: 0.8035762

00:45:21.891 --> 00:45:24.717 when we knocked down or Tencent.

NOTE Confidence: 0.80430764

00:45:26.880 --> 00:45:29.877 OK, so Chris bring out the New York Times

NOTE Confidence: 0.80430764

00:45:29.877 --> 00:45:32.955 and Gene in specifically the PDT tibial.

NOTE Confidence: 0.80430764

00:45:32.960 --> 00:45:34.860 A population reduces decoding accuracy

NOTE Confidence: 0.80430764

00:45:34.860 --> 00:45:36.760 of behavior from feeling relativity,

NOTE Confidence: 0.80430764

00:45:36.760 --> 00:45:37.900 so control animals.

NOTE Confidence: 0.80430764

00:45:37.900 --> 00:45:41.369 Once the Q comes on, it's very clear

NOTE Confidence: 0.80430764

00:45:41.369 --> 00:45:45.030 like what what trial type it was.

NOTE Confidence: 0.80430764

00:45:45.030 --> 00:45:47.396 However, if we do this with crisper

NOTE Confidence: 0.80430764

00:45:47.396 --> 00:45:49.344 animals and this is, you know,

NOTE Confidence: 0.80430764

00:45:49.344 --> 00:45:51.004 training with controls testing controls,

NOTE Confidence: 0.80430764

00:45:51.010 --> 00:45:52.334 you know different different

NOTE Confidence: 0.80430764

00:45:52.334 --> 00:45:53.989 training and testing of course.

NOTE Confidence: 0.80430764

00:45:53.990 --> 00:45:55.650 But from the same group.

NOTE Confidence: 0.7999176

00:45:58.080 --> 00:46:01.056 If we train and test on crisper animals,

NOTE Confidence: 0.7999176

00:46:01.060 --> 00:46:02.930 they perform significantly less well,

NOTE Confidence: 0.7999176

00:46:02.930 --> 00:46:05.906 but still are able to code above chance.

NOTE Confidence: 0.7999176

00:46:05.910 --> 00:46:08.208 Importantly, if we train the decoder

NOTE Confidence: 0.7999176

00:46:08.208 --> 00:46:10.939 with data from the control and then

NOTE Confidence: 0.7999176

00:46:10.939 --> 00:46:13.571 test on crisper or train with CRISPER

NOTE Confidence: 0.7999176

00:46:13.643 --> 00:46:16.355 data and then test on the control data,

NOTE Confidence: 0.7999176

00:46:16.360 --> 00:46:18.632 we get chance essentially.

NOTE Confidence: 0.7999176

00:46:18.632 --> 00:46:21.472 Suggesting that crisper and control

NOTE Confidence: 0.7999176

00:46:21.472 --> 00:46:24.640 animals are using different coding rules

NOTE Confidence: 0.7999176

00:46:24.640 --> 00:46:27.748 to determine what's going on. OK Anna.

NOTE Confidence: 0.7999176

00:46:27.748 --> 00:46:30.904 Nice ball in my lab who has has done a

NOTE Confidence: 0.7999176

00:46:30.904 --> 00:46:33.431 lot of work on another project relating

NOTE Confidence: 0.7999176

00:46:33.431 --> 00:46:36.395 to a real time Alpha tracker which I

NOTE Confidence: 0.7999176

00:46:36.395 --> 00:46:39.200 don't have time to talk about right now.

NOTE Confidence: 0.7999176

00:46:39.200 --> 00:46:40.732 Explored this for analyzing,

NOTE Confidence: 0.7999176

00:46:40.732 --> 00:46:42.647 analyzing BLTS with more regularity

NOTE Confidence: 0.7999176

00:46:42.647 --> 00:46:44.697 here and so this is pretty simple.

NOTE Confidence: 0.7999176

00:46:44.700 --> 00:46:46.425 We're looking at reward trials

NOTE Confidence: 0.7999176

00:46:46.425 --> 00:46:47.460 and shock trials.

NOTE Confidence: 0.7999176

00:46:47.460 --> 00:46:48.832 Should be simple, right?

NOTE Confidence: 0.7999176

00:46:48.832 --> 00:46:50.204 Just punishment and reward,

NOTE Confidence: 0.7999176

00:46:50.210 --> 00:46:51.992 but yet, even with the responses

NOTE Confidence: 0.7999176

00:46:51.992 --> 00:46:54.339 that we get from punishment reward,

NOTE Confidence: 0.7999176

00:46:54.340 --> 00:46:55.736 there are different responses.

NOTE Confidence: 0.7999176

00:46:55.736 --> 00:46:57.830 For example in with shock conditioning.

NOTE Confidence: 0.7999176

00:46:57.830 --> 00:46:59.979 You could either get freezing a passive,

NOTE Confidence: 0.7999176

00:46:59.980 --> 00:47:01.204 you know coping state,

NOTE Confidence: 0.7999176

00:47:01.204 --> 00:47:02.734 or you can get darting,

NOTE Confidence: 0.7999176

00:47:02.740 --> 00:47:05.248 which might be thought of as

NOTE Confidence: 0.7999176

00:47:05.248 --> 00:47:06.920 a more active state.

NOTE Confidence: 0.7999176

00:47:06.920 --> 00:47:07.276 Similarly,

NOTE Confidence: 0.7999176

00:47:07.276 --> 00:47:09.412 this is true for reward trials

NOTE Confidence: 0.7999176

00:47:09.412 --> 00:47:10.790 could be hanging out,

NOTE Confidence: 0.7999176

00:47:10.790 --> 00:47:12.902 or you can come and actively

NOTE Confidence: 0.7999176

00:47:12.902 --> 00:47:13.958 approach the port.

NOTE Confidence: 0.8637464

00:47:16.120 --> 00:47:19.416 So what we found here is that the

NOTE Confidence: 0.8637464

00:47:19.416 --> 00:47:21.570 neural responses to the rewards,

NOTE Confidence: 0.8637464

00:47:21.570 --> 00:47:24.330 yes, or the shocks, yes.

NOTE Confidence: 0.8637464

00:47:24.330 --> 00:47:29.270 For each type each behavioral.

NOTE Confidence: 0.8637464

00:47:29.270 --> 00:47:31.587 Type of response is is blunted overall,

NOTE Confidence: 0.8637464

00:47:31.590 --> 00:47:33.250 but specific to each type,

NOTE Confidence: 0.8637464

00:47:33.250 --> 00:47:34.910 and if we quantify this,

NOTE Confidence: 0.8637464

00:47:34.910 --> 00:47:37.022 what you can see.

NOTE Confidence: 0.8637464

00:47:37.022 --> 00:47:40.945 Is that there's a greater impact of

NOTE Confidence: 0.8637464

00:47:40.945 --> 00:47:44.165 Christopher ING out near attention

NOTE Confidence: 0.8637464

00:47:44.165 --> 00:47:48.153 in these low motivation States and

NOTE Confidence: 0.8637464

00:47:48.153 --> 00:47:51.398 or active avoidance states here.

NOTE Confidence: 0.8637464

00:47:51.400 --> 00:47:53.848 OK, so back to the outline.

NOTE Confidence: 0.8637464

00:47:53.850 --> 00:47:56.220 Where does circuits you know encoding

NOTE Confidence: 0.8637464

00:47:56.220 --> 00:47:58.340 positive and negative balance diverge?

NOTE Confidence: 0.8637464

00:47:58.340 --> 00:48:00.380 The basil lateral make list

NOTE Confidence: 0.8637464

00:48:00.380 --> 00:48:02.420 one of these prime targets,

NOTE Confidence: 0.8637464

00:48:02.420 --> 00:48:06.083 but now you know what criteria to look for.

NOTE Confidence: 0.8637464

00:48:06.090 --> 00:48:08.130 What are the local interactions?

NOTE Confidence: 0.8637464

00:48:08.130 --> 00:48:10.752 There are absolutely lots of microcircuit

NOTE Confidence: 0.8637464

00:48:10.752 --> 00:48:12.873 interactions of inhibition and or

NOTE Confidence: 0.8637464

00:48:12.873 --> 00:48:15.001 facilitation locally at the level of the

NOTE Confidence: 0.8637464

00:48:15.001 --> 00:48:17.918 lay of these functionally distinct circuits.

NOTE Confidence: 0.8637464

00:48:17.920 --> 00:48:20.235 And now we're beginning to

NOTE Confidence: 0.8637464

00:48:20.235 --> 00:48:22.087 explore how narrow modulation.

NOTE Confidence: 0.8637464

00:48:22.090 --> 00:48:24.904 Can play a role in balance assignment

NOTE Confidence: 0.8637464

00:48:24.904 --> 00:48:27.839 specially in these sort of initial trials,

NOTE Confidence: 0.8637464

00:48:27.840 --> 00:48:30.372 and so I don't really think

NOTE Confidence: 0.8637464

00:48:30.372 --> 00:48:32.060 neuromodulatory systems or neuropeptides

NOTE Confidence: 0.8637464

00:48:32.123 --> 00:48:34.415 will contribute within trial per say,

NOTE Confidence: 0.8637464

00:48:34.420 --> 00:48:37.748 but between trials, certainly.

NOTE Confidence: 0.8637464

00:48:37.750 --> 00:48:40.396 OK, so where are we now?

