WEBVTT

NOTE duration:"01:11:16.6080000"

NOTE language:en-us

NOTE Confidence: 0.8314021

00:00:00.000 --> 00:00:02.328 Because my introduction is much less

NOTE Confidence: 0.8314021

00:00:02.328 --> 00:00:04.220 important than Doctor Calipari's talk,

NOTE Confidence: 0.8314021

00:00:04.220 --> 00:00:06.670 which will be eagerly awaiting.

NOTE Confidence: 0.8314021

00:00:06.670 --> 00:00:09.772 So it's it's my absolute pleasure

NOTE Confidence: 0.8314021

00:00:09.772 --> 00:00:12.573 to introduce Doctor Erin Calipari

NOTE Confidence: 0.8314021

00:00:12.573 --> 00:00:15.768 who's today's grand round speaker.

NOTE Confidence: 0.8314021

00:00:15.770 --> 00:00:18.934 She is someone who has really been

NOTE Confidence: 0.8314021

00:00:18.934 --> 00:00:21.653 a pioneer and incredibly prolific

NOTE Confidence: 0.8314021

00:00:21.653 --> 00:00:25.439 scientists already in the area of

NOTE Confidence: 0.8314021

00:00:25.439 --> 00:00:29.819 addiction and using a rodent models to

NOTE Confidence: 0.8314021

00:00:29.819 --> 00:00:32.231 understand the neurobiological basis

NOTE Confidence: 0.8314021

00:00:32.231 --> 00:00:34.625 of important constructs underlying

NOTE Confidence: 0.8314021

00:00:34.625 --> 00:00:37.600 addiction that are relevant to.

NOTE Confidence: 0.8314021

00:00:37.600 --> 00:00:39.705 Human subjects she did her

NOTE Confidence: 0.8314021

00:00:39.705 --> 00:00:41.810 undergraduate degree at the University

NOTE Confidence: 0.8314021

00:00:41.876 --> 00:00:43.688 of Massachusetts in Amherst,

NOTE Confidence: 0.8314021

00:00:43.690 --> 00:00:46.876 where she has got her BS in both psychology

NOTE Confidence: 0.8314021

00:00:46.876 --> 00:00:49.717 and biology and already began working

NOTE Confidence: 0.8314021

00:00:49.717 --> 00:00:53.259 with Doctor Gerald Meyer using rodent models.

NOTE Confidence: 0.8314021

00:00:53.260 --> 00:00:56.824 And then she did her graduate work at Wake

NOTE Confidence: 0.8314021

00:00:56.824 --> 00:01:00.217 Forest School of Medicine with Sarah Jones,

NOTE Confidence: 0.8314021

00:01:00.220 --> 00:01:03.288 where she began to.

NOTE Confidence: 0.8314021

00:01:03.290 --> 00:01:06.146 It really immerse herself and neurochemistry,

NOTE Confidence: 0.8314021

00:01:06.150 --> 00:01:09.496 an other aspects of in vivo manipulations

NOTE Confidence: 0.8314021

00:01:09.496 --> 00:01:11.880 and measurements related to behavior.

NOTE Confidence: 0.8314021

00:01:11.880 --> 00:01:15.384 She then went on as a postdoctoral fellow

NOTE Confidence: 0.8314021

00:01:15.384 --> 00:01:19.410 and then a instructor at the Mount Sinai's

NOTE Confidence: 0.8314021

00:01:19.410 --> 00:01:22.848 Icahn School of Medicine at Mount Sinai,

NOTE Confidence: 0.8314021

00:01:22.850 --> 00:01:25.706 where she worked with Eric Nestler.

NOTE Confidence: 0.8314021

00:01:25.710 --> 00:01:28.410 And there she began to develop

NOTE Confidence: 0.8314021

00:01:28.410 --> 00:01:31.429 a number of lines of research,

NOTE Confidence: 0.8314021

00:01:31.430 --> 00:01:33.224 including examination of.

NOTE Confidence: 0.8314021

00:01:33.224 --> 00:01:35.018 Particularly molecular consequences

NOTE Confidence: 0.8314021

00:01:35.018 --> 00:01:36.812 of drug addiction,

NOTE Confidence: 0.8314021

00:01:36.820 --> 00:01:38.761 and particularly intracellular

NOTE Confidence: 0.8314021

00:01:38.761 --> 00:01:42.643 signaling as a consequence of drug

NOTE Confidence: 0.8314021

00:01:42.643 --> 00:01:46.316 addiction that may maintain long term

NOTE Confidence: 0.8314021

00:01:46.316 --> 00:01:48.664 structural and behavioral adaptations

NOTE Confidence: 0.8314021

00:01:48.664 --> 00:01:51.935 to drugs of abuse and also was really

NOTE Confidence: 0.8314021

00:01:51.935 --> 00:01:55.214 key in a number of important papers

NOTE Confidence: 0.8314021

00:01:55.214 --> 00:01:58.460 on sex specific effects of addictive,

NOTE Confidence: 0.8314021

00:01:58.460 --> 00:02:01.260 addictive substances like cocaine and

NOTE Confidence: 0.8314021

00:02:01.260 --> 00:02:03.500 those experiments are particularly

NOTE Confidence: 0.8314021

00:02:03.500 --> 00:02:05.040 notable because they.

NOTE Confidence: 0.8314021

00:02:05.040 --> 00:02:07.440 Involved many, many levels of evaluation,

NOTE Confidence: 0.8314021

00:02:07.440 --> 00:02:10.240 not only in rodents but also in

NOTE Confidence: 0.8314021

00:02:10.240 --> 00:02:11.040 human subjects.

NOTE Confidence: 0.8314021

00:02:11.040 --> 00:02:14.240 She has won a number of awards already.

NOTE Confidence: 0.8314021

00:02:14.240 --> 00:02:17.440 I want to note a few notable ones.

NOTE Confidence: 0.8314021

00:02:17.440 --> 00:02:21.040 In particular she is an awardee of the DP.

NOTE Confidence: 0.8314021

00:02:21.040 --> 00:02:23.040 One Avenir Award in genetics,

NOTE Confidence: 0.8314021

00:02:23.040 --> 00:02:25.040 and epigenetics from the National

NOTE Confidence: 0.8314021

00:02:25.040 --> 00:02:26.640 Institute on Drug Abuse,

NOTE Confidence: 0.8314021

00:02:26.640 --> 00:02:29.028 and that's someone who the director

NOTE Confidence: 0.8314021

00:02:29.028 --> 00:02:31.984 of Naida pulls out as having research

NOTE Confidence: 0.8314021

00:02:31.984 --> 00:02:34.124 that is extremely innovative and

NOTE Confidence: 0.8314021

00:02:34.124 --> 00:02:35.939 at the edge of the.

NOTE Confidence: 0.8314021

00:02:35.940 --> 00:02:37.648 Molecular basis of addiction.

NOTE Confidence: 0.8314021

00:02:37.648 --> 00:02:40.700 She's an associate member of the AC NP.

NOTE Confidence: 0.8314021

00:02:40.700 --> 00:02:42.814 Oh I should have noted that she's

NOTE Confidence: 0.8314021

00:02:42.814 --> 00:02:44.688 also an assistant professor in

NOTE Confidence: 0.8314021

00:02:44.688 --> 00:02:46.492 the department's particularly in

NOTE Confidence: 0.8314021

00:02:46.492 --> 00:02:48.296 the Department of Pharmacology

NOTE Confidence: 0.8314021

00:02:48.356 --> 00:02:49.838 at Vanderbilt University,

NOTE Confidence: 0.8314021

00:02:49.840 --> 00:02:51.615 but also has appointments in

NOTE Confidence: 0.8314021

00:02:51.615 --> 00:02:53.035 the departments of Psychiatry

NOTE Confidence: 0.8314021

00:02:53.035 --> 00:02:54.599 and Behavioral Sciences.

NOTE Confidence: 0.8314021

00:02:54.600 --> 00:02:56.634 Of course relevant to our Department

NOTE Confidence: 0.8314021

00:02:56.634 --> 00:02:58.579 and the Department of Molecular

NOTE Confidence: 0.8314021

00:02:58.579 --> 00:03:00.157 Physiology and Biophysics.

NOTE Confidence: 0.8314021

00:03:00.160 --> 00:03:02.536 So again, even with her appointments,

NOTE Confidence: 0.8314021

00:03:02.540 --> 00:03:05.753 you can see how her work spans areas of

NOTE Confidence: 0.8314021

00:03:05.753 --> 00:03:08.040 investigation from the very molecular

NOTE Confidence: 0.8314021

00:03:08.040 --> 00:03:10.830 and cellular through the pharmacological too.

NOTE Confidence: 0.8314021

00:03:10.830 --> 00:03:13.010 The area of drug addiction

NOTE Confidence: 0.8314021

00:03:13.010 --> 00:03:14.754 relevant to psychiatric illness.

NOTE Confidence: 0.8314021

00:03:14.760 --> 00:03:16.950 So back to her awards.

NOTE Confidence: 0.8314021

00:03:16.950 --> 00:03:20.009 Just because they're so notable she is,

NOTE Confidence: 0.8314021

00:03:20.010 --> 00:03:22.680 has been awarded a Whitehall Foundation

NOTE Confidence: 0.8314021

00:03:22.680 --> 00:03:25.306 research grant and are said Young

NOTE Confidence: 0.8314021

00:03:25.306 --> 00:03:27.628 Investigator Award and a K99 to

NOTE Confidence: 0.8314021

00:03:27.628 --> 00:03:30.059 R00 pathway to Independence Award,

NOTE Confidence: 0.8314021

00:03:30.060 --> 00:03:32.682 and even back in her days

NOTE Confidence: 0.8314021

00:03:32.682 --> 00:03:34.430 as a graduate student.

NOTE Confidence: 0.8314021

00:03:34.430 --> 00:03:36.170 The Knighted Director's Award,

NOTE Confidence: 0.8314021

00:03:36.170 --> 00:03:37.910 which acknowledged her innovative

NOTE Confidence: 0.8314021

00:03:37.910 --> 00:03:39.670 work from the beginning,

NOTE Confidence: 0.8314021

00:03:39.670 --> 00:03:40.538 an addiction.

NOTE Confidence: 0.8314021

00:03:40.538 --> 00:03:42.708 She's an editorial boards relevant

NOTE Confidence: 0.8314021

00:03:42.708 --> 00:03:44.010 to this Department.

NOTE Confidence: 0.8314021

00:03:44.010 --> 00:03:45.700 Both the editorial board of

NOTE Confidence: 0.8314021

00:03:45.700 --> 00:03:46.376 Neuropsychopharmacology and

NOTE Confidence: 0.8314021

00:03:46.376 --> 00:03:48.070 the Journal of Neuroscience,

NOTE Confidence: 0.8314021

00:03:48.070 --> 00:03:49.490 and she's been incredibly

NOTE Confidence: 0.8314021

00:03:49.490 --> 00:03:51.620 prolific at every stage of her

NOTE Confidence: 0.87306535

00:03:51.686 --> 00:03:54.212 career, showing how which I love that

NOTE Confidence: 0.87306535

00:03:54.212 --> 00:03:56.929 not only does she have great ideas,

NOTE Confidence: 0.87306535

00:03:56.930 --> 00:03:59.354 but she carries them through all the way

NOTE Confidence: 0.87306535

00:03:59.354 --> 00:04:01.720 to really publishing beautiful papers,

NOTE Confidence: 0.87306535

00:04:01.720 --> 00:04:03.904 and it's been exciting to watch

NOTE Confidence: 0.87306535

00:04:03.904 --> 00:04:05.780 the evolution of the work.

NOTE Confidence: 0.87306535

00:04:05.780 --> 00:04:08.370 Do you want to say something that

NOTE Confidence: 0.87306535

00:04:08.370 --> 00:04:10.265 is not exactly science related,

NOTE Confidence: 0.87306535

00:04:10.265 --> 00:04:12.390 as she was recounting during?

NOTE Confidence: 0.87306535

00:04:12.390 --> 00:04:14.686 The first discussion she does have one area

NOTE Confidence: 0.87306535

00:04:14.686 --> 00:04:17.070 that she's interested in outside of science,

NOTE Confidence: 0.87306535

00:04:17.070 --> 00:04:18.813 or that she's able to devote time

NOTE Confidence: 0.87306535

00:04:18.813 --> 00:04:20.809 to as an assistant professor,

NOTE Confidence: 0.87306535

00:04:20.810 --> 00:04:23.612 and that is she is a powerlifter and

NOTE Confidence: 0.87306535

00:04:23.612 --> 00:04:27.300 I have seen a video of her doing.

NOTE Confidence: 0.87306535

00:04:27.300 --> 00:04:29.456 Plus, which I'm very, very envious of,

NOTE Confidence: 0.87306535

00:04:29.460 --> 00:04:32.244 but I do want to highlight that her most

NOTE Confidence: 0.87306535

00:04:32.244 --> 00:04:33.787 recent achievement in powerlifting is

NOTE Confidence: 0.87306535

00:04:33.787 --> 00:04:35.950 that she has just deadlifted 300 pounds.

NOTE Confidence: 0.87306535

00:04:35.950 --> 00:04:37.810 Now if that isn't an achievement,

NOTE Confidence: 0.87306535

00:04:37.810 --> 00:04:39.350 I don't know what is.

NOTE Confidence: 0.87306535

00:04:39.350 --> 00:04:41.513 So thank you very much for being

NOTE Confidence: 0.87306535

00:04:41.513 --> 00:04:42.440 with us here.

NOTE Confidence: 0.87306535

00:04:42.440 --> 00:04:42.992 Erin Dr.

NOTE Confidence: 0.87306535

00:04:42.992 --> 00:04:43.268 Calipari,

NOTE Confidence: 0.87306535

00:04:43.268 --> 00:04:45.200 it is a pleasure to welcome you

NOTE Confidence: 0.87306535

00:04:45.257 --> 00:04:47.177 to the Department and I'm looking

NOTE Confidence: 0.87306535

00:04:47.177 --> 00:04:49.161 forward to hearing we're all looking

NOTE Confidence: 0.87306535

00:04:49.161 --> 00:04:50.776 forward to hearing your talk.

NOTE Confidence: 0.87306535

00:04:50.780 --> 00:04:51.710 Thank you so

NOTE Confidence: 0.86387175

00:04:51.710 --> 00:04:53.260 much. That was so nice.

NOTE Confidence: 0.86387175

00:04:53.260 --> 00:04:55.416 And yeah, I know I tried it.

NOTE Confidence: 0.86387175

00:04:55.420 --> 00:04:57.025 You know the pandemic has

NOTE Confidence: 0.86387175

00:04:57.025 --> 00:04:59.259 made me start to try to find.

NOTE Confidence: 0.86387175

00:04:59.260 --> 00:05:01.311 Things to occupy my time that aren't

NOTE Confidence: 0.86387175

00:05:01.311 --> 00:05:03.423 just sitting at home and working and

NOTE Confidence: 0.86387175

00:05:03.423 --> 00:05:05.580 so that's that's what I've been doing.

NOTE Confidence: 0.86387175

00:05:05.580 --> 00:05:07.296 But I'm I'm actually really excited

NOTE Confidence: 0.86387175

00:05:07.296 --> 00:05:09.489 to present for a number of reasons.

NOTE Confidence: 0.86387175

00:05:09.490 --> 00:05:11.826 One, because I get to see some people

NOTE Confidence: 0.86387175

00:05:11.826 --> 00:05:14.310 outside of my immediate family in my lab.

NOTE Confidence: 0.86387175

00:05:14.310 --> 00:05:16.846 But to this, this work is some kind

NOTE Confidence: 0.86387175

00:05:16.846 --> 00:05:19.062 of work that's been developing in

NOTE Confidence: 0.86387175

00:05:19.062 --> 00:05:22.060 my lab of the last couple of years.

NOTE Confidence: 0.86387175

00:05:22.060 --> 00:05:24.268 That focuses on kind of what

NOTE Confidence: 0.86387175

00:05:24.268 --> 00:05:25.372 dopamine is doing,

NOTE Confidence: 0.86387175

00:05:25.380 --> 00:05:28.071 and so I think you know for somebody who

NOTE Confidence: 0.86387175

00:05:28.071 --> 00:05:30.548 studies addiction and psychiatric disease.

NOTE Confidence: 0.86387175

00:05:30.550 --> 00:05:32.866 The reason this is so important

NOTE Confidence: 0.86387175

00:05:32.866 --> 00:05:35.164 is because domains at the core

NOTE Confidence: 0.86387175

00:05:35.164 --> 00:05:37.186 of a lot of these disorders,

NOTE Confidence: 0.86387175

00:05:37.190 --> 00:05:38.930 and you know specifically addiction

NOTE Confidence: 0.86387175

00:05:38.930 --> 00:05:41.250 where you see deficits in dopamine,

NOTE Confidence: 0.86387175

00:05:41.250 --> 00:05:43.386 and I think it's really important

NOTE Confidence: 0.86387175

00:05:43.386 --> 00:05:45.258 to understand for people what

NOTE Confidence: 0.86387175

00:05:45.258 --> 00:05:46.410 those deficits mean.

NOTE Confidence: 0.86387175

00:05:46.410 --> 00:05:48.426 You know if dopamine is encoding

NOTE Confidence: 0.86387175

00:05:48.426 --> 00:05:50.260 reward and reduction in dopamine

NOTE Confidence: 0.86387175

00:05:50.260 --> 00:05:52.410 may mean something very different.

NOTE Confidence: 0.86387175

00:05:52.410 --> 00:05:54.174 Then if it don't mean is encoding

NOTE Confidence: 0.86387175

00:05:54.174 --> 00:05:55.968 some other aspect of learned behavior,

NOTE Confidence: 0.86387175

00:05:55.970 --> 00:05:59.634 which I'm probably going to show you today.

NOTE Confidence: 0.86387175

00:05:59.640 --> 00:06:00.465 So you know,

NOTE Confidence: 0.86387175

00:06:00.465 --> 00:06:03.079 I'll kind of show some stuff in the weeds,

NOTE Confidence: 0.86387175

00:06:03.080 --> 00:06:05.264 but also kind of tide into big

NOTE Confidence: 0.86387175

00:06:05.264 --> 00:06:07.292 picture and so please like stop

NOTE Confidence: 0.86387175

00:06:07.292 --> 00:06:09.672 me if things aren't clear or you

NOTE Confidence: 0.86387175

00:06:09.741 --> 00:06:12.170 have thoughts or comments as we go.

NOTE Confidence: 0.86387175

00:06:12.170 --> 00:06:12.525 OK,

NOTE Confidence: 0.86387175

00:06:12.525 --> 00:06:15.365 so the focus of my lab is really

NOTE Confidence: 0.86387175

00:06:15.365 --> 00:06:17.994 understanding if you can see my slides right.

NOTE Confidence: 0.86387175

00:06:18.000 --> 00:06:18.354 OK,

NOTE Confidence: 0.86387175

00:06:18.354 --> 00:06:20.124 good is understanding how neural

NOTE Confidence: 0.86387175

00:06:20.124 --> 00:06:21.976 experience or how neural circuits

NOTE Confidence: 0.86387175

00:06:21.976 --> 00:06:23.464 integrate experiences to drive

NOTE Confidence: 0.86387175

00:06:23.464 --> 00:06:25.963 behavior and so you know in life

NOTE Confidence: 0.86387175

00:06:25.963 --> 00:06:27.993 or in animals you know we have

NOTE Confidence: 0.86387175

00:06:27.993 --> 00:06:29.810 experiences that have negative outcomes.

NOTE Confidence: 0.86387175

00:06:29.810 --> 00:06:31.710 Things that have positive outcomes

NOTE Confidence: 0.86387175

00:06:31.710 --> 00:06:33.776 and what happens is that these

NOTE Confidence: 0.86387175

00:06:33.776 --> 00:06:35.765 experiences change the way our brain

NOTE Confidence: 0.86387175

00:06:35.765 --> 00:06:37.949 response to stimuli in the future to

NOTE Confidence: 0.86387175

00:06:37.949 --> 00:06:39.654 increase the probability of behaviors

NOTE Confidence: 0.86387175

00:06:39.654 --> 00:06:41.444 that result in good outcomes.

NOTE Confidence: 0.86387175

00:06:41.450 --> 00:06:43.405 And decrease the probability of

NOTE Confidence: 0.86387175

00:06:43.405 --> 00:06:45.970 behaviors that result in negative outcomes.

NOTE Confidence: 0.86387175

00:06:45.970 --> 00:06:48.562 And the reason I'm so interested

NOTE Confidence: 0.86387175

00:06:48.562 --> 00:06:51.727 in this is because this is kind of,

NOTE Confidence: 0.86387175

00:06:51.730 --> 00:06:52.552 you know,

NOTE Confidence: 0.86387175

00:06:52.552 --> 00:06:55.018 the fundamental core of how we

NOTE Confidence: 0.86387175

00:06:55.018 --> 00:06:55.840 make decisions.

NOTE Confidence: 0.86387175

00:06:55.840 --> 00:06:57.484 But it's also dysregulated,

NOTE Confidence: 0.86387175

00:06:57.484 --> 00:06:59.950 and almost every psychiatric disease state,

NOTE Confidence: 0.86387175

00:06:59.950 --> 00:07:02.410 and so you know for somebody

NOTE Confidence: 0.86387175

00:07:02.410 --> 00:07:03.640 who studies addiction,

NOTE Confidence: 0.86387175

00:07:03.640 --> 00:07:05.700 you know drug associated stimuli,

NOTE Confidence: 0.86387175

00:07:05.700 --> 00:07:07.344 or overvalued relative to

NOTE Confidence: 0.86387175

00:07:07.344 --> 00:07:08.166 negative consequences.

NOTE Confidence: 0.86387175

00:07:08.170 --> 00:07:09.810 An alternative reinforcers depression.

NOTE Confidence: 0.86387175

00:07:09.810 --> 00:07:11.450 You have reduced motivation.

NOTE Confidence: 0.86387175

00:07:11.450 --> 00:07:12.470 Valuation of rewards.

NOTE Confidence: 0.86387175

00:07:12.470 --> 00:07:14.170 Reward learning or things like

NOTE Confidence: 0.86387175

00:07:14.170 --> 00:07:16.052 anxiety and stress disorders where

NOTE Confidence: 0.86387175

00:07:16.052 --> 00:07:17.962 these negative outcomes may be

NOTE Confidence: 0.86387175

00:07:17.962 --> 00:07:20.168 overgeneralized to neutral cues and contexts,

NOTE Confidence: 0.86387175

00:07:20.170 --> 00:07:20.878 which is,

NOTE Confidence: 0.86387175

00:07:20.878 --> 00:07:22.648 you know things like PTSD,

NOTE Confidence: 0.86387175

00:07:22.650 --> 00:07:25.030 and so you know this kind of

NOTE Confidence: 0.86387175

00:07:25.030 --> 00:07:26.897 fundamental process by which we

NOTE Confidence: 0.86387175

00:07:26.897 --> 00:07:29.219 attribute value to things that our

NOTE Confidence: 0.86387175

00:07:29.219 --> 00:07:31.344 environment is really a core of

NOTE Confidence: 0.86387175

00:07:31.344 --> 00:07:33.264 how we should be thinking about

NOTE Confidence: 0.86387175

00:07:33.270 --> 00:07:35.350 treating people with disorders

NOTE Confidence: 0.86387175

00:07:35.350 --> 00:07:37.430 where this is dysregulated.

NOTE Confidence: 0.86387175

00:07:37.430 --> 00:07:39.116 So you know, I'm, you know,

NOTE Confidence: 0.86387175

00:07:39.120 --> 00:07:40.806 going way back to the simple,

NOTE Confidence: 0.86387175

00:07:40.810 --> 00:07:42.784 you know half of my lab studies.

NOTE Confidence: 0.86387175

00:07:42.790 --> 00:07:45.038 You know how to drug change the brain,

NOTE Confidence: 0.86387175

00:07:45.040 --> 00:07:46.726 but the other half of my

NOTE Confidence: 0.86387175

00:07:46.726 --> 00:07:47.850 labs that he's just

NOTE Confidence: 0.87806416

00:07:47.918 --> 00:07:49.840 kind of. How do these same systems

NOTE Confidence: 0.87806416

00:07:49.840 --> 00:07:51.250 work in a normal situation?

NOTE Confidence: 0.87806416

00:07:51.250 --> 00:07:53.498 And so the first thing is kind of,

NOTE Confidence: 0.87806416

00:07:53.500 --> 00:07:55.670 you know, how do we learn to

NOTE Confidence: 0.87806416

00:07:55.670 --> 00:07:57.320 make these adaptive decisions?

NOTE Confidence: 0.87806416

00:07:57.320 --> 00:07:59.448 And so we use things in our

NOTE Confidence: 0.87806416

00:07:59.448 --> 00:08:00.940 Virat environment to do this.

NOTE Confidence: 0.87806416

00:08:00.940 --> 00:08:02.415 So maybe there's contextual cues

NOTE Confidence: 0.87806416

00:08:02.415 --> 00:08:04.553 that help you figure out when things

NOTE Confidence: 0.87806416

00:08:04.553 --> 00:08:06.377 are dangerous and when they aren't,

NOTE Confidence: 0.87806416

00:08:06.380 --> 00:08:08.708 and so if you have something like the

NOTE Confidence: 0.87806416

00:08:08.708 --> 00:08:11.033 sound of a helicopter in a hometown

NOTE Confidence: 0.87806416

00:08:11.033 --> 00:08:13.577 may be very different than the cell of

NOTE Confidence: 0.87806416

00:08:13.577 --> 00:08:15.741 sound of a helicopter in a war zone.

NOTE Confidence: 0.87806416

00:08:15.741 --> 00:08:17.547 We have things like discrete cues,

NOTE Confidence: 0.87806416

00:08:17.550 --> 00:08:19.489 which would be the sound of a

NOTE Confidence: 0.87806416

00:08:19.489 --> 00:08:21.179 helicopter itself with drug addiction.

NOTE Confidence: 0.87806416

00:08:21.180 --> 00:08:22.818 It's these cues that are associated

NOTE Confidence: 0.87806416

00:08:22.818 --> 00:08:24.500 with the drug taking experience,

NOTE Confidence: 0.87806416

00:08:24.500 --> 00:08:26.607 and so we learn to associate those.

NOTE Confidence: 0.87806416

00:08:26.610 --> 00:08:28.548 And then there's also, you know.

NOTE Confidence: 0.87806416

00:08:28.550 --> 00:08:30.886 What we do in response to these stimuli,

NOTE Confidence: 0.87806416

00:08:30.890 --> 00:08:32.535 and so you know my background is

NOTE Confidence: 0.87806416

00:08:32.535 --> 00:08:33.619 really focused on reinforcement

NOTE Confidence: 0.87806416

00:08:33.619 --> 00:08:35.569 learning and how these stimuli in

NOTE Confidence: 0.87806416

00:08:35.569 --> 00:08:37.226 the environment drive animals to

NOTE Confidence: 0.87806416

00:08:37.226 --> 00:08:38.806 make decisions in different context.

NOTE Confidence: 0.87806416

00:08:38.810 --> 00:08:40.854 So what are they going to do?

NOTE Confidence: 0.87806416

00:08:40.860 --> 00:08:42.606 Are they going to, you know,

NOTE Confidence: 0.87806416

00:08:42.610 --> 00:08:43.441 are they reinforce?

NOTE Confidence: 0.87806416

00:08:43.441 --> 00:08:45.380 Are they going to do something or

NOTE Confidence: 0.87806416

00:08:45.439 --> 00:08:47.009 they going to avoid something?

NOTE Confidence: 0.87806416

00:08:47.010 --> 00:08:49.579 And how we can understand the neural

NOTE Confidence: 0.87806416

00:08:49.579 --> 00:08:51.056 circuitry that underlies this

NOTE Confidence: 0.87806416

00:08:51.056 --> 00:08:53.560 decision to kind of seek out or avoid

NOTE Confidence: 0.87806416

00:08:53.560 --> 00:08:55.498 different things in the environment?

NOTE Confidence: 0.87806416

00:08:55.500 --> 00:08:56.564 And so you know,

NOTE Confidence: 0.87806416

00:08:56.564 --> 00:08:59.270 I think this is a really important thing,

NOTE Confidence: 0.87806416

00:08:59.270 --> 00:08:59.570 right?

NOTE Confidence: 0.87806416

00:08:59.570 --> 00:09:01.970 Is that we learn to make predictions and

NOTE Confidence: 0.87806416

00:09:01.970 --> 00:09:04.605 so our actions have some sort of outcome.

NOTE Confidence: 0.87806416

00:09:04.610 --> 00:09:06.794 It changes the state of our

NOTE Confidence: 0.87806416

00:09:06.794 --> 00:09:08.564 environment and basically what we

NOTE Confidence: 0.87806416

00:09:08.564 --> 00:09:10.572 do is we learn to do something and

NOTE Confidence: 0.87806416

00:09:10.572 --> 00:09:12.765 so this is kind of guiding these.

NOTE Confidence: 0.87806416

00:09:12.770 --> 00:09:14.340 These associations aren't just there,

NOTE Confidence: 0.87806416

00:09:14.340 --> 00:09:16.490 they're guiding how we navigate

NOTE Confidence: 0.87806416

00:09:16.490 --> 00:09:18.358 an environment. And so.

NOTE Confidence: 0.87806416

00:09:18.358 --> 00:09:20.878 How do we do this?

