WEBVTT

NOTE duration:"01:00:40.2880000"

NOTE language:en-us

NOTE Confidence: 0.88865805

00:00:00.000 --> 00:00:02.040 You did in order to receive

NOTE Confidence: 0.88865805

00:00:02.040 --> 00:00:03.400 CME credit for attendance,

NOTE Confidence: 0.88865805

00:00:03.400 --> 00:00:05.745 please see the chat room for instructions.

NOTE Confidence: 0.88865805

00:00:05.750 --> 00:00:08.470 You can text the unique ID for this

NOTE Confidence: 0.88865805

00:00:08.470 --> 00:00:10.790 conference anytime between 1:45 and 3:15 PM,

NOTE Confidence: 0.88865805

00:00:10.790 --> 00:00:12.470 and if you're not already

NOTE Confidence: 0.88865805

00:00:12.470 --> 00:00:14.150 registered with the LC me,

NOTE Confidence: 0.88865805

00:00:14.150 --> 00:00:16.495 you will need to do that first.

NOTE Confidence: 0.88865805

00:00:16.500 --> 00:00:18.180 If you have any questions

NOTE Confidence: 0.88865805

00:00:18.180 --> 00:00:19.188 during the presentation,

NOTE Confidence: 0.88865805

00:00:19.190 --> 00:00:21.178 I encourage you to make use of

NOTE Confidence: 0.88865805

00:00:21.178 --> 00:00:23.241 the chat room throughout the hour

NOTE Confidence: 0.88865805

00:00:23.241 --> 00:00:25.527 and we will either read those

NOTE Confidence: 0.88865805

00:00:25.527 --> 00:00:27.620 questions allowed at the end or

NOTE Confidence: 0.88865805

00:00:27.620 --> 00:00:29.656 invite you to unmute yourself at

NOTE Confidence: 0.88865805

00:00:29.656 --> 00:00:31.586 the close of the presentation.

NOTE Confidence: 0.88865805

00:00:31.590 --> 00:00:33.135 Recorded versions of these lectures

NOTE Confidence: 0.88865805

00:00:33.135 --> 00:00:35.240 will be available on line within two

NOTE Confidence: 0.88865805

00:00:35.240 --> 00:00:37.264 weeks at the link provided in the chat.

NOTE Confidence: 0.88865805

00:00:37.270 --> 00:00:37.836 And finally,

NOTE Confidence: 0.88865805

00:00:37.836 --> 00:00:39.534 please feel free to share the

NOTE Confidence: 0.88865805

00:00:39.534 --> 00:00:40.655 announcements for our weekly

NOTE Confidence: 0.88865805

00:00:40.655 --> 00:00:41.905 lecture series to anyone else

NOTE Confidence: 0.88865805

00:00:41.905 --> 00:00:43.230 who might be interested,

NOTE Confidence: 0.88865805

00:00:43.230 --> 00:00:44.625 or contact Debbie Lovejoy to

NOTE Confidence: 0.88865805

00:00:44.625 --> 00:00:46.360 be added to our email list.

NOTE Confidence: 0.88865805

00:00:46.360 --> 00:00:48.528 So with that I'm going to turn it

NOTE Confidence: 0.88865805

00:00:48.528 --> 00:00:51.088 over to Brian Minor who is going

NOTE Confidence: 0.88865805

00:00:51.088 --> 00:00:53.038 to be introducing today's speaker.

NOTE Confidence: 0.88865805

00:00:53.040 --> 00:00:54.528 OK, good afternoon everyone.

NOTE Confidence: 0.88865805

00:00:54.528 --> 00:00:56.760 When you first join the conference,

NOTE Confidence: 0.88865805

00:00:56.760 --> 00:00:58.284 you might have noticed,

NOTE Confidence: 0.88865805

00:00:58.284 --> 00:01:00.850 but I'll just draw attention to it.

NOTE Confidence: 0.88865805

00:01:00.850 --> 00:01:03.010 Our next joint Yale Harvard Sleep

NOTE Confidence: 0.88865805

00:01:03.010 --> 00:01:05.319 Medicine Seminar will be on Wednesday,

NOTE Confidence: 0.88865805

00:01:05.320 --> 00:01:06.044 December 9th,

NOTE Confidence: 0.88865805

00:01:06.044 --> 00:01:08.578 same time 2:00 o'clock and the speaker

NOTE Confidence: 0.88865805

00:01:08.578 --> 00:01:11.268 for that talk will be Janet Mollington,

NOTE Confidence: 0.88865805

00:01:11.270 --> 00:01:13.130 who's a professor in neurology

NOTE Confidence: 0.88865805

00:01:13.130 --> 00:01:14.618 at Harvard Medical School,

NOTE Confidence: 0.88865805

00:01:14.620 --> 00:01:17.154 and she's going to be talking about

NOTE Confidence: 0.88865805

00:01:17.154 --> 00:01:19.790 the cost of insufficient sleep.