NOTE Confidence: 0.8637464

00:48:40.400 --> 00:48:40.840 What?

NOTE Confidence: 0.8637464

00:48:40.840 --> 00:48:43.040 What can we take away?

NOTE Confidence: 0.8637464

00:48:43.040 --> 00:48:45.686 What's the takeaway message from a,

NOTE Confidence: 0.8637464

00:48:45.690 --> 00:48:47.890 you know therapeutic standpoint here.

NOTE Confidence: 0.8637464

00:48:47.890 --> 00:48:49.778 Well, just that identifying

NOTE Confidence: 0.8637464

00:48:49.778 --> 00:48:51.666 differentially expressed genes and

NOTE Confidence: 0.8637464

00:48:51.666 --> 00:48:53.047 functionally characterized functionally

NOTE Confidence: 0.8637464

00:48:53.047 --> 00:48:54.957 distinct circuits can be leveraged

NOTE Confidence: 0.8637464

00:48:54.957 --> 00:48:57.599 for selective control of neuronal population.

NOTE Confidence: 0.8637464

00:48:57.600 --> 00:49:01.120 So instead of a shooting in the dark,

NOTE Confidence: 0.8637464

00:49:01.120 --> 00:49:02.884 like trial and error

NOTE Confidence: 0.8637464

00:49:02.884 --> 00:49:04.648 strategy for drug discovery,

NOTE Confidence: 0.8637464

00:49:04.650 --> 00:49:07.807 why don't we use a circuit based?

NOTE Confidence: 0.8637464

00:49:07.810 --> 00:49:09.781 Just drug discovery.

NOTE Confidence: 0.8637464

00:49:09.781 --> 00:49:13.723 Find small molecule targets on circuit

NOTE Confidence: 0.8637464

00:49:13.723 --> 00:49:16.359 components with known function.

NOTE Confidence: 0.8637464

00:49:16.360 --> 00:49:19.736 So again, this is just bringing things back.

NOTE Confidence: 0.8637464

00:49:19.740 --> 00:49:21.436 We've in the amygdala,

NOTE Confidence: 0.8637464

00:49:21.436 --> 00:49:22.934 Howley, Praneeth, Ambrian,

NOTE Confidence: 0.8637464

00:49:22.934 --> 00:49:26.156 Jake Olson are contributing to understanding

NOTE Confidence: 0.8637464

00:49:26.156 --> 00:49:29.100 the role of Neuromodulatory gang.

NOTE Confidence: 0.8637464

00:49:29.100 --> 00:49:29.554 OK,

NOTE Confidence: 0.8637464

00:49:29.554 --> 00:49:33.640 so why should you even care about all this?

NOTE Confidence: 0.8637464

00:49:33.640 --> 00:49:36.818 How does this ultimately matter for people?

NOTE Confidence: 0.8637464

00:49:36.820 --> 00:49:37.319 Well,

NOTE Confidence: 0.8637464

00:49:37.319 --> 00:49:40.313 despite the prevalence of anxiety disorders

NOTE Confidence: 0.8637464

00:49:40.313 --> 00:49:43.179 and other mental health disorders.

NOTE Confidence: 0.8637464

00:49:43.180 --> 00:49:44.770 Current treatments are not effective

NOTE Confidence: 0.8637464

00:49:44.770 --> 00:49:46.360 for the entire patient population,

NOTE Confidence: 0.8637464

00:49:46.360 --> 00:49:49.314 or at least have a lot of

NOTE Confidence: 0.8637464

00:49:49.314 --> 00:49:50.580 undesirable side effects.

NOTE Confidence: 0.8637464

00:49:50.580 --> 00:49:53.600 So how do we get to where we are now?

NOTE Confidence: 0.8637464

00:49:53.600 --> 00:49:55.378 From you know where we are now

NOTE Confidence: 0.8637464

00:49:55.378 --> 00:49:57.335 with with these sort of no no

NOTE Confidence: 0.8637464

00:49:57.335 --> 00:49:58.750 treatment is perfect that works.

NOTE Confidence: 0.8637464

00:49:58.750 --> 00:50:00.991 There's no such thing as a team that works

NOTE Confidence: 0.8637464

00:50:00.991 --> 00:50:03.357 for everyone that is free of side effects.

NOTE Confidence: 0.8637464

00:50:03.360 --> 00:50:05.208 How do we get from that to something

NOTE Confidence: 0.8637464

00:50:05.208 --> 00:50:06.945 where that is possible with every

NOTE Confidence: 0.8637464

00:50:06.945 --> 00:50:08.775 single individual will find a treatment

NOTE Confidence: 0.8637464

00:50:08.829 --> 00:50:10.425 that is effective for them that

NOTE Confidence: 0.8637464

00:50:10.425 --> 00:50:12.320 lasts and doesn't have side effects?

NOTE Confidence: 0.8637464

00:50:12.320 --> 00:50:13.150 Sounds like.

NOTE Confidence: 0.8637464

00:50:13.150 --> 00:50:14.776 You know, far away,

NOTE Confidence: 0.8637464

00:50:14.776 --> 00:50:16.766 how do we get there?

NOTE Confidence: 0.8637464

00:50:16.770 --> 00:50:17.168 Well,

NOTE Confidence: 0.8637464

00:50:17.168 --> 00:50:19.954 we have to change our current approach,

NOTE Confidence: 0.8637464

00:50:19.960 --> 00:50:21.684 which currently involves testing

NOTE Confidence: 0.8637464

00:50:21.684 --> 00:50:23.408 drugs that act nonspecifically

NOTE Confidence: 0.8637464

00:50:23.408 --> 00:50:25.548 throughout the entire brain and body,

NOTE Confidence: 0.8637464

00:50:25.550 --> 00:50:28.189 and doing so in a sort of

NOTE Confidence: 0.8637464

00:50:28.189 --> 00:50:30.339 again trial and error way.

NOTE Confidence: 0.8637464

00:50:30.340 --> 00:50:32.566 I think another huge problem with

NOTE Confidence: 0.8637464

00:50:32.566 --> 00:50:35.129 the way that we're tackling this.

NOTE Confidence: 0.8637464

00:50:35.130 --> 00:50:36.722 This challenge is poor

NOTE Confidence: 0.8637464

00:50:36.722 --> 00:50:37.518 disease classification,

NOTE Confidence: 0.8637464

00:50:37.520 --> 00:50:39.515 poor understanding of what actually

NOTE Confidence: 0.8637464

00:50:39.515 --> 00:50:41.510 gives rise to the disease,

NOTE Confidence: 0.8637464

00:50:41.510 --> 00:50:44.178 comorbidity that we see.

NOTE Confidence: 0.8637464

00:50:44.180 --> 00:50:46.035 We currently rely on symptom

NOTE Confidence: 0.8637464

00:50:46.035 --> 00:50:47.519 based categorical definitions of

NOTE Confidence: 0.8637464

00:50:47.519 --> 00:50:49.148 mental illness and this is just

NOTE Confidence: 0.8637464

00:50:49.148 --> 00:50:50.348 a barrier to a true

NOTE Confidence: 0.794893600000001

00:50:50.405 --> 00:50:52.041 biological understanding of psychiatric

NOTE Confidence: 0.794893600000001

00:50:52.041 --> 00:50:54.495 diseases as researchers are sort of

NOTE Confidence: 0.794893600000001

00:50:54.500 --> 00:50:56.220 discouraged from exploring comorbid

NOTE Confidence: 0.794893600000001

00:50:56.220 --> 00:50:58.800 Lee Express symptoms when they may

NOTE Confidence: 0.794893600000001

00:50:58.864 --> 00:51:00.814 in fact be meaningful clues that

NOTE Confidence: 0.794893600000001

00:51:00.814 --> 00:51:02.654 guide us to distinct ideologies

NOTE Confidence: 0.794893600000001

00:51:02.654 --> 00:51:05.009 that call for different treatments.

NOTE Confidence: 0.794893600000001

00:51:05.010 --> 00:51:08.216 All these issues route back to the

NOTE Confidence: 0.794893600000001

00:51:08.216 --> 00:51:10.025 inadequate understanding that we

NOTE Confidence: 0.794893600000001

00:51:10.025 --> 00:51:12.173 currently have of how the brain

NOTE Confidence: 0.794893600000001

00:51:12.173 --> 00:51:14.180 even gives rise to behavior.

NOTE Confidence: 0.794893600000001

00:51:14.180 --> 00:51:16.050 Super BASIC, but fortunately we

NOTE Confidence: 0.794893600000001

00:51:16.050 --> 00:51:18.436 now have the ability to identify

NOTE Confidence: 0.794893600000001

00:51:18.436 --> 00:51:20.676 specific neuronal or synaptic targets

NOTE Confidence: 0.794893600000001

00:51:20.676 --> 00:51:23.360 and test their role in behavior.

NOTE Confidence: 0.794893600000001

00:51:23.360 --> 00:51:25.028 That's what modern neuroscience

NOTE Confidence: 0.794893600000001

00:51:25.028 --> 00:51:26.279 technologies will allow,

NOTE Confidence: 0.794893600000001

00:51:26.280 --> 00:51:28.460 and perhaps high rates of

NOTE Confidence: 0.794893600000001

00:51:28.460 --> 00:51:30.640 comorbidity can be explained by

NOTE Confidence: 0.794893600000001

00:51:30.723 --> 00:51:33.479 common neural circuit perturbations.