NOTE Confidence: 0.87806416

00:09:20.880 --> 00:09:21.227 Well,

NOTE Confidence: 0.87806416

00:09:21.227 --> 00:09:23.656 we need to encode the value or

NOTE Confidence: 0.87806416

00:09:23.656 --> 00:09:26.153 salience salience is kind of like how

NOTE Confidence: 0.87806416

00:09:26.153 --> 00:09:27.888 attention grabbing something is of

NOTE Confidence: 0.87806416

00:09:27.955 --> 00:09:30.843 unexpected outcomes and so you get ice cream.

NOTE Confidence: 0.87806416

00:09:30.850 --> 00:09:31.688 That's great.

NOTE Confidence: 0.87806416

00:09:31.688 --> 00:09:32.526 It's awesome.

NOTE Confidence: 0.87806416

00:09:32.526 --> 00:09:35.406 We need to know whether it's good

NOTE Confidence: 0.87806416

00:09:35.406 --> 00:09:37.962 or bad and how good or bad it is.

NOTE Confidence: 0.87806416

00:09:37.970 --> 00:09:40.458 How attention, yes, are you advancing slides?

NOTE Confidence: 0.87806416

00:09:40.460 --> 00:09:41.194 Yes, sorry,

NOTE Confidence: 0.87806416

00:09:41.194 --> 00:09:43.763 this has happened to me before and

NOTE Confidence: 0.87806416

00:09:43.763 --> 00:09:46.509 I have no idea why it does this.

NOTE Confidence: 0.87806416

00:09:46.510 --> 00:09:48.950 Let me try this again.

NOTE Confidence: 0.87806416

00:09:48.950 --> 00:09:50.987 It's OK if you guys followed them.

NOTE Confidence: 0.857993

00:09:50.990 --> 00:09:53.609 Yeah, I thought the intro was all very clear,

NOTE Confidence: 0.857993

00:09:53.610 --> 00:09:55.644 but I thought maybe you were dancing.

NOTE Confidence: 0.857993

00:09:55.644 --> 00:09:57.390 We didn't know. Yeah, this is

NOTE Confidence: 0.857993

00:09:57.390 --> 00:10:00.502 this is happened to me before. I have no.

NOTE Confidence: 0.857993

00:10:00.502 --> 00:10:03.680 Idea when or why this does this?

NOTE Confidence: 0.857993

00:10:03.680 --> 00:10:06.074 Let me try this one more time.

NOTE Confidence: 0.857993

00:10:06.080 --> 00:10:08.824 So where I made it 'cause it's on,

NOTE Confidence: 0.857993

00:10:08.830 --> 00:10:10.828 zoom on the shorter side because

NOTE Confidence: 0.857993

00:10:10.828 --> 00:10:12.923 I don't think people love watching

NOTE Confidence: 0.857993

00:10:12.923 --> 00:10:15.074 zoom for two hours. So OK.

NOTE Confidence: 0.857993

00:10:15.074 --> 00:10:19.019 So now if I move the slides they move OK.

NOTE Confidence: 0.857993

00:10:19.020 --> 00:10:20.778 Well, there were pictures you guys

NOTE Confidence: 0.857993

00:10:20.778 --> 00:10:22.700 have experience with all of this stuff,

NOTE Confidence: 0.857993

00:10:22.700 --> 00:10:23.588 so that's fine.

NOTE Confidence: 0.857993

00:10:23.588 --> 00:10:25.364 So now we're into the important

NOTE Confidence: 0.857993

00:10:25.364 --> 00:10:27.512 bit so it's good you saw this. OK,

NOTE Confidence: 0.857993

00:10:27.512 --> 00:10:29.768 so nothing like this is like pandemic level.

NOTE Confidence: 0.857993

00:10:29.770 --> 00:10:30.336 Like everything,

NOTE Confidence: 0.857993

00:10:30.336 --> 00:10:32.317 something has to go wrong every time.

NOTE Confidence: 0.857993

00:10:32.320 --> 00:10:34.018 Otherwise, like you know, it's not.

NOTE Confidence: 0.857993

00:10:34.020 --> 00:10:35.430 It's not real, so OK,

NOTE Confidence: 0.857993

00:10:35.430 --> 00:10:37.418 so you have to encode some information.

NOTE Confidence: 0.857993

00:10:37.420 --> 00:10:39.352 We need to know whether it's good

NOTE Confidence: 0.857993

00:10:39.352 --> 00:10:41.377 or bad and how intense it is.

NOTE Confidence: 0.857993

00:10:41.380 --> 00:10:42.790 Is this something we should

NOTE Confidence: 0.857993

00:10:42.790 --> 00:10:43.918 really pay attention to?

NOTE Confidence: 0.857993

00:10:43.920 --> 00:10:46.184 Or is this something that's not as important?

NOTE Confidence: 0.857993

00:10:46.190 --> 00:10:47.665 We need to make predictions

NOTE Confidence: 0.857993

00:10:47.665 --> 00:10:49.530 about when that's going to occur.

NOTE Confidence: 0.857993

00:10:49.530 --> 00:10:52.330 And so you know you have an ice cream truck.

NOTE Confidence: 0.857993

00:10:52.330 --> 00:10:53.730 You predict whether the ice

NOTE Confidence: 0.857993

00:10:53.730 --> 00:10:55.410 cream will be there or not.

NOTE Confidence: 0.857993

00:10:55.410 --> 00:10:57.930 But not only do we need to make predictions,

NOTE Confidence: 0.857993

00:10:57.930 --> 00:10:59.750 we need to be able to update

NOTE Confidence: 0.857993

00:10:59.750 --> 00:11:01.010 these when they change.

NOTE Confidence: 0.857993

00:11:01.010 --> 00:11:02.970 So when something no longer is associated,

NOTE Confidence: 0.857993

00:11:02.970 --> 00:11:04.930 we need to be able to adapt.

NOTE Confidence: 0.857993

00:11:04.930 --> 00:11:07.027 If the update this so that we can change

NOTE Confidence: 0.857993

00:11:07.027 --> 00:11:08.670 our behavior when the environment is

NOTE Confidence: 0.857993

00:11:08.670 --> 00:11:11.089 not the same as we learned previously,

NOTE Confidence: 0.857993

00:11:11.090 --> 00:11:13.510 and so this is a really, really critical

NOTE Confidence: 0.857993

00:11:13.510 --> 00:11:15.360 aspect of learning and behavior.

NOTE Confidence: 0.857993

00:11:15.360 --> 00:11:17.236 So I'm going to kind of go.

NOTE Confidence: 0.857993

00:11:17.240 --> 00:11:19.376 There's going to be some computation in here,

NOTE Confidence: 0.857993

00:11:19.380 --> 00:11:21.060 but what I'll tell you is most of

NOTE Confidence: 0.857993

00:11:21.060 --> 00:11:23.125 it is is more of a framework for

NOTE Confidence: 0.857993

00:11:23.125 --> 00:11:24.921 how people think about how these

NOTE Confidence: 0.857993

00:11:24.921 --> 00:11:26.616 these computations are being done,

NOTE Confidence: 0.857993

00:11:26.620 --> 00:11:28.756 and if you don't care about the computation,

NOTE Confidence: 0.857993

00:11:28.760 --> 00:11:30.636 which I've met, many people who say,

NOTE Confidence: 0.857993

00:11:30.640 --> 00:11:30.907 oh,

NOTE Confidence: 0.857993

00:11:30.907 --> 00:11:32.242 whatever we've used these to

NOTE Confidence: 0.857993

00:11:32.242 --> 00:11:32.776 design experiments,

NOTE Confidence: 0.857993

00:11:32.780 --> 00:11:34.322 and so it's not like you

NOTE Confidence: 0.857993

00:11:34.322 --> 00:11:35.730 need to know the math.

NOTE Confidence: 0.857993

00:11:35.730 --> 00:11:37.585 It's more of a kind of framework

NOTE Confidence: 0.857993

00:11:37.585 --> 00:11:39.740 for how we designed experiments.

NOTE Confidence: 0.857993

00:11:39.740 --> 00:11:41.540 So this kind of prediction

NOTE Confidence: 0.857993

00:11:41.540 --> 00:11:42.980 based learning was formalized.

NOTE Confidence: 0.857993

00:11:42.980 --> 00:11:43.700 You know,

NOTE Confidence: 0.857993

00:11:43.700 --> 00:11:45.860 originally by Rescorla Wagner in 1972,

NOTE Confidence: 0.857993

00:11:45.860 --> 00:11:48.380 and there's been a bunch of kind

NOTE Confidence: 0.857993

00:11:48.380 --> 00:11:50.588 of adaptations of this and allow

NOTE Confidence: 0.857993

00:11:50.588 --> 00:11:52.700 the model to do other things.

NOTE Confidence: 0.857993

00:11:52.700 --> 00:11:53.406 But really,

NOTE Confidence: 0.857993

00:11:53.406 --> 00:11:55.877 what this is is it's a mathematical

NOTE Confidence: 0.857993

00:11:55.877 --> 00:11:58.100 model that allows us to kind

NOTE Confidence: 0.857993

00:11:58.100 --> 00:11:59.900 of formalize how animals learn,

NOTE Confidence: 0.857993

00:11:59.900 --> 00:12:01.965 and So what happens in this model

NOTE Confidence: 0.857993

00:12:01.965 --> 00:12:04.252 is that if you have something

NOTE Confidence: 0.857993

00:12:04.252 --> 00:12:06.020 like an unexpected outcome,

NOTE Confidence: 0.857993

00:12:06.020 --> 00:12:08.180 that is an error in prediction,

NOTE Confidence: 0.857993

00:12:08.180 --> 00:12:10.436 you predicted nothing, something was there.

NOTE Confidence: 0.857993

00:12:10.440 --> 00:12:12.827 You made an error and what happens

NOTE Confidence: 0.857993

00:12:12.827 --> 00:12:14.770 overtime is your prediction gets

NOTE Confidence: 0.857993

00:12:14.770 --> 00:12:17.326 better and then there's less error.

NOTE Confidence: 0.857993

00:12:17.330 --> 00:12:19.742 So essentially what happens is the

NOTE Confidence: 0.857993

00:12:19.742 --> 00:12:21.796 associative strength or how well

NOTE Confidence: 0.857993

00:12:21.796 --> 00:12:23.676 you how well something predicts

NOTE Confidence: 0.857993

00:12:23.676 --> 00:12:26.321 something goes up and the error in

NOTE Confidence: 0.857993

00:12:26.321 --> 00:12:28.463 that prediction goes down and so

NOTE Confidence: 0.857993

00:12:28.463 --> 00:12:30.818 basically the way the model works is

NOTE Confidence: 0.857993

00:12:30.818 --> 00:12:33.519 that as you learn the prediction of

NOTE Confidence: 0.857993

00:12:33.519 --> 00:12:36.093 that Q and the outcome increases.

NOTE Confidence: 0.857993

00:12:36.100 --> 00:12:38.865 But any errors you make go down

NOTE Confidence: 0.857993

00:12:38.865 --> 00:12:40.050 and so essentially

NOTE Confidence: 0.87582153

00:12:40.132 --> 00:12:42.138 you get this. Increase in the

NOTE Confidence: 0.87582153

00:12:42.138 --> 00:12:44.094 predictive response and a decrease in

NOTE Confidence: 0.87582153

00:12:44.094 --> 00:12:46.309 the error or the mistakes from that,

NOTE Confidence: 0.87582153

00:12:46.310 --> 00:12:49.208 and so this is kind of how animals learn.

NOTE Confidence: 0.87582153

00:12:49.210 --> 00:12:50.956 It can map learning rates in

NOTE Confidence: 0.87582153

00:12:50.956 --> 00:12:52.750 a lot of different contexts.

NOTE Confidence: 0.87582153

00:12:52.750 --> 00:12:54.038 You know learning about

NOTE Confidence: 0.87582153

00:12:54.038 --> 00:12:55.004 Accuen award extinction.

NOTE Confidence: 0.87582153

00:12:55.010 --> 00:12:58.090 All of these and so people have really

NOTE Confidence: 0.87582153

00:12:58.090 --> 00:13:00.529 been searching for what is a circuit

NOTE Confidence: 0.87582153

00:13:00.529 --> 00:13:02.929 in the brain that does this math.

NOTE Confidence: 0.87582153

00:13:02.930 --> 00:13:05.538 And that's been a kind of really big

NOTE Confidence: 0.87582153

00:13:05.538 --> 00:13:08.578 focus of specifically the dopamine field.

NOTE Confidence: 0.87582153

00:13:08.580 --> 00:13:09.536 And other fields too.

NOTE Confidence: 0.87582153

00:13:09.536 --> 00:13:11.328 I think a lot of people are

NOTE Confidence: 0.87582153

00:13:11.328 --> 00:13:13.414 starting to see that these kinds of

NOTE Confidence: 0.87582153

00:13:13.414 --> 00:13:15.178 computations are done in a variety

NOTE Confidence: 0.87582153

00:13:15.178 --> 00:13:16.568 of circuits across the brain.

NOTE Confidence: 0.87582153

00:13:16.570 --> 00:13:18.826 So the dopamine system is important

NOTE Confidence: 0.87582153

00:13:18.826 --> 00:13:21.260 for any a lot of reasons.

NOTE Confidence: 0.87582153

00:13:21.260 --> 00:13:24.108 These neurons you know that we focus on

NOTE Confidence: 0.87582153

00:13:24.108 --> 00:13:26.738 originate in the ventral tegmental area,

NOTE Confidence: 0.87582153

00:13:26.740 --> 00:13:29.068 so we're focusing on more reward

NOTE Confidence: 0.87582153

00:13:29.068 --> 00:13:31.068 associated circuits rather than things

NOTE Confidence: 0.87582153

00:13:31.068 --> 00:13:32.988 that are associated with motor.

NOTE Confidence: 0.87582153

00:13:32.990 --> 00:13:35.336 So we're looking in for this

NOTE Confidence: 0.87582153

00:13:35.336 --> 00:13:36.118 particular project.

NOTE Confidence: 0.87582153

00:13:36.120 --> 00:13:37.293 The nucleus accumbens,

NOTE Confidence: 0.87582153

00:13:37.293 --> 00:13:38.466 the core region,

NOTE Confidence: 0.87582153

00:13:38.470 --> 00:13:40.672 and So what these dopamine neurons

NOTE Confidence: 0.87582153

00:13:40.672 --> 00:13:42.770 are really important for survival.

NOTE Confidence: 0.87582153

00:13:42.770 --> 00:13:44.334 Lesioning them present prevents

NOTE Confidence: 0.87582153

00:13:44.334 --> 00:13:46.289 this kind of associative learning.

NOTE Confidence: 0.87582153

00:13:46.290 --> 00:13:48.990 An also reinforcement learning.

NOTE Confidence: 0.87582153

00:13:48.990 --> 00:13:51.566 And the thing people been kind of really

NOTE Confidence: 0.87582153

00:13:51.566 --> 00:13:54.019 focus on is that this domain neurons

NOTE Confidence: 0.87582153

00:13:54.019 --> 00:13:56.619 respond in a fashion that mimics this.

NOTE Confidence: 0.87582153

00:13:56.620 --> 00:13:59.049 This mathematical model I just showed you,

NOTE Confidence: 0.87582153

00:13:59.050 --> 00:14:01.048 and so essentially this kind of

NOTE Confidence: 0.87582153

00:14:01.048 --> 00:14:03.516 originated and within a lots of other

NOTE Confidence: 0.87582153

00:14:03.516 --> 00:14:05.296 people have shown these patterns.

NOTE Confidence: 0.87582153

00:14:05.300 --> 00:14:07.388 So this originative with Wolfram Schultz

NOTE Confidence: 0.87582153

00:14:07.388 --> 00:14:09.808 and I'm just showing the the original.

NOTE Confidence: 0.87582153

00:14:09.810 --> 00:14:11.520 But people within the domain

NOTE Confidence: 0.87582153

00:14:11.520 --> 00:14:13.643 field have done this with all

NOTE Confidence: 0.87582153

00:14:13.643 --> 00:14:15.707 kinds of other approaches as well.

NOTE Confidence: 0.87582153

00:14:15.710 --> 00:14:17.710 But essentially what they see

NOTE Confidence: 0.87582153

00:14:17.710 --> 00:14:20.200 is this kind of same math.

NOTE Confidence: 0.87582153

00:14:20.200 --> 00:14:22.578 We went hoping that this didn't

NOTE Confidence: 0.87582153

00:14:22.580 --> 00:14:24.160 just move because OK,

NOTE Confidence: 0.87582153

00:14:24.160 --> 00:14:26.511 the slides are still advancing, right?

NOTE Confidence: 0.87582153

00:14:26.511 --> 00:14:27.624 Yeah, OK, OK.

NOTE Confidence: 0.87582153

00:14:27.624 --> 00:14:29.479 So essentially what happens is

NOTE Confidence: 0.87582153

00:14:29.479 --> 00:14:31.679 you have an unexpected reward.

NOTE Confidence: 0.87582153

00:14:31.680 --> 00:14:33.596 Dopamine firing goes up.

NOTE Confidence: 0.87582153

00:14:33.596 --> 00:14:36.470 You predict that reward dopamine firing

NOTE Confidence: 0.87582153

00:14:36.546 --> 00:14:39.687 now goes up to the queue that predicts it,

NOTE Confidence: 0.87582153

00:14:39.690 --> 00:14:41.066 but not the reward,

NOTE Confidence: 0.87582153

00:14:41.066 --> 00:14:42.786 because the prediction of that

NOTE Confidence: 0.87582153

00:14:42.786 --> 00:14:44.468 reward is basically perfect.

NOTE Confidence: 0.87582153

00:14:44.470 --> 00:14:47.046 And now if the reward is omitted,

NOTE Confidence: 0.87582153

00:14:47.050 --> 00:14:48.935 what happens is the dopamine

NOTE Confidence: 0.87582153

00:14:48.935 --> 00:14:51.100 response to the queue goes up,

NOTE Confidence: 0.87582153

00:14:51.100 --> 00:14:53.884 but there is now a decrease in that

NOTE Confidence: 0.87582153

00:14:53.884 --> 00:14:55.878 domain response when it's omitted,

NOTE Confidence: 0.87582153

00:14:55.880 --> 00:14:57.720 signaling the negative error that,

NOTE Confidence: 0.87582153

00:14:57.720 --> 00:14:59.400 uh, from that prediction.

NOTE Confidence: 0.87582153

00:14:59.400 --> 00:15:01.500 And so this is they.

NOTE Confidence: 0.87582153

00:15:01.500 --> 00:15:02.836 You know, originally this,

NOTE Confidence: 0.87582153

00:15:02.836 --> 00:15:03.838 this first paper.

NOTE Confidence: 0.87582153

00:15:03.840 --> 00:15:04.845 They said, wow,

NOTE Confidence: 0.87582153

00:15:04.845 --> 00:15:07.190 that looks a lot like reward prediction,

NOTE Confidence: 0.87582153

00:15:07.190 --> 00:15:07.820 error learning,

NOTE Confidence: 0.87582153

00:15:07.820 --> 00:15:10.340 and so this is kind of formed the

NOTE Confidence: 0.87582153

00:15:10.408 --> 00:15:12.994 basis of the domain field dopamine

NOTE Confidence: 0.87582153

00:15:12.994 --> 00:15:14.718 does reward prediction learning.

NOTE Confidence: 0.87582153

00:15:14.720 --> 00:15:18.770 So here's the kind of maybe issue with that.

NOTE Confidence: 0.87582153

00:15:18.770 --> 00:15:21.020 If you do stress work,

NOTE Confidence: 0.87582153

00:15:21.020 --> 00:15:23.492 anything else you know the domain

NOTE Confidence: 0.87582153

00:15:23.492 --> 00:15:26.240 does not only respond to rewards

NOTE Confidence: 0.87582153

00:15:26.240 --> 00:15:27.770 and reward predictions,

NOTE Confidence: 0.87582153

00:15:27.770 --> 00:15:30.470 it's involved in things like punishment,

NOTE Confidence: 0.87582153

00:15:30.470 --> 00:15:33.170 which is an aversive learning parameter.

NOTE Confidence: 0.87582153

00:15:33.170 --> 00:15:35.454 Motivation, fear, safety transitions,

NOTE Confidence: 0.87582153

00:15:35.454 --> 00:15:36.596 aversive learning.

NOTE Confidence: 0.87582153

00:15:36.600 --> 00:15:38.250 All kinds of there's been a

NOTE Confidence: 0.87582153

00:15:38.250 --> 00:15:39.075 lot of Association,

NOTE Confidence: 0.87582153

00:15:39.080 --> 00:15:40.184 aversive learning and these

NOTE Confidence: 0.87582153

00:15:40.184 --> 00:15:41.564 fields have been kind of.

NOTE Confidence: 0.87582153

00:15:41.570 --> 00:15:42.674 It was a separate,

NOTE Confidence: 0.87582153

00:15:42.674 --> 00:15:44.330 but there's kind of the reward.

NOTE Confidence: 0.87582153

00:15:44.330 --> 00:15:45.705 Prediction people and then the

NOTE Confidence: 0.87582153

00:15:45.705 --> 00:15:46.805 people who studied anxiety,

NOTE Confidence: 0.83455783

00:15:46.810 --> 00:15:47.910 depression looking at Microdialysis,

NOTE Confidence: 0.83455783

00:15:47.910 --> 00:15:49.010 showing that dopamine does

NOTE Confidence: 0.83455783

00:15:49.010 --> 00:15:50.400 go up to aversive stimuli,

NOTE Confidence: 0.83455783

00:15:50.400 --> 00:15:52.488 and so these kind of have been a

NOTE Confidence: 0.83455783

00:15:52.488 --> 00:15:54.539 little bit at odds with each other.

NOTE Confidence: 0.83455783

00:15:54.540 --> 00:15:55.920 But they kind of are,

NOTE Confidence: 0.83455783

00:15:55.920 --> 00:15:57.304 you know, different fields,

NOTE Confidence: 0.83455783

00:15:57.304 --> 00:15:59.034 so people haven't really looked

NOTE Confidence: 0.83455783

00:15:59.034 --> 00:16:00.837 at them in the same context.

NOTE Confidence: 0.83455783

00:16:00.840 --> 00:16:01.728 And so essentially,

NOTE Confidence: 0.83455783

00:16:01.728 --> 00:16:03.800 I think some of the disconnect also

NOTE Confidence: 0.83455783

00:16:03.857 --> 00:16:05.759 comes from this kind of fundamental

NOTE Confidence: 0.83455783

00:16:05.759 --> 00:16:07.520 process of about domain neurons.

NOTE Confidence: 0.83455783

00:16:07.520 --> 00:16:09.200 That's actually my favorite

NOTE Confidence: 0.83455783

00:16:09.200 --> 00:16:10.880 part of GOP neurons.

NOTE Confidence: 0.83455783

00:16:10.880 --> 00:16:12.352 Many studies have looked

NOTE Confidence: 0.83455783

00:16:12.352 --> 00:16:14.192 at VTA cell body firing.

NOTE Confidence: 0.83455783

00:16:14.200 --> 00:16:15.337 They use electrophysiology.

NOTE Confidence: 0.83455783

00:16:15.337 --> 00:16:18.260 They say we don't need it goes up.

NOTE Confidence: 0.83455783

00:16:18.260 --> 00:16:19.265 It goes down.

NOTE Confidence: 0.83455783

00:16:19.265 --> 00:16:20.940 And there's this inference that

NOTE Confidence: 0.83455783

00:16:20.940 --> 00:16:22.690 that means dopamine release.

NOTE Confidence: 0.83455783

00:16:22.690 --> 00:16:23.424 That is,

NOTE Confidence: 0.83455783

00:16:23.424 --> 00:16:25.993 projection targets is going to be the

NOTE Confidence: 0.83455783

00:16:25.993 --> 00:16:28.585 same as what the firing looks like.

NOTE Confidence: 0.83455783

00:16:28.590 --> 00:16:30.912 But dopamine terminals are so cool

NOTE Confidence: 0.83455783

00:16:30.912 --> 00:16:32.850 because they're regulated at the

NOTE Confidence: 0.83455783

00:16:32.850 --> 00:16:34.490 terminal level by **** synaptic.

NOTE Confidence: 0.83455783

00:16:34.490 --> 00:16:37.010 So things that are regulated by Domi

NOTE Confidence: 0.83455783

00:16:37.010 --> 00:16:38.928 itself but also header, synaptic,

NOTE Confidence: 0.83455783

00:16:38.928 --> 00:16:40.400 regulators things like glutamate,

NOTE Confidence: 0.83455783

00:16:40.400 --> 00:16:40.766 GABA.

NOTE Confidence: 0.83455783

00:16:40.766 --> 00:16:42.596 A favorite of this Department,

NOTE Confidence: 0.83455783

00:16:42.600 --> 00:16:43.960 acetylcholine and so these.

NOTE Confidence: 0.83455783

00:16:43.960 --> 00:16:45.660 These things actually can elicit

NOTE Confidence: 0.83455783

00:16:45.660 --> 00:16:47.389 dopamine release from the terminals,

NOTE Confidence: 0.83455783

00:16:47.390 --> 00:16:48.506 independent of cymatic firing.

NOTE Confidence: 0.83455783

00:16:48.506 --> 00:16:50.642 And so if you want to understand

NOTE Confidence: 0.83455783

00:16:50.642 --> 00:16:52.262 what dopamine release another

NOTE Confidence: 0.83455783

00:16:52.262 --> 00:16:53.882 projection target is doing,

NOTE Confidence: 0.83455783

00:16:53.890 --> 00:16:55.600 you need to actually record

NOTE Confidence: 0.83455783

00:16:55.600 --> 00:16:57.310 dopamine and the ultimate wrists.

NOTE Confidence: 0.83455783

00:16:57.310 --> 00:17:00.038 You have a few of those as well,

NOTE Confidence: 0.83455783

00:17:00.040 --> 00:17:03.118 have been doing this for a really long time,

NOTE Confidence: 0.83455783

00:17:03.120 --> 00:17:05.752 but there's a lot of kind of

NOTE Confidence: 0.83455783

00:17:05.752 --> 00:17:07.552 limitations to voltammetry and we'll

NOTE Confidence: 0.83455783

00:17:07.552 --> 00:17:09.960 kind of talk about those as we go,

NOTE Confidence: 0.83455783

00:17:09.960 --> 00:17:12.498 but our goal was really too.

NOTE Confidence: 0.83455783

00:17:12.500 --> 00:17:13.152 Record dopamine,

NOTE Confidence: 0.83455783

00:17:13.152 --> 00:17:14.782 but be able to dissociate

NOTE Confidence: 0.83455783

00:17:14.782 --> 00:17:16.230 these kind of things.

NOTE Confidence: 0.83455783

00:17:16.230 --> 00:17:18.234 People have seen in the aversive

NOTE Confidence: 0.83455783

00:17:18.234 --> 00:17:19.972 field with the things people

NOTE Confidence: 0.83455783

00:17:19.972 --> 00:17:21.988 have seen in the reward fields.

NOTE Confidence: 0.83455783

00:17:21.990 --> 00:17:24.433 Why is dopamine look like it's doing

NOTE Confidence: 0.83455783

00:17:24.433 --> 00:17:26.737 both of these at the same time?

NOTE Confidence: 0.83455783

00:17:26.740 --> 00:17:28.505 So my background isn't reinforcement

NOTE Confidence: 0.83455783

00:17:28.505 --> 00:17:31.207 learning and what we did is we we

NOTE Confidence: 0.83455783

00:17:31.207 --> 00:17:32.947 like to develop behavioral tasks to

NOTE Confidence: 0.83455783

00:17:32.947 --> 00:17:35.206 parse the things that we're interested.

NOTE Confidence: 0.83455783

00:17:35.210 --> 00:17:36.910 So we developed this task,

NOTE Confidence: 0.83455783

00:17:36.910 --> 00:17:38.434 which is not really the task

NOTE Confidence: 0.83455783

00:17:38.434 --> 00:17:39.997 itself is an innovative behavioral

NOTE Confidence: 0.83455783

00:17:39.997 --> 00:17:41.989 pharmacology and reinforcement learning.

NOTE Confidence: 0.83455783

00:17:41.990 --> 00:17:44.769 People have been doing this for years.

NOTE Confidence: 0.83455783

00:17:44.770 --> 00:17:46.234 Essentially what we do is we

NOTE Confidence: 0.83455783

00:17:46.234 --> 00:17:47.739 have a queue that comes on.

NOTE Confidence: 0.83455783

00:17:47.740 --> 00:17:48.649 In one phase,

NOTE Confidence: 0.83455783

00:17:48.649 --> 00:17:50.467 that tells animals if they know

NOTE Confidence: 0.83455783

00:17:50.467 --> 00:17:52.284 spoke during this Q and in

NOTE Confidence: 0.83455783

00:17:52.284 --> 00:17:53.739 this example is white noise.

NOTE Confidence: 0.83455783

00:17:53.740 --> 00:17:55.240 But we counterbalance and change

NOTE Confidence: 0.83455783

00:17:55.240 --> 00:17:56.740 that they will get sucrose.

NOTE Confidence: 0.83455783

00:17:56.740 --> 00:17:58.540 This is like normal positive reinforcement.

NOTE Confidence: 0.83455783

00:17:58.540 --> 00:18:00.640 You know you treat your teacher dog,

NOTE Confidence: 0.83455783

00:18:00.640 --> 00:18:03.310 that's it. They get a reward.

NOTE Confidence: 0.83455783

00:18:03.310 --> 00:18:04.936 What we taught the animals in

NOTE Confidence: 0.83455783

00:18:04.936 --> 00:18:06.911 the other face is that a separate

NOTE Confidence: 0.83455783

00:18:06.911 --> 00:18:08.573 queue comes on and they have

NOTE Confidence: 0.83455783

00:18:08.573 --> 00:18:10.350 the same behavioral response.