NOTE Confidence: 0.794893600000001

00:51:33.480 --> 00:51:35.670 And then to translate our basic

NOTE Confidence: 0.794893600000001

00:51:35.670 --> 00:51:38.278 insights into a better type of therapy,

NOTE Confidence: 0.794893600000001

00:51:38.280 --> 00:51:40.492 we will need to apply the knowledge

NOTE Confidence: 0.794893600000001

00:51:40.492 --> 00:51:41.916 we gained informed therapeutic

NOTE Confidence: 0.794893600000001

00:51:41.916 --> 00:51:43.576 development and take advantage

NOTE Confidence: 0.794893600000001

00:51:43.576 --> 00:51:45.651 of we know about plasticity,

NOTE Confidence: 0.794893600000001

00:51:45.660 --> 00:51:47.330 resilience and the new adaptations

NOTE Confidence: 0.794893600000001

00:51:47.330 --> 00:51:49.000 that occur with stress and

NOTE Confidence: 0.794893600000001

00:51:49.055 --> 00:51:51.461 basically focus on a neural circuit

NOTE Confidence: 0.794893600000001

00:51:51.461 --> 00:51:52.664 based therapeutic development.

NOTE Confidence: 0.794893600000001

00:51:52.670 --> 00:51:54.142 It may be pharmacological,

NOTE Confidence: 0.794893600000001

00:51:54.142 --> 00:51:55.614 it may not be.

NOTE Confidence: 0.88645333

00:51:58.130 --> 00:52:00.302 OK, so regardless of if you're

NOTE Confidence: 0.88645333

00:52:00.302 --> 00:52:02.170 listening to this talk with,

NOTE Confidence: 0.88645333

00:52:02.170 --> 00:52:03.634 you know translation here

NOTE Confidence: 0.88645333

00:52:03.634 --> 00:52:05.098 or basic science here.

NOTE Confidence: 0.88645333

00:52:05.100 --> 00:52:08.306 I guess I would say from a

NOTE Confidence: 0.88645333

00:52:08.306 --> 00:52:09.680 basic science perspective.

NOTE Confidence: 0.88645333

00:52:09.680 --> 00:52:11.335 If we can't understand simple

NOTE Confidence: 0.88645333

00:52:11.335 --> 00:52:13.590 circuits like those in the amygdala,

NOTE Confidence: 0.88645333

00:52:13.590 --> 00:52:15.122 and simple questions like,

NOTE Confidence: 0.88645333

00:52:15.122 --> 00:52:18.559 how do we tell if something is good or bad?

NOTE Confidence: 0.88645333

00:52:18.560 --> 00:52:21.032 How are we going to understand more complex

NOTE Confidence: 0.88645333

00:52:21.032 --> 00:52:23.305 circuits and more complex questions and

NOTE Confidence: 0.88645333

00:52:23.305 --> 00:52:25.300 then from a translational perspective,

NOTE Confidence: 0.88645333

00:52:25.300 --> 00:52:27.430 the amygdala has been so well

NOTE Confidence: 0.88645333

00:52:27.430 --> 00:52:28.495 conserved across evolution,

NOTE Confidence: 0.88645333

00:52:28.500 --> 00:52:29.388 and you know,

NOTE Confidence: 0.88645333

00:52:29.388 --> 00:52:31.460 a lot of these circuits are still

NOTE Confidence: 0.88645333

00:52:31.531 --> 00:52:33.516 consistent in species that have

NOTE Confidence: 0.88645333

00:52:33.516 --> 00:52:35.950 scarcely changed for 70 million years.

NOTE Confidence: 0.88645333

00:52:35.950 --> 00:52:39.145 This this gives this lens a lot of hope,

NOTE Confidence: 0.88645333

00:52:39.150 --> 00:52:39.746 that the.

NOTE Confidence: 0.88645333

00:52:39.746 --> 00:52:42.130 The changes that we see in in mice

NOTE Confidence: 0.88645333

00:52:42.204 --> 00:52:44.580 will also have relevance to humans,

NOTE Confidence: 0.88645333

00:52:44.580 --> 00:52:46.612 given the common homology.

NOTE Confidence: 0.88645333

00:52:46.612 --> 00:52:49.250 OK, so with that I will thank

NOTE Confidence: 0.88645333

00:52:49.250 --> 00:52:51.703 all the members of my laboratory

NOTE Confidence: 0.88645333

00:52:51.703 --> 00:52:54.068 and you for your attention.

NOTE Confidence: 0.88645333

00:52:54.070 --> 00:52:54.890 My collaborators,

NOTE Confidence: 0.88645333

00:52:54.890 --> 00:52:56.120 my funding sources,

NOTE Confidence: 0.88645333

00:52:56.120 --> 00:52:59.382 and thanks for listening and I believe

NOTE Confidence: 0.88645333

00:52:59.382 --> 00:53:03.210 I will take some questions right now.

NOTE Confidence: 0.88645333

00:53:03.210 --> 00:53:03.780 Thanks.

NOTE Confidence: 0.8451138

00:53:09.420 --> 00:53:11.604 Thank you very much everyone

NOTE Confidence: 0.8451138

00:53:11.604 --> 00:53:14.220 for joining us for the talk.

NOTE Confidence: 0.8451138

00:53:14.220 --> 00:53:17.265 Thank you Kate for a great talk.

NOTE Confidence: 0.8451138

00:53:17.270 --> 00:53:21.450 I believe that we are going to have to wait

NOTE Confidence: 0.8451138

00:53:21.556 --> 00:53:25.543 a few moments for Doctor Tide to join us.

NOTE Confidence: 0.8451138

00:53:25.550 --> 00:53:29.474 She is in California and is on a delay.

NOTE Confidence: 0.8451138

00:53:29.480 --> 00:53:32.819 I do see that there is one message in

NOTE Confidence: 0.8451138

00:53:32.819 --> 00:53:36.188 the chat from Doctor Clayton Barnes.

NOTE Confidence: 0.8451138

00:53:36.190 --> 00:53:38.087 But if you have any other questions,

NOTE Confidence: 0.8451138

00:53:38.090 --> 00:53:39.734 please add them in.

NOTE Confidence: 0.8451138

00:53:39.734 --> 00:53:41.730 And Trisha, if you can,

NOTE Confidence: 0.8451138

00:53:41.730 --> 00:53:44.820 let me know when Doctor Ty joins us.

NOTE Confidence: 0.8451138

00:53:44.820 --> 00:53:47.190 We will switch to the question

NOTE Confidence: 0.8451138

00:53:47.190 --> 00:53:49.466 and answer portion of the talk.

NOTE Confidence: 0.8451138

00:53:49.466 --> 00:53:51.788 And there are a couple of

NOTE Confidence: 0.8451138

00:53:51.788 --> 00:53:54.110 questions for you in the chat.

NOTE Confidence: 0.8451138

00:53:54.110 --> 00:53:57.756 If I can read them out to you, I will.

NOTE Confidence: 0.8451138

00:53:57.756 --> 00:54:00.399 I will start out by has the KAYTIE has

NOTE Confidence: 0.8451138

00:54:00.399 --> 00:54:02.703 that I lab thought about developing

NOTE Confidence: 0.8451138

00:54:02.703 --> 00:54:05.395 a dynamical systems model of the

NOTE Confidence: 0.8451138

00:54:05.395 --> 00:54:06.862 interactions between projection

NOTE Confidence: 0.8451138

00:54:06.862 --> 00:54:09.200 specific subpopulations in the VLA.

NOTE Confidence: 0.7905622

00:54:11.990 --> 00:54:14.380 And you're muted.

NOTE Confidence: 0.7905622

00:54:14.380 --> 00:54:15.444 Thank you, great question.

NOTE Confidence: 0.7905622

00:54:15.444 --> 00:54:17.040 I think we've approached looking at

NOTE Confidence: 0.7905622

00:54:17.083 --> 00:54:18.967 predicted dynamical models in other systems.

NOTE Confidence: 0.7905622

00:54:18.970 --> 00:54:21.218 We have not yet begun to build one

NOTE Confidence: 0.7905622

00:54:21.218 --> 00:54:23.274 in the DLA, but we absolutely should.

NOTE Confidence: 0.7905622

00:54:23.274 --> 00:54:24.704 I think you're absolutely right.

NOTE Confidence: 0.7905622

00:54:24.710 --> 00:54:26.432 Like you know there are these

NOTE Confidence: 0.7905622

00:54:26.432 --> 00:54:27.293 projections that exist.

NOTE Confidence: 0.7905622

00:54:27.300 --> 00:54:29.295 There are neurons that have hard wiring,

NOTE Confidence: 0.7905622

00:54:29.300 --> 00:54:31.404 but you can think of that as the

NOTE Confidence: 0.7905622

00:54:31.404 --> 00:54:33.223 roads that exist and we want

NOTE Confidence: 0.7905622

00:54:33.223 --> 00:54:34.753 to think about the traffic.

NOTE Confidence: 0.7905622

00:54:34.760 --> 00:54:37.630 So coming to that is something we want to do.

NOTE Confidence: 0.7905622

00:54:37.630 --> 00:54:40.158 We started to do that in the prefrontal

NOTE Confidence: 0.7905622

00:54:40.158 --> 00:54:42.410 cortex and you know we're able to

NOTE Confidence: 0.7905622

00:54:42.410 --> 00:54:44.470 predict a lot of different people.

NOTE Confidence: 0.7905622

00:54:44.470 --> 00:54:46.518 Cortex VLA data is a little bit different.

NOTE Confidence: 0.7905622

00:54:46.520 --> 00:54:49.960 Not to say that we couldn't do it, but.

NOTE Confidence: 0.7905622

00:54:49.960 --> 00:54:51.320 We haven't done it yet,

NOTE Confidence: 0.7905622

00:54:51.320 --> 00:54:52.400 but we we absolutely

NOTE Confidence: 0.847146100555556

00:54:52.400 --> 00:54:53.675 should. Thanks Kate,

NOTE Confidence: 0.847146100555556

00:54:53.675 --> 00:54:56.225 the next question is about the

NOTE Confidence: 0.847146100555556

00:54:56.225 --> 00:54:58.885 recruitment of the central amygdala

NOTE Confidence: 0.847146100555556

00:54:58.885 --> 00:55:01.045 projections during rewarding conditions.

NOTE Confidence: 0.847146100555556

00:55:01.050 --> 00:55:04.210 It looks like it might be a check

NOTE Confidence: 0.847146100555556

00:55:04.210 --> 00:55:06.929 on reward behaviors are there?

NOTE Confidence: 0.847146100555556

00:55:06.930 --> 00:55:08.975 Is there evidence of deficits

NOTE Confidence: 0.847146100555556

00:55:08.975 --> 00:55:10.611 in central amygdala projections

NOTE Confidence: 0.847146100555556

00:55:10.611 --> 00:55:12.809 in unchecked reward behaviors,

NOTE Confidence: 0.847146100555556

00:55:12.810 --> 00:55:14.160 like an addiction?

NOTE Confidence: 0.821512054

00:55:15.440 --> 00:55:18.200 Well, interesting. Interesting, you know.

NOTE Confidence: 0.821512054

00:55:18.200 --> 00:55:20.544 So first the projections to Central

NOTE Confidence: 0.821512054

00:55:20.544 --> 00:55:22.584 central itself is super complicated

NOTE Confidence: 0.821512054

00:55:22.584 --> 00:55:25.317 and I think of it as a ministrator.

NOTE Confidence: 0.821512054

00:55:25.320 --> 00:55:27.195 There's so many different mirror

NOTE Confidence: 0.821512054

00:55:27.195 --> 00:55:28.320 peptidergic neurons there,

NOTE Confidence: 0.821512054

00:55:28.320 --> 00:55:30.791 and we found a lot of different

NOTE Confidence: 0.821512054

00:55:30.791 --> 00:55:33.199 roles from central amygdala that are,

NOTE Confidence: 0.821512054

00:55:33.200 --> 00:55:35.762 you know, widely varying from, you know,

NOTE Confidence: 0.821512054

00:55:35.762 --> 00:55:37.492 aversive behavior to social behavior

NOTE Confidence: 0.821512054

00:55:37.492 --> 00:55:40.860 and other other components, but.

NOTE Confidence: 0.821512054

00:55:40.860 --> 00:55:42.765 Or the specific projection from

NOTE Confidence: 0.821512054

00:55:42.765 --> 00:55:45.170 the PLA to the central limit,

NOTE Confidence: 0.821512054

00:55:45.170 --> 00:55:47.914 which is predominantly coding for a version,

NOTE Confidence: 0.821512054

00:55:47.920 --> 00:55:50.266 but it's not exclusively doing so.

NOTE Confidence: 0.821512054

00:55:50.270 --> 00:55:52.230 We haven't seen that in.

NOTE Confidence: 0.821512054

00:55:52.230 --> 00:55:54.190 We haven't looked in addiction

NOTE Confidence: 0.821512054

00:55:54.190 --> 00:55:56.150 to see if it is,

NOTE Confidence: 0.821512054

00:55:56.150 --> 00:55:58.430 it is specifically modified in terms

NOTE Confidence: 0.821512054

00:55:58.430 --> 00:56:00.849 of firing rates we have looked.

NOTE Confidence: 0.7812509

00:56:04.910 --> 00:56:07.045 Look and actually this is something I

NOTE Confidence: 0.7812509

00:56:07.045 --> 00:56:09.357 didn't talk about in this particular talk.

NOTE Confidence: 0.7812509

00:56:09.360 --> 00:56:10.632 It's pretty new data,

NOTE Confidence: 0.7812509

00:56:10.632 --> 00:56:11.904 but with social isolation,

NOTE Confidence: 0.7812509

00:56:11.910 --> 00:56:14.238 a stress in this can potentiate the minerals

NOTE Confidence: 0.7812509

00:56:14.238 --> 00:56:16.038 and correlate's with increased drinking.

NOTE Confidence: 0.7812509

00:56:16.040 --> 00:56:17.870 So when we stimulate the light

NOTE Confidence: 0.7812509

00:56:17.870 --> 00:56:19.540 inputs to the prefrontal cortex,

NOTE Confidence: 0.7812509

00:56:19.540 --> 00:56:21.964 we now find that this this is sufficient

NOTE Confidence: 0.7812509

00:56:21.964 --> 00:56:23.869 to drive alcohol drinking as opposed

NOTE Confidence: 0.7812509

00:56:23.869 --> 00:56:26.220 to water in a 2 bottle choice.

NOTE Confidence: 0.7812509

00:56:26.220 --> 00:56:27.810 So that's something, but it's,

NOTE Confidence: 0.7812509

00:56:27.810 --> 00:56:29.335 you know, still super preliminary

NOTE Confidence: 0.7812509

00:56:29.335 --> 00:56:30.860 and thinking about this particular

NOTE Confidence: 0.7812509

00:56:30.912 --> 00:56:32.260 projection from DLA decentral,

NOTE Confidence: 0.7812509

00:56:32.260 --> 00:56:34.920 we haven't studied that one.

NOTE Confidence: 0.7812509

00:56:34.920 --> 00:56:37.656 In in the in the context of addiction,

NOTE Confidence: 0.7812509

00:56:37.660 --> 00:56:39.706 it is sort of this projection.

NOTE Confidence: 0.7812509

00:56:39.710 --> 00:56:43.038 These neurons have the capacity to sort of.

NOTE Confidence: 0.7812509

00:56:43.040 --> 00:56:44.910 Ubiquitously inhibit

NOTE Confidence: 0.7881507

00:56:48.500 --> 00:56:50.030 birthday very broadly, and had,

NOTE Confidence: 0.7881507

00:56:50.030 --> 00:56:52.158 of course also recruit another local network,

NOTE Confidence: 0.7881507

00:56:52.160 --> 00:56:53.760 but the local feedforward inhibition

NOTE Confidence: 0.7881507

00:56:53.760 --> 00:56:55.688 coming from the latest central England

NOTE Confidence: 0.7881507

00:56:55.688 --> 00:56:57.655 is is much more potent than other

NOTE Confidence: 0.7881507

00:56:57.655 --> 00:56:59.179 other productions that we've studied.

NOTE Confidence: 0.7881507

00:56:59.180 --> 00:57:01.000 So I guess I don't know the

NOTE Confidence: 0.7881507

00:57:01.000 --> 00:57:02.839 answer to that question either.

NOTE Confidence: 0.7881507

00:57:02.840 --> 00:57:04.060 That's a great question.

NOTE Confidence: 0.7881507

00:57:04.060 --> 00:57:05.890 We haven't done that specific experiment.

NOTE Confidence: 0.8657458

00:57:06.990 --> 00:57:10.174 Next question is sort of related to that.

NOTE Confidence: 0.8657458

00:57:10.180 --> 00:57:13.180 Do you see individual differences among.

NOTE Confidence: 0.8657458

00:57:13.180 --> 00:57:14.760 Subjects in the balance

NOTE Confidence: 0.8657458

00:57:14.760 --> 00:57:16.340 between the two circuits.

NOTE Confidence: 0.8657458

00:57:16.340 --> 00:57:18.940 Have you been able to match that in

NOTE Confidence: 0.8657458

00:57:18.940 --> 00:57:21.869 any way to susceptible ability versus

NOTE Confidence: 0.856353

00:57:21.870 --> 00:57:23.450 resilience for stress disorders?

NOTE Confidence: 0.856353

00:57:23.450 --> 00:57:25.030 That's a great question.

NOTE Confidence: 0.856353

00:57:25.030 --> 00:57:27.400 That's great, but so we definitely

NOTE Confidence: 0.856353

00:57:27.400 --> 00:57:28.980 do see individual variability.

NOTE Confidence: 0.856353

00:57:28.980 --> 00:57:31.265 We have not systematically correlated

NOTE Confidence: 0.856353

00:57:31.265 --> 00:57:33.093 that with pre-existing behavioral.

NOTE Confidence: 0.856353

00:57:33.100 --> 00:57:35.266 Features, but we should do that.