NOTE Confidence: 0.83455783

00:18:10.350 --> 00:18:11.166 They know spoke,

NOTE Confidence: 0.83455783

00:18:11.166 --> 00:18:13.070 but they know spoke to prevent a

NOTE Confidence: 0.83455783

00:18:13.128 --> 00:18:15.240 series of shocks from being delivered,

NOTE Confidence: 0.83455783

00:18:15.240 --> 00:18:17.920 so it's called negative reinforcement.

NOTE Confidence: 0.83455783

00:18:17.920 --> 00:18:20.240 The reason that using these is so cool

NOTE Confidence: 0.83455783

00:18:20.240 --> 00:18:22.779 is because they have the exact same action.

NOTE Confidence: 0.83455783

00:18:22.780 --> 00:18:24.305 So if dopamine just encodes

NOTE Confidence: 0.83455783

00:18:24.305 --> 00:18:25.220 the motivated response,

NOTE Confidence: 0.83455783

00:18:25.220 --> 00:18:27.600 these will look the same.

NOTE Confidence: 0.83455783

00:18:27.600 --> 00:18:29.538 They have the same outcome value.

NOTE Confidence: 0.83455783

00:18:29.540 --> 00:18:30.836 The outcome is positive.

NOTE Confidence: 0.83455783

00:18:30.836 --> 00:18:32.456 Avoiding something negative is positive.

NOTE Confidence: 0.83455783

00:18:32.460 --> 00:18:34.080 Getting something positive is positive,

NOTE Confidence: 0.83455783

00:18:34.080 --> 00:18:35.860 but there's different stimuli maintaining

NOTE Confidence: 0.83455783

00:18:35.860 --> 00:18:37.640 these behavioral events and so

NOTE Confidence: 0.865027

00:18:37.692 --> 00:18:39.558 essentially what we've associated here is

NOTE Confidence: 0.865027

00:18:39.558 --> 00:18:41.731 the kind of motivated action from this

NOTE Confidence: 0.865027

00:18:41.731 --> 00:18:43.477 stimulus value in the outcome value,

NOTE Confidence: 0.865027

00:18:43.480 --> 00:18:45.888 and the question is in this sounds

NOTE Confidence: 0.865027

00:18:45.888 --> 00:18:47.360 more complicated than it is,

NOTE Confidence: 0.865027

00:18:47.360 --> 00:18:49.560 and I'm going to tell you the story

NOTE Confidence: 0.865027

00:18:49.560 --> 00:18:52.407 is that we're going to be able to see

NOTE Confidence: 0.865027

00:18:52.407 --> 00:18:54.542 if dopamine responds to just rewards

NOTE Confidence: 0.865027

00:18:54.542 --> 00:18:56.756 if it's just involved in motivation,

NOTE Confidence: 0.865027

00:18:56.760 --> 00:18:59.756 or if it's doing something maybe slightly.

NOTE Confidence: 0.865027

00:18:59.760 --> 00:19:01.464 It's a more complicated,

NOTE Confidence: 0.865027

00:19:01.464 --> 00:19:03.168 but it's actually simpler.

NOTE Confidence: 0.865027

00:19:03.170 --> 00:19:05.508 We need a way to record dopamine

NOTE Confidence: 0.865027

00:19:05.508 --> 00:19:06.510 during this task.

NOTE Confidence: 0.865027

00:19:06.510 --> 00:19:08.676 Aversive foot shocks are electrical signals.

NOTE Confidence: 0.865027

00:19:08.680 --> 00:19:10.762 All of the previous domain recording

NOTE Confidence: 0.865027

00:19:10.762 --> 00:19:12.588 techniques on fast time scales

NOTE Confidence: 0.865027

00:19:12.588 --> 00:19:14.468 were used on electrical systems,

NOTE Confidence: 0.865027

00:19:14.470 --> 00:19:16.934 and so the problem with this is all

NOTE Confidence: 0.865027

00:19:16.934 --> 00:19:18.407 the voltammetry techniques people

NOTE Confidence: 0.865027

00:19:18.407 --> 00:19:20.397 use before you couldn't record

NOTE Confidence: 0.865027

00:19:20.397 --> 00:19:22.080 responses to foot shocks,

NOTE Confidence: 0.865027

00:19:22.080 --> 00:19:24.502 and So what we've been using is

NOTE Confidence: 0.865027

00:19:24.502 --> 00:19:26.060 a fluorescent dopamine sensor.

NOTE Confidence: 0.865027

00:19:26.060 --> 00:19:27.870 This one is called delight.

NOTE Confidence: 0.865027

00:19:27.870 --> 00:19:30.362 It was developed at UC Davis by

NOTE Confidence: 0.865027

00:19:30.362 --> 00:19:32.983 Lindsay Angela and what this is is

NOTE Confidence: 0.865027

00:19:32.983 --> 00:19:35.203 it's a modified D1 dopamine receptor

NOTE Confidence: 0.865027

00:19:35.278 --> 00:19:37.700 that when it binds to dopamine it.

NOTE Confidence: 0.865027

00:19:37.700 --> 00:19:38.378 Laura says.

NOTE Confidence: 0.865027

00:19:38.378 --> 00:19:40.412 And so this fluorescent sensor is

NOTE Confidence: 0.865027

00:19:40.412 --> 00:19:42.205 really great because we can inject

NOTE Confidence: 0.865027

00:19:42.205 --> 00:19:44.429 it in with a virus into the brain.

NOTE Confidence: 0.865027

00:19:44.430 --> 00:19:45.960 We build fiber, photometry, systems.

NOTE Confidence: 0.865027

00:19:45.960 --> 00:19:48.714 I know a lot of people are using these,

NOTE Confidence: 0.865027

00:19:48.720 --> 00:19:50.890 but what it allows us to do is in awake

NOTE Confidence: 0.865027

00:19:50.953 --> 00:19:52.878 and behaving animals during these

NOTE Confidence: 0.865027

00:19:52.878 --> 00:19:55.140 discrete aspects of this behavioral task,

NOTE Confidence: 0.865027

00:19:55.140 --> 00:19:56.868 is record fluctuations in joking that

NOTE Confidence: 0.865027

00:19:56.868 --> 00:19:58.769 happened through this kind of fluorescent

NOTE Confidence: 0.865027

00:19:58.769 --> 00:20:00.177 response that isn't interfering?

NOTE Confidence: 0.865027

00:20:00.180 --> 00:20:01.715 Electrical signals and also the

NOTE Confidence: 0.865027

00:20:01.715 --> 00:20:03.250 great thing about these optical

NOTE Confidence: 0.865027

00:20:03.300 --> 00:20:04.848 sensors is they have really great

NOTE Confidence: 0.865027

00:20:04.848 --> 00:20:06.904 signal to noise and so you can get

NOTE Confidence: 0.865027

00:20:06.904 --> 00:20:08.119 single trial responses which with

NOTE Confidence: 0.865027

00:20:08.119 --> 00:20:10.008 a lot of voltammetry in the past,

NOTE Confidence: 0.865027

00:20:10.010 --> 00:20:11.914 which is my backgrounds you didn't get,

NOTE Confidence: 0.865027

00:20:11.920 --> 00:20:13.600 you had to average responses and

NOTE Confidence: 0.865027

00:20:13.600 --> 00:20:15.848 what I'll show you is a lot of what

NOTE Confidence: 0.865027

00:20:15.848 --> 00:20:17.603 we see is these really rapid changes

NOTE Confidence: 0.865027

00:20:17.603 --> 00:20:19.481 in dopamine that are happening on

NOTE Confidence: 0.865027

00:20:19.481 --> 00:20:21.290 the trial by trial basis that we

NOTE Confidence: 0.865027

00:20:21.290 --> 00:20:22.470 think are really critical for

NOTE Confidence: 0.865027

00:20:22.522 --> 00:20:23.659 this behavioral response.

NOTE Confidence: 0.85444176

00:20:25.850 --> 00:20:27.225 So we started with kind

NOTE Confidence: 0.85444176

00:20:27.225 --> 00:20:28.600 of what everyone is done.

NOTE Confidence: 0.85444176

00:20:28.600 --> 00:20:30.497 Before this you know it's always good

NOTE Confidence: 0.85444176

00:20:30.497 --> 00:20:32.534 when you start with like new tools to

NOTE Confidence: 0.85444176

00:20:32.534 --> 00:20:34.649 make sure you see what everybody else's.

NOTE Confidence: 0.85444176

00:20:34.650 --> 00:20:36.882 And So what we did is we recorded domain

NOTE Confidence: 0.85444176

00:20:36.882 --> 00:20:38.778 responses during the pre training session.

NOTE Confidence: 0.85444176

00:20:38.780 --> 00:20:40.614 The first time the animals had been

NOTE Confidence: 0.85444176

00:20:40.614 --> 00:20:42.322 in these operating chambers and post

NOTE Confidence: 0.85444176

00:20:42.322 --> 00:20:44.068 training after the animals had learned

NOTE Confidence: 0.85444176

00:20:44.068 --> 00:20:45.981 and so not surprising animals learn to

NOTE Confidence: 0.85444176

00:20:45.981 --> 00:20:48.094 know spoke during a queue for sucrose we

NOTE Confidence: 0.85444176

00:20:48.094 --> 00:20:50.303 can change the length of the queue to

NOTE Confidence: 0.85444176

00:20:50.303 --> 00:20:52.242 make the task more or less difficult.

NOTE Confidence: 0.85444176

00:20:52.250 --> 00:20:54.572 We kind of did this so we had some

NOTE Confidence: 0.85444176

00:20:54.572 --> 00:20:56.749 dynamic range of whether they did the.

NOTE Confidence: 0.85444176

00:20:56.750 --> 00:20:57.642 Miss trials or not,

NOTE Confidence: 0.85444176

00:20:57.642 --> 00:20:59.470 and so we did some machine learning.

NOTE Confidence: 0.85444176

00:20:59.470 --> 00:21:00.700 I won't show you then.

NOTE Confidence: 0.85444176

00:21:00.700 --> 00:21:01.935 This was actually a really

NOTE Confidence: 0.85444176

00:21:01.935 --> 00:21:02.923 great tool for that,

NOTE Confidence: 0.85444176

00:21:02.930 --> 00:21:05.270 but what we do is we see kind of the

NOTE Confidence: 0.85444176

00:21:05.335 --> 00:21:07.477 same thing everyone else is seen.

NOTE Confidence: 0.85444176

00:21:07.480 --> 00:21:08.120 Early on,

NOTE Confidence: 0.85444176

00:21:08.120 --> 00:21:10.680 when the animals go into the sucrose port,

NOTE Confidence: 0.85444176

00:21:10.680 --> 00:21:12.787 so red in here this is more

NOTE Confidence: 0.85444176

00:21:12.787 --> 00:21:14.200 domain response over trials.

NOTE Confidence: 0.85444176

00:21:14.200 --> 00:21:16.440 When they go into the Super sport,

NOTE Confidence: 0.85444176

00:21:16.440 --> 00:21:18.475 you get this robust domain

NOTE Confidence: 0.85444176

00:21:18.475 --> 00:21:20.103 response to the sucrose.

NOTE Confidence: 0.85444176

00:21:20.110 --> 00:21:21.034 Overtraining this signal

NOTE Confidence: 0.85444176

00:21:21.034 --> 00:21:22.574 moves back to the cube.

NOTE Confidence: 0.85444176

00:21:22.580 --> 00:21:23.492 That's very predictive.

NOTE Confidence: 0.85444176

00:21:23.492 --> 00:21:25.620 So now you get this really robust

NOTE Confidence: 0.85444176

00:21:25.673 --> 00:21:27.218 domain response to the queue,

NOTE Confidence: 0.85444176

00:21:27.220 --> 00:21:29.782 but not as much of a domain

NOTE Confidence: 0.85444176

00:21:29.782 --> 00:21:31.650 response to the sucrose.

NOTE Confidence: 0.85444176

00:21:31.650 --> 00:21:33.918 Great, it looks just like that equation.

NOTE Confidence: 0.85444176

00:21:33.920 --> 00:21:34.886 I showed you.

NOTE Confidence: 0.85444176

00:21:34.886 --> 00:21:37.388 Dopamine goes up to the Q goes

NOTE Confidence: 0.85444176

00:21:37.388 --> 00:21:39.590 down to the error signal.

NOTE Confidence: 0.85444176

00:21:39.590 --> 00:21:42.558 All is well in the reward domain

NOTE Confidence: 0.85444176

00:21:42.558 --> 00:21:45.189 does reward based learning field.

NOTE Confidence: 0.85444176

00:21:45.190 --> 00:21:47.262 But then we moved on to this

NOTE Confidence: 0.85444176

00:21:47.262 --> 00:21:48.150 other behavioral task.

NOTE Confidence: 0.85444176

00:21:48.150 --> 00:21:48.778 So again,

NOTE Confidence: 0.85444176

00:21:48.778 --> 00:21:50.348 the animals can know spoke

NOTE Confidence: 0.85444176

00:21:50.348 --> 00:21:52.609 during this Q and they do it to

NOTE Confidence: 0.85444176

00:21:52.609 --> 00:21:54.370 avoid a series of foot shocks.

NOTE Confidence: 0.85444176

00:21:54.370 --> 00:21:55.984 So if they don't press during

NOTE Confidence: 0.85444176

00:21:55.984 --> 00:21:57.620 the Q they get shocked.

NOTE Confidence: 0.85444176

00:21:57.620 --> 00:21:59.330 There's a series of shocks they

NOTE Confidence: 0.85444176

00:21:59.330 --> 00:22:00.830 can press anytime during this

NOTE Confidence: 0.85444176

00:22:00.830 --> 00:22:02.355 series to terminate the shocks,

NOTE Confidence: 0.85444176

00:22:02.360 --> 00:22:04.362 and so we did the same thing

NOTE Confidence: 0.85444176

00:22:04.362 --> 00:22:05.909 we recorded early in Leanne.

NOTE Confidence: 0.85444176

00:22:05.910 --> 00:22:07.058 Learning animals actually learn.

NOTE Confidence: 0.85444176

00:22:07.058 --> 00:22:09.760 When I started my lab a bunch of behavior.

NOTE Confidence: 0.85444176

00:22:09.760 --> 00:22:11.235 People told me that animals

NOTE Confidence: 0.85444176

00:22:11.235 --> 00:22:12.415 will never do this.

NOTE Confidence: 0.85444176

00:22:12.420 --> 00:22:13.900 Mice do this really great.

NOTE Confidence: 0.85444176

00:22:13.900 --> 00:22:15.084 They'll learn really rapidly

NOTE Confidence: 0.85444176

00:22:15.084 --> 00:22:16.564 to press on the nose,

NOTE Confidence: 0.85444176

00:22:16.570 --> 00:22:18.130 poke that active know spoke

NOTE Confidence: 0.85444176

00:22:18.130 --> 00:22:19.378 to avoid the shocks.

NOTE Confidence: 0.85444176

00:22:19.380 --> 00:22:20.904 And they actually at the end

NOTE Confidence: 0.85444176

00:22:20.904 --> 00:22:22.559 of these trials are doing this,

NOTE Confidence: 0.85444176

00:22:22.560 --> 00:22:24.680 that they are not getting shots at all,

NOTE Confidence: 0.85444176

00:22:24.680 --> 00:22:26.535 and so they learn this very fast.

NOTE Confidence: 0.85444176

00:22:26.540 --> 00:22:28.868 And it's actually really robust task

NOTE Confidence: 0.85444176

00:22:28.868 --> 00:22:30.420 for generating motivated behavior.

NOTE Confidence: 0.85444176

00:22:30.420 --> 00:22:30.762 Um?

NOTE Confidence: 0.85444176

00:22:30.762 --> 00:22:31.104 OK,

NOTE Confidence: 0.85444176

00:22:31.104 --> 00:22:33.840 so the first thing we saw which goes

NOTE Confidence: 0.85444176

00:22:33.927 --> 00:22:36.357 in the face of dopamine encoding

NOTE Confidence: 0.85444176

00:22:36.357 --> 00:22:39.390 rewards is that you get this really

NOTE Confidence: 0.85444176

00:22:39.390 --> 00:22:42.498 robust positive response to a foot shock.

NOTE Confidence: 0.85444176

00:22:42.500 --> 00:22:45.270 So dopamine goes up when

NOTE Confidence: 0.85444176

00:22:45.270 --> 00:22:47.486 aversive stimuli are encountered.

NOTE Confidence: 0.85444176

00:22:47.490 --> 00:22:47.786 Um,

NOTE Confidence: 0.85444176

00:22:47.786 --> 00:22:49.266 other people have seen this,

NOTE Confidence: 0.85444176

00:22:49.270 --> 00:22:51.004 but what's really interesting is I'll

NOTE Confidence: 0.85444176

00:22:51.004 --> 00:22:53.408 remind you of what that model looked like.

NOTE Confidence: 0.85444176

00:22:53.410 --> 00:22:56.189 If dopamine is doing reward based learning.

NOTE Confidence: 0.85444176

00:22:56.190 --> 00:22:58.170 We didn't get this robust

NOTE Confidence: 0.85444176

00:22:58.170 --> 00:23:01.876 response to the Q like we did with

NOTE Confidence: 0.85444176

00:23:01.876 --> 00:23:02.966 sucrose overlearning.

NOTE Confidence: 0.85444176

00:23:02.970 --> 00:23:05.466 We did get a decrease in the response.

NOTE Confidence: 0.85444176

00:23:05.470 --> 00:23:06.680 We have the safety queue

NOTE Confidence: 0.85444176

00:23:06.680 --> 00:23:07.890 that came on when the

NOTE Confidence: 0.8690799

00:23:07.952 --> 00:23:10.167 animals avoided the negative consequences.

NOTE Confidence: 0.8690799

00:23:10.170 --> 00:23:13.040 So at the end of the trial.

NOTE Confidence: 0.8690799

00:23:13.040 --> 00:23:14.909 It did go down over learning like

NOTE Confidence: 0.8690799

00:23:14.909 --> 00:23:16.640 you'd expect of an error signal,

NOTE Confidence: 0.8690799

00:23:16.640 --> 00:23:17.792 but here's the problem.

NOTE Confidence: 0.8690799

00:23:17.792 --> 00:23:19.232 The safety queue domain response

NOTE Confidence: 0.8690799

00:23:19.232 --> 00:23:20.888 was the biggest on the first

NOTE Confidence: 0.8690799

00:23:20.888 --> 00:23:22.208 trial they ever encountered it

NOTE Confidence: 0.8690799

00:23:22.256 --> 00:23:23.840 before they could know its value,

NOTE Confidence: 0.8690799

00:23:23.840 --> 00:23:25.928 and so we were kind of a little

NOTE Confidence: 0.8690799

00:23:25.928 --> 00:23:27.170 bit hesitant about that.

NOTE Confidence: 0.8690799

00:23:27.170 --> 00:23:29.940 But we said OK, but maybe this looks kind of.

NOTE Confidence: 0.8690799

00:23:29.940 --> 00:23:30.903 Maybe it fits.

NOTE Confidence: 0.8690799

00:23:30.903 --> 00:23:33.610 But then what we found was that Adobe

NOTE Confidence: 0.8690799

00:23:33.610 --> 00:23:35.914 response to the foot shot during

NOTE Confidence: 0.8690799

00:23:35.914 --> 00:23:38.398 these trials was not only positive,

NOTE Confidence: 0.8690799

00:23:38.400 --> 00:23:39.720 it actually increases.

NOTE Confidence: 0.8690799

00:23:39.720 --> 00:23:43.110 Animals got better at the task and so.

NOTE Confidence: 0.8690799

00:23:43.110 --> 00:23:44.650 We've looked and we said,

NOTE Confidence: 0.8690799

00:23:44.650 --> 00:23:46.190 OK, this doesn't really fit.

NOTE Confidence: 0.8690799

00:23:46.190 --> 00:23:48.255 People had seen this safety Q response

NOTE Confidence: 0.8690799

00:23:48.255 --> 00:23:50.142 before and said look doping doesn't

NOTE Confidence: 0.8690799

00:23:50.142 --> 00:23:52.032 work of RP in aversive contexts.

NOTE Confidence: 0.8690799

00:23:52.040 --> 00:23:54.623 But we looked at the other parameters

NOTE Confidence: 0.8690799

00:23:54.623 --> 00:23:57.010 that this doesn't really make sense.

NOTE Confidence: 0.8690799

00:23:57.010 --> 00:23:59.740 So now we have this situation

NOTE Confidence: 0.8690799

00:23:59.740 --> 00:24:02.266 where dopamine responses in the

NOTE Confidence: 0.8690799

00:24:02.266 --> 00:24:04.750 nucleus accumbens track these

NOTE Confidence: 0.8690799

00:24:04.750 --> 00:24:07.234 prediction error based computations.

NOTE Confidence: 0.8690799

00:24:07.240 --> 00:24:09.662 But only in contexts that are reward

NOTE Confidence: 0.8690799

00:24:09.662 --> 00:24:12.501 based and so everyone has really kind

NOTE Confidence: 0.8690799

00:24:12.501 --> 00:24:15.087 of design these experiments to parse

NOTE Confidence: 0.8690799

00:24:15.163 --> 00:24:17.634 weather domain does RP not does all

NOTE Confidence: 0.8690799

00:24:17.634 --> 00:24:21.000 of what doping does fit these computations.

NOTE Confidence: 0.8690799

00:24:21.000 --> 00:24:23.875 So we had a problem.

NOTE Confidence: 0.8690799

00:24:23.880 --> 00:24:25.930 This reward based Association model

NOTE Confidence: 0.8690799

00:24:25.930 --> 00:24:28.399 was just too simplistic to account

NOTE Confidence: 0.8690799

00:24:28.399 --> 00:24:31.199 for what domain was doing in the same

NOTE Confidence: 0.8690799

00:24:31.199 --> 00:24:33.210 animals in his behavioral tasks.

NOTE Confidence: 0.8690799

00:24:33.210 --> 00:24:35.022 And what we started looking through

NOTE Confidence: 0.8690799

00:24:35.022 --> 00:24:37.058 the literature is a lot of people.

NOTE Confidence: 0.8690799

00:24:37.060 --> 00:24:39.337 What they did is once we have this RP

NOTE Confidence: 0.8690799

00:24:39.337 --> 00:24:40.910 hypothesis reward prediction error.

NOTE Confidence: 0.8690799

00:24:40.910 --> 00:24:42.390 Apophysis people started saying OK,

NOTE Confidence: 0.8690799

00:24:42.390 --> 00:24:44.160 well reward fish based dictionary does.

NOTE Confidence: 0.8690799

00:24:44.160 --> 00:24:45.936 This. Does dopamine look like this?

NOTE Confidence: 0.8690799

00:24:45.940 --> 00:24:47.788 And the issue with that is that

NOTE Confidence: 0.8690799

00:24:47.788 --> 00:24:49.934 dopamine does a lot of stuff that

NOTE Confidence: 0.8690799

00:24:49.934 --> 00:24:51.554 reward prediction error cannot do,

NOTE Confidence: 0.8690799

00:24:51.560 --> 00:24:53.562 and so we ended up doing all

NOTE Confidence: 0.8690799

00:24:53.562 --> 00:24:54.820 this broad prediction error.

NOTE Confidence: 0.8690799

00:24:54.820 --> 00:24:56.300 Modeling those that math cannot

NOTE Confidence: 0.8690799

00:24:56.300 --> 00:24:57.188 do negative reinforcement.

NOTE Confidence: 0.8690799

00:24:57.190 --> 00:24:59.054 So we ended up at this problem where

NOTE Confidence: 0.8690799

00:24:59.054 --> 00:25:01.334 if we wanted to understand what domain

NOTE Confidence: 0.8690799

00:25:01.334 --> 00:25:03.480 was doing from a computational model.

NOTE Confidence: 0.8690799

00:25:03.480 --> 00:25:05.545 These models didn't even make

NOTE Confidence: 0.8690799

00:25:05.545 --> 00:25:07.197 the computations we needed.

NOTE Confidence: 0.8690799

00:25:07.200 --> 00:25:07.658 So.

NOTE Confidence: 0.8690799

00:25:07.658 --> 00:25:10.406 We decided to I have a

NOTE Confidence: 0.8690799

00:25:10.406 --> 00:25:11.780 postdoc who's fantastic,

NOTE Confidence: 0.8690799

00:25:11.780 --> 00:25:13.108 who's a computational psychologist.

NOTE Confidence: 0.8690799

00:25:13.108 --> 00:25:15.100 I will not take credit for

NOTE Confidence: 0.8690799

00:25:15.155 --> 00:25:16.280 developing the model.

NOTE Confidence: 0.8690799

00:25:16.280 --> 00:25:18.010 This is not my backgrounds,

NOTE Confidence: 0.8690799

00:25:18.010 --> 00:25:20.086 but we've had a really great

NOTE Confidence: 0.8690799

00:25:20.086 --> 00:25:20.778 synergistic relationship.

NOTE Confidence: 0.8690799

00:25:20.780 --> 00:25:23.498 And So what we did is we created a

NOTE Confidence: 0.8690799

00:25:23.498 --> 00:25:25.970 complex model of learning and memory.

NOTE Confidence: 0.8690799

00:25:25.970 --> 00:25:27.950 You have the theoretical components of

NOTE Confidence: 0.8690799

00:25:27.950 --> 00:25:30.468 this model that are developed from site.

NOTE Confidence: 0.8690799

00:25:30.470 --> 00:25:32.196 Many years of psychology research

NOTE Confidence: 0.8690799

00:25:32.196 --> 00:25:35.186 and then what we can do is we can

NOTE Confidence: 0.8690799

00:25:35.186 --> 00:25:37.231 record domain responses and many many

NOTE Confidence: 0.8690799

00:25:37.231 --> 00:25:40.290 Contacts and we can map the domain responses.

NOTE Confidence: 0.8690799

00:25:40.290 --> 00:25:42.439 On to the parameters of this model

NOTE Confidence: 0.8690799

00:25:42.439 --> 00:25:44.997 that we know is capable of modeling

NOTE Confidence: 0.8690799

00:25:44.997 --> 00:25:46.957 the behavioral outputs we have.

NOTE Confidence: 0.8690799

00:25:46.960 --> 00:25:48.962 So I'm not going to go into

NOTE Confidence: 0.8690799

00:25:48.962 --> 00:25:50.390 details like super details,

NOTE Confidence: 0.8690799

00:25:50.390 --> 00:25:52.441 but I'm really happy for people if

NOTE Confidence: 0.8690799

00:25:52.441 --> 00:25:54.188 they have questions to talk more

NOTE Confidence: 0.8690799

00:25:54.188 --> 00:25:55.814 essentially with the model does is

NOTE Confidence: 0.8690799

00:25:55.814 --> 00:25:57.879 it models the behavioral responses,

NOTE Confidence: 0.8690799

00:25:57.880 --> 00:25:58.504 the outcomes,

NOTE Confidence: 0.8690799

00:25:58.504 --> 00:26:00.688 the predictions like people have done before.

NOTE Confidence: 0.8690799

00:26:00.690 --> 00:26:02.245 We actually have those prediction

NOTE Confidence: 0.8690799

00:26:02.245 --> 00:26:03.178 based learning algorithms.

NOTE Confidence: 0.85464823

00:26:03.180 --> 00:26:05.259 But one thing it has that's actually

NOTE Confidence: 0.85464823

00:26:05.259 --> 00:26:07.547 was been has been found over years.

NOTE Confidence: 0.85464823

00:26:07.550 --> 00:26:09.734 So you really critical component of learning.

NOTE Confidence: 0.85464823

00:26:09.740 --> 00:26:11.300 Is this perceived salience term?

NOTE Confidence: 0.85464823

00:26:11.300 --> 00:26:13.559 And so this is kind of you know how

NOTE Confidence: 0.85464823

00:26:13.559 --> 00:26:15.229 attention grabbing something is and

NOTE Confidence: 0.85464823

00:26:15.229 --> 00:26:17.269 so it's really highly influenced by

NOTE Confidence: 0.85464823

00:26:17.332 --> 00:26:19.510 things in the environment like novelty.

NOTE Confidence: 0.85464823

00:26:19.510 --> 00:26:21.554 The first time you experience an unexpected

NOTE Confidence: 0.85464823

00:26:21.554 --> 00:26:23.090 aversive foot shock or something,

NOTE Confidence: 0.85464823

00:26:23.090 --> 00:26:24.620 it's it's more attention grabbing

NOTE Confidence: 0.85464823

00:26:24.620 --> 00:26:26.360 the 10th time you present it,

NOTE Confidence: 0.85464823

00:26:26.360 --> 00:26:28.344 and so this that with this term does

NOTE Confidence: 0.85464823

00:26:28.344 --> 00:26:30.591 is it influences how we learn based

NOTE Confidence: 0.85464823

00:26:30.591 --> 00:26:32.636 on these other factors that are

NOTE Confidence: 0.85464823

00:26:32.636 --> 00:26:34.412 not included in these other models

NOTE Confidence: 0.85464823

00:26:34.412 --> 00:26:37.230 and what it does is it's able to

NOTE Confidence: 0.85464823

00:26:37.230 --> 00:26:39.160 make really accurate predictions of

NOTE Confidence: 0.85464823

00:26:39.234 --> 00:26:41.649 what animals will do in the future.

NOTE Confidence: 0.85464823

00:26:41.650 --> 00:26:43.594 Again, we use this model to figure out

NOTE Confidence: 0.85464823

00:26:43.594 --> 00:26:45.086 what experiments would dissociate these

NOTE Confidence: 0.85464823

00:26:45.086 --> 00:26:46.686 different factors from one another.