NOTE Confidence: 0.856353

00:57:35.270 --> 00:57:37.075 That's a very good expansion

NOTE Confidence: 0.856353

00:57:37.075 --> 00:57:39.600 that's I love that idea. The next

NOTE Confidence: 0.8713635

00:57:39.600 --> 00:57:41.124 question is more clinical,

NOTE Confidence: 0.8713635

00:57:41.124 --> 00:57:44.206 so I will actually ask John Crystal to

NOTE Confidence: 0.8713635

00:57:44.206 --> 00:57:47.086 jump in and help or ask other clinicians

NOTE Confidence: 0.8713635

00:57:47.160 --> 00:57:49.344 in the audience to help with K.

NOTE Confidence: 0.8713635

00:57:49.350 --> 00:57:51.150 You may have some ideas.

NOTE Confidence: 0.8713635

00:57:51.150 --> 00:57:53.250 So the question is help me translate

NOTE Confidence: 0.8713635

00:57:53.250 --> 00:57:55.499 this into clinical practice of patient

NOTE Confidence: 0.8713635

00:57:55.499 --> 00:57:57.649 presents with generalized anxiety disorder.

NOTE Confidence: 0.8713635

00:57:57.650 --> 00:57:59.842 How do you know whether the treatment of

NOTE Confidence: 0.8713635

00:57:59.842 --> 00:58:01.979 choice is pharmacology psychoanalysis,

NOTE Confidence: 0.8713635

00:58:01.980 --> 00:58:03.492 cognitive therapy, behavioral therapy?

NOTE Confidence: 0.8713635

00:58:03.492 --> 00:58:04.248 Learning theory,

NOTE Confidence: 0.8713635

00:58:04.250 --> 00:58:07.170 or a combination of all of these approaches,

NOTE Confidence: 0.8713635

00:58:07.170 --> 00:58:09.830 with the theories that you put forward

NOTE Confidence: 0.8713635

00:58:09.830 --> 00:58:12.941 around looking at a circuit analysis help to

NOTE Confidence: 0.8713635

00:58:12.941 --> 00:58:15.927 make those kinds of decisions I know not now,

NOTE Confidence: 0.8713635

00:58:15.930 --> 00:58:17.760 but perhaps in the future,

NOTE Confidence: 0.8713635

00:58:17.760 --> 00:58:19.944 and I will recruit John to

NOTE Confidence: 0.8713635

00:58:19.944 --> 00:58:22.498 help back you up on this one.

NOTE Confidence: 0.8713635

00:58:22.500 --> 00:58:23.595 Yeah, it's John.

NOTE Confidence: 0.8713635

00:58:23.595 --> 00:58:25.785 Do you want to start her?

NOTE Confidence: 0.8713635

00:58:25.790 --> 00:58:26.150 I

NOTE Confidence: 0.8536046

00:58:26.150 --> 00:58:29.070 have go ahead, go ahead once you start.

NOTE Confidence: 0.8536046

00:58:29.070 --> 00:58:31.990 I mean it's so some of this work.

NOTE Confidence: 0.8536046

00:58:31.990 --> 00:58:34.636 I'm actually referring to colleagues work so.

NOTE Confidence: 0.8536046

00:58:34.640 --> 00:58:37.310 I'm thinking of Amy Atkin, for example.

NOTE Confidence: 0.8536046

00:58:37.310 --> 00:58:39.900 We've had a lot of interesting conversy

NOTE Confidence: 0.8536046

00:58:39.900 --> 00:58:42.336 thinking about different types of anxiety,

NOTE Confidence: 0.8536046

00:58:42.340 --> 00:58:44.758 different types of you know psychiatric

NOTE Confidence: 0.8536046

00:58:44.758 --> 00:58:47.117 conditions where you're you're put into

NOTE Confidence: 0.8536046

00:58:47.117 --> 00:58:49.658 buckets with some symptoms, but that's not.

NOTE Confidence: 0.7798303

00:58:53.440 --> 00:58:55.210 Basically, with the biological perturbations,

NOTE Confidence: 0.7798303

00:58:55.210 --> 00:58:56.662 so using resting state,

NOTE Confidence: 0.7798303

00:58:56.662 --> 00:58:59.588 fMRI is is something that a meeting has

NOTE Confidence: 0.7798303

00:58:59.588 --> 00:59:02.268 been able to do to sort of predict,

NOTE Confidence: 0.7798303

00:59:02.270 --> 00:59:03.845 you know what treatment strategy

NOTE Confidence: 0.7798303

00:59:03.845 --> 00:59:05.420 would be most successful with

NOTE Confidence: 0.7798303

00:59:05.476 --> 00:59:06.850 this particular individual.

NOTE Confidence: 0.7798303

00:59:06.850 --> 00:59:08.968 I'm a big proponent of individual

NOTE Confidence: 0.7798303

00:59:08.968 --> 00:59:09.674 individualized medicine.

NOTE Confidence: 0.7798303

00:59:09.680 --> 00:59:11.088 I understand us residency.

NOTE Confidence: 0.7798303

00:59:11.088 --> 00:59:13.232 fMRI might not be, you know.

NOTE Confidence: 0.7798303

00:59:13.232 --> 00:59:14.696 We need something that

NOTE Confidence: 0.7798303

00:59:14.696 --> 00:59:16.160 could be more affordable,

NOTE Confidence: 0.7798303

00:59:16.160 --> 00:59:17.714 more easily applicable to a broader

NOTE Confidence: 0.7798303

00:59:17.714 --> 00:59:19.379 population that can be rapidly used,

NOTE Confidence: 0.7798303

00:59:19.380 --> 00:59:20.988 so I understand that's sort of,

NOTE Confidence: 0.7798303

00:59:20.990 --> 00:59:22.598 you know, a proof of principle,

NOTE Confidence: 0.7798303

00:59:22.600 --> 00:59:24.100 maybe not the immediate thing that

NOTE Confidence: 0.7798303

00:59:24.100 --> 00:59:25.809 we would put right into practice,

NOTE Confidence: 0.7798303

00:59:25.810 --> 00:59:27.658 but that's sort of what I would

NOTE Confidence: 0.7798303

00:59:27.658 --> 00:59:29.993 love to see happen in the future

NOTE Confidence: 0.7798303

00:59:29.993 --> 00:59:31.469 of mental health treatment.

NOTE Confidence: 0.7798303

00:59:31.470 --> 00:59:33.318 Go ahead, John.

NOTE Confidence: 0.7798303

00:59:33.320 --> 00:59:36.750 Well first K, What an amazing awesome,

NOTE Confidence: 0.7798303

00:59:36.750 --> 00:59:38.220 fantastic, wonderful, stupendous,

NOTE Confidence: 0.7798303

00:59:38.220 --> 00:59:39.200 exceptional presentation.

NOTE Confidence: 0.7798303

00:59:39.200 --> 00:59:41.650 It was just so enlightening.

NOTE Confidence: 0.7798303

00:59:41.650 --> 00:59:45.080 And and and such a great example

NOTE Confidence: 0.7798303

00:59:45.080 --> 00:59:49.929 of the way you approach this work.

NOTE Confidence: 0.7798303

00:59:49.930 --> 00:59:52.328 And and because it was so fantastic,

NOTE Confidence: 0.7798303

00:59:52.330 --> 00:59:54.871 it's about 10 years of head of

NOTE Confidence: 0.7798303

00:59:54.871 --> 00:59:57.259 anything that we're able to to do

NOTE Confidence: 0.7798303

00:59:57.259 --> 00:59:59.530 in the clinic while you were away.

NOTE Confidence: 0.7798303

00:59:59.530 --> 01:00:00.906 The thought of we,

NOTE Confidence: 0.7798303

01:00:00.906 --> 01:00:03.650 we got into a little discussion about how,

NOTE Confidence: 0.7798303

01:00:03.650 --> 01:00:05.711 how could we even think about

NOTE Confidence: 0.7798303

01:00:05.711 --> 01:00:07.416 developing biomarkers of new retention

NOTE Confidence: 0.7798303

01:00:07.416 --> 01:00:09.140 signaling in the human brain,

NOTE Confidence: 0.7798303

01:00:09.140 --> 01:00:11.044 and which would be kind of the

NOTE Confidence: 0.7798303

01:00:11.044 --> 01:00:13.337 first step in guiding a precision

NOTE Confidence: 0.7798303

01:00:13.337 --> 01:00:14.277 medicine approach.

NOTE Confidence: 0.7798303

01:00:14.280 --> 01:00:17.045 But we're all in with you on

NOTE Confidence: 0.7798303

01:00:17.045 --> 01:00:18.830 on the idea that.

NOTE Confidence: 0.7798303

01:00:18.830 --> 01:00:22.190 That if we we treat illnesses,

NOTE Confidence: 0.7798303

01:00:22.190 --> 01:00:24.836 we treat pathology in other areas

NOTE Confidence: 0.7798303

01:00:24.836 --> 01:00:27.994 of medicine and we treat people in

NOTE Confidence: 0.7798303

01:00:27.994 --> 01:00:31.508 in psychiatry and we need to be able

NOTE Confidence: 0.7798303

01:00:31.508 --> 01:00:33.698 to incorporate an understanding of

NOTE Confidence: 0.7798303

01:00:33.698 --> 01:00:35.961 the pathology that people actually

NOTE Confidence: 0.7798303

01:00:35.961 --> 01:00:39.066 have if we want to get better

NOTE Confidence: 0.7798303

01:00:39.066 --> 01:00:40.839 and more specific treatments.