NOTE Confidence: 0.85464823

00:26:46.690 --> 00:26:48.370 So after I show you this,

NOTE Confidence: 0.85464823

00:26:48.370 --> 00:26:49.966 you can ignore the model stuff

NOTE Confidence: 0.85464823

00:26:49.966 --> 00:26:52.244 if you want and just look at the

NOTE Confidence: 0.85464823

00:26:52.244 --> 00:26:53.689 experiments we run to parse.

NOTE Confidence: 0.85464823

00:26:53.690 --> 00:26:56.210 Kind of what's going on.

NOTE Confidence: 0.85464823

00:26:56.210 --> 00:26:58.226 The really important thing about this

NOTE Confidence: 0.85464823

00:26:58.226 --> 00:27:00.440 model is the simulations from the model.

NOTE Confidence: 0.85464823

00:27:00.440 --> 00:27:01.412 The behavioral output

NOTE Confidence: 0.85464823

00:27:01.412 --> 00:27:02.708 simulations are in grey,

NOTE Confidence: 0.85464823

00:27:02.710 --> 00:27:04.235 and the behavioral data itself

NOTE Confidence: 0.85464823

00:27:04.235 --> 00:27:07.002 is in blue and you can see it can

NOTE Confidence: 0.85464823

00:27:07.002 --> 00:27:08.760 start to model these things that

NOTE Confidence: 0.85464823

00:27:08.825 --> 00:27:10.509 couldn't be modeled before,

NOTE Confidence: 0.85464823

00:27:10.510 --> 00:27:12.652 so things like the animals to train

NOTE Confidence: 0.85464823

00:27:12.652 --> 00:27:14.961 to know spoke for sucrose and then

NOTE Confidence: 0.85464823

00:27:14.961 --> 00:27:16.947 we have we introduce an aversive

NOTE Confidence: 0.85464823

00:27:17.014 --> 00:27:18.639 foot shock all the sudden.

NOTE Confidence: 0.85464823

00:27:18.640 --> 00:27:20.260 The animals responding goes down.

NOTE Confidence: 0.85464823

00:27:20.260 --> 00:27:21.890 That's what the model suggests.

NOTE Confidence: 0.85464823

00:27:21.890 --> 00:27:24.221 We can model how animals will learn

NOTE Confidence: 0.85464823

00:27:24.221 --> 00:27:25.618 and negative reinforcement Contacts

NOTE Confidence: 0.85464823

00:27:25.618 --> 00:27:27.688 the removal of an aversive stimulus.

NOTE Confidence: 0.85464823

00:27:27.690 --> 00:27:30.682 And so we're now able to model the

NOTE Confidence: 0.85464823

00:27:30.682 --> 00:27:32.646 behavioral outcomes of these more

NOTE Confidence: 0.85464823

00:27:32.646 --> 00:27:34.932 complex behaviors but use these same

NOTE Confidence: 0.85464823

00:27:34.932 --> 00:27:38.018 kind of computations to not punch to me so.

NOTE Confidence: 0.85464823

00:27:38.020 --> 00:27:40.004 What I'm going to show you is that

NOTE Confidence: 0.85464823

00:27:40.004 --> 00:27:41.606 dopamine does not track reward

NOTE Confidence: 0.85464823

00:27:41.606 --> 00:27:42.308 prediction error.

NOTE Confidence: 0.85464823

00:27:42.310 --> 00:27:43.570 It tracks perceived salience,

NOTE Confidence: 0.85464823

00:27:43.570 --> 00:27:45.865 which is just kind of like how

NOTE Confidence: 0.85464823

00:27:45.865 --> 00:27:47.600 attention grabbing a stimulus is.

NOTE Confidence: 0.85464823

00:27:47.600 --> 00:27:50.510 Perceived salience is the perception

NOTE Confidence: 0.85464823

00:27:50.510 --> 00:27:52.250 of housing question.

NOTE Confidence: 0.85464823

00:27:52.250 --> 00:27:52.830 Yes,

NOTE Confidence: 0.77778655

00:27:52.830 --> 00:27:55.030 just a quick question.

NOTE Confidence: 0.77778655

00:27:55.030 --> 00:27:58.330 How different is this model from

NOTE Confidence: 0.77778655

00:27:58.436 --> 00:28:01.536 Pierce Hall Macintosh model of?

NOTE Confidence: 0.83179504

00:28:02.200 --> 00:28:03.690 It's it's actually very similar,

NOTE Confidence: 0.83179504

00:28:03.690 --> 00:28:04.734 so it includes the.

NOTE Confidence: 0.83179504

00:28:04.734 --> 00:28:06.630 So the thing about the Pearsall Macintosh

NOTE Confidence: 0.83179504

00:28:06.630 --> 00:28:08.838 models for the people who don't know is

NOTE Confidence: 0.83179504

00:28:08.838 --> 00:28:10.807 they include these attentional terms,

NOTE Confidence: 0.83179504

00:28:10.810 --> 00:28:12.295 which are really actually important

NOTE Confidence: 0.83179504

00:28:12.295 --> 00:28:13.780 for things like Leighton ambition,

NOTE Confidence: 0.83179504

00:28:13.780 --> 00:28:15.859 things that these other models can't do.

NOTE Confidence: 0.83179504

00:28:15.860 --> 00:28:17.642 It includes the same kind of

NOTE Confidence: 0.83179504

00:28:17.642 --> 00:28:19.182 computational terms, and this perceived

NOTE Confidence: 0.83179504

00:28:19.182 --> 00:28:20.752 salience term is essentially kind

NOTE Confidence: 0.83179504

00:28:20.752 --> 00:28:22.689 of what was added to that model.

NOTE Confidence: 0.83179504

00:28:22.690 --> 00:28:24.769 It's based on a neural net model,

NOTE Confidence: 0.83179504

00:28:24.770 --> 00:28:27.443 so it's a little bit different in the math,

NOTE Confidence: 0.83179504

00:28:27.450 --> 00:28:29.515 but it's the same kind of idea,

NOTE Confidence: 0.83179504

00:28:29.520 --> 00:28:31.040 and that's it that the

NOTE Confidence: 0.83179504

00:28:31.040 --> 00:28:32.256 attentional value of things.

NOTE Confidence: 0.83179504

00:28:32.260 --> 00:28:33.988 Are going to influence the associative

NOTE Confidence: 0.83179504

00:28:33.988 --> 00:28:35.460 strength and how animals learn,

NOTE Confidence: 0.83179504

00:28:35.460 --> 00:28:37.532 and so that's that's what we're adding

NOTE Confidence: 0.83179504

00:28:37.532 --> 00:28:39.538 that allows us to do these things.

NOTE Confidence: 0.83179504

00:28:39.540 --> 00:28:42.144 And then on top of that, we've added these.

NOTE Confidence: 0.83179504

00:28:42.144 --> 00:28:43.584 They operate probabilistic responses because

NOTE Confidence: 0.83179504

00:28:43.584 --> 00:28:45.357 pavlovi and learning is not probabilistic,

NOTE Confidence: 0.83179504

00:28:45.360 --> 00:28:47.390 and so we've added that to that.

NOTE Confidence: 0.83179504

00:28:47.390 --> 00:28:48.850 To that kind of framework.

NOTE Confidence: 0.83179504

00:28:48.850 --> 00:28:50.880 So it's very, very similar to that.

NOTE Confidence: 0.83179504

00:28:50.880 --> 00:28:52.340 Thank you for that question.

NOTE Confidence: 0.83179504

00:28:52.340 --> 00:28:54.476 I don't go into too much detail 'cause

NOTE Confidence: 0.83179504

00:28:54.476 --> 00:28:56.697 people don't always know about these models,

NOTE Confidence: 0.83179504

00:28:56.700 --> 00:28:58.482 but that's actually kind of the

NOTE Confidence: 0.83179504

00:28:58.482 --> 00:29:00.199 framework by which we're using it.

NOTE Confidence: 0.83179504

00:29:00.200 --> 00:29:01.940 More appears Hall that the Macintosh,

NOTE Confidence: 0.83179504

00:29:01.940 --> 00:29:04.200 though.

NOTE Confidence: 0.83179504

00:29:04.200 --> 00:29:06.999 OK, so we can model the behavior we need,

NOTE Confidence: 0.83179504

00:29:07.000 --> 00:29:07.840 so so again,

NOTE Confidence: 0.83179504

00:29:07.840 --> 00:29:09.520 this perceived salience is kind of

NOTE Confidence: 0.83179504

00:29:09.520 --> 00:29:11.174 like a driving animals attention

NOTE Confidence: 0.83179504

00:29:11.174 --> 00:29:13.148 towards States and so it's really

NOTE Confidence: 0.83179504

00:29:13.202 --> 00:29:15.074 highly affected by the in physical

NOTE Confidence: 0.83179504

00:29:15.074 --> 00:29:17.042 intensity of a stimulus and the

NOTE Confidence: 0.83179504

00:29:17.042 --> 00:29:18.466 novelty and environment that

NOTE Confidence: 0.83179504

00:29:18.466 --> 00:29:20.739 changes how you attend to stimulate.

NOTE Confidence: 0.83179504

00:29:20.740 --> 00:29:23.676 And So what we did is we started.

NOTE Confidence: 0.83179504

00:29:23.680 --> 00:29:24.784 We said OK,

NOTE Confidence: 0.83179504

00:29:24.784 --> 00:29:26.992 if it's tracking just the saliency,

NOTE Confidence: 0.83179504

00:29:27.000 --> 00:29:28.835 it should increase with physical

NOTE Confidence: 0.83179504

00:29:28.835 --> 00:29:30.303 intensity of a stimulus.

NOTE Confidence: 0.83179504

00:29:30.310 --> 00:29:32.150 Whether it's positive or negative.

NOTE Confidence: 0.83179504

00:29:32.150 --> 00:29:34.412 And so this is a increasing

NOTE Confidence: 0.83179504

00:29:34.412 --> 00:29:36.929 series of foot shocks on the left.

NOTE Confidence: 0.83179504

00:29:36.930 --> 00:29:37.678 That is,

NOTE Confidence: 0.83179504

00:29:37.678 --> 00:29:39.548 the simulations from that perceived

NOTE Confidence: 0.83179504

00:29:39.548 --> 00:29:41.350 salience term of our model,

NOTE Confidence: 0.83179504

00:29:41.350 --> 00:29:43.996 and on the right is the actual

NOTE Confidence: 0.83179504

00:29:43.996 --> 00:29:45.566 dopamine recorded responses to

NOTE Confidence: 0.83179504

00:29:45.566 --> 00:29:47.421 increasing intensities of foot shocks

NOTE Confidence: 0.83179504

00:29:47.421 --> 00:29:50.269 and what you see is that dopamine

NOTE Confidence: 0.83179504

00:29:50.269 --> 00:29:52.424 increases with foot shock intensity.

NOTE Confidence: 0.83179504

00:29:52.430 --> 00:29:54.850 It also increases when we

NOTE Confidence: 0.83179504

00:29:54.850 --> 00:29:57.270 increase the volume of sucrose.

NOTE Confidence: 0.83179504

00:29:57.270 --> 00:30:00.258 So a better than expected appetitive.

NOTE Confidence: 0.83179504

00:30:00.260 --> 00:30:02.430 Reward or the volume of quiet Night,

NOTE Confidence: 0.83179504

00:30:02.430 --> 00:30:04.290 which is a bitter taste scent,

NOTE Confidence: 0.83179504

00:30:04.290 --> 00:30:05.840 and so everyone always asks.

NOTE Confidence: 0.83179504

00:30:05.840 --> 00:30:07.390 And it's a great question.

NOTE Confidence: 0.83179504

00:30:07.390 --> 00:30:08.940 Foot shocks are kind of

NOTE Confidence: 0.83179504

00:30:08.940 --> 00:30:09.870 weird aversive stimuli,

NOTE Confidence: 0.83179504

00:30:09.870 --> 00:30:12.022 so for many of these tasks we have

NOTE Confidence: 0.83179504

00:30:12.022 --> 00:30:14.518 worked in other things that are aversive.

NOTE Confidence: 0.83179504

00:30:14.520 --> 00:30:15.760 But not, you know,

NOTE Confidence: 0.83179504

00:30:15.760 --> 00:30:16.070 painful.

NOTE Confidence: 0.83179504

00:30:16.070 --> 00:30:18.093 We can argue all day about whether

NOTE Confidence: 0.83179504

00:30:18.093 --> 00:30:20.408 foot shock is pain or something else,

NOTE Confidence: 0.83179504

00:30:20.410 --> 00:30:22.181 but we see the same pattern with

NOTE Confidence: 0.83179504

00:30:22.181 --> 00:30:24.130 other types of aversive stimulation,

NOTE Confidence: 0.83179504

00:30:24.130 --> 00:30:26.300 and so this is ruling out simple,

NOTE Confidence: 0.83179504

00:30:26.300 --> 00:30:27.612 rewarding coding by dopamine,

NOTE Confidence: 0.83179504

00:30:27.612 --> 00:30:29.252 because dopamine in the incumbents

NOTE Confidence: 0.83179504

00:30:29.252 --> 00:30:31.136 is going up to both appetitive

NOTE Confidence: 0.83179504

00:30:31.136 --> 00:30:32.036 and aversive stimuli.

NOTE Confidence: 0.83179504

00:30:32.040 --> 00:30:34.188 So it cannot be just rewards.

NOTE Confidence: 0.84336776

00:30:36.420 --> 00:30:38.766 So the other thing that influences

NOTE Confidence: 0.84336776

00:30:38.766 --> 00:30:40.330 perceived salience is novelty.

NOTE Confidence: 0.84336776

00:30:40.330 --> 00:30:41.894 So how much experience

NOTE Confidence: 0.84336776

00:30:41.894 --> 00:30:43.458 you have with something.

NOTE Confidence: 0.84336776

00:30:43.460 --> 00:30:46.164 So what we did is we took foot

NOTE Confidence: 0.84336776

00:30:46.164 --> 00:30:48.539 shocks of the same intensity.

NOTE Confidence: 0.84336776

00:30:48.540 --> 00:30:51.172 Intensity is not changed and we repeated

NOTE Confidence: 0.84336776

00:30:51.172 --> 00:30:54.408 them in a series on a fixed interval,

NOTE Confidence: 0.84336776

00:30:54.410 --> 00:30:56.320 so every every 60 seconds

NOTE Confidence: 0.84336776

00:30:56.320 --> 00:30:58.710 the animals got a foot shot.

NOTE Confidence: 0.84336776

00:30:58.710 --> 00:31:01.502 What we found is that doping goes down

NOTE Confidence: 0.84336776

00:31:01.502 --> 00:31:04.368 to the foot shots even though the

NOTE Confidence: 0.84336776

00:31:04.368 --> 00:31:07.010 intensity of the foot shock stays.

NOTE Confidence: 0.84336776

00:31:07.010 --> 00:31:09.980 Constant, so it's also not just

NOTE Confidence: 0.84336776

00:31:09.980 --> 00:31:11.960 encoding only the intensity,

NOTE Confidence: 0.84336776

00:31:11.960 --> 00:31:13.940 it's encoding other aspects

NOTE Confidence: 0.84336776

00:31:13.940 --> 00:31:15.920 like novelty as well,

NOTE Confidence: 0.84336776

00:31:15.920 --> 00:31:19.310 and so you get decreased domain

NOTE Confidence: 0.84336776

00:31:19.310 --> 00:31:21.570 responses to repeated exposures

NOTE Confidence: 0.84336776

00:31:21.666 --> 00:31:24.090 of stimulate both aversive.

NOTE Confidence: 0.84336776

00:31:24.090 --> 00:31:25.245 And neutral simulate,

NOTE Confidence: 0.84336776

00:31:25.245 --> 00:31:27.940 and so this is an auditory tone,

NOTE Confidence: 0.84336776

00:31:27.940 --> 00:31:30.250 so we've done this with tones,

NOTE Confidence: 0.84336776

00:31:30.250 --> 00:31:31.750 lights, and white noise.

NOTE Confidence: 0.84336776

00:31:31.750 --> 00:31:34.490 This is an example from white noise,

NOTE Confidence: 0.84336776

00:31:34.490 --> 00:31:36.626 but what you see which is

NOTE Confidence: 0.84336776

00:31:36.626 --> 00:31:38.546 important is the first exposure

NOTE Confidence: 0.84336776

00:31:38.546 --> 00:31:41.030 of a stimulus that is neutral,

NOTE Confidence: 0.84336776

00:31:41.030 --> 00:31:43.515 elicits dopamine and repeated exposures

NOTE Confidence: 0.84336776

00:31:43.515 --> 00:31:46.780 of that stimulus go down overtime.

NOTE Confidence: 0.84336776

00:31:46.780 --> 00:31:48.840 So you're getting decreased dopamine

NOTE Confidence: 0.84336776

00:31:48.840 --> 00:31:50.900 when animals are exposed repeatedly

NOTE Confidence: 0.84336776

00:31:50.962 --> 00:31:52.677 to stimuli in the environment,

NOTE Confidence: 0.84336776

00:31:52.680 --> 00:31:54.640 regardless of whether they have

NOTE Confidence: 0.84336776

00:31:54.640 --> 00:31:56.584 positive value, negative value,

NOTE Confidence: 0.84336776

00:31:56.584 --> 00:32:01.200 or are what we think of as neutral.

NOTE Confidence: 0.84336776

00:32:01.200 --> 00:32:01.727 I'm.

NOTE Confidence: 0.84336776

00:32:01.727 --> 00:32:04.889 So another aspect that I think,

NOTE Confidence: 0.84336776

00:32:04.890 --> 00:32:06.816 and this is really important experiment

NOTE Confidence: 0.84336776

00:32:06.816 --> 00:32:08.851 because it really rules out this

NOTE Confidence: 0.84336776

00:32:08.851 --> 00:32:10.596 reward prediction error based learning.

NOTE Confidence: 0.84336776

00:32:10.600 --> 00:32:13.120 So what we did is we trained animals to

NOTE Confidence: 0.84336776

00:32:13.120 --> 00:32:15.636 know spoke during a discriminative cue.

NOTE Confidence: 0.84336776

00:32:15.640 --> 00:32:17.320 So auditory cue comes on.

NOTE Confidence: 0.84336776

00:32:17.320 --> 00:32:20.848 If they respond they get sucrose.

NOTE Confidence: 0.84336776

00:32:20.850 --> 00:32:21.924 Without any signal,

NOTE Confidence: 0.84336776

00:32:21.924 --> 00:32:25.479 we now switch it to the same auditory cue.

NOTE Confidence: 0.84336776

00:32:25.480 --> 00:32:26.638 If they press,

NOTE Confidence: 0.84336776

00:32:26.638 --> 00:32:27.796 they get shocked,

NOTE Confidence: 0.84336776

00:32:27.800 --> 00:32:30.404 so we're switching that the Q is

NOTE Confidence: 0.84336776

00:32:30.404 --> 00:32:33.103 the same and it now represents

NOTE Confidence: 0.84336776

00:32:33.103 --> 00:32:35.588 a worse than expected outcome.

NOTE Confidence: 0.84336776

00:32:35.590 --> 00:32:36.270 And so.

NOTE Confidence: 0.84336776

00:32:36.270 --> 00:32:38.310 What should happen in a task

NOTE Confidence: 0.84336776

00:32:38.310 --> 00:32:40.767 like this is that the animals

NOTE Confidence: 0.84336776

00:32:40.767 --> 00:32:42.467 in this grezar simulation,

NOTE Confidence: 0.84336776

00:32:42.470 --> 00:32:44.434 the animal should reduce

NOTE Confidence: 0.84336776

00:32:44.434 --> 00:32:45.907 their behavioral responding.

NOTE Confidence: 0.84336776

00:32:45.910 --> 00:32:46.994 They do not surprisingly,

NOTE Confidence: 0.84336776

00:32:46.994 --> 00:32:48.349 this is a traditional kind

NOTE Confidence: 0.84336776

00:32:48.349 --> 00:32:49.469 of punishment task.

NOTE Confidence: 0.84336776

00:32:49.470 --> 00:32:51.830 Animals will reduce their behavior.

NOTE Confidence: 0.84336776

00:32:51.830 --> 00:32:53.750 But what our model predicts,

NOTE Confidence: 0.84336776

00:32:53.750 --> 00:32:55.402 this perceived salience model.

NOTE Confidence: 0.84336776

00:32:55.402 --> 00:32:57.467 Is that because there's unexpected

NOTE Confidence: 0.84336776

00:32:57.467 --> 00:32:58.739 information and it's novel?

NOTE Confidence: 0.84336776

00:32:58.740 --> 00:33:00.588 There should be increase

NOTE Confidence: 0.84336776

00:33:00.588 --> 00:33:02.898 in dopamine to this Q.

NOTE Confidence: 0.84336776

00:33:02.900 --> 00:33:04.680 Prediction error responding with

NOTE Confidence: 0.84336776

00:33:04.680 --> 00:33:07.350 say it should be decreased because

NOTE Confidence: 0.84336776

00:33:07.422 --> 00:33:09.750 it's a worse than expected outcome.

NOTE Confidence: 0.84336776

00:33:09.750 --> 00:33:12.006 A reward prediction error, excuse me.

NOTE Confidence: 0.84336776

00:33:12.010 --> 00:33:13.990 So what we're going to look

NOTE Confidence: 0.84336776

00:33:13.990 --> 00:33:15.550 at here is this Q,

NOTE Confidence: 0.84336776

00:33:15.550 --> 00:33:18.126 which is the last Q that predicted sucrose,

NOTE Confidence: 0.84336776

00:33:18.130 --> 00:33:20.062 so this is before the animals

NOTE Confidence: 0.84336776

00:33:20.062 --> 00:33:21.028 got gotten shocked.

NOTE Confidence: 0.84336776

00:33:21.030 --> 00:33:23.598 So this Q still has that predict sucrose,

NOTE Confidence: 0.84336776

00:33:23.600 --> 00:33:26.822 and then we're going to look at the next

NOTE Confidence: 0.84336776

00:33:26.822 --> 00:33:30.086 Q right after the first foot shock.

NOTE Confidence: 0.84336776

00:33:30.090 --> 00:33:32.688 And what we find is first,

NOTE Confidence: 0.84336776

00:33:32.690 --> 00:33:34.850 this foot shock causes a

NOTE Confidence: 0.84336776

00:33:34.850 --> 00:33:36.146 positive domain response.

NOTE Confidence: 0.84336776

00:33:36.150 --> 00:33:39.614 So it doesn't matter what kind of task,

NOTE Confidence: 0.84336776

00:33:39.620 --> 00:33:42.104 but shocks are being presented and

NOTE Confidence: 0.84336776

00:33:42.104 --> 00:33:43.760 they're always words resulting

NOTE Confidence: 0.84336776

00:33:43.830 --> 00:33:45.678 in positive domain responses.

NOTE Confidence: 0.84336776

00:33:45.680 --> 00:33:48.374 What the dopamine response to this

NOTE Confidence: 0.84336776

00:33:48.374 --> 00:33:50.440 discriminative cue actually goes up,

NOTE Confidence: 0.84336776

00:33:50.440 --> 00:33:53.134 even though it's it represents a

NOTE Confidence: 0.84336776

00:33:53.134 --> 00:33:55.458 worse than expected outcomes and

NOTE Confidence: 0.84336776

00:33:55.458 --> 00:33:57.703 so dopamine is increasing anytime

NOTE Confidence: 0.84336776

00:33:57.703 --> 00:33:59.984 information is novel or salient

NOTE Confidence: 0.84336776

00:33:59.984 --> 00:34:01.199 to the animal.

NOTE Confidence: 0.84336776

00:34:01.200 --> 00:34:02.940 And it's increasing even if

NOTE Confidence: 0.84336776

00:34:02.940 --> 00:34:04.680 the outcome is worse than

NOTE Confidence: 0.85146016

00:34:04.750 --> 00:34:06.920 expected or better than expected,

NOTE Confidence: 0.85146016

00:34:06.920 --> 00:34:09.840 and one of the key aspects of this

NOTE Confidence: 0.85146016

00:34:09.840 --> 00:34:12.247 experiment is dopamine is going up,

NOTE Confidence: 0.85146016

00:34:12.250 --> 00:34:13.774 even though the animal's

NOTE Confidence: 0.85146016

00:34:13.774 --> 00:34:15.298 behavior is going down,

NOTE Confidence: 0.85146016

00:34:15.300 --> 00:34:17.322 so increases in dopamine don't just

NOTE Confidence: 0.85146016

00:34:17.322 --> 00:34:19.118 mean motivated behavior or approach

NOTE Confidence: 0.85146016

00:34:19.118 --> 00:34:21.073 because we're getting increases in

NOTE Confidence: 0.85146016

00:34:21.073 --> 00:34:23.532 dopamine here that correlate with animals

NOTE Confidence: 0.85146016

00:34:23.532 --> 00:34:25.200 inhibiting a behavioral response,

NOTE Confidence: 0.85146016

00:34:25.200 --> 00:34:27.486 and so this kind of saliency.

NOTE Confidence: 0.85146016

00:34:27.490 --> 00:34:30.698 What it'll do, is it helps animals make

NOTE Confidence: 0.85146016

00:34:30.698 --> 00:34:32.839 adaptive updating of responses were.

NOTE Confidence: 0.85146016

00:34:32.840 --> 00:34:35.568 List of what the context of those responses

NOTE Confidence: 0.85146016

00:34:35.568 --> 00:34:38.640 are or the behavioral response necessary.

NOTE Confidence: 0.85146016

00:34:38.640 --> 00:34:41.292 So I'm gonna show I think

NOTE Confidence: 0.85146016

00:34:41.292 --> 00:34:43.060 I've one more experiment,

NOTE Confidence: 0.85146016

00:34:43.060 --> 00:34:44.824 so this experiment is

NOTE Confidence: 0.85146016

00:34:44.824 --> 00:34:46.147 actually really important,

NOTE Confidence: 0.85146016

00:34:46.150 --> 00:34:49.406 because it's kind of shows how much these

NOTE Confidence: 0.85146016

00:34:49.406 --> 00:34:52.930 kind of novel salients events that don't

NOTE Confidence: 0.85146016

00:34:52.930 --> 00:34:56.300 necessarily acquire value R to animals.

NOTE Confidence: 0.85146016

00:34:56.300 --> 00:34:59.288 So what we did is we did an experiment

NOTE Confidence: 0.85146016

00:34:59.288 --> 00:35:02.416 where we associated ECU with a foot shock,

NOTE Confidence: 0.85146016

00:35:02.420 --> 00:35:03.968 so just fear conditioning.

NOTE Confidence: 0.85146016

00:35:03.968 --> 00:35:07.180 But what we did is on some of

NOTE Confidence: 0.85146016

00:35:07.180 --> 00:35:10.001 the trials we just put a random

NOTE Confidence: 0.85146016

00:35:10.001 --> 00:35:11.699 irrelevant house light on.

NOTE Confidence: 0.85146016

00:35:11.700 --> 00:35:14.076 And what the model predicts is that because

NOTE Confidence: 0.85146016

00:35:14.076 --> 00:35:16.278 there is novelty in the environment,

NOTE Confidence: 0.85146016

00:35:16.280 --> 00:35:18.422 there will be an increase in dopamine

NOTE Confidence: 0.85146016

00:35:18.422 --> 00:35:20.489 response on these trials where novel

NOTE Confidence: 0.85146016

00:35:20.489 --> 00:35:22.661 information is added even though previous

NOTE Confidence: 0.85146016

00:35:22.661 --> 00:35:24.949 work has shown that novel irrelevant

NOTE Confidence: 0.85146016

00:35:24.949 --> 00:35:26.814 information will not acquire value.

NOTE Confidence: 0.85146016

00:35:26.820 --> 00:35:29.444 So the Q that we're adding this random

NOTE Confidence: 0.85146016

00:35:29.444 --> 00:35:31.437 irrelevant light won't acquire value

NOTE Confidence: 0.85146016

00:35:31.437 --> 00:35:33.557 because the animals already associated

NOTE Confidence: 0.85146016

00:35:33.557 --> 00:35:35.716 the previous Q with the foot shot.

NOTE Confidence: 0.85146016

00:35:35.720 --> 00:35:38.312 And So what we find is on trials

NOTE Confidence: 0.85146016

00:35:38.312 --> 00:35:40.700 where we add this novel light.

NOTE Confidence: 0.85146016

00:35:40.700 --> 00:35:42.836 There is a very large increase

NOTE Confidence: 0.85146016

00:35:42.836 --> 00:35:44.260 in the domain response,

NOTE Confidence: 0.85146016

00:35:44.260 --> 00:35:46.040 even though that novel light

NOTE Confidence: 0.85146016

00:35:46.040 --> 00:35:47.464 won't acquire value itself.

NOTE Confidence: 0.85146016

00:35:47.470 --> 00:35:49.798 And So what this does is it rules

NOTE Confidence: 0.85146016

00:35:49.798 --> 00:35:51.966 out the simple Attribution of some

NOTE Confidence: 0.85146016

00:35:51.966 --> 00:35:54.704 sort of balance to a queue or

NOTE Confidence: 0.85146016

00:35:54.704 --> 00:35:56.719 associative strength of that Q.

NOTE Confidence: 0.85146016

00:35:56.720 --> 00:35:58.570 It means that you're getting

NOTE Confidence: 0.85146016

00:35:58.570 --> 00:36:00.050 increases in dopamine responses.

NOTE Confidence: 0.85146016

00:36:00.050 --> 00:36:02.490 They don't necessarily correspond with

NOTE Confidence: 0.85146016

00:36:02.490 --> 00:36:04.930 the animal making Association between

NOTE Confidence: 0.85146016

00:36:04.996 --> 00:36:07.628 that queue and the outcome in some cases.

NOTE Confidence: 0.86010796

00:36:10.660 --> 00:36:12.274 The last thing, which again for

NOTE Confidence: 0.86010796

00:36:12.274 --> 00:36:14.059 people who are are really deep

NOTE Confidence: 0.86010796

00:36:14.059 --> 00:36:15.674 in the prediction based field.

NOTE Confidence: 0.86010796

00:36:15.680 --> 00:36:17.155 One thing that people can

NOTE Confidence: 0.86010796

00:36:17.155 --> 00:36:18.901 say at this point is, well,

NOTE Confidence: 0.86010796

00:36:18.901 --> 00:36:20.527 maybe doping is doing prediction error

NOTE Confidence: 0.86010796

00:36:20.527 --> 00:36:22.170 but not reward prediction error.

NOTE Confidence: 0.86010796

00:36:22.170 --> 00:36:23.760 So it's going up every time

NOTE Confidence: 0.86010796

00:36:23.760 --> 00:36:25.710 there is an error in prediction.

NOTE Confidence: 0.86010796

00:36:25.710 --> 00:36:27.992 This is actually really good good thought

NOTE Confidence: 0.86010796

00:36:27.992 --> 00:36:30.429 and we thought this too and we said OK.

NOTE Confidence: 0.86010796

00:36:30.430 --> 00:36:32.670 Well let's let's see if that is the

NOTE Confidence: 0.86010796

00:36:32.670 --> 00:36:35.148 case and we were kind of Gnostic here.

NOTE Confidence: 0.86010796

00:36:35.150 --> 00:36:36.302 We were saying, OK,

NOTE Confidence: 0.86010796

00:36:36.302 --> 00:36:38.390 let's just figure out what it does.

NOTE Confidence: 0.86010796

00:36:38.390 --> 00:36:39.534 We're not trying to.

NOTE Confidence: 0.86010796

00:36:39.534 --> 00:36:41.128 Pusha theory we're saying, well,

NOTE Confidence: 0.86010796

00:36:41.128 --> 00:36:43.816 how does the data fit together?

NOTE Confidence: 0.86010796

00:36:43.820 --> 00:36:45.810 So saliency or perceived salience?

NOTE Confidence: 0.86010796

00:36:45.810 --> 00:36:48.372 What it would suggest is that when

NOTE Confidence: 0.86010796

00:36:48.372 --> 00:36:51.759 you have a stimulus like a foot shock,

NOTE Confidence: 0.86010796

00:36:51.760 --> 00:36:54.539 you should have the biggest opening response,

NOTE Confidence: 0.86010796

00:36:54.540 --> 00:36:56.375 because when the stimulus is

NOTE Confidence: 0.86010796

00:36:56.375 --> 00:36:58.725 present and there it's the most

NOTE Confidence: 0.86010796

00:36:58.725 --> 00:37:00.489 salient 'cause most intense.

NOTE Confidence: 0.86010796

00:37:00.490 --> 00:37:03.178 But if you have a prediction of

NOTE Confidence: 0.86010796

00:37:03.178 --> 00:37:05.260 that during extinction or omission,

NOTE Confidence: 0.86010796

00:37:05.260 --> 00:37:07.636 there should still be a positive

NOTE Confidence: 0.86010796

00:37:07.636 --> 00:37:08.428 doping response,

NOTE Confidence: 0.86010796

00:37:08.430 --> 00:37:11.174 but it should be lower than when the

NOTE Confidence: 0.86010796

00:37:11.174 --> 00:37:14.078 stimulus is physically there a prediction.

NOTE Confidence: 0.86010796

00:37:14.080 --> 00:37:15.760 Error hypothesis would be that

NOTE Confidence: 0.86010796

00:37:15.760 --> 00:37:17.440 when you have an omission,

NOTE Confidence: 0.86010796

00:37:17.440 --> 00:37:19.095 this response should be higher

NOTE Confidence: 0.86010796

00:37:19.095 --> 00:37:21.145 than when the stimulus is there

NOTE Confidence: 0.86010796

00:37:21.145 --> 00:37:22.820 because it signals an error.

NOTE Confidence: 0.8327354

00:37:25.250 --> 00:37:26.610 We did this experiment.

NOTE Confidence: 0.8327354

00:37:26.610 --> 00:37:29.065 What we found was that there's a

NOTE Confidence: 0.8327354

00:37:29.065 --> 00:37:31.141 positive domain response at the time

NOTE Confidence: 0.8327354

00:37:31.141 --> 00:37:33.346 of the predicted foot shock when

NOTE Confidence: 0.8327354

00:37:33.346 --> 00:37:35.348 it's omitted, so it's not there,

NOTE Confidence: 0.8327354

00:37:35.348 --> 00:37:37.711 but the response of the foot shock

NOTE Confidence: 0.8327354

00:37:37.711 --> 00:37:40.427 itself is higher than when it's omitted.

NOTE Confidence: 0.8327354

00:37:40.430 --> 00:37:42.548 And so this also rules out

NOTE Confidence: 0.8327354

00:37:42.548 --> 00:37:43.607 other competing theories,

NOTE Confidence: 0.8327354

00:37:43.610 --> 00:37:45.370 which is that domain does

NOTE Confidence: 0.8327354

00:37:45.370 --> 00:37:46.426 prediction error learning,

NOTE Confidence: 0.8327354

00:37:46.430 --> 00:37:48.200 but it's not reward based.

NOTE Confidence: 0.835218896

00:37:50.470 --> 00:37:54.340 So. And I showed you a lot of stuff and,

NOTE Confidence: 0.835218896

00:37:54.340 --> 00:37:56.364 well, I kind of rule kind of come

NOTE Confidence: 0.835218896

00:37:56.364 --> 00:37:58.678 back and say like why should you care?

NOTE Confidence: 0.835218896

00:37:58.680 --> 00:38:00.512 So essentially what we did is we did

NOTE Confidence: 0.835218896

00:38:00.512 --> 00:38:02.500 a number of experiments to rule out

NOTE Confidence: 0.835218896

00:38:02.500 --> 00:38:04.586 these kind of competing factors of what

NOTE Confidence: 0.835218896

00:38:04.586 --> 00:38:06.525 dopamine is doing in learning and memory.

NOTE Confidence: 0.835218896

00:38:06.530 --> 00:38:07.890 Don't mean release is doing.

NOTE Confidence: 0.835218896

00:38:07.890 --> 00:38:09.516 I'm not saying the VTA cell

NOTE Confidence: 0.835218896

00:38:09.516 --> 00:38:10.600 bodies don't do this.

NOTE Confidence: 0.835218896

00:38:10.600 --> 00:38:11.449 Maybe they do,

NOTE Confidence: 0.835218896

00:38:11.449 --> 00:38:12.864 but there's integration of information

NOTE Confidence: 0.835218896

00:38:12.864 --> 00:38:14.828 at the level of the terminal that

NOTE Confidence: 0.835218896

00:38:14.828 --> 00:38:16.173 dictates how doing is actually

NOTE Confidence: 0.835218896

00:38:16.225 --> 00:38:17.475 releasing these brain regions and

NOTE Confidence: 0.835218896

00:38:17.475 --> 00:38:19.272 what I am saying is that dopamine

NOTE Confidence: 0.835218896

00:38:19.272 --> 00:38:20.627 release in the nucleus accumbens,

NOTE Confidence: 0.835218896

00:38:20.630 --> 00:38:22.050 core Maps on true perceived.

NOTE Confidence: 0.835218896

00:38:22.050 --> 00:38:24.600 Salience not prediction error or value.

NOTE Confidence: 0.8711132

00:38:26.760 --> 00:38:28.250 Our models are modeled behavior,

NOTE Confidence: 0.8711132

00:38:28.250 --> 00:38:30.112 we just use it to generate experiments

NOTE Confidence: 0.8711132

00:38:30.112 --> 00:38:31.972 we should run to parse different

NOTE Confidence: 0.8711132

00:38:31.972 --> 00:38:33.316 aspects of domain encoding,

NOTE Confidence: 0.8711132

00:38:33.320 --> 00:38:35.152 and So what you can do is use

NOTE Confidence: 0.8711132

00:38:35.152 --> 00:38:37.114 these kind of predictions to make

NOTE Confidence: 0.8711132

00:38:37.114 --> 00:38:39.280 experiments with other circuits as well,

NOTE Confidence: 0.8711132

00:38:39.280 --> 00:38:42.136 which I think is kind of an interesting

NOTE Confidence: 0.8711132

00:38:42.136 --> 00:38:44.638 way to approach the question.

NOTE Confidence: 0.8711132

00:38:44.640 --> 00:38:46.698 But what I'm showing you is that

NOTE Confidence: 0.8711132

00:38:46.698 --> 00:38:48.080 even in reinforcement context,

NOTE Confidence: 0.8711132

00:38:48.080 --> 00:38:49.019 pavlovi in context,

NOTE Confidence: 0.8711132

00:38:49.019 --> 00:38:51.210 this isn't a value based prediction signal,

NOTE Confidence: 0.8711132

00:38:51.210 --> 00:38:52.525 and these same signals are

NOTE Confidence: 0.8711132

00:38:52.525 --> 00:38:53.840 there in punishment tasks in

NOTE Confidence: 0.8711132

00:38:53.891 --> 00:38:55.280 negative reinforcement tasks,

NOTE Confidence: 0.8711132

00:38:55.280 --> 00:38:56.845 and so it's actually really

NOTE Confidence: 0.8711132

00:38:56.845 --> 00:38:58.097 interesting that you're seeing

NOTE Confidence: 0.8711132

00:38:58.097 --> 00:38:59.657 this kind of dopamine signal.

NOTE Confidence: 0.8711132

00:38:59.660 --> 00:39:01.538 It's very critical in driving behaviors,

NOTE Confidence: 0.8711132

00:39:01.540 --> 00:39:04.494 just not in the way that I

NOTE Confidence: 0.8711132

00:39:04.494 --> 00:39:06.520 think we predicted before.

NOTE Confidence: 0.8711132

00:39:06.520 --> 00:39:08.350 So why should we care?

NOTE Confidence: 0.8711132

00:39:08.350 --> 00:39:10.522 I think understanding what domain is

NOTE Confidence: 0.8711132

00:39:10.522 --> 00:39:12.729 doing is really important for disease,

NOTE Confidence: 0.8711132

00:39:12.730 --> 00:39:15.442 and so if you want to understand what

NOTE Confidence: 0.8711132

00:39:15.442 --> 00:39:18.032 dopamine is doing and what deficits in

NOTE Confidence: 0.8711132

00:39:18.032 --> 00:39:21.120 dopamine in a patient mean for that patient,

NOTE Confidence: 0.8711132

00:39:21.120 --> 00:39:23.310 it really requires a kind of

NOTE Confidence: 0.8711132

00:39:23.310 --> 00:39:24.040 holistic understanding.

NOTE Confidence: 0.8711132

00:39:24.040 --> 00:39:26.284 What domains doing across contexts and

NOTE Confidence: 0.8711132

00:39:26.284 --> 00:39:28.420 internal States and things like that,

NOTE Confidence: 0.8711132

00:39:28.420 --> 00:39:31.520 and so you know when you have a model and

NOTE Confidence: 0.8711132

00:39:31.601 --> 00:39:34.625 you say doesken dopamine fit this model,

NOTE Confidence: 0.8711132

00:39:34.630 --> 00:39:36.540 the answer might be yes.

NOTE Confidence: 0.8711132

00:39:36.540 --> 00:39:39.483 But it kind of leaves out that aspect of.

NOTE Confidence: 0.8711132

00:39:39.490 --> 00:39:41.702 But what is domain doing in other

NOTE Confidence: 0.8711132

00:39:41.702 --> 00:39:44.266 contexts of the model can't fit and

NOTE Confidence: 0.8711132

00:39:44.266 --> 00:39:46.201 so understanding the components that

NOTE Confidence: 0.8711132

00:39:46.201 --> 00:39:48.806 dry of these behaviors is really

NOTE Confidence: 0.8711132

00:39:48.806 --> 00:39:50.526 critical to understanding this.

NOTE Confidence: 0.8711132

00:39:50.530 --> 00:39:52.672 But I think that maybe more

NOTE Confidence: 0.8711132

00:39:52.672 --> 00:39:54.810 important thing for for kind of

NOTE Confidence: 0.8711132

00:39:54.810 --> 00:39:57.046 human health is is from, you know,

NOTE Confidence: 0.8711132

00:39:57.046 --> 00:39:58.636 my primary field which is

NOTE Confidence: 0.8711132

00:39:58.636 --> 00:40:00.320 addiction an it's understand.

NOTE Confidence: 0.8711132

00:40:00.320 --> 00:40:01.960 The difference between a dopamine

NOTE Confidence: 0.8711132

00:40:01.960 --> 00:40:03.600 signal that signals were worn

NOTE Confidence: 0.8711132

00:40:03.660 --> 00:40:05.328 and what a salience signal does.

NOTE Confidence: 0.8711132

00:40:05.330 --> 00:40:06.510 So a reward signal.

NOTE Confidence: 0.8711132

00:40:06.510 --> 00:40:09.400 If you have a deficits in a reward signal,

NOTE Confidence: 0.8711132

00:40:09.400 --> 00:40:11.206 you may say you know we don't

NOTE Confidence: 0.8711132

00:40:11.206 --> 00:40:13.138 want to increase those and people

NOTE Confidence: 0.8711132

00:40:13.138 --> 00:40:14.963 suffering from substance use disorder

NOTE Confidence: 0.8711132

00:40:14.963 --> 00:40:17.269 because if we do that may increase

NOTE Confidence: 0.8711132

00:40:17.269 --> 00:40:18.784 the rewarding value of stimuli

NOTE Confidence: 0.8711132

00:40:18.790 --> 00:40:21.150 in the environment like drugs.

NOTE Confidence: 0.8711132

00:40:21.150 --> 00:40:24.446 But the issue is with the salience signal.

NOTE Confidence: 0.8711132

00:40:24.450 --> 00:40:25.882 If you have deficits,

NOTE Confidence: 0.8711132

00:40:25.882 --> 00:40:29.073 it's going to slow the rate of learning

NOTE Confidence: 0.8711132

00:40:29.073 --> 00:40:31.478 for everything in the environment,

NOTE Confidence: 0.8711132

00:40:31.480 --> 00:40:33.766 so it could explain why people

NOTE Confidence: 0.8711132

00:40:33.766 --> 00:40:35.826 are compulsive because they don't

NOTE Confidence: 0.8711132

00:40:35.826 --> 00:40:37.670 respond to negative outcomes.

NOTE Confidence: 0.8711132

00:40:37.670 --> 00:40:40.554 It would explain why they have trouble

NOTE Confidence: 0.8711132

00:40:40.554 --> 00:40:42.209 learning. The adaptive alternatives.

NOTE Confidence: 0.8711132

00:40:42.209 --> 00:40:43.448 Are there an?

NOTE Confidence: 0.8711132

00:40:43.450 --> 00:40:45.515 It would explain why extinguishing

NOTE Confidence: 0.8711132

00:40:45.515 --> 00:40:47.580 drug associations is much slower,

NOTE Confidence: 0.8711132

00:40:47.580 --> 00:40:50.884 and so in if it's a saliency signal,

NOTE Confidence: 0.8711132

00:40:50.890 --> 00:40:52.142 we may want to.

NOTE Confidence: 0.8711132

00:40:52.142 --> 00:40:54.020 Increased opening so that people can

NOTE Confidence: 0.8711132

00:40:54.081 --> 00:40:56.608 learn adaptively in all of these contexts.

NOTE Confidence: 0.8711132

00:40:56.610 --> 00:40:57.522 And so again,

NOTE Confidence: 0.8711132

00:40:57.522 --> 00:40:59.650 I'm not saying that like you know,

NOTE Confidence: 0.8711132

00:40:59.650 --> 00:41:01.891 this is the end all be all dopamine is

NOTE Confidence: 0.8711132

00:41:01.891 --> 00:41:04.135 in lots of projection targets and it

NOTE Confidence: 0.8711132

00:41:04.135 --> 00:41:06.640 does lots of things in different areas.

NOTE Confidence: 0.8711132

00:41:06.640 --> 00:41:08.470 And we're in one single area,

NOTE Confidence: 0.8711132

00:41:08.470 --> 00:41:10.254 but I think kind of taking a step

NOTE Confidence: 0.8711132

00:41:10.254 --> 00:41:12.137 back and thinking about what these

NOTE Confidence: 0.8711132

00:41:12.137 --> 00:41:13.517 domains signatures really mean

NOTE Confidence: 0.8711132

00:41:13.517 --> 00:41:15.284 and what those deficits would

NOTE Confidence: 0.8711132

00:41:15.284 --> 00:41:16.979 mean to a behaving individual,

NOTE Confidence: 0.8711132

00:41:16.980 --> 00:41:19.290 as I think it's really important

NOTE Confidence: 0.8711132

00:41:19.290 --> 00:41:20.445 component of conceptualizing

NOTE Confidence: 0.8711132

00:41:20.445 --> 00:41:22.246 what these you know psychiatric

NOTE Confidence: 0.8711132

00:41:22.246 --> 00:41:24.274 deficits mean to people and how

NOTE Confidence: 0.842202

00:41:24.340 --> 00:41:25.448 to best treat them.

NOTE Confidence: 0.842202

00:41:25.450 --> 00:41:27.010 Anyway, so with that I'll

NOTE Confidence: 0.842202

00:41:27.010 --> 00:41:28.570 end with thanking my lab,

NOTE Confidence: 0.842202

00:41:28.570 --> 00:41:30.130 so Ganesh clue his background

NOTE Confidence: 0.842202

00:41:30.130 --> 00:41:31.378 is in computational psychology,

NOTE Confidence: 0.842202

00:41:31.380 --> 00:41:33.578 so he's like the modeler and he's

NOTE Confidence: 0.842202

00:41:33.578 --> 00:41:35.430 really like driven this you know.

NOTE Confidence: 0.842202

00:41:35.430 --> 00:41:36.990 Together he's a Pavlovian guy.

NOTE Confidence: 0.842202

00:41:36.990 --> 00:41:38.550 I was a reinforcement person.

NOTE Confidence: 0.842202

00:41:38.550 --> 00:41:40.419 I think this was like one of

NOTE Confidence: 0.842202

00:41:40.419 --> 00:41:42.243 those projects that was this great

NOTE Confidence: 0.842202

00:41:42.243 --> 00:41:43.853 synergism between two people who

NOTE Confidence: 0.842202

00:41:43.853 --> 00:41:45.728 just we're really excited about.

NOTE Confidence: 0.842202

00:41:45.730 --> 00:41:47.907 Kind of figuring out what's going on.

NOTE Confidence: 0.842202

00:41:47.910 --> 00:41:49.860 Jennifer, Zachary and Patrick and

NOTE Confidence: 0.842202

00:41:49.860 --> 00:41:51.810 Stephanie were are grad students

NOTE Confidence: 0.842202

00:41:51.874 --> 00:41:53.542 that were working on this project

NOTE Confidence: 0.842202

00:41:53.542 --> 00:41:55.657 and put a lot of time into it.

NOTE Confidence: 0.842202

00:41:55.660 --> 00:41:57.886 Cody Siciliano and Lindsay Ann Lynn

NOTE Confidence: 0.842202

00:41:57.886 --> 00:42:00.945 was was really nice and was helping us

NOTE Confidence: 0.842202

00:42:00.945 --> 00:42:03.207 get the delight these optical sensors

NOTE Confidence: 0.842202

00:42:03.282 --> 00:42:05.543 up and running in the lab fairly

NOTE Confidence: 0.842202

00:42:05.543 --> 00:42:07.459 early in Cody's at optical engineer.

NOTE Confidence: 0.842202

00:42:07.459 --> 00:42:10.164 So he helps a lot at Vanderbilt with

NOTE Confidence: 0.842202

00:42:10.164 --> 00:42:11.948 getting these working correctly,

NOTE Confidence: 0.842202

00:42:11.950 --> 00:42:14.316 validating them an my funding and I

NOTE Confidence: 0.842202

00:42:14.316 --> 00:42:17.020 can take any questions you may have.

NOTE Confidence: 0.842202

00:42:17.020 --> 00:42:18.830 So thank you so much.

NOTE Confidence: 0.8725846

00:42:21.530 --> 00:42:23.130 Thank you so much Aaron.

NOTE Confidence: 0.8725846

00:42:23.130 --> 00:42:25.020 If anybody doesn't want to pipe

NOTE Confidence: 0.8725846

00:42:25.086 --> 00:42:27.228 up with the just asking questions,

NOTE Confidence: 0.8725846

00:42:27.230 --> 00:42:30.093 please put them in the chat and

NOTE Confidence: 0.8725846

00:42:30.093 --> 00:42:33.267 I can read them out for Aaron.

NOTE Confidence: 0.8725846

00:42:33.270 --> 00:42:35.116 Like can I start with one?

NOTE Confidence: 0.8725846

00:42:35.116 --> 00:42:38.356 Go for it. So in terms of those

NOTE Confidence: 0.8725846

00:42:38.356 --> 00:42:39.800 projections you were discussing

NOTE Confidence: 0.8725846

00:42:39.869 --> 00:42:41.867 and you're looking in the core,

NOTE Confidence: 0.8725846

00:42:41.870 --> 00:42:44.152 do you think that just with predictions

NOTE Confidence: 0.8725846

00:42:44.152 --> 00:42:47.045 of what the core versus shell of the

NOTE Confidence: 0.8725846

00:42:47.045 --> 00:42:49.323 incumbents does in activations of the

NOTE Confidence: 0.8725846

00:42:49.323 --> 00:42:51.459 core versus Shell does to behavior?

NOTE Confidence: 0.8725846

00:42:51.460 --> 00:42:53.798 Do you think that one might be

NOTE Confidence: 0.8725846

00:42:53.798 --> 00:42:56.002 more important than the other in

NOTE Confidence: 0.8725846

00:42:56.002 --> 00:42:57.136 the prediction error?

NOTE Confidence: 0.8725846

00:42:57.140 --> 00:42:58.556 This is actually really

NOTE Confidence: 0.8725846

00:42:58.556 --> 00:43:00.326 great question an I should

NOTE Confidence: 0.8017342

00:43:00.330 --> 00:43:01.395 have pasted this.

NOTE Confidence: 0.8017342

00:43:01.395 --> 00:43:03.525 Actually I can do it now.

NOTE Confidence: 0.8017342

00:43:03.530 --> 00:43:06.106 I we have shell data so so.

NOTE Confidence: 0.8017342

00:43:06.110 --> 00:43:09.094 The answer is probably yes in some contexts,

NOTE Confidence: 0.8017342

00:43:09.100 --> 00:43:12.184 although when we we started to

NOTE Confidence: 0.8017342

00:43:12.184 --> 00:43:14.830 look through the shell data.

NOTE Confidence: 0.8017342

00:43:14.830 --> 00:43:17.245 So I just wanted to side when

NOTE Confidence: 0.8017342

00:43:17.245 --> 00:43:19.541 we started to look through the

NOTE Confidence: 0.8017342

00:43:19.541 --> 00:43:21.893 new data or the shell data.

NOTE Confidence: 0.8017342

00:43:21.900 --> 00:43:24.132 It did not look like what

NOTE Confidence: 0.8017342

00:43:24.132 --> 00:43:25.620 I would expect either.

NOTE Confidence: 0.83395291

00:43:27.900 --> 00:43:30.640 Basically. It still doesn't

NOTE Confidence: 0.83395291

00:43:30.640 --> 00:43:33.380 look like prediction error.

NOTE Confidence: 0.83395291

00:43:33.380 --> 00:43:36.026 So we still get a positive

NOTE Confidence: 0.83395291

00:43:36.026 --> 00:43:38.420 domain response to the shock.

NOTE Confidence: 0.83395291

00:43:38.420 --> 00:43:40.800 We get some scaling with stimulus intensity.

NOTE Confidence: 0.83395291

00:43:40.800 --> 00:43:43.848 Not quite as much.

NOTE Confidence: 0.83395291

00:43:43.850 --> 00:43:46.208 People have shown decreases in dopamine

NOTE Confidence: 0.83395291

00:43:46.208 --> 00:43:48.712 and to aversive stimuli and we have

NOTE Confidence: 0.83395291

00:43:48.712 --> 00:43:51.101 been working out why that would be when

NOTE Confidence: 0.83395291

00:43:51.101 --> 00:43:53.285 we aren't seeing them and we think.

NOTE Confidence: 0.83395291

00:43:53.290 --> 00:43:55.162 And so basically we did show

NOTE Confidence: 0.83395291

00:43:55.162 --> 00:43:57.329 decreases in domain in some contexts.

NOTE Confidence: 0.83395291

00:43:57.330 --> 00:43:59.520 Dopamine goes down when animals don't

NOTE Confidence: 0.83395291

00:43:59.520 --> 00:44:02.390 have to do anything or they have to wait.

NOTE Confidence: 0.83395291

00:44:02.390 --> 00:44:04.560 So what we did is we design

NOTE Confidence: 0.83395291

00:44:04.560 --> 00:44:06.299 this other experiment that I'm

NOTE Confidence: 0.83395291

00:44:06.299 --> 00:44:07.775 like really excited about.

NOTE Confidence: 0.83395291

00:44:07.780 --> 00:44:10.615 What we did is we trained animals to know

NOTE Confidence: 0.83395291

00:44:10.615 --> 00:44:13.240 smoker sucrose and then we switched the

NOTE Confidence: 0.83395291

00:44:13.240 --> 00:44:15.588 contingency so that they had to with.

NOTE Confidence: 0.83395291

00:44:15.590 --> 00:44:17.886 Hold a response and wait to get sucrose.

NOTE Confidence: 0.83395291

00:44:17.890 --> 00:44:20.203 So this is kind of like the same reciprocal

NOTE Confidence: 0.83395291

00:44:20.203 --> 00:44:21.929 thing to fear conditioning right?

NOTE Confidence: 0.83395291

00:44:21.930 --> 00:44:22.986 You have a queue.

NOTE Confidence: 0.83395291

00:44:22.986 --> 00:44:25.090 The animal just waits to get shocked.

NOTE Confidence: 0.83395291

00:44:25.090 --> 00:44:26.242 There's nothing they can

NOTE Confidence: 0.83395291

00:44:26.242 --> 00:44:27.394 do during that period.

NOTE Confidence: 0.83395291

00:44:27.400 --> 00:44:28.052 They wait,

NOTE Confidence: 0.83395291

00:44:28.052 --> 00:44:30.008 we see decreases in dopamine to

NOTE Confidence: 0.83395291

00:44:30.008 --> 00:44:31.430 fear conditioning Q and two AQ,

NOTE Confidence: 0.83395291

00:44:31.430 --> 00:44:33.726 where the animal gets sucrose at the end,

NOTE Confidence: 0.83395291

00:44:33.730 --> 00:44:36.794 but they have to wait to do it.

NOTE Confidence: 0.83395291

00:44:36.800 --> 00:44:39.401 And So what we think is happening is a

NOTE Confidence: 0.83395291

00:44:39.401 --> 00:44:41.915 lot of these decreases in domain people

NOTE Confidence: 0.83395291

00:44:41.915 --> 00:44:45.010 have seen or not necessarily just value.

NOTE Confidence: 0.83395291

00:44:45.010 --> 00:44:47.110 They have to do with what animals

NOTE Confidence: 0.83395291

00:44:47.110 --> 00:44:49.091 are doing and what novelty in

NOTE Confidence: 0.83395291

00:44:49.091 --> 00:44:50.781 salience do in an environment

NOTE Confidence: 0.83395291

00:44:50.781 --> 00:44:52.870 is they increase exploration.

NOTE Confidence: 0.83395291

00:44:52.870 --> 00:44:55.229 So if you need to decrease exploration

NOTE Confidence: 0.83395291

00:44:55.229 --> 00:44:57.857 and just wait for something to happen,

NOTE Confidence: 0.83395291

00:44:57.860 --> 00:44:58.934 domain goes down.

NOTE Confidence: 0.83395291

00:44:58.934 --> 00:45:01.440 So we get doping reductions even when

NOTE Confidence: 0.83395291

00:45:01.508 --> 00:45:04.056 the outcome is positive when the task

NOTE Confidence: 0.83395291

00:45:04.056 --> 00:45:06.437 design mimics that of the aversive

NOTE Confidence: 0.83395291

00:45:06.437 --> 00:45:08.867 tasks where people have seen reductions.

NOTE Confidence: 0.83395291

00:45:08.870 --> 00:45:11.174 And a lot of the like you know,

NOTE Confidence: 0.83395291

00:45:11.180 --> 00:45:13.175 there's a lot of great work from

NOTE Confidence: 0.83395291

00:45:13.175 --> 00:45:14.948 like Mitchell White Men looking at

NOTE Confidence: 0.83395291

00:45:14.948 --> 00:45:16.664 aversive like wine in the mouth.

NOTE Confidence: 0.83395291

00:45:16.670 --> 00:45:17.248 It's unavoidable.

NOTE Confidence: 0.83395291

00:45:17.248 --> 00:45:19.560 The animals are just waiting there as well.