NOTE Confidence: 0.7798303

01:00:40.840 --> 01:00:43.060 So that's that's clearly a

NOTE Confidence: 0.7798303

01:00:43.060 --> 01:00:45.280 critical step in the pathway.

NOTE Confidence: 0.7798303

01:00:45.280 --> 01:00:47.495 So what a wonderful lecture

NOTE Confidence: 0.7798303

01:00:47.495 --> 01:00:48.824 really appreciate it.

NOTE Confidence: 0.7798303

01:00:48.830 --> 01:00:49.436 Thank you.

NOTE Confidence: 0.7798303

01:00:49.436 --> 01:00:49.739 Yeah,

NOTE Confidence: 0.7798303

01:00:49.739 --> 01:00:52.284 I mean I this also didn't make it

NOTE Confidence: 0.7798303

01:00:52.284 --> 01:00:54.438 into the seminar because it's still.

NOTE Confidence: 0.8208675

01:00:58.550 --> 01:01:00.818 Have collected so recently but we are.

NOTE Confidence: 0.8208675

01:01:00.820 --> 01:01:02.435 We've now started using the

NOTE Confidence: 0.8208675

01:01:02.435 --> 01:01:03.727 tensor from you lonely.

NOTE Confidence: 0.8208675

01:01:03.730 --> 01:01:05.350 You along these lab created.

NOTE Confidence: 0.8208675

01:01:05.350 --> 01:01:07.744 You know all of his tools work so well

NOTE Confidence: 0.8208675

01:01:07.744 --> 01:01:10.128 and he created a new retention sensor

NOTE Confidence: 0.8208675

01:01:10.128 --> 01:01:12.650 and so obviously you know I'm not

NOTE Confidence: 0.8208675

01:01:12.650 --> 01:01:14.774 necessarily a proponent of, you know.

NOTE Confidence: 0.8208675

01:01:14.774 --> 01:01:17.133 I think there's a lot of safety

NOTE Confidence: 0.8208675

01:01:17.133 --> 01:01:19.609 testing that needs to be put in place.

NOTE Confidence: 0.8208675

01:01:19.610 --> 01:01:21.978 You know long term effects of of using

NOTE Confidence: 0.8208675

01:01:21.978 --> 01:01:24.149 viral or genetic tools in humans,

NOTE Confidence: 0.8208675

01:01:24.150 --> 01:01:25.835 even though there's systemic administration

NOTE Confidence: 0.8208675

01:01:25.835 --> 01:01:27.520 potentially possible long term effects.

NOTE Confidence: 0.8208675

01:01:27.520 --> 01:01:29.984 I'm just having a transgene and creating

NOTE Confidence: 0.8208675

01:01:29.984 --> 01:01:32.288 proteins needs to be something that is

NOTE Confidence: 0.8208675

01:01:32.288 --> 01:01:34.620 dealt with a great amount of caution,

NOTE Confidence: 0.8208675

01:01:34.620 --> 01:01:36.979 so I will make that big disclaimer.

NOTE Confidence: 0.8208675

01:01:36.980 --> 01:01:38.332 Circle it underline highlight.

NOTE Confidence: 0.8208675

01:01:38.332 --> 01:01:39.478 However, you know,

NOTE Confidence: 0.8208675

01:01:39.478 --> 01:01:41.902 potentially you could see you know

NOTE Confidence: 0.8208675

01:01:41.902 --> 01:01:44.591 this isn't this is one way that you

NOTE Confidence: 0.8208675

01:01:44.591 --> 01:01:47.336 could be able to to sort of say what

NOTE Confidence: 0.8208675

01:01:47.336 --> 01:01:49.575 is going on in terms of the dynamics

NOTE Confidence: 0.8208675

01:01:49.575 --> 01:01:51.948 and so it offers some some window into

NOTE Confidence: 0.8208675

01:01:51.948 --> 01:01:53.550 potentially using neurotransmitters.

NOTE Confidence: 0.8208675

01:01:53.550 --> 01:01:55.115 Biomarker even this really needs

NOTE Confidence: 0.8208675

01:01:55.115 --> 01:01:57.260 to be stressed out and approved.

NOTE Confidence: 0.7894718

01:02:01.050 --> 01:02:03.642 Away from that, but that's sort of my long

NOTE Confidence: 0.7894718

01:02:03.642 --> 01:02:05.950 term forward looking view. Thanks John.

NOTE Confidence: 0.84375924

01:02:06.620 --> 01:02:08.940 I want to apologize that I haven't been

NOTE Confidence: 0.84375924

01:02:08.940 --> 01:02:11.236 reading out the names of the questioners,

NOTE Confidence: 0.84375924

01:02:11.240 --> 01:02:13.970 so I will try to start reading out the names

NOTE Confidence: 0.84375924

01:02:14.041 --> 01:02:16.777 of the questioners as I asked the questions.

NOTE Confidence: 0.84375924

01:02:16.780 --> 01:02:19.244 I also want to sort of echo Johns

NOTE Confidence: 0.84375924

01:02:19.244 --> 01:02:20.476 phenomenal work. Phenomenal talk.

NOTE Confidence: 0.84375924

01:02:20.476 --> 01:02:22.940 Thank you so much for being with us.

NOTE Confidence: 0.84375924

01:02:22.940 --> 01:02:25.092 Kay Ann. I want to introduce you again

NOTE Confidence: 0.84375924

01:02:25.092 --> 01:02:27.254 to Doctor Flynn's daughter, Sarah Flynn,

NOTE Confidence: 0.84375924

01:02:27.254 --> 01:02:29.403 who's been able to join us today,

NOTE Confidence: 0.84375924

01:02:29.410 --> 01:02:31.914 and it's really been a pleasure to have

NOTE Confidence: 0.84375924

01:02:31.914 --> 01:02:33.717 a representative of the Flynn family.

NOTE Confidence: 0.84375924

01:02:33.720 --> 01:02:38.348 Hi Sarah. Icera it's an honor.

NOTE Confidence: 0.84375924

01:02:38.350 --> 01:02:41.406 So the next question is from Doctor Tech,

NOTE Confidence: 0.84375924

01:02:41.410 --> 01:02:43.040 both the function and structure

NOTE Confidence: 0.84375924

01:02:43.040 --> 01:02:45.223 of amygdala seem to be impaired

NOTE Confidence: 0.84375924

01:02:45.223 --> 01:02:47.159 in subjects with schizophrenia.

NOTE Confidence: 0.84375924

01:02:47.160 --> 01:02:48.412 Have you ever used,

NOTE Confidence: 0.84375924

01:02:48.412 --> 01:02:51.448 or do you plan to use any models

NOTE Confidence: 0.84375924

01:02:51.448 --> 01:02:52.520 of schizophrenia,

NOTE Confidence: 0.84375924

01:02:52.520 --> 01:02:55.070 and in this preclinical work such

NOTE Confidence: 0.84375924

01:02:55.070 --> 01:02:56.345 as phencyclidine administration

NOTE Confidence: 0.84375924

01:02:56.345 --> 01:02:58.648 or some other way of getting it,

NOTE Confidence: 0.84375924

01:02:58.650 --> 01:02:59.799 that that link?

NOTE Confidence: 0.84009415

01:03:01.710 --> 01:03:05.060 I have not. I guess the short answer is no.

NOTE Confidence: 0.84009415

01:03:05.060 --> 01:03:06.740 I have not done that,

NOTE Confidence: 0.84009415

01:03:06.740 --> 01:03:09.252 but I think when I think about schizophrenia

NOTE Confidence: 0.84009415

01:03:09.252 --> 01:03:11.430 and what what is really happening,

NOTE Confidence: 0.84009415

01:03:11.430 --> 01:03:13.509 I guess the the way that I've

NOTE Confidence: 0.84009415

01:03:13.509 --> 01:03:16.360 thought about the most is sort of a

NOTE Confidence: 0.84009415

01:03:16.360 --> 01:03:17.938 computational framework, you know,

NOTE Confidence: 0.84009415

01:03:17.938 --> 01:03:20.392 kind of drawing from like roles

NOTE Confidence: 0.84009415

01:03:20.392 --> 01:03:22.220 and and oppression.

NOTE Confidence: 0.84009415

01:03:22.220 --> 01:03:23.336 With Patricia Coleman,

NOTE Confidence: 0.84009415

01:03:23.336 --> 01:03:25.940 rookies excuse me and thinking about just

NOTE Confidence: 0.84009415

01:03:26.004 --> 01:03:28.097 how do you modulate signal to noise?

NOTE Confidence: 0.84009415

01:03:28.100 --> 01:03:31.346 How do neuromodulators are near peptides?

NOTE Confidence: 0.84009415

01:03:31.350 --> 01:03:31.675 Influence.

NOTE Confidence: 0.84009415

01:03:31.675 --> 01:03:33.625 You know where you draw the

NOTE Confidence: 0.84009415

01:03:33.625 --> 01:03:35.280 line for spike threshold,

NOTE Confidence: 0.84009415

01:03:35.280 --> 01:03:36.678 so you know there's always going

NOTE Confidence: 0.84009415

01:03:36.678 --> 01:03:38.139 to be some noise of inputs.

NOTE Confidence: 0.84009415

01:03:38.140 --> 01:03:39.556 There's going to be some signal,

NOTE Confidence: 0.84009415

01:03:39.560 --> 01:03:42.386 and one way that I think about this is.