NOTE Confidence: 0.83395291

00:45:19.560 --> 00:45:21.288 And so I think there's also

NOTE Confidence: 0.83395291

00:45:21.288 --> 00:45:22.152 differences in relative,

NOTE Confidence: 0.83395291

00:45:22.160 --> 00:45:22.742 you know,

NOTE Confidence: 0.83395291

00:45:22.742 --> 00:45:24.779 in his designs he has positive and

NOTE Confidence: 0.83395291

00:45:24.779 --> 00:45:26.497 negative stimuli in the same task,

NOTE Confidence: 0.83395291

00:45:26.500 --> 00:45:28.132 which are a little bit different

NOTE Confidence: 0.83395291

00:45:28.132 --> 00:45:29.680 than having an animal behaves.

NOTE Confidence: 0.83395291

00:45:29.680 --> 00:45:31.216 So obviously there's there is some

NOTE Confidence: 0.83395291

00:45:31.216 --> 00:45:32.860 sort of value based computation,

NOTE Confidence: 0.83395291

00:45:32.860 --> 00:45:34.588 but we think they're done and

NOTE Confidence: 0.83395291

00:45:34.588 --> 00:45:35.452 really specific context.

NOTE Confidence: 0.90038413

00:45:37.530 --> 00:45:38.790 Thank you.

NOTE Confidence: 0.90038413

00:45:38.790 --> 00:45:43.770 I think the other question go ahead.

NOTE Confidence: 0.90038413

00:45:43.770 --> 00:45:46.374 But they are zoom etiquette.

NOTE Confidence: 0.90038413

00:45:46.374 --> 00:45:48.560 Go ahead, I'll jump in after you.

NOTE Confidence: 0.90038413

00:45:48.560 --> 00:45:50.120 OK, thanks for bringing talker

NOTE Confidence: 0.90038413

00:45:50.120 --> 00:45:51.996 and that was really really cool.

NOTE Confidence: 0.90038413

00:45:51.996 --> 00:45:54.536 So one thing that you can do with

NOTE Confidence: 0.90038413

00:45:54.536 --> 00:45:56.986 these models is sort of see if they

NOTE Confidence: 0.90038413

00:45:56.986 --> 00:45:58.230 can predict particular phenomena

NOTE Confidence: 0.90038413

00:45:58.230 --> 00:46:00.730 and one of the ideas I think that's

NOTE Confidence: 0.90038413

00:46:00.730 --> 00:46:02.298 becoming more and more prevalent

NOTE Confidence: 0.90038413

00:46:02.298 --> 00:46:04.194 about a sort of teleological idea

NOTE Confidence: 0.90038413

00:46:04.194 --> 00:46:05.726 about what the dopamine system

NOTE Confidence: 0.90038413

00:46:05.726 --> 00:46:07.598 might be for is not rewards,

NOTE Confidence: 0.90038413

00:46:07.598 --> 00:46:09.153 not punishments as you've argued,

NOTE Confidence: 0.90038413

00:46:09.153 --> 00:46:10.404 but actually the causal

NOTE Confidence: 0.90038413

00:46:10.404 --> 00:46:11.652 structure of the world.

NOTE Confidence: 0.90038413

00:46:11.652 --> 00:46:13.521 Yeah, and so does your model

NOTE Confidence: 0.90038413

00:46:13.521 --> 00:46:14.765 predict things like sensory

NOTE Confidence: 0.90038413

00:46:14.765 --> 00:46:15.500 preconditioning where?

NOTE Confidence: 0.90038413

00:46:15.500 --> 00:46:16.340 There was

NOTE Confidence: 0.81181043

00:46:16.340 --> 00:46:17.628 no value at all.

NOTE Confidence: 0.81181043

00:46:17.628 --> 00:46:19.238 Initially you use that information

NOTE Confidence: 0.81181043

00:46:19.240 --> 00:46:21.124 later to imbue or impede value.

NOTE Confidence: 0.81181043

00:46:21.124 --> 00:46:23.203 Yes, yes, so actually this is one

NOTE Confidence: 0.81181043

00:46:23.203 --> 00:46:25.349 of the other powers of this model is

NOTE Confidence: 0.81181043

00:46:25.349 --> 00:46:27.610 it can do sensory preconditioning,

NOTE Confidence: 0.81181043

00:46:27.610 --> 00:46:28.194 Layton addition,

NOTE Confidence: 0.81181043

00:46:28.194 --> 00:46:30.530 so these are two things that that even

NOTE Confidence: 0.81181043

00:46:30.589 --> 00:46:32.767 the temporal difference models cannot do,

NOTE Confidence: 0.81181043

00:46:32.770 --> 00:46:35.787 and the problem is dopamine does them.

NOTE Confidence: 0.81181043

00:46:35.790 --> 00:46:37.495 So if dopamine does these

NOTE Confidence: 0.81181043

00:46:37.495 --> 00:46:38.859 in a computational model,

NOTE Confidence: 0.81181043

00:46:38.860 --> 00:46:40.565 can't that cannot be the

NOTE Confidence: 0.81181043

00:46:40.565 --> 00:46:41.929 computation domain is doing,

NOTE Confidence: 0.81181043

00:46:41.930 --> 00:46:44.634 and so we we have our next at

NOTE Confidence: 0.81181043

00:46:44.634 --> 00:46:47.040 once we get this out the door.

NOTE Confidence: 0.81181043

00:46:47.040 --> 00:46:48.744 I'm trying to find my.

NOTE Confidence: 0.81181043

00:46:48.744 --> 00:46:50.450 We haven't started doing sensory

NOTE Confidence: 0.81181043

00:46:50.450 --> 00:46:52.938 preconditioning yet because of the fact that

NOTE Confidence: 0.81181043

00:46:52.938 --> 00:46:56.250 it's a little bit more of a pain in mice,

NOTE Confidence: 0.81181043

00:46:56.250 --> 00:46:58.230 and I think we're going to

NOTE Confidence: 0.81181043

00:46:58.230 --> 00:47:00.000 have to switch to rats.

NOTE Confidence: 0.81181043

00:47:00.000 --> 00:47:02.094 Mice aren't like the best set

NOTE Confidence: 0.81181043

00:47:02.094 --> 00:47:03.750 like attending to things so,

NOTE Confidence: 0.81181043

00:47:03.750 --> 00:47:04.576 so lame.

NOTE Confidence: 0.81181043

00:47:04.576 --> 00:47:06.228 Inhibition is something that

NOTE Confidence: 0.81181043

00:47:06.228 --> 00:47:07.880 our model does do.

NOTE Confidence: 0.81181043

00:47:07.880 --> 00:47:09.560 So late inhibition is actually

NOTE Confidence: 0.81181043

00:47:09.560 --> 00:47:10.904 this really interesting novelty

NOTE Confidence: 0.81181043

00:47:10.904 --> 00:47:12.506 based learning constructs were

NOTE Confidence: 0.81181043

00:47:12.506 --> 00:47:14.118 essentially pre exposed stimuli,

NOTE Confidence: 0.81181043

00:47:14.120 --> 00:47:15.950 acquire values slower than simulated.

NOTE Confidence: 0.81181043

00:47:15.950 --> 00:47:18.218 Have not been pre exposed so familiar

NOTE Confidence: 0.81181043

00:47:18.218 --> 00:47:20.494 stimuli take longer to because you're

NOTE Confidence: 0.81181043

00:47:20.494 --> 00:47:22.559 basically unlearning the no Association.

NOTE Confidence: 0.81181043

00:47:22.560 --> 00:47:24.891 So a lot of these different models

NOTE Confidence: 0.81181043

00:47:24.891 --> 00:47:27.699 you know we brought this up earlier.

NOTE Confidence: 0.81181043

00:47:27.700 --> 00:47:30.269 I was asked about Pierce Hall Macintosh.

NOTE Confidence: 0.81181043

00:47:30.270 --> 00:47:32.562 Like all of these models have

NOTE Confidence: 0.81181043

00:47:32.562 --> 00:47:34.821 added these components to do this

NOTE Confidence: 0.81181043

00:47:34.821 --> 00:47:37.110 and our model does this and the

NOTE Confidence: 0.81181043

00:47:37.110 --> 00:47:38.620 sensory preconditioning.

NOTE Confidence: 0.81181043

00:47:38.620 --> 00:47:40.642 I showed you the dobine goes

NOTE Confidence: 0.81181043

00:47:40.642 --> 00:47:41.990 down to repeated shocks.

NOTE Confidence: 0.81181043

00:47:41.990 --> 00:47:42.354 Um?

NOTE Confidence: 0.81181043

00:47:42.354 --> 00:47:44.902 We can get pre exposed stimuli to

NOTE Confidence: 0.81181043

00:47:44.902 --> 00:47:47.285 have less associative value and

NOTE Confidence: 0.81181043

00:47:47.285 --> 00:47:49.915 what's really interesting is that

NOTE Confidence: 0.81181043

00:47:49.915 --> 00:47:52.751 the dopamine response to these pre

NOTE Confidence: 0.81181043

00:47:52.751 --> 00:47:55.713 exposed stimuli is much lower and it

NOTE Confidence: 0.81181043

00:47:55.713 --> 00:47:58.534 also tracks over the pre exposure period.

NOTE Confidence: 0.81181043

00:47:58.540 --> 00:48:01.380 So these these kind of non value based

NOTE Confidence: 0.81181043

00:48:01.380 --> 00:48:02.898 learning constructs were previous

NOTE Confidence: 0.81181043

00:48:02.898 --> 00:48:05.136 experience is changing the way that

NOTE Confidence: 0.81181043

00:48:05.136 --> 00:48:07.360 stimuli can drive future behavior

NOTE Confidence: 0.81181043

00:48:07.360 --> 00:48:09.715 or sensory preconditioning were two

NOTE Confidence: 0.81181043

00:48:09.715 --> 00:48:11.500 irrelevant simulate form associations

NOTE Confidence: 0.81181043

00:48:11.500 --> 00:48:14.020 that can then be associated later.

NOTE Confidence: 0.81181043

00:48:14.020 --> 00:48:15.012 Our model does it,

NOTE Confidence: 0.81181043

00:48:15.012 --> 00:48:16.500 and dopamine still Maps onto that

NOTE Confidence: 0.81181043

00:48:16.547 --> 00:48:18.545 perceived salience term in those contexts.

NOTE Confidence: 0.81181043

00:48:18.550 --> 00:48:21.380 And this is actually why we were so set on.

NOTE Confidence: 0.81181043

00:48:21.380 --> 00:48:21.934 You know,

NOTE Confidence: 0.81181043

00:48:21.934 --> 00:48:23.319 the first experiments really well

NOTE Confidence: 0.81181043

00:48:23.319 --> 00:48:25.058 it could be other things too,

NOTE Confidence: 0.81181043

00:48:25.060 --> 00:48:26.240 and then we started going

NOTE Confidence: 0.81181043

00:48:26.240 --> 00:48:27.420 into these latent addition and

NOTE Confidence: 0.81181043

00:48:27.471 --> 00:48:28.740 sensory preconditioning ideas,

NOTE Confidence: 0.81181043

00:48:28.740 --> 00:48:30.714 because those really can't be other things.

NOTE Confidence: 0.81181043

00:48:30.720 --> 00:48:31.286 I mean,

NOTE Confidence: 0.81181043

00:48:31.286 --> 00:48:33.550 it could be there's other components of it,

NOTE Confidence: 0.81181043

00:48:33.550 --> 00:48:35.426 but I think it is more strong

NOTE Confidence: 0.81181043

00:48:35.426 --> 00:48:36.660 with the other stuff.

NOTE Confidence: 0.81181043

00:48:36.660 --> 00:48:38.916 It does too, that that's what it's doing.

NOTE Confidence: 0.81181043

00:48:38.920 --> 00:48:40.830 But it's that's a great, I think.

NOTE Confidence: 0.81181043

00:48:40.830 --> 00:48:42.545 Those are like the killer like knife

NOTE Confidence: 0.81181043

00:48:42.545 --> 00:48:44.345 in the coffin experiments, right?

NOTE Confidence: 0.81181043

00:48:44.345 --> 00:48:45.320 Because they just.

NOTE Confidence: 0.81181043

00:48:45.320 --> 00:48:47.270 Those other models cannot do them,

NOTE Confidence: 0.81181043

00:48:47.270 --> 00:48:49.510 so yeah, that's a great great point.

NOTE Confidence: 0.7855291

00:48:50.600 --> 00:48:52.238 I think we had a question,

NOTE Confidence: 0.7855291

00:48:52.240 --> 00:48:54.109 thanks. Those are really great talk here

NOTE Confidence: 0.7855291

00:48:54.109 --> 00:48:56.348 and thanks for taking us through all that.

NOTE Confidence: 0.7855291

00:48:56.350 --> 00:48:58.272 And you have touched on my question

NOTE Confidence: 0.7855291

00:48:58.272 --> 00:48:59.912 a little bit because you started.

NOTE Confidence: 0.7855291

00:48:59.912 --> 00:49:01.556 I mean, even with the default

NOTE Confidence: 0.7855291

00:49:01.556 --> 00:49:02.928 Pomeranians when he starts to

NOTE Confidence: 0.7855291

00:49:02.928 --> 00:49:04.298 look at nucleus accumbens shell.

NOTE Confidence: 0.7855291

00:49:04.300 --> 00:49:06.765 But one thing I was curious about with your

NOTE Confidence: 0.7855291

00:49:06.765 --> 00:49:09.505 model is how how global do you think it is?

NOTE Confidence: 0.7855291

00:49:09.505 --> 00:49:11.695 And you hinted as we talked about the

NOTE Confidence: 0.7855291

00:49:11.695 --> 00:49:13.620 VTA component as well. So you know,

NOTE Confidence: 0.7855291

00:49:13.620 --> 00:49:15.524 going back to some of the Bromberg,

NOTE Confidence: 0.7855291

00:49:15.530 --> 00:49:16.902 Martin work about different VTA

NOTE Confidence: 0.7855291

00:49:16.902 --> 00:49:17.724 neurons responding differently

NOTE Confidence: 0.7855291

00:49:17.724 --> 00:49:18.820 to balance versus silence.

NOTE Confidence: 0.7855291

00:49:18.820 --> 00:49:20.782 You think this Maps onto multiple regions

NOTE Confidence: 0.7855291

00:49:20.782 --> 00:49:22.654 using this sub regions within the.

NOTE Confidence: 0.7855291

00:49:22.660 --> 00:49:24.884 The common score is a global number

NOTE Confidence: 0.7855291

00:49:24.884 --> 00:49:26.797 as a discrete to specific places.

NOTE Confidence: 0.7855291

00:49:26.797 --> 00:49:29.074 Yeah, so this is a great question,

NOTE Confidence: 0.7855291

00:49:29.074 --> 00:49:31.944 so I'm lucky to have married very well in

NOTE Confidence: 0.7855291

00:49:31.944 --> 00:49:35.058 my life and my partner is a two photon guide.

NOTE Confidence: 0.7855291

00:49:35.060 --> 00:49:35.966 When he does,

NOTE Confidence: 0.7855291

00:49:35.966 --> 00:49:38.560 he does 2 photon imaging through grin lenses,

NOTE Confidence: 0.7855291

00:49:38.560 --> 00:49:40.444 cranial windows, you name it and

NOTE Confidence: 0.7855291

00:49:40.444 --> 00:49:42.689 so one thing we're working on now.

NOTE Confidence: 0.7855291

00:49:42.690 --> 00:49:45.091 The really power of of these kind

NOTE Confidence: 0.7855291

00:49:45.091 --> 00:49:46.838 of optical imaging approaches is

NOTE Confidence: 0.7855291

00:49:46.838 --> 00:49:49.099 that you can record as small as

NOTE Confidence: 0.7855291

00:49:49.099 --> 00:49:51.274 you want or as big as you want,

NOTE Confidence: 0.7855291

00:49:51.280 --> 00:49:52.920 and so depending on your.

NOTE Confidence: 0.7855291

00:49:52.920 --> 00:49:54.100 Microscope and resolution so

NOTE Confidence: 0.7855291

00:49:54.100 --> 00:49:55.280 we're moving into these.

NOTE Confidence: 0.7855291

00:49:55.280 --> 00:49:56.760 Either I love slice work.

NOTE Confidence: 0.7855291

00:49:56.760 --> 00:49:58.620 This is like my background so

NOTE Confidence: 0.7855291

00:49:58.620 --> 00:50:00.390 we're moving into these kind of.

NOTE Confidence: 0.7855291

00:50:00.390 --> 00:50:02.352 In vivo in slice imaging approaches

NOTE Confidence: 0.7855291

00:50:02.352 --> 00:50:03.660 to understand better domain

NOTE Confidence: 0.7855291

00:50:03.715 --> 00:50:05.689 regulation across big and small areas.

NOTE Confidence: 0.7855291

00:50:05.690 --> 00:50:07.345 Because the thing about domain

NOTE Confidence: 0.7855291

00:50:07.345 --> 00:50:09.000 neurons that so you know,

NOTE Confidence: 0.7855291

00:50:09.000 --> 00:50:10.655 like kind of weird about

NOTE Confidence: 0.7855291

00:50:10.655 --> 00:50:11.979 them is their projection.

NOTE Confidence: 0.7855291

00:50:11.980 --> 00:50:13.960 Like you know, Arborization is insane.

NOTE Confidence: 0.7855291

00:50:13.960 --> 00:50:16.651 If you fill a single domain on the PTA

NOTE Confidence: 0.7855291

00:50:16.651 --> 00:50:19.586 and look at the field that it populates,

NOTE Confidence: 0.7855291

00:50:19.590 --> 00:50:21.570 it's like half the straight up.

NOTE Confidence: 0.7855291

00:50:21.570 --> 00:50:24.130 But then if you look at these specific

NOTE Confidence: 0.7855291

00:50:24.130 --> 00:50:25.880 release sites on these neurons,

NOTE Confidence: 0.7855291

00:50:25.880 --> 00:50:27.204 it's not releasing dopamine

NOTE Confidence: 0.7855291

00:50:27.204 --> 00:50:28.528 at everywhere every time.

NOTE Confidence: 0.7855291

00:50:28.530 --> 00:50:30.840 It's depending on all these different things.

NOTE Confidence: 0.7855291

00:50:30.840 --> 00:50:31.500 So this.

NOTE Confidence: 0.7855291

00:50:31.500 --> 00:50:33.480 Release structure is so complicated and

NOTE Confidence: 0.7855291

00:50:33.480 --> 00:50:35.833 I think part of the reason people have

NOTE Confidence: 0.7855291

00:50:35.833 --> 00:50:37.668 been so like oh volume transmission

NOTE Confidence: 0.7855291

00:50:37.668 --> 00:50:40.404 is our ability to really look at these

NOTE Confidence: 0.7855291

00:50:40.410 --> 00:50:41.666 granularities between these components.

NOTE Confidence: 0.7855291

00:50:41.666 --> 00:50:43.550 And so we're starting to go,

NOTE Confidence: 0.7855291

00:50:43.550 --> 00:50:44.806 you know, start big.

NOTE Confidence: 0.7855291

00:50:44.806 --> 00:50:45.748 We're just saying,

NOTE Confidence: 0.7855291

00:50:45.750 --> 00:50:46.020 OK,

NOTE Confidence: 0.7855291

00:50:46.020 --> 00:50:48.450 if we do image in a bigger field or

NOTE Confidence: 0.7855291

00:50:48.524 --> 00:50:51.086 with multiple sites at the same time,

NOTE Confidence: 0.7855291

00:50:51.090 --> 00:50:52.250 are we seeing differences?

NOTE Confidence: 0.7855291

00:50:52.250 --> 00:50:54.659 We do see differences so I think there

NOTE Confidence: 0.7855291

00:50:54.659 --> 00:50:56.801 are differences in these VTA neurons in

NOTE Confidence: 0.7855291

00:50:56.801 --> 00:50:59.245 what what they're doing in different areas.

NOTE Confidence: 0.7855291

00:50:59.250 --> 00:51:01.834 So I don't think like all dopamine is.

NOTE Confidence: 0.7855291

00:51:01.840 --> 00:51:04.500 This I think don't mean to the core is this,

NOTE Confidence: 0.7855291

00:51:04.500 --> 00:51:06.068 but it also makes sense that domain

NOTE Confidence: 0.7855291

00:51:06.068 --> 00:51:08.273 in the core that's been tide more to

NOTE Confidence: 0.7855291

00:51:08.273 --> 00:51:10.090 instrumental responding than like the shell.

NOTE Confidence: 0.7855291

00:51:10.090 --> 00:51:11.122 That's like these acquisition.

NOTE Confidence: 0.7855291

00:51:11.122 --> 00:51:12.982 And like Valeant space kind of learning

NOTE Confidence: 0.7855291

00:51:12.982 --> 00:51:14.865 would look like a perceived salience term,

NOTE Confidence: 0.7855291

00:51:14.870 --> 00:51:15.109 right?

NOTE Confidence: 0.7855291

00:51:15.109 --> 00:51:16.782 That makes way more sense for something

NOTE Confidence: 0.7855291

00:51:16.782 --> 00:51:18.330 that is involved in punishment,

NOTE Confidence: 0.7855291

00:51:18.330 --> 00:51:18.862 negative reinforcement,

NOTE Confidence: 0.7855291

00:51:18.862 --> 00:51:19.394 positive reinforcement,

NOTE Confidence: 0.7855291

00:51:19.394 --> 00:51:20.990 which are the same motivated responses,

NOTE Confidence: 0.7855291

00:51:20.990 --> 00:51:21.512 independent violence.

NOTE Confidence: 0.7855291

00:51:21.512 --> 00:51:23.600 So we're doing some more stuff in the

NOTE Confidence: 0.81092066

00:51:23.654 --> 00:51:25.733 shell. You know, I'm not sold that the

NOTE Confidence: 0.81092066

00:51:25.733 --> 00:51:27.974 shell doesn't do value because I don't think

NOTE Confidence: 0.81092066

00:51:27.974 --> 00:51:30.299 foot shocks are the best way to do stuff.

NOTE Confidence: 0.81092066

00:51:30.300 --> 00:51:32.238 I think foot shocks are weird.

NOTE Confidence: 0.81092066

00:51:32.240 --> 00:51:34.166 Stimulus that are really powerful initially,

NOTE Confidence: 0.81092066

00:51:34.170 --> 00:51:35.780 but we didn't really evolve

NOTE Confidence: 0.81092066

00:51:35.780 --> 00:51:37.390 to respond to foot shocks,

NOTE Confidence: 0.81092066

00:51:37.390 --> 00:51:39.412 so we're starting to go in

NOTE Confidence: 0.81092066

00:51:39.412 --> 00:51:41.260 more with things like Quy 9.

NOTE Confidence: 0.81092066

00:51:41.260 --> 00:51:42.235 We've been developing.

NOTE Confidence: 0.81092066

00:51:42.235 --> 00:51:44.800 You can make them liquor lic ometer hot,

NOTE Confidence: 0.81092066

00:51:44.800 --> 00:51:46.726 so we've been doing like thermal,

NOTE Confidence: 0.81092066

00:51:46.730 --> 00:51:48.530 like not pain, but thermal sensitivity

NOTE Confidence: 0.81092066

00:51:48.530 --> 00:51:51.156 curves so that you can look at thermal

NOTE Confidence: 0.81092066

00:51:51.156 --> 00:51:52.524 stimuli that reduced responding.

NOTE Confidence: 0.81092066

00:51:52.530 --> 00:51:54.777 But without this, like foot shot component,

NOTE Confidence: 0.81092066

00:51:54.780 --> 00:51:57.027 so we're trying to parse this out.

NOTE Confidence: 0.81092066

00:51:57.030 --> 00:51:58.302 I'm not sold that,

NOTE Confidence: 0.81092066

00:51:58.302 --> 00:52:00.210 it's just like every dopamine responses

NOTE Confidence: 0.81092066

00:52:00.269 --> 00:52:02.189 that I think it's more complicated,

NOTE Confidence: 0.81092066

00:52:02.190 --> 00:52:04.843 but I think we need better resolution

NOTE Confidence: 0.81092066

00:52:04.843 --> 00:52:06.770 techniques to really parse that.

NOTE Confidence: 0.81092066

00:52:06.770 --> 00:52:08.578 And hopefully over the next I don't know.

NOTE Confidence: 0.81092066

00:52:08.580 --> 00:52:09.745 However long my career last

NOTE Confidence: 0.81092066

00:52:09.745 --> 00:52:11.289 will see will start to get it.

NOTE Confidence: 0.81092066

00:52:11.290 --> 00:52:12.430 Some of those questions and

NOTE Confidence: 0.81092066

00:52:12.430 --> 00:52:13.780 other people are doing that too.

NOTE Confidence: 0.81092066

00:52:13.780 --> 00:52:14.206 I mean,

NOTE Confidence: 0.81092066

00:52:14.206 --> 00:52:15.271 there's some really great work

NOTE Confidence: 0.81092066

00:52:15.271 --> 00:52:16.428 coming out where people are

NOTE Confidence: 0.81092066

00:52:16.428 --> 00:52:17.618 using those like single synapse.

NOTE Confidence: 0.81092066

00:52:17.620 --> 00:52:18.062 You know,

NOTE Confidence: 0.81092066

00:52:18.062 --> 00:52:19.388 you know Uncaging and Eli and

NOTE Confidence: 0.81092066

00:52:19.388 --> 00:52:20.560 all kinds of crazy stuff,

NOTE Confidence: 0.81092066

00:52:20.560 --> 00:52:22.585 so I'm excited to see where the field goes.

NOTE Confidence: 0.81092066

00:52:22.590 --> 00:52:22.815 Yeah,

NOTE Confidence: 0.81092066

00:52:22.815 --> 00:52:23.715 that's really excited how

NOTE Confidence: 0.81092066

00:52:23.715 --> 00:52:24.615 great you are looking

NOTE Confidence: 0.81791025

00:52:24.620 --> 00:52:25.755 at. I'm glad you're looking

NOTE Confidence: 0.81791025

00:52:25.755 --> 00:52:28.010 into it. Sounds like

NOTE Confidence: 0.81791025

00:52:26.660 --> 00:52:29.370 you thought about it already. Definitely

NOTE Confidence: 0.81791025

00:52:28.010 --> 00:52:29.370 I went a little bit. Now

NOTE Confidence: 0.81791025

00:52:29.370 --> 00:52:30.987 the question is just like do we

NOTE Confidence: 0.81791025

00:52:30.987 --> 00:52:32.562 have the tools and then the next

NOTE Confidence: 0.81791025

00:52:32.562 --> 00:52:34.312 thing is do we have the month of

NOTE Confidence: 0.81791025

00:52:34.312 --> 00:52:35.915 money and the people that do it?

NOTE Confidence: 0.81791025

00:52:35.920 --> 00:52:37.720 And so it's like you know.

NOTE Confidence: 0.81791025

00:52:37.720 --> 00:52:39.472 You you see what you can do and

NOTE Confidence: 0.81791025

00:52:39.472 --> 00:52:41.180 with the resources you have so.

NOTE Confidence: 0.8302632

00:52:44.360 --> 00:52:46.504 There is a question in the chat by

NOTE Confidence: 0.8302632

00:52:46.504 --> 00:52:47.892 from Denise, Baghdad and Denise.

NOTE Confidence: 0.8302632

00:52:47.892 --> 00:52:50.183 Do you want to read it out or

NOTE Confidence: 0.8302632

00:52:50.183 --> 00:52:51.856 would you like me to ask it?

NOTE Confidence: 0.7900004

00:52:53.460 --> 00:52:55.780 Good morning, great talk,

NOTE Confidence: 0.7900004

00:52:55.780 --> 00:52:59.840 so I just wanted to understand something.

NOTE Confidence: 0.7900004

00:52:59.840 --> 00:53:03.320 Maybe it's not a great question.

NOTE Confidence: 0.7900004

00:53:03.320 --> 00:53:06.220 Let me just say it.

NOTE Confidence: 0.7900004

00:53:06.220 --> 00:53:08.540 So nicotine reinforcement is

NOTE Confidence: 0.7900004

00:53:08.540 --> 00:53:10.860 generally considered as positive

NOTE Confidence: 0.7900004

00:53:10.860 --> 00:53:12.020 reinforcement enforcement.

NOTE Confidence: 0.7900004

00:53:12.020 --> 00:53:14.340 However, it's also discussed

NOTE Confidence: 0.7900004

00:53:14.340 --> 00:53:16.660 about like the weather.

NOTE Confidence: 0.7900004

00:53:16.660 --> 00:53:18.400 Nicotine reinforcement is

NOTE Confidence: 0.7900004

00:53:18.400 --> 00:53:19.560 negative reinforcement.

NOTE Confidence: 0.7900004

00:53:19.560 --> 00:53:21.944 Becausw of nicotine withdrawal.

NOTE Confidence: 0.7900004

00:53:21.944 --> 00:53:23.168 The compost.

NOTE Confidence: 0.7900004

00:53:23.168 --> 00:53:26.840 Open intake and taking is actually

NOTE Confidence: 0.7900004

00:53:26.840 --> 00:53:29.111 contributes to nicotine reinforcement,

NOTE Confidence: 0.7900004

00:53:29.111 --> 00:53:33.082 so I am interested in whether your

NOTE Confidence: 0.7900004

00:53:33.082 --> 00:53:36.496 model could dissect the positive or

NOTE Confidence: 0.7900004

00:53:36.496 --> 00:53:39.326 negative reinforcement for the nicotine.

NOTE Confidence: 0.7900004

00:53:39.330 --> 00:53:43.730 It's I know it's your.

NOTE Confidence: 0.7900004

00:53:43.730 --> 00:53:46.867 Shock, but this is the one molecule.

NOTE Confidence: 0.7900004

00:53:46.867 --> 00:53:49.429 You know, so could have both.

NOTE Confidence: 0.7900004

00:53:49.430 --> 00:53:51.398 So how we put the fact

NOTE Confidence: 0.7900004

00:53:51.398 --> 00:53:52.710 that's a great question.

NOTE Confidence: 0.7900004

00:53:52.710 --> 00:53:54.886 So one of the things in the addiction

NOTE Confidence: 0.7900004

00:53:54.886 --> 00:53:57.409 field is that there are all these

NOTE Confidence: 0.7900004

00:53:57.409 --> 00:53:59.268 series of negative reinforcement, right?

NOTE Confidence: 0.7900004

00:53:59.268 --> 00:54:00.580 Like opioid withdrawal alcohol,

NOTE Confidence: 0.7900004

00:54:00.580 --> 00:54:00.907 withdrawal.

NOTE Confidence: 0.7900004

00:54:00.907 --> 00:54:02.542 All of these are negative

NOTE Confidence: 0.7900004

00:54:02.542 --> 00:54:03.196 reinforcement concepts,

NOTE Confidence: 0.7900004

00:54:03.200 --> 00:54:04.840 but no one actually does

NOTE Confidence: 0.7900004

00:54:04.840 --> 00:54:05.496 negative reinforcement.

NOTE Confidence: 0.7900004

00:54:05.500 --> 00:54:08.125 We make the inference that is negative

NOTE Confidence: 0.7900004

00:54:08.125 --> 00:54:10.344 reinforcement from the fact that it

NOTE Confidence: 0.7900004

00:54:10.344 --> 00:54:12.064 causes withdrawn animals are taking

NOTE Confidence: 0.7900004

00:54:12.064 --> 00:54:14.597 it with during the withdrawal period.

NOTE Confidence: 0.7900004

00:54:14.600 --> 00:54:15.310 It's OK,

NOTE Confidence: 0.7900004

00:54:15.310 --> 00:54:17.085 so it's a hard question.

NOTE Confidence: 0.7900004

00:54:17.090 --> 00:54:18.746 I think the first step would

NOTE Confidence: 0.7900004

00:54:18.746 --> 00:54:21.758 be to look at how you know if

NOTE Confidence: 0.7900004

00:54:21.758 --> 00:54:23.138 negative reinforcement processes,

NOTE Confidence: 0.7900004

00:54:23.140 --> 00:54:24.564 like for avoiding shocks,

NOTE Confidence: 0.7900004

00:54:24.564 --> 00:54:25.988 are changed after nicotine.

NOTE Confidence: 0.7900004

00:54:25.990 --> 00:54:27.950 So one of the things that we're

NOTE Confidence: 0.7900004

00:54:27.950 --> 00:54:30.003 working with with Cody Siciliano is

NOTE Confidence: 0.7900004

00:54:30.003 --> 00:54:32.301 looking at how alcohol changes animals

NOTE Confidence: 0.7900004

00:54:32.301 --> 00:54:34.179 motivation for negative reinforcers,

NOTE Confidence: 0.7900004

00:54:34.180 --> 00:54:36.665 and so that's like the first step.

NOTE Confidence: 0.7900004

00:54:36.670 --> 00:54:38.674 I think this is like it's

NOTE Confidence: 0.7900004

00:54:38.674 --> 00:54:40.590 a hard thing to parse.

NOTE Confidence: 0.7900004

00:54:40.590 --> 00:54:44.640 Nicotine is also, I know it's like I do.

NOTE Confidence: 0.7900004

00:54:44.640 --> 00:54:45.588 A cholinergic regulation

NOTE Confidence: 0.7900004

00:54:45.588 --> 00:54:46.536 of dopamine terminals.

NOTE Confidence: 0.7900004

00:54:46.540 --> 00:54:48.745 So nicotine is like in my mind,

NOTE Confidence: 0.7900004

00:54:48.750 --> 00:54:50.646 but like we don't do nicotine

NOTE Confidence: 0.7900004

00:54:50.646 --> 00:54:51.278 reinforcement stuff.

NOTE Confidence: 0.7900004

00:54:51.280 --> 00:54:52.950 It's also this really interesting

NOTE Confidence: 0.7900004

00:54:52.950 --> 00:54:54.286 molecule because it regulates

NOTE Confidence: 0.7900004

00:54:54.286 --> 00:54:55.829 like how dopamine is released

NOTE Confidence: 0.7900004

00:54:55.829 --> 00:54:57.274 in a really interesting way.

NOTE Confidence: 0.7900004

00:54:57.280 --> 00:54:58.860 That's not just like up,

NOTE Confidence: 0.7900004

00:54:58.860 --> 00:55:00.440 it's changing like phasic responses

NOTE Confidence: 0.7900004

00:55:00.440 --> 00:55:02.020 to stimuli in the environment.

NOTE Confidence: 0.7900004

00:55:02.020 --> 00:55:03.600 And so thinking about the

NOTE Confidence: 0.7900004

00:55:03.600 --> 00:55:04.548 interaction between those,

NOTE Confidence: 0.7900004

00:55:04.550 --> 00:55:06.596 it's like we're doing some work

NOTE Confidence: 0.7900004

00:55:06.596 --> 00:55:08.345 with sex differences in that

NOTE Confidence: 0.7900004

00:55:08.345 --> 00:55:10.241 system is like so much more

NOTE Confidence: 0.7900004

00:55:10.241 --> 00:55:12.128 complicated than I want it to be.

NOTE Confidence: 0.7900004

00:55:12.130 --> 00:55:13.117 Like with cocaine,

NOTE Confidence: 0.7900004

00:55:13.117 --> 00:55:15.420 it's like it binds to the transporter.

NOTE Confidence: 0.7900004

00:55:15.420 --> 00:55:16.680 Show me goes up.

NOTE Confidence: 0.7900004

00:55:16.680 --> 00:55:19.287 Can we reduce that nicotine is like Oh

NOTE Confidence: 0.7900004

00:55:19.287 --> 00:55:21.541 well in some cases domain goes down

NOTE Confidence: 0.7900004

00:55:21.541 --> 00:55:23.810 some cases it goes up and so it's

NOTE Confidence: 0.7900004

00:55:23.810 --> 00:55:25.190 just such a complicated question.

NOTE Confidence: 0.7900004

00:55:25.190 --> 00:55:27.185 I think the behavioral stuff we do

NOTE Confidence: 0.7900004

00:55:27.185 --> 00:55:29.122 can start to parse how processes and

NOTE Confidence: 0.7900004

00:55:29.122 --> 00:55:30.670 animals are changing by exposure,

NOTE Confidence: 0.7900004

00:55:30.670 --> 00:55:32.602 and I think that's the first step

NOTE Confidence: 0.7900004

00:55:32.602 --> 00:55:34.697 and then the next step is trying.

NOTE Confidence: 0.7900004

00:55:34.700 --> 00:55:36.155 We're trying to develop task

NOTE Confidence: 0.7900004

00:55:36.155 --> 00:55:38.150 to figure out how to do this.

NOTE Confidence: 0.7900004

00:55:38.150 --> 00:55:40.580 So one thing we've been thinking

NOTE Confidence: 0.7900004

00:55:40.580 --> 00:55:41.795 about is doing.

NOTE Confidence: 0.7900004

00:55:41.800 --> 00:55:43.810 Old school drag discrimination so

NOTE Confidence: 0.7900004

00:55:43.810 --> 00:55:45.820 animals will actually press before

NOTE Confidence: 0.7900004

00:55:45.885 --> 00:55:47.621 like to tell you an internal state

NOTE Confidence: 0.7900004

00:55:47.621 --> 00:55:50.005 is X or Y and what we want to do

NOTE Confidence: 0.7900004

00:55:50.005 --> 00:55:51.568 is we've been thinking about doing

NOTE Confidence: 0.7900004

00:55:51.568 --> 00:55:52.801 this with optogenetics, right?

NOTE Confidence: 0.7900004

00:55:52.801 --> 00:55:54.847 Does an optical stimulation of a

NOTE Confidence: 0.7900004

00:55:54.847 --> 00:55:56.574 circuit substitute for X drug X

NOTE Confidence: 0.7900004

00:55:56.574 --> 00:55:58.466 state and I think that some of these

NOTE Confidence: 0.7900004

00:55:58.466 --> 00:56:00.446 withdrawal effects you could see if,

NOTE Confidence: 0.7900004

00:56:00.450 --> 00:56:01.338 like nicotine withdrawal,

NOTE Confidence: 0.7900004

00:56:01.338 --> 00:56:03.410 substituted for some of these other things,

NOTE Confidence: 0.8238095

00:56:03.410 --> 00:56:05.391 and if that was a critical component

NOTE Confidence: 0.8238095

00:56:05.391 --> 00:56:06.960 of reinforcement isn't hard question.

NOTE Confidence: 0.8238095

00:56:06.960 --> 00:56:08.736 I think that that's it can

NOTE Confidence: 0.8238095

00:56:08.736 --> 00:56:09.920 start answering that question,

NOTE Confidence: 0.8238095

00:56:09.920 --> 00:56:12.120 but I've been thinking about this a lot

NOTE Confidence: 0.8238095

00:56:12.120 --> 00:56:14.438 and I'm not sure how to specifically.

NOTE Confidence: 0.8238095

00:56:14.440 --> 00:56:16.533 Parse when an animal is doing something

NOTE Confidence: 0.8238095

00:56:16.533 --> 00:56:18.428 for two things at the same time.

NOTE Confidence: 0.8238095

00:56:18.430 --> 00:56:19.860 What component is what I?

NOTE Confidence: 0.8238095

00:56:19.860 --> 00:56:21.570 I wish I had better answer.

NOTE Confidence: 0.8238095

00:56:21.570 --> 00:56:22.990 I'm excited about the question,

NOTE Confidence: 0.8238095

00:56:22.990 --> 00:56:25.270 but I don't have the answer for you.

NOTE Confidence: 0.6433553

00:56:29.430 --> 00:56:31.642 Is there time for one more Marina

NOTE Confidence: 0.6433553

00:56:31.642 --> 00:56:34.317 or do we directly is that Beth?

NOTE Confidence: 0.6433553

00:56:34.320 --> 00:56:36.670 No, it's less less sorry.

NOTE Confidence: 0.6433553

00:56:36.670 --> 00:56:41.728 I had one too. OK first Liz then Jane.

NOTE Confidence: 0.6433553

00:56:41.730 --> 00:56:43.417 So Aaron, that was such a beautiful

NOTE Confidence: 0.6433553

00:56:43.417 --> 00:56:45.592 talk and I love all the different

NOTE Confidence: 0.6433553

00:56:45.592 --> 00:56:46.642 behavioral experiments that

NOTE Confidence: 0.6433553

00:56:46.642 --> 00:56:48.330 were inspired by your model.

NOTE Confidence: 0.6433553

00:56:48.330 --> 00:56:50.297 And one of the powers of this

NOTE Confidence: 0.6433553

00:56:50.297 --> 00:56:51.838 model is obviously you could

NOTE Confidence: 0.6433553

00:56:51.838 --> 00:56:53.428 take that salience term out.

NOTE Confidence: 0.6433553

00:56:53.430 --> 00:56:55.158 And guess how behavior would be

NOTE Confidence: 0.6433553

00:56:55.158 --> 00:56:57.030 altered by it in the future.

NOTE Confidence: 0.6433553

00:56:57.030 --> 00:56:58.638 So I'm curious whether you're going

NOTE Confidence: 0.6433553

00:56:58.638 --> 00:57:00.435 to start looking at blocking these

NOTE Confidence: 0.6433553

00:57:00.435 --> 00:57:02.115 signals and seeing whether they

NOTE Confidence: 0.6433553

00:57:02.115 --> 00:57:03.734 match the expectations that the

NOTE Confidence: 0.6433553

00:57:03.734 --> 00:57:05.124 model would make in particular,

NOTE Confidence: 0.6433553

00:57:05.130 --> 00:57:06.985 that when you were showing the responses

NOTE Confidence: 0.6433553

00:57:06.985 --> 00:57:09.030 to the light cue during conditioning,

NOTE Confidence: 0.6433553

00:57:09.030 --> 00:57:11.178 which shouldn't be involving any learning

NOTE Confidence: 0.6433553

00:57:11.178 --> 00:57:13.519 like what's the point of that signal?

NOTE Confidence: 0.6433553

00:57:13.520 --> 00:57:15.446 Our behavior could come from it.

NOTE Confidence: 0.6433553

00:57:15.450 --> 00:57:15.770 I'm

NOTE Confidence: 0.8257919

00:57:15.770 --> 00:57:18.338 so excited to just ask me this one.

NOTE Confidence: 0.8257919

00:57:18.340 --> 00:57:20.599 OK, so there's.

NOTE Confidence: 0.8257919

00:57:20.600 --> 00:57:22.154 I'm lazy and I don't want to.

NOTE Confidence: 0.8257919

00:57:22.160 --> 00:57:23.504 Maybe I'll do this why I

NOTE Confidence: 0.8257919

00:57:23.504 --> 00:57:24.840 should have put these in here.

NOTE Confidence: 0.8257919

00:57:24.840 --> 00:57:26.616 I didn't think people were going to have.

NOTE Confidence: 0.8257919

00:57:26.620 --> 00:57:27.958 Not that I didn't think you

NOTE Confidence: 0.8257919

00:57:27.958 --> 00:57:28.850 would have great questions,

NOTE Confidence: 0.8257919

00:57:28.850 --> 00:57:31.550 but I didn't think you guys were to ask

NOTE Confidence: 0.8257919

00:57:31.550 --> 00:57:33.994 questions that I had like specific data for.

NOTE Confidence: 0.8257919

00:57:34.000 --> 00:57:37.430 OK, so two things. First thing first.

NOTE Confidence: 0.8257919

00:57:37.430 --> 00:57:38.630 Wow, that looks terrible.

NOTE Confidence: 0.8257919

00:57:38.630 --> 00:57:40.130 We did do experiments to

NOTE Confidence: 0.8257919

00:57:40.130 --> 00:57:41.090 eliminate this signal.

NOTE Confidence: 0.8257919

00:57:41.090 --> 00:57:43.835 You can see I'm like really crafty with this.

NOTE Confidence: 0.8257919

00:57:43.840 --> 00:57:46.890 This is not my OK so we First things first.

NOTE Confidence: 0.8257919

00:57:46.890 --> 00:57:48.969 Yes, I'll tell you what I think

NOTE Confidence: 0.8257919

00:57:48.969 --> 00:57:51.159 that signal is doing and then two.

NOTE Confidence: 0.8257919

00:57:51.160 --> 00:57:51.770 Well, two.

NOTE Confidence: 0.8257919

00:57:51.770 --> 00:57:53.600 I'll show you the optic Jenner.

NOTE Confidence: 0.8257919

00:57:53.600 --> 00:57:54.554 Other we're not.

NOTE Confidence: 0.8257919

00:57:54.554 --> 00:57:56.144 We're almost done with the

NOTE Confidence: 0.8257919

00:57:56.144 --> 00:57:57.869 Histology so take this with it.

NOTE Confidence: 0.8257919

00:57:57.870 --> 00:58:00.050 This is preliminary preliminary ish.

NOTE Confidence: 0.8257919

00:58:00.050 --> 00:58:01.940 We did two experiments where we

NOTE Confidence: 0.8257919

00:58:01.940 --> 00:58:03.898 inhibited the signal using what our

NOTE Confidence: 0.8257919

00:58:03.898 --> 00:58:05.818 model would predict as the condition

NOTE Confidence: 0.8257919

00:58:05.818 --> 00:58:07.264 response that would dissociate

NOTE Confidence: 0.8257919

00:58:07.264 --> 00:58:09.124 it from these other components.

NOTE Confidence: 0.8257919

00:58:09.130 --> 00:58:10.655 Injected Halo rhodopsin in TH

NOTE Confidence: 0.8257919

00:58:10.655 --> 00:58:12.586 positive neurons in the VTA and

NOTE Confidence: 0.8257919

00:58:12.586 --> 00:58:13.958 then inhibited the terminal.

NOTE Confidence: 0.8257919

00:58:13.960 --> 00:58:15.244 So we're only inhibiting

NOTE Confidence: 0.8257919

00:58:15.244 --> 00:58:16.207 dopamine releasing terminals.

NOTE Confidence: 0.8257919

00:58:16.210 --> 00:58:17.634 Any comments?

NOTE Confidence: 0.8257919

00:58:17.634 --> 00:58:21.906 We either inhibited during a Q

NOTE Confidence: 0.8257919

00:58:21.906 --> 00:58:25.000 predicting fear conditioning.

NOTE Confidence: 0.8257919

00:58:25.000 --> 00:58:26.504 Or we inhibited or?

NOTE Confidence: 0.8257919

00:58:26.504 --> 00:58:28.384 We know we stimulated during.

NOTE Confidence: 0.8257919

00:58:28.390 --> 00:58:30.280 Sorry this is my fault.

NOTE Confidence: 0.8257919

00:58:30.280 --> 00:58:32.160 We stimulated during these are

NOTE Confidence: 0.8257919

00:58:32.160 --> 00:58:33.288 two different things.

NOTE Confidence: 0.8257919

00:58:33.290 --> 00:58:35.606 We stimulated during a fear conditioning

NOTE Confidence: 0.8257919

00:58:35.606 --> 00:58:37.720 Q or we stimulated channelrhodopsin

NOTE Confidence: 0.8257919

00:58:37.720 --> 00:58:40.744 during an emitted but expected shock.

NOTE Confidence: 0.8257919

00:58:40.750 --> 00:58:43.060 If you stimulate and this gets

NOTE Confidence: 0.8257919

00:58:43.060 --> 00:58:44.820 your questions during a Q,

NOTE Confidence: 0.8257919

00:58:44.820 --> 00:58:46.300 that's a fair condition.

NOTE Confidence: 0.8257919

00:58:46.300 --> 00:58:48.520 Q You actually get less freezing,

NOTE Confidence: 0.8257919

00:58:48.520 --> 00:58:50.976 so this is the opposite of what you

NOTE Confidence: 0.8257919

00:58:50.976 --> 00:58:53.328 would expect from associative strength,

NOTE Confidence: 0.8257919

00:58:53.330 --> 00:58:55.180 but it kind of person.

NOTE Confidence: 0.8257919

00:58:55.180 --> 00:58:57.735 We basically points to this question when

NOTE Confidence: 0.8257919

00:58:57.735 --> 00:58:59.990 there's novel stimuli in the environment,

NOTE Confidence: 0.8257919

00:58:59.990 --> 00:59:01.100 you increase exploration.

NOTE Confidence: 0.8257919

00:59:01.100 --> 00:59:02.580 All of our data,

NOTE Confidence: 0.8257919

00:59:02.580 --> 00:59:03.948 like the novel Q.

NOTE Confidence: 0.8257919

00:59:03.948 --> 00:59:06.000 All of our data show that

NOTE Confidence: 0.8257919

00:59:06.086 --> 00:59:07.758 when you add novelty,

NOTE Confidence: 0.8257919

00:59:07.760 --> 00:59:09.950 you increase dopamine and the increased

NOTE Confidence: 0.8257919

00:59:09.950 --> 00:59:12.400 dopamine is associated with more exploration.

NOTE Confidence: 0.8257919

00:59:12.400 --> 00:59:13.459 And less freezing.

NOTE Confidence: 0.8257919

00:59:13.459 --> 00:59:15.224 And so these novelty terms,

NOTE Confidence: 0.8257919

00:59:15.230 --> 00:59:16.855 what they're doing is they're

NOTE Confidence: 0.8257919

00:59:16.855 --> 00:59:18.155 helping animals to adaptively

NOTE Confidence: 0.8257919

00:59:18.155 --> 00:59:19.829 learn by increasing exploration.

NOTE Confidence: 0.8257919

00:59:19.830 --> 00:59:21.600 And like here, decreasing freezing.

NOTE Confidence: 0.8257919

00:59:21.600 --> 00:59:23.370 So in the same animal,

NOTE Confidence: 0.8257919

00:59:23.370 --> 00:59:25.946 the queue that wasn't stimulated has just

NOTE Confidence: 0.8257919

00:59:25.946 --> 00:59:28.330 as much freezing is the wifey group,

NOTE Confidence: 0.8257919

00:59:28.330 --> 00:59:30.738 and when it's stimulated they freeze less

NOTE Confidence: 0.8257919

00:59:30.738 --> 00:59:33.290 and that's what our model would predict.

NOTE Confidence: 0.8257919

00:59:33.290 --> 00:59:35.610 The other thing we did is we show

NOTE Confidence: 0.8257919

00:59:35.610 --> 00:59:37.888 that we can prevent extinction,

NOTE Confidence: 0.8257919

00:59:37.890 --> 00:59:38.949 freezing extinction by

NOTE Confidence: 0.8257919

00:59:38.949 --> 00:59:40.714 stimulating dopamine to the Q,

NOTE Confidence: 0.8257919

00:59:40.720 --> 00:59:43.348 and so we both prevent extinction.

NOTE Confidence: 0.8257919

00:59:43.350 --> 00:59:45.235 We prevent extinction by basically

NOTE Confidence: 0.8257919

00:59:45.235 --> 00:59:47.456 like increasing the salience of that

NOTE Confidence: 0.8257919

00:59:47.456 --> 00:59:49.353 event so that it doesn't go away,

NOTE Confidence: 0.8257919

00:59:49.360 --> 00:59:51.640 which is not the same as you'd expect

NOTE Confidence: 0.8257919

00:59:51.640 --> 00:59:53.699 by these prediction error terms.

NOTE Confidence: 0.8257919

00:59:53.700 --> 00:59:55.338 So what we think is happening

NOTE Confidence: 0.8257919

00:59:55.338 --> 00:59:56.889 is that these novel stimuli

NOTE Confidence: 0.8257919

00:59:56.889 --> 00:59:58.473 are increasing dopamine that

NOTE Confidence: 0.8257919

00:59:58.473 --> 01:00:00.453 increase in dopamine promotes and.

NOTE Confidence: 0.8257919

01:00:00.460 --> 01:00:01.136 Exploration term,

NOTE Confidence: 0.8257919

01:00:01.136 --> 01:00:04.300 we also did some like deep lab cut based,

NOTE Confidence: 0.8257919

01:00:04.300 --> 01:00:04.998 you know,

NOTE Confidence: 0.8257919

01:00:04.998 --> 01:00:06.394 machine learning algorithms to

NOTE Confidence: 0.8257919

01:00:06.394 --> 01:00:07.790 look at orienting responses.

NOTE Confidence: 0.8257919

01:00:07.790 --> 01:00:09.182 It's not associated with

NOTE Confidence: 0.8257919

01:00:09.182 --> 01:00:10.226 general motor activity,

NOTE Confidence: 0.8257919

01:00:10.230 --> 01:00:11.622 it's associated with orientation

NOTE Confidence: 0.8257919

01:00:11.622 --> 01:00:13.014 towards the novel stimulus.

NOTE Confidence: 0.8432272

01:00:13.020 --> 01:00:15.162 And so we think that these these

NOTE Confidence: 0.8432272

01:00:15.162 --> 01:00:17.049 this saliency term in the Commons

NOTE Confidence: 0.8432272

01:00:17.049 --> 01:00:19.149 is changing the way the animals are

NOTE Confidence: 0.8432272

01:00:19.218 --> 01:00:20.926 interacting with the environment

NOTE Confidence: 0.8432272

01:00:20.926 --> 01:00:23.488 rather than just the associated value.

NOTE Confidence: 0.8432272

01:00:23.490 --> 01:00:25.688 But the problem is these are such

NOTE Confidence: 0.8432272

01:00:25.688 --> 01:00:27.680 complex things to dissociate that.

NOTE Confidence: 0.8432272

01:00:27.680 --> 01:00:29.455 I understand why people solve

NOTE Confidence: 0.8432272

01:00:29.455 --> 01:00:30.875 the data before instead.

NOTE Confidence: 0.8432272

01:00:30.880 --> 01:00:33.016 Oh, it's that balance goes up to rewards,

NOTE Confidence: 0.8432272

01:00:33.020 --> 01:00:34.882 goes down to a fear conditioning Q

NOTE Confidence: 0.8432272

01:00:34.882 --> 01:00:36.750 that looks like violence to me too.

NOTE Confidence: 0.8432272

01:00:36.750 --> 01:00:38.352 You only start to see that

NOTE Confidence: 0.8432272

01:00:38.352 --> 01:00:39.420 it can't be balanced.

NOTE Confidence: 0.8432272

01:00:39.420 --> 01:00:41.044 When you do these kind of really

NOTE Confidence: 0.8432272

01:00:41.044 --> 01:00:42.708 in the weeds like someone showed

NOTE Confidence: 0.8432272

01:00:42.708 --> 01:00:44.223 this in 1950 in psychology,

NOTE Confidence: 0.8432272

01:00:44.230 --> 01:00:46.225 we're gonna do this again with optogenetics

NOTE Confidence: 0.8432272

01:00:46.225 --> 01:00:47.968 kinds of experiments which I don't know.

NOTE Confidence: 0.8432272

01:00:47.970 --> 01:00:49.839 I think those are the fun experiments,

NOTE Confidence: 0.8432272

01:00:49.840 --> 01:00:51.440 but does that answer your question?

NOTE Confidence: 0.8432272

01:00:51.440 --> 01:00:52.508 Yes, thank you, awesome.

NOTE Confidence: 0.80182445

01:00:52.510 --> 01:00:55.310 I think James next and then Rick.

NOTE Confidence: 0.80182445

01:00:55.310 --> 01:00:58.748 Hi that was a great talk.

NOTE Confidence: 0.80182445

01:00:58.748 --> 01:01:02.359 So my question is.

NOTE Confidence: 0.80182445

01:01:02.360 --> 01:01:04.650 You talk about increasing dopamine,

NOTE Confidence: 0.80182445

01:01:04.650 --> 01:01:07.681 and in most of your experiments where

NOTE Confidence: 0.80182445

01:01:07.681 --> 01:01:09.670 you're actually measuring dopamine,

NOTE Confidence: 0.80182445

01:01:09.670 --> 01:01:12.400 you're looking at.

NOTE Confidence: 0.80182445

01:01:12.400 --> 01:01:15.595 Using Delight an if you go back to the

NOTE Confidence: 0.80182445

01:01:15.595 --> 01:01:18.658 not the old psychology experiments,

NOTE Confidence: 0.80182445

01:01:18.660 --> 01:01:20.890 but the 80s dopamine literature.

NOTE Confidence: 0.80182445

01:01:20.890 --> 01:01:23.578 People think about tonic versus phasic,

NOTE Confidence: 0.80182445

01:01:23.580 --> 01:01:26.457 dopamine and a lot of your experiments

NOTE Confidence: 0.80182445

01:01:26.457 --> 01:01:29.687 seem to be focused more on what

NOTE Confidence: 0.80182445

01:01:29.687 --> 01:01:32.067 the phasic dopamine signal is.

NOTE Confidence: 0.80182445

01:01:32.070 --> 01:01:34.748 An I'm wondering whether you have

NOTE Confidence: 0.80182445

01:01:34.750 --> 01:01:37.516 some way that you can simultaneously

NOTE Confidence: 0.80182445

01:01:37.516 --> 01:01:40.301 look at dopamine tone because it

NOTE Confidence: 0.80182445

01:01:40.301 --> 01:01:42.863 may be that things like novelty.

NOTE Confidence: 0.80182445

01:01:42.870 --> 01:01:44.712 Might actually be linked to some

NOTE Confidence: 0.80182445

01:01:44.712 --> 01:01:47.142 of those and you get you know

NOTE Confidence: 0.80182445

01:01:47.142 --> 01:01:48.650 interactions between the two,

NOTE Confidence: 0.80182445

01:01:48.650 --> 01:01:51.030 and you know when you're you're seeing

NOTE Confidence: 0.80182445

01:01:51.030 --> 01:01:52.730 your increase with the delight.

NOTE Confidence: 0.80182445

01:01:52.730 --> 01:01:54.430 What baseline is that on?

NOTE Confidence: 0.80182445

01:01:54.430 --> 01:01:55.110 This is,

NOTE Confidence: 0.80182445

01:01:55.110 --> 01:01:56.470 I'm like you guys

NOTE Confidence: 0.8477508

01:01:56.470 --> 01:01:58.170 are like making my day.

NOTE Confidence: 0.8477508

01:01:58.170 --> 01:02:00.210 I have like I'm this is

NOTE Confidence: 0.8477508

01:02:00.210 --> 01:02:01.570 such a great question.

NOTE Confidence: 0.8477508

01:02:01.570 --> 01:02:04.290 So this is like our first like thing.

NOTE Confidence: 0.8477508

01:02:04.290 --> 01:02:05.990 We're getting out the door.

NOTE Confidence: 0.8477508

01:02:05.990 --> 01:02:08.978 We have a bunch of extra data where what

NOTE Confidence: 0.8477508

01:02:08.978 --> 01:02:11.766 we've been doing and this is the thing.

NOTE Confidence: 0.8477508

01:02:11.770 --> 01:02:13.120 OK, so voltammetry.

NOTE Confidence: 0.8477508

01:02:13.120 --> 01:02:14.470 Is background subtracted?

NOTE Confidence: 0.8477508

01:02:14.470 --> 01:02:16.906 So you can't really get both tonan,

NOTE Confidence: 0.8477508

01:02:16.910 --> 01:02:18.998 phasic stuff in the same experiment.

NOTE Confidence: 0.8477508

01:02:19.000 --> 01:02:21.100 So what people historically done as

NOTE Confidence: 0.8477508

01:02:21.100 --> 01:02:22.554 they said, microanalysis histone,

NOTE Confidence: 0.8477508

01:02:22.554 --> 01:02:24.439 gigha Ruth and voltammetry is

NOTE Confidence: 0.8477508

01:02:24.439 --> 01:02:26.678 is phasic an my the 80s domain.