NOTE Confidence: 0.84009415

01:03:42.390 --> 01:03:43.398 Pattern completion there's

NOTE Confidence: 0.84009415

01:03:43.398 --> 01:03:45.414 always going to be some noise,

NOTE Confidence: 0.84009415

01:03:45.420 --> 01:03:47.448 and when there's more noise and.

NOTE Confidence: 0.34992766

01:03:50.100 --> 01:03:53.456 No. You know membrane potentials are closer,

NOTE Confidence: 0.34992766

01:03:53.460 --> 01:03:53.996 despite thresholds.

NOTE Confidence: 0.34992766

01:03:53.996 --> 01:03:55.604 Then you might just get spiking

NOTE Confidence: 0.34992766

01:03:55.604 --> 01:03:56.969 and therefore pattern completion,

NOTE Confidence: 0.34992766

01:03:56.970 --> 01:03:58.425 and that's what the brain's

NOTE Confidence: 0.34992766

01:03:58.425 --> 01:03:59.589 really good at doing.

NOTE Confidence: 0.34992766

01:03:59.590 --> 01:04:01.348 This is not just limited Nicola.

NOTE Confidence: 0.34992766

01:04:01.350 --> 01:04:02.810 I'm thinking of amygdala, hippocampus,

NOTE Confidence: 0.34992766

01:04:02.810 --> 01:04:04.556 prefrontal cortex as a connected circuit,

NOTE Confidence: 0.34992766

01:04:04.560 --> 01:04:06.268 but this is something this is sort

NOTE Confidence: 0.34992766

01:04:06.268 --> 01:04:08.323 of the way I've been thinking about

NOTE Confidence: 0.34992766

01:04:08.323 --> 01:04:09.898 how schizophrenia can can come

NOTE Confidence: 0.34992766

01:04:09.898 --> 01:04:12.097 to be in the context of dopamine

NOTE Confidence: 0.34992766

01:04:12.097 --> 01:04:13.720 and other neuropeptides as well.

NOTE Confidence: 0.34992766

01:04:13.720 --> 01:04:16.920 But the signal to noise concept is really.

NOTE Confidence: 0.34992766

01:04:16.920 --> 01:04:18.136 Gotten into the infected,

NOTE Confidence: 0.34992766

01:04:18.136 --> 01:04:20.320 my brain and an I've been thinking

NOTE Confidence: 0.34992766

01:04:20.320 --> 01:04:22.108 about a lot in that terms.

NOTE Confidence: 0.34992766

01:04:22.110 --> 01:04:24.112 It makes a lot of intuitive sense

NOTE Confidence: 0.34992766

01:04:24.112 --> 01:04:26.378 to me how you could get there.

NOTE Confidence: 0.34992766

01:04:26.380 --> 01:04:28.270 So just just how hallucination is

NOTE Confidence: 0.34992766

01:04:28.270 --> 01:04:29.730 constructed is fascinating to me,

NOTE Confidence: 0.34992766

01:04:29.730 --> 01:04:31.560 but we haven't done those experiments.

NOTE Confidence: 0.80241287

01:04:32.720 --> 01:04:35.793 Yeah, that that's an active area of

NOTE Confidence: 0.80241287

01:04:35.793 --> 01:04:38.609 investigation in the in the department.

NOTE Confidence: 0.80241287

01:04:38.610 --> 01:04:41.928 Jane Taylor and Phil Corlette are working

NOTE Confidence: 0.80241287

01:04:41.928 --> 01:04:45.898 on models that really do sort of address

NOTE Confidence: 0.80241287

01:04:45.898 --> 01:04:48.700 some of those behavioral aspects of.

NOTE Confidence: 0.80241287

01:04:48.700 --> 01:04:50.428 Not necessarily pattern completion,

NOTE Confidence: 0.80241287

01:04:50.428 --> 01:04:53.407 but I I like that idea of

NOTE Confidence: 0.80241287

01:04:53.407 --> 01:04:54.957 signal to noise a lot.

NOTE Confidence: 0.80241287

01:04:54.960 --> 01:04:57.306 So John Crystal asks in humans

NOTE Confidence: 0.80241287

01:04:57.306 --> 01:04:58.870 emotions are quite differentiated.

NOTE Confidence: 0.80241287

01:04:58.870 --> 01:05:00.820 So for example fear is

NOTE Confidence: 0.80241287

01:05:00.820 --> 01:05:01.990 different from discussed,

NOTE Confidence: 0.80241287

01:05:01.990 --> 01:05:04.461 which of course we do have discussed

NOTE Confidence: 0.80241287

01:05:04.461 --> 01:05:07.699 circuits in the brain stem of mice that

NOTE Confidence: 0.80241287

01:05:07.699 --> 01:05:09.804 are differentiated from fear circuits.

NOTE Confidence: 0.80241287

01:05:09.810 --> 01:05:11.298 There different from frustration,

NOTE Confidence: 0.80241287

01:05:11.298 --> 01:05:13.530 which of course we can distinguish

NOTE Confidence: 0.80241287

01:05:13.586 --> 01:05:14.900 behaviourally in humans.

NOTE Confidence: 0.80241287

01:05:14.900 --> 01:05:16.920 This higher level differentiation of

NOTE Confidence: 0.80241287

01:05:16.920 --> 01:05:19.410 emotional states seems to involve insula.

NOTE Confidence: 0.80241287

01:05:19.410 --> 01:05:20.892 And have you thought about how

NOTE Confidence: 0.80241287

01:05:20.892 --> 01:05:22.389 the insula might fit in with

NOTE Confidence: 0.80241287

01:05:22.389 --> 01:05:23.769 the story that you told today?

NOTE Confidence: 0.79308337

01:05:24.660 --> 01:05:25.904 That's an excellent question.

NOTE Confidence: 0.79308337

01:05:25.904 --> 01:05:28.459 I am not presently working on the insulin,

NOTE Confidence: 0.79308337

01:05:28.460 --> 01:05:31.277 but my first postdoc from the lab on a

NOTE Confidence: 0.79308337

01:05:31.277 --> 01:05:34.167 Baylor who now has her own lab in Bordeaux,

NOTE Confidence: 0.79308337

01:05:34.170 --> 01:05:36.072 has focused a lot on the

NOTE Confidence: 0.79308337

01:05:36.072 --> 01:05:37.340 insula and amygdala circuitry,

NOTE Confidence: 0.79308337

01:05:37.340 --> 01:05:39.820 so I guess I would encourage you to

NOTE Confidence: 0.79308337

01:05:39.820 --> 01:05:41.900 check out her work, but absolutely,

NOTE Confidence: 0.79308337

01:05:41.900 --> 01:05:44.180 it's in its intricately involved in

NOTE Confidence: 0.79308337

01:05:44.180 --> 01:05:45.691 reciprocally connected with a lot

NOTE Confidence: 0.79308337

01:05:45.691 --> 01:05:47.482 of the different sort of, you know,

NOTE Confidence: 0.79308337

01:05:47.482 --> 01:05:49.384 the emotional triad circuitry, I think.

NOTE Confidence: 0.79308337

01:05:49.384 --> 01:05:51.920 Also Nadine Gogol's work in the insula is.

NOTE Confidence: 0.8155253

01:05:55.620 --> 01:05:58.836 But I haven't done that, but there is

NOTE Confidence: 0.8155253

01:05:58.836 --> 01:06:01.650 beautiful work being done by a number

NOTE Confidence: 0.8155253

01:06:01.650 --> 01:06:03.660 of rising stars in the

NOTE Confidence: 0.8155253

01:06:03.660 --> 01:06:06.066 field. And Mark Anderman also has

NOTE Confidence: 0.8155253

01:06:06.070 --> 01:06:08.457 some market as well. Yes, absolutely.

NOTE Confidence: 0.8155253

01:06:08.457 --> 01:06:11.096 So another question from the chat allcare

NOTE Confidence: 0.8155253

01:06:11.096 --> 01:06:13.120 asks or says behavioral activation

NOTE Confidence: 0.8155253

01:06:13.120 --> 01:06:15.532 is 1 therapeutic form of activation

NOTE Confidence: 0.8155253

01:06:15.532 --> 01:06:17.652 of positive valence neurons using

NOTE Confidence: 0.8155253

01:06:17.652 --> 01:06:20.136 psychotherapy which is used to treat

NOTE Confidence: 0.8155253

01:06:20.140 --> 01:06:22.150 negative balance disorders like depression.

NOTE Confidence: 0.8155253

01:06:22.150 --> 01:06:24.160 And he asks, you might,

NOTE Confidence: 0.8155253

01:06:24.160 --> 01:06:27.114 if you think this might rely on

NOTE Confidence: 0.8155253

01:06:27.114 --> 01:06:29.079 the competition between the BLA.

NOTE Confidence: 0.8155253

01:06:29.080 --> 01:06:30.650 Nucleus incumbents in the BL.

NOTE Confidence: 0.8155253

01:06:30.650 --> 01:06:33.154 A central amygdala circuits and I would add.

NOTE Confidence: 0.8155253

01:06:33.160 --> 01:06:35.360 If so, how might you measure that in

NOTE Confidence: 0.8155253

01:06:35.360 --> 01:06:37.559 a person who is undergoing therapy?