NOTE Confidence: 0.8477508

01:02:26.680 --> 01:02:28.666 Literatures like where I started my

NOTE Confidence: 0.8477508

01:02:28.666 --> 01:02:31.218 career so I'm very excited about that.

NOTE Confidence: 0.8477508

01:02:31.220 --> 01:02:33.772 Do you like this kind of nice because

NOTE Confidence: 0.8477508

01:02:33.772 --> 01:02:36.031 you have some photobleaching but you

NOTE Confidence: 0.8477508

01:02:36.031 --> 01:02:38.756 can control for that and you don't

NOTE Confidence: 0.8477508

01:02:38.756 --> 01:02:41.031 know what the the problem with it

NOTE Confidence: 0.8477508

01:02:41.031 --> 01:02:43.510 is that you don't know the number.

NOTE Confidence: 0.8477508

01:02:43.510 --> 01:02:45.617 So with microdialysis you get an amount.

NOTE Confidence: 0.8477508

01:02:45.620 --> 01:02:47.420 With voltammetry you calibrate your probe,

NOTE Confidence: 0.8477508

01:02:47.420 --> 01:02:50.710 you have an estimated amount with delight.

NOTE Confidence: 0.8477508

01:02:50.710 --> 01:02:52.642 I haven't found a great way to

NOTE Confidence: 0.8477508

01:02:52.642 --> 01:02:54.378 figure out what the number is,

NOTE Confidence: 0.8477508

01:02:54.380 --> 01:02:56.642 but you can look at relative

NOTE Confidence: 0.8477508

01:02:56.642 --> 01:02:58.150 changes over the session.

NOTE Confidence: 0.8477508

01:02:58.150 --> 01:03:00.526 I don't have this data up and is easier

NOTE Confidence: 0.8477508

01:03:00.526 --> 01:03:02.451 way because we're putting it into

NOTE Confidence: 0.8477508

01:03:02.451 --> 01:03:04.889 something so we have a manuscript that

NOTE Confidence: 0.8477508

01:03:04.889 --> 01:03:07.211 we're getting together and its focus

NOTE Confidence: 0.8477508

01:03:07.211 --> 01:03:09.630 on novelty based changes and joking signals,

NOTE Confidence: 0.8477508

01:03:09.630 --> 01:03:12.246 and so it's focused on Lane in addition,

NOTE Confidence: 0.8477508

01:03:12.250 --> 01:03:14.158 But what we're looking at is

NOTE Confidence: 0.8477508

01:03:14.158 --> 01:03:15.430 the phasic response relative

NOTE Confidence: 0.8477508

01:03:15.493 --> 01:03:17.168 to longer changes in dopamine,

NOTE Confidence: 0.8477508

01:03:17.170 --> 01:03:19.642 and I don't want to call it tone

NOTE Confidence: 0.8477508

01:03:19.642 --> 01:03:21.768 because it's over like 10 minutes.

NOTE Confidence: 0.8477508

01:03:21.770 --> 01:03:22.724 Not like ours,

NOTE Confidence: 0.8477508

01:03:22.724 --> 01:03:24.632 but it's definitely not what you

NOTE Confidence: 0.8477508

01:03:24.632 --> 01:03:26.690 would call a phasic fast response.

NOTE Confidence: 0.8477508

01:03:26.690 --> 01:03:28.790 What novelty in the environment does?

NOTE Confidence: 0.8477508

01:03:28.790 --> 01:03:30.668 Is it increases that phasic response?

NOTE Confidence: 0.8477508

01:03:30.670 --> 01:03:32.230 But then it does it.

NOTE Confidence: 0.8477508

01:03:32.230 --> 01:03:33.800 The baseline is much higher.

NOTE Confidence: 0.8477508

01:03:33.800 --> 01:03:36.000 So what you have is this shift and

NOTE Confidence: 0.8477508

01:03:36.000 --> 01:03:38.394 what we think is happening is that

NOTE Confidence: 0.8477508

01:03:38.394 --> 01:03:40.825 the novelty is changing the state of

NOTE Confidence: 0.8477508

01:03:40.825 --> 01:03:43.185 the system so that if the next thing

NOTE Confidence: 0.8477508

01:03:43.190 --> 01:03:44.715 that's encountered in that situation

NOTE Confidence: 0.8477508

01:03:44.715 --> 01:03:46.630 the domain response will be bigger.

NOTE Confidence: 0.8477508

01:03:46.630 --> 01:03:48.793 Now one of the things I've always

NOTE Confidence: 0.8477508

01:03:48.793 --> 01:03:50.670 been interested in over my career

NOTE Confidence: 0.8477508

01:03:50.670 --> 01:03:52.749 is what matters for the animal that

NOTE Confidence: 0.8477508

01:03:52.809 --> 01:03:54.765 change from baseline or the peak.

NOTE Confidence: 0.8477508

01:03:54.770 --> 01:03:57.266 And so we're trying to get into that.

NOTE Confidence: 0.8477508

01:03:57.270 --> 01:03:59.734 Now to say like, OK, that increasing.

NOTE Confidence: 0.8477508

01:03:59.734 --> 01:04:02.863 Slide does that just increase the peak?

NOTE Confidence: 0.8477508

01:04:02.870 --> 01:04:05.246 Or does that actually still amplify

NOTE Confidence: 0.8477508

01:04:05.246 --> 01:04:08.733 more this signal to noise and so these

NOTE Confidence: 0.8477508

01:04:08.733 --> 01:04:11.013 novelty terms are definitely changing.

NOTE Confidence: 0.8477508

01:04:11.020 --> 01:04:12.832 What I would call.

NOTE Confidence: 0.8477508

01:04:12.832 --> 01:04:14.644 I don't want to,

NOTE Confidence: 0.8477508

01:04:14.650 --> 01:04:16.340 but they are definitely changing

NOTE Confidence: 0.8477508

01:04:16.340 --> 01:04:18.030 these slower baseline fluctuations in

NOTE Confidence: 0.8477508

01:04:18.082 --> 01:04:19.870 dopamine over longer periods of time,

NOTE Confidence: 0.8477508

01:04:19.870 --> 01:04:21.760 and we think that's really important

NOTE Confidence: 0.8477508

01:04:21.760 --> 01:04:23.750 for the effects of novelty on

NOTE Confidence: 0.8477508

01:04:23.750 --> 01:04:25.086 other types of learning,

NOTE Confidence: 0.8477508

01:04:25.090 --> 01:04:26.390 and so this dopamine,

NOTE Confidence: 0.8477508

01:04:26.390 --> 01:04:27.040 perceived salience,

NOTE Confidence: 0.8477508

01:04:27.040 --> 01:04:28.996 perceived failings is influenced by novelty,

NOTE Confidence: 0.8477508

01:04:29.000 --> 01:04:30.630 so anything that changes novelty

NOTE Confidence: 0.8477508

01:04:30.630 --> 01:04:32.260 will change this as well,

NOTE Confidence: 0.8477508

01:04:32.260 --> 01:04:34.432 and so it's really important in

NOTE Confidence: 0.8477508

01:04:34.432 --> 01:04:35.880 these novelty based learning

NOTE Confidence: 0.8477508

01:04:35.950 --> 01:04:38.064 things on these both slow and fast

NOTE Confidence: 0.8477508

01:04:38.064 --> 01:04:39.760 timescales in a way that is,

NOTE Confidence: 0.8477508

01:04:39.760 --> 01:04:40.378 I think,

NOTE Confidence: 0.8477508

01:04:40.378 --> 01:04:42.232 consistent with what people have seen

NOTE Confidence: 0.8477508

01:04:42.232 --> 01:04:43.669 with microdialysis and voltammetry,

NOTE Confidence: 0.8477508

01:04:43.670 --> 01:04:46.250 but in a more you are able to more granularly

NOTE Confidence: 0.861912214285714

01:04:46.308 --> 01:04:48.070 relate them with this, But again,

NOTE Confidence: 0.861912214285714

01:04:48.070 --> 01:04:50.320 you don't have the amount, so I kind of,

NOTE Confidence: 0.861912214285714

01:04:50.320 --> 01:04:52.085 you know, it's hard because there's no

NOTE Confidence: 0.861912214285714

01:04:52.085 --> 01:04:53.570 like calibration like you can't say,

NOTE Confidence: 0.861912214285714

01:04:53.570 --> 01:04:54.820 oh, this is the amount,

NOTE Confidence: 0.861912214285714

01:04:54.820 --> 01:04:56.521 and I think that's where I hesitate

NOTE Confidence: 0.861912214285714

01:04:56.521 --> 01:04:58.567 a little bit to make these really

NOTE Confidence: 0.861912214285714

01:04:58.567 --> 01:05:00.142 strong conclusions about like what.

NOTE Confidence: 0.861912214285714

01:05:00.150 --> 01:05:02.214 It is, I know that it's changed from

NOTE Confidence: 0.861912214285714

01:05:02.214 --> 01:05:03.890 the minute one of this session.

NOTE Confidence: 0.861912214285714

01:05:03.890 --> 01:05:06.018 The question is like exactly what is that?

NOTE Confidence: 0.861912214285714

01:05:06.020 --> 01:05:07.980 But there are those changes and I think

NOTE Confidence: 0.861912214285714

01:05:07.980 --> 01:05:09.758 that's a great point that people.

NOTE Confidence: 0.861912214285714

01:05:09.760 --> 01:05:12.118 I think a lot of people have gone into

NOTE Confidence: 0.861912214285714

01:05:12.118 --> 01:05:14.706 these kind of optical measurements and they.

NOTE Confidence: 0.861912214285714

01:05:14.710 --> 01:05:15.901 That was ignored,

NOTE Confidence: 0.861912214285714

01:05:15.901 --> 01:05:18.680 but they're not necessarily rooted in these,

NOTE Confidence: 0.861912214285714

01:05:18.680 --> 01:05:19.476 like microdialysis.

NOTE Confidence: 0.861912214285714

01:05:19.476 --> 01:05:20.670 Will Tanistry fields,

NOTE Confidence: 0.861912214285714

01:05:20.670 --> 01:05:22.908 and so they don't understand that

NOTE Confidence: 0.861912214285714

01:05:22.908 --> 01:05:26.133 there has been a ton of work parsing

NOTE Confidence: 0.861912214285714

01:05:26.133 --> 01:05:28.203 what these tonic changes mean?

NOTE Confidence: 0.861912214285714

01:05:28.210 --> 01:05:30.658 How tonic dopamine is regulated relative

NOTE Confidence: 0.861912214285714

01:05:30.658 --> 01:05:33.370 to like fast release like the domain

NOTE Confidence: 0.8083617

01:05:33.370 --> 01:05:35.350 transporters? My favorite protein because

NOTE Confidence: 0.8083617

01:05:35.350 --> 01:05:38.932 I guess the question I guess I'm asking is,

NOTE Confidence: 0.8083617

01:05:38.932 --> 01:05:41.739 would you see some more reward evidence

NOTE Confidence: 0.8083617

01:05:41.739 --> 01:05:44.641 of more reward prediction error if

NOTE Confidence: 0.8083617

01:05:44.641 --> 01:05:47.061 you somehow subtracted what the?

NOTE Confidence: 0.8083617

01:05:47.070 --> 01:05:49.950 Basil Change is an are you missing some

NOTE Confidence: 0.8083617

01:05:49.950 --> 01:05:52.110 of that? Because your tonic salience?

NOTE Confidence: 0.8083617

01:05:52.110 --> 01:05:55.441 I mean, you started out talking a lot about

NOTE Confidence: 0.8083617

01:05:55.441 --> 01:05:58.228 how dopamine could be doing this and that,

NOTE Confidence: 0.8083617

01:05:58.230 --> 01:06:01.470 but it also could be doing all of it.

NOTE Confidence: 0.8083617

01:06:01.470 --> 01:06:03.630 You know it's not mutually exclusive.

NOTE Confidence: 0.8083617

01:06:03.630 --> 01:06:04.710 It could be.

NOTE Confidence: 0.8695758

01:06:04.710 --> 01:06:06.510 It could be let me.

NOTE Confidence: 0.8695758

01:06:06.510 --> 01:06:08.806 I do have a data that answers

NOTE Confidence: 0.8695758

01:06:08.806 --> 01:06:10.650 that question because actually a

NOTE Confidence: 0.8695758

01:06:10.650 --> 01:06:12.625 really astute reviewer asked us.

NOTE Confidence: 0.8695758

01:06:12.630 --> 01:06:16.728 Now I need to find it. It wasn't me.

NOTE Confidence: 0.8695758

01:06:16.730 --> 01:06:18.476 They they they asked us saying,

NOTE Confidence: 0.8695758

01:06:18.480 --> 01:06:20.524 oh, there it is, we did this,

NOTE Confidence: 0.8695758

01:06:20.530 --> 01:06:22.276 so this is actually a really,

NOTE Confidence: 0.8695758

01:06:22.280 --> 01:06:23.153 really good question.

NOTE Confidence: 0.8695758

01:06:23.153 --> 01:06:24.608 Why is this coming up?

NOTE Confidence: 0.8695758

01:06:24.610 --> 01:06:27.238 Oh I'm like not looking at the right file.

NOTE Confidence: 0.8695758

01:06:27.240 --> 01:06:29.580 Maybe if I can get it in like

NOTE Confidence: 0.8695758

01:06:29.580 --> 01:06:31.335 2 seconds I'm going to write,

NOTE Confidence: 0.8695758

01:06:31.335 --> 01:06:33.105 But basically we did what you

NOTE Confidence: 0.8695758

01:06:33.105 --> 01:06:34.829 your question is a good one.

NOTE Confidence: 0.8695758

01:06:34.830 --> 01:06:37.458 I think one of the things that they ask,

NOTE Confidence: 0.8695758

01:06:37.460 --> 01:06:38.920 which is a great question.

NOTE Confidence: 0.8695758

01:06:38.920 --> 01:06:40.380 We'd already been thinking about

NOTE Confidence: 0.8695758

01:06:40.380 --> 01:06:42.698 this so we were like, OK, cool was.

NOTE Confidence: 0.8695758

01:06:42.698 --> 01:06:44.700 If these changes in baseline are the

NOTE Confidence: 0.8695758

01:06:44.766 --> 01:06:46.656 reason that we don't see changes.

NOTE Confidence: 0.8695758

01:06:46.660 --> 01:06:50.635 In in a, let's see file new release.

NOTE Confidence: 0.8695758

01:06:50.640 --> 01:06:55.420 All these will be in here now. Insert.

NOTE Confidence: 0.8695758

01:06:55.420 --> 01:07:01.448 Side OK. OK, So what we did here?

NOTE Confidence: 0.8695758

01:07:01.450 --> 01:07:03.598 Is we had that repeated shock

NOTE Confidence: 0.8695758

01:07:03.598 --> 01:07:05.030 experiment and their question

NOTE Confidence: 0.8695758

01:07:05.096 --> 01:07:06.979 was kind of what yours is like.

NOTE Confidence: 0.8695758

01:07:06.980 --> 01:07:09.248 Well, maybe the difference is the baseline,

NOTE Confidence: 0.8695758

01:07:09.250 --> 01:07:11.434 like the baseline is changing overtime

NOTE Confidence: 0.8695758

01:07:11.434 --> 01:07:13.895 and so we calculated the shocks in

NOTE Confidence: 0.8695758

01:07:13.895 --> 01:07:16.093 the original stuff I showed from like

NOTE Confidence: 0.8695758

01:07:16.161 --> 01:07:18.142 a 2 second window before the event

NOTE Confidence: 0.8695758

01:07:18.142 --> 01:07:20.252 and then we went back and calculated

NOTE Confidence: 0.8695758

01:07:20.252 --> 01:07:22.523 all the shocks from a global baseline

NOTE Confidence: 0.8695758

01:07:22.523 --> 01:07:24.847 at the very beginning of each trial.

NOTE Confidence: 0.8695758

01:07:24.850 --> 01:07:26.800 And what we found is that

NOTE Confidence: 0.8695758

01:07:26.800 --> 01:07:28.100 the data is correlated,

NOTE Confidence: 0.8695758

01:07:28.100 --> 01:07:29.296 like very highly correlated.

NOTE Confidence: 0.8695758

01:07:29.296 --> 01:07:32.110 And if we look at the baseline change.

NOTE Confidence: 0.8695758

01:07:32.110 --> 01:07:33.965 Over that trial it is not changing,

NOTE Confidence: 0.8695758

01:07:33.970 --> 01:07:35.825 so it can't explain all of it.

NOTE Confidence: 0.8695758

01:07:35.830 --> 01:07:36.571 Like I understand,

NOTE Confidence: 0.8695758

01:07:36.571 --> 01:07:38.922 I do agree that there is a lot of

NOTE Confidence: 0.8695758

01:07:38.922 --> 01:07:40.602 baseline stuff that's this where we

NOTE Confidence: 0.8695758

01:07:40.602 --> 01:07:43.029 are like kind of taking out here that I

NOTE Confidence: 0.8695758

01:07:43.029 --> 01:07:44.826 think does paint a more complex picture,

NOTE Confidence: 0.8695758

01:07:44.826 --> 01:07:46.965 but I think for a lot of these

NOTE Confidence: 0.8695758

01:07:46.965 --> 01:07:48.340 things that would say OK,

NOTE Confidence: 0.8695758

01:07:48.340 --> 01:07:49.930 this is definitely not our PE.

NOTE Confidence: 0.8695758

01:07:49.930 --> 01:07:51.562 The baseline is not the factor

NOTE Confidence: 0.8695758

01:07:51.562 --> 01:07:52.860 that's driving all of it,

NOTE Confidence: 0.8695758

01:07:52.860 --> 01:07:54.390 but I think that's something actually

NOTE Confidence: 0.8695758

01:07:54.390 --> 01:07:55.714 that people should be thinking

NOTE Confidence: 0.8695758

01:07:55.714 --> 01:07:57.268 about in these papers and everyone

NOTE Confidence: 0.8695758

01:07:57.268 --> 01:07:58.928 does imaging now and they're all

NOTE Confidence: 0.8695758

01:07:58.928 --> 01:08:00.040 doing everything is baseline,

NOTE Confidence: 0.8695758

01:08:00.040 --> 01:08:01.415 But there's like slower changes

NOTE Confidence: 0.8695758

01:08:01.415 --> 01:08:03.229 that are totally left out of that.

NOTE Confidence: 0.8695758

01:08:03.230 --> 01:08:04.904 They're going to change the way

NOTE Confidence: 0.8695758

01:08:04.904 --> 01:08:06.020 you interpret the data.

NOTE Confidence: 0.8695758

01:08:06.020 --> 01:08:07.956 But that's I mean it's a great question.

NOTE Confidence: 0.8695758

01:08:07.960 --> 01:08:09.430 It will look into this more

NOTE Confidence: 0.8695758

01:08:09.430 --> 01:08:10.880 'cause I think maybe it does.

NOTE Confidence: 0.8695758

01:08:10.880 --> 01:08:12.926 All of that is totally reasonable.

NOTE Confidence: 0.8695758

01:08:12.930 --> 01:08:14.722 Explanation and it might be like nice at

NOTE Confidence: 0.8695758

01:08:14.722 --> 01:08:16.376 a different synapses and the same area,

NOTE Confidence: 0.8695758

01:08:16.380 --> 01:08:17.990 and so like how to parse those.

NOTE Confidence: 0.8695758

01:08:17.990 --> 01:08:18.910 I think it's important.

NOTE Confidence: 0.85778123

01:08:21.240 --> 01:08:23.114 Last question from Rick.

NOTE Confidence: 0.85778123

01:08:23.114 --> 01:08:24.660 The outstanding thank you.

NOTE Confidence: 0.85778123

01:08:24.660 --> 01:08:26.585 Very much so this is I'm not

NOTE Confidence: 0.85778123

01:08:26.585 --> 01:08:28.298 sure exactly this question,

NOTE Confidence: 0.85778123

01:08:28.300 --> 01:08:30.280 but since there's so much regulation

NOTE Confidence: 0.85778123

01:08:30.280 --> 01:08:32.576 and release at terminals Strike and dip

NOTE Confidence: 0.85778123

01:08:32.576 --> 01:08:34.412 compared to mean cell body activity,

NOTE Confidence: 0.85778123

01:08:34.420 --> 01:08:36.346 do you think that other neurotransmitters

NOTE Confidence: 0.85778123

01:08:36.346 --> 01:08:37.636 responsible for the specific

NOTE Confidence: 0.85778123

01:08:37.636 --> 01:08:39.216 components of your learning model

NOTE Confidence: 0.85778123

01:08:39.216 --> 01:08:41.100 and like dopamine release the end

NOTE Confidence: 0.85778123

01:08:41.163 --> 01:08:42.792 result and integration of those?

NOTE Confidence: 0.85778123

01:08:42.792 --> 01:08:44.726 And can you speak this one?

NOTE Confidence: 0.85778123

01:08:44.726 --> 01:08:47.296 I can think of right off the bat.

NOTE Confidence: 0.85778123

01:08:47.300 --> 01:08:49.498 So one thing we think is really

NOTE Confidence: 0.85778123

01:08:49.498 --> 01:08:51.508 important for this is acetylcholine

NOTE Confidence: 0.85778123

01:08:51.508 --> 01:08:53.516 regulation of dopamine release.

NOTE Confidence: 0.85778123

01:08:53.520 --> 01:08:55.806 We we have started to do some of this

NOTE Confidence: 0.85778123

01:08:55.806 --> 01:08:58.145 where we're starting on the slice level

NOTE Confidence: 0.85778123

01:08:58.145 --> 01:08:59.997 trying to workout these parameters

NOTE Confidence: 0.85778123

01:08:59.997 --> 01:09:02.212 because it's like calling regulation

NOTE Confidence: 0.85778123

01:09:02.212 --> 01:09:04.318 of domain releases actually really

NOTE Confidence: 0.85778123

01:09:04.318 --> 01:09:05.958 kind of cool regulatory mechanism

NOTE Confidence: 0.85778123

01:09:05.958 --> 01:09:08.792 because it's one of the few that really

NOTE Confidence: 0.85778123

01:09:08.792 --> 01:09:10.617 robustly releases domain from terminals,

NOTE Confidence: 0.85778123

01:09:10.620 --> 01:09:12.720 totally independent of the semantic activity.

NOTE Confidence: 0.85778123

01:09:12.720 --> 01:09:15.037 And you can even get this in

NOTE Confidence: 0.85778123

01:09:15.037 --> 01:09:16.550 isolated terminals and slices.

NOTE Confidence: 0.85778123

01:09:16.550 --> 01:09:19.350 And so we think that there is probably,

NOTE Confidence: 0.85778123

01:09:19.350 --> 01:09:21.090 you know, maybe it's the.

NOTE Confidence: 0.85778123

01:09:21.090 --> 01:09:22.534 Maybe it's both questions.

NOTE Confidence: 0.85778123

01:09:22.534 --> 01:09:23.978 Maybe Domain was released.

NOTE Confidence: 0.85778123

01:09:23.980 --> 01:09:25.790 In response to RP signals,

NOTE Confidence: 0.85778123

01:09:25.790 --> 01:09:27.230 but also attentional signals

NOTE Confidence: 0.85778123

01:09:27.230 --> 01:09:29.030 that are coming from these,

NOTE Confidence: 0.85778123

01:09:29.030 --> 01:09:31.790 maybe like that's the first thing I think

NOTE Confidence: 0.85778123

01:09:31.790 --> 01:09:34.090 of acetylcholine is like attention arousal,

NOTE Confidence: 0.85778123

01:09:34.090 --> 01:09:35.534 but here's the thing.

NOTE Confidence: 0.85778123

01:09:35.534 --> 01:09:36.978 Those are all integrated.

NOTE Confidence: 0.85778123

01:09:36.980 --> 01:09:39.140 What the domain signature finally is,

NOTE Confidence: 0.85778123

01:09:39.140 --> 01:09:41.373 and so I think that it is

NOTE Confidence: 0.85778123

01:09:41.373 --> 01:09:43.470 probably both in some contexts,

NOTE Confidence: 0.85778123

01:09:43.470 --> 01:09:43.859 right?

NOTE Confidence: 0.85778123

01:09:43.859 --> 01:09:45.415 It's probably both acetylcholine

NOTE Confidence: 0.85778123

01:09:45.415 --> 01:09:47.360 regulated domain release and RPE

NOTE Confidence: 0.85778123

01:09:47.418 --> 01:09:49.093 regulated cymatic activity that leads

NOTE Confidence: 0.85778123

01:09:49.093 --> 01:09:51.419 to this kind of saliency based term.

NOTE Confidence: 0.85778123

01:09:51.420 --> 01:09:53.220 One thing I'll tell you some

NOTE Confidence: 0.85778123

01:09:53.220 --> 01:09:55.889 ants about it as we see pretty

NOTE Confidence: 0.85778123

01:09:55.889 --> 01:09:57.290 interesting sex differences.

NOTE Confidence: 0.85778123

01:09:57.290 --> 01:09:58.385 In terminal regulatory

NOTE Confidence: 0.85778123

01:09:58.385 --> 01:10:00.210 mechanisms through the A4 beta,

NOTE Confidence: 0.85778123

01:10:00.210 --> 01:10:01.670 two containing nicotinic receptors

NOTE Confidence: 0.85778123

01:10:01.670 --> 01:10:03.495 that are on those terminals,

NOTE Confidence: 0.85778123

01:10:03.500 --> 01:10:06.100 and So what we're trying to do first

NOTE Confidence: 0.85778123

01:10:06.100 --> 01:10:08.627 is outline the mechanism or how this

NOTE Confidence: 0.85778123

01:10:08.627 --> 01:10:10.895 is different and then take that

NOTE Confidence: 0.85778123

01:10:10.895 --> 01:10:13.660 model into this and say do those

NOTE Confidence: 0.85778123

01:10:13.660 --> 01:10:14.841 differences predict differences

NOTE Confidence: 0.85778123

01:10:14.841 --> 01:10:16.405 in these learning parameters

NOTE Confidence: 0.85778123

01:10:16.405 --> 01:10:18.829 because it's really hard to get it.

NOTE Confidence: 0.85778123

01:10:18.830 --> 01:10:20.625 Don't mean terminal regulation by

NOTE Confidence: 0.85778123

01:10:20.625 --> 01:10:22.420 acetylcholine in vivo because it's

NOTE Confidence: 0.85778123

01:10:22.475 --> 01:10:24.245 your calling regulates other cell

NOTE Confidence: 0.85778123

01:10:24.245 --> 01:10:26.490 types that also regulate dopamine release.

NOTE Confidence: 0.85778123

01:10:26.490 --> 01:10:28.400 So it regulates GABA release.

NOTE Confidence: 0.85778123

01:10:28.400 --> 01:10:30.280 That regulates terminals and so,

NOTE Confidence: 0.85778123

01:10:30.280 --> 01:10:32.835 like without some sort of like biological

NOTE Confidence: 0.85778123

01:10:32.835 --> 01:10:35.149 system that you know is different.

NOTE Confidence: 0.85778123

01:10:35.150 --> 01:10:37.340 It's really hard to isolate just

NOTE Confidence: 0.85778123

01:10:37.340 --> 01:10:39.938 the effects of cetyl choline from

NOTE Confidence: 0.85778123

01:10:39.938 --> 01:10:42.593 the effects of acetylcholine media

NOTE Confidence: 0.85778123

01:10:42.593 --> 01:10:44.186 dopamine terminal regulation.

NOTE Confidence: 0.85778123

01:10:44.190 --> 01:10:45.490 I hope tools come along.

NOTE Confidence: 0.85778123

01:10:45.490 --> 01:10:46.790 There's like darts and stuff

NOTE Confidence: 0.85778123

01:10:46.790 --> 01:10:47.570 which are awesome.

NOTE Confidence: 0.85778123

01:10:47.570 --> 01:10:49.390 Those are coming and like we'll see.

NOTE Confidence: 0.85778123

01:10:49.390 --> 01:10:51.397 But like anyway I'm like this is a that's

NOTE Confidence: 0.85778123

01:10:51.397 --> 01:10:53.550 a great question I'm excited about so.

NOTE Confidence: 0.87011683

01:10:54.730 --> 01:10:56.802 Well thank you were coming up to 11:30

NOTE Confidence: 0.87011683

01:10:56.802 --> 01:10:58.838 and we peppered you with questions

NOTE Confidence: 0.87011683

01:10:58.838 --> 01:11:01.016 we really appreciate the great talk

NOTE Confidence: 0.87011683

01:11:01.081 --> 01:11:03.153 and the time that you spent with us.

NOTE Confidence: 0.87011683

01:11:03.160 --> 01:11:05.281 Thank you to everyone for your attention

NOTE Confidence: 0.87011683

01:11:05.281 --> 01:11:07.718 and we hope to hear more about the

NOTE Confidence: 0.87011683

01:11:07.718 --> 01:11:09.480 next steps in the research. Yeah,

NOTE Confidence: 0.87011683

01:11:09.480 --> 01:11:10.980 thank you guys so much.

NOTE Confidence: 0.87011683

01:11:10.980 --> 01:11:12.490 These questions were awesome man.

NOTE Confidence: 0.87011683

01:11:12.490 --> 01:11:13.995 I had a great time

NOTE Confidence: 0.87011683

01:11:13.995 --> 01:11:15.199 chatting with everybody so

NOTE Confidence: 0.87011683

01:11:15.200 --> 01:11:16.607 thanks. Thanks Erin.