NOTE Confidence: 0.8155253

01:06:37.560 --> 01:06:38.190 Oh, oh,

NOTE Confidence: 0.794027

01:06:38.190 --> 01:06:40.068 the second part of your question.

NOTE Confidence: 0.794027

01:06:40.070 --> 01:06:42.860 I'm going to come back to that that in a

NOTE Confidence: 0.794027

01:06:42.930 --> 01:06:45.714 moment I think this is a great question.

NOTE Confidence: 0.794027

01:06:45.720 --> 01:06:47.808 It it actually brings us back to Harkins

NOTE Confidence: 0.794027

01:06:47.808 --> 01:06:50.295 back to a few questions ago regarding

NOTE Confidence: 0.794027

01:06:50.295 --> 01:06:53.040 clinical treatment, and I think.

NOTE Confidence: 0.794027

01:06:53.040 --> 01:06:58.440 The reality is. That that.

NOTE Confidence: 0.794027

01:06:58.440 --> 01:06:59.905 I've been told that pharmacological

NOTE Confidence: 0.794027

01:06:59.905 --> 01:07:01.660 treatment, in my opinion not specific,

NOTE Confidence: 0.794027

01:07:01.660 --> 01:07:03.418 and so this is. It's not.

NOTE Confidence: 0.794027

01:07:03.420 --> 01:07:05.298 It's never going to be maximally

NOTE Confidence: 0.794027

01:07:05.298 --> 01:07:07.229 effective in my opinion on its own.

NOTE Confidence: 0.794027

01:07:07.230 --> 01:07:08.630 I think pharmacological treatments are

NOTE Confidence: 0.794027

01:07:08.630 --> 01:07:10.987 always going to be better in combination with

NOTE Confidence: 0.794027

01:07:10.987 --> 01:07:12.799 some form of cognitive behavioral therapy,

NOTE Confidence: 0.794027

01:07:12.800 --> 01:07:14.468 and I'm using that a very

NOTE Confidence: 0.794027

01:07:14.468 --> 01:07:16.020 very broad term and again,

NOTE Confidence: 0.794027

01:07:16.020 --> 01:07:18.050 of course I'm not a medical professional

NOTE Confidence: 0.794027

01:07:18.050 --> 01:07:20.118 and not qualified to give medical advice,

NOTE Confidence: 0.794027

01:07:20.120 --> 01:07:21.872 but my perception and my understanding

NOTE Confidence: 0.794027

01:07:21.872 --> 01:07:23.961 of the circuitry would suggest this dual

NOTE Confidence: 0.794027

01:07:23.961 --> 01:07:25.689 approach would be what is necessary.

NOTE Confidence: 0.794027

01:07:25.690 --> 01:07:27.754 I do think it's very likely that there's

NOTE Confidence: 0.794027

01:07:27.754 --> 01:07:30.018 going to be competition between circuits.

NOTE Confidence: 0.794027

01:07:30.020 --> 01:07:32.715 There's going to be interaction because both.

NOTE Confidence: 0.794027

01:07:32.720 --> 01:07:34.091 BLANECNBLICE central amygdala

NOTE Confidence: 0.794027

01:07:34.091 --> 01:07:36.376 neurons are not only rip,

NOTE Confidence: 0.794027

01:07:36.380 --> 01:07:38.208 typically connected model synaptically

NOTE Confidence: 0.794027

01:07:38.208 --> 01:07:39.579 with excitatory connections,

NOTE Confidence: 0.794027

01:07:39.580 --> 01:07:42.110 but also through feedforward connections

NOTE Confidence: 0.794027

01:07:42.110 --> 01:07:45.086 and that dual connectivity allows a

NOTE Confidence: 0.794027

01:07:45.086 --> 01:07:47.342 lot of opportunity for regulation of

NOTE Confidence: 0.794027

01:07:47.342 --> 01:07:49.974 the net strength of connections between

NOTE Confidence: 0.794027

01:07:49.974 --> 01:07:52.364 those two populations of neurons,

NOTE Confidence: 0.794027

01:07:52.370 --> 01:07:56.474 and so we do see a lot of plus.

NOTE Confidence: 0.8349331

01:08:00.360 --> 01:08:03.136 I did not object into that study today,

NOTE Confidence: 0.8349331

01:08:03.140 --> 01:08:05.908 but but we have seen that and simple

NOTE Confidence: 0.8349331

01:08:05.908 --> 01:08:06.964 manipulations, food deprivation,

NOTE Confidence: 0.8349331

01:08:06.964 --> 01:08:08.724 social isolation of these things

NOTE Confidence: 0.8349331

01:08:08.724 --> 01:08:11.180 will change the balance of, you know,

NOTE Confidence: 0.8349331

01:08:11.180 --> 01:08:13.460 the the plasticity between these two

NOTE Confidence: 0.8349331

01:08:13.460 --> 01:08:15.840 populations of neurons in their ability to

NOTE Confidence: 0.8349331

01:08:15.840 --> 01:08:18.136 affect each other in a very qualitative

NOTE Confidence: 0.8349331

01:08:18.136 --> 01:08:21.177 way where you know it can become from a

NOTE Confidence: 0.8349331

01:08:21.177 --> 01:08:23.259 suppression to a facilitation based on,

NOTE Confidence: 0.8349331

01:08:23.260 --> 01:08:24.692 for example, food deprivation.

NOTE Confidence: 0.8349331

01:08:24.692 --> 01:08:27.080 And so this is something this is.

NOTE Confidence: 0.8349331

01:08:27.080 --> 01:08:28.830 Gwendolyn calhouns.

NOTE Confidence: 0.8349331

01:08:28.830 --> 01:08:30.125 A study that's that's been

NOTE Confidence: 0.8349331

01:08:30.125 --> 01:08:31.420 bar by archive for awhile.

NOTE Confidence: 0.8349331

01:08:31.420 --> 01:08:32.974 But yeah, I think I think that's

NOTE Confidence: 0.8349331

01:08:32.974 --> 01:08:34.590 kind of how I would imagine

NOTE Confidence: 0.8349331

01:08:34.590 --> 01:08:36.075 this circuitry playing into it,

NOTE Confidence: 0.8349331

01:08:36.080 --> 01:08:38.144 but it's going to be broader than that.

NOTE Confidence: 0.8349331

01:08:38.150 --> 01:08:39.138 Of course, you know,

NOTE Confidence: 0.8349331

01:08:39.138 --> 01:08:41.693 I don't think this is the end all and be

NOTE Confidence: 0.8349331

01:08:41.693 --> 01:08:43.590 all of Dylan's processing by any means.

NOTE Confidence: 0.8349331

01:08:43.590 --> 01:08:45.150 I don't mean to imply that.

NOTE Confidence: 0.821403

01:08:49.270 --> 01:08:51.146 And a representative of how the brain

NOTE Confidence: 0.821403

01:08:51.146 --> 01:08:52.382 will apply biological implementational

NOTE Confidence: 0.821403

01:08:52.382 --> 01:08:54.277 strategies to solve this problem.

NOTE Confidence: 0.821403

01:08:54.280 --> 01:08:56.310 And I think we'll see that motif

NOTE Confidence: 0.821403

01:08:56.310 --> 01:08:58.539 appear again and again in different in

NOTE Confidence: 0.821403

01:08:58.539 --> 01:09:00.850 different circuits as well as the glow.

NOTE Confidence: 0.7463192

01:09:04.910 --> 01:09:05.530 Therefore.

NOTE Confidence: 0.861282

01:09:06.950 --> 01:09:09.134 That's all the questions from the chat,

NOTE Confidence: 0.861282

01:09:09.140 --> 01:09:10.705 except for some comments to

NOTE Confidence: 0.861282

01:09:10.705 --> 01:09:11.644 say brilliant presentation.

NOTE Confidence: 0.861282

01:09:11.650 --> 01:09:13.195 Does anyone else have any

NOTE Confidence: 0.861282

01:09:13.195 --> 01:09:15.090 questions they'd like to ask live?

NOTE Confidence: 0.843655

01:09:19.050 --> 01:09:22.034 Well, if not thank you so much Kay,

NOTE Confidence: 0.843655

01:09:22.040 --> 01:09:24.984 for being with us with a 3 hour

NOTE Confidence: 0.843655

01:09:24.984 --> 01:09:27.215 difference in time early early on

NOTE Confidence: 0.843655

01:09:27.215 --> 01:09:30.179 the West Coast it was a pleasure to

NOTE Confidence: 0.843655

01:09:30.179 --> 01:09:33.251 be able to hear about your work and

NOTE Confidence: 0.843655

01:09:33.260 --> 01:09:35.912 particularly to have our audience that

NOTE Confidence: 0.843655

01:09:35.912 --> 01:09:38.047 involves everything from a molecule

NOTE Confidence: 0.843655

01:09:38.047 --> 01:09:40.738 to a patient to to be able to stab.

NOTE Confidence: 0.843655

01:09:40.740 --> 01:09:42.990 Your synthesis has been really helpful,

NOTE Confidence: 0.843655

01:09:42.990 --> 01:09:45.204 so thanks so much everyone in

NOTE Confidence: 0.843655

01:09:45.204 --> 01:09:47.469 Marina for hosting and having me.

NOTE Confidence: 0.38562948

01:09:49.500 --> 01:09:51.264 Wonderful God care.