NOTE Confidence: 0.88865805

00:01:19.790 --> 00:01:22.527 So today it is my pleasure to

NOTE Confidence: 0.88865805

00:01:22.527 --> 00:01:24.210 introduce doctor Brendan Lucey,

NOTE Confidence: 0.88865805

00:01:24.210 --> 00:01:26.926 who has become a close colleague of

NOTE Confidence: 0.88865805

00:01:26.926 --> 00:01:30.240 mine in the field of sleep and aging.

NOTE Confidence: 0.88865805

00:01:30.240 --> 00:01:31.784 Doctor Lucy completed his

NOTE Confidence: 0.88865805

00:01:31.784 --> 00:01:33.714 undergraduate work at the University

NOTE Confidence: 0.88865805

00:01:33.714 --> 00:01:35.468 of Vermont in Burlington,

NOTE Confidence: 0.88865805

00:01:35.470 --> 00:01:38.179 where he graduated summa cum Lau Dai

NOTE Confidence: 0.88865805

00:01:38.179 --> 00:01:40.688 before going on to Johns Hopkins,

NOTE Confidence: 0.88865805

00:01:40.690 --> 00:01:43.876 where he got his medical degree.

NOTE Confidence: 0.88865805

00:01:43.880 --> 00:01:46.538 This was followed by postgraduate training,

NOTE Confidence: 0.88865805

00:01:46.540 --> 00:01:49.908 first as a resident in neurology at the

NOTE Confidence: 0.88865805

00:01:49.908 --> 00:01:52.740 Barnes Jewish hospital in Saint Louis.

NOTE Confidence: 0.88865805

00:01:52.740 --> 00:01:55.212 He did a fellowship in clinical

NOTE Confidence: 0.88865805

00:01:55.212 --> 00:01:56.448 neurophysiology at Brigham

NOTE Confidence: 0.88865805

00:01:56.448 --> 00:01:58.060 and Women's Hospital,

NOTE Confidence: 0.88865805

00:01:58.060 --> 00:02:01.126 and he's also completed a Masters of

NOTE Confidence: 0.88865805

00:02:01.126 --> 00:02:03.600 Science and clinical investigation.

NOTE Confidence: 0.88865805

00:02:03.600 --> 00:02:05.136 After his postgraduate training,

NOTE Confidence: 0.88865805

00:02:05.136 --> 00:02:08.184 he spent four years as chief of neurology

NOTE Confidence: 0.88865805

00:02:08.184 --> 00:02:10.536 on Nellis Air Force Base in Nevada,

NOTE Confidence: 0.88865805

00:02:10.540 --> 00:02:13.300 and he rose to the rank of major

NOTE Confidence: 0.88865805

00:02:13.300 --> 00:02:16.208 in the United States Air Force.

NOTE Confidence: 0.88865805

00:02:16.210 --> 00:02:18.632 And then he came back to Washington

NOTE Confidence: 0.88865805

00:02:18.632 --> 00:02:20.120 University in Saint Louis,

NOTE Confidence: 0.88865805

00:02:20.120 --> 00:02:22.885 where he is now a tenured associate

NOTE Confidence: 0.88865805

00:02:22.885 --> 00:02:25.392 professor of neurology and the director

NOTE Confidence: 0.88865805

00:02:25.392 --> 00:02:27.477 of their Sleep Medicine Section.

NOTE Confidence: 0.88865805

00:02:27.480 --> 00:02:29.600 With respect to his research,

NOTE Confidence: 0.88865805

00:02:29.600 --> 00:02:32.568 he's been well funded by the NIH,

NOTE Confidence: 0.88865805

00:02:32.570 --> 00:02:35.108 especially the National Institute on aging,

NOTE Confidence: 0.88865805

00:02:35.110 --> 00:02:37.546 as well as some non governmental

NOTE Confidence: 0.88865805

00:02:37.546 --> 00:02:39.576 organizations for his work which

NOTE Confidence: 0.88865805

00:02:39.576 --> 00:02:41.226 is really focused on looking

NOTE Confidence: 0.88865805

00:02:41.226 --> 00:02:43.796 at sleep as a potential novel

NOTE Confidence: 0.88865805

00:02:43.796 --> 00:02:46.140 modulator of Alzheimer's pathology.

NOTE Confidence: 0.88865805

00:02:46.140 --> 00:02:48.170 He's received two very prestigious

NOTE Confidence: 0.88865805

00:02:48.170 --> 00:02:51.219 awards from the N IAD Gemstar Ward,

NOTE Confidence: 0.88865805

00:02:51.220 --> 00:02:54.292 which is focused on some specialists

NOTE Confidence: 0.88865805

00:02:54.292 --> 00:02:56.822 who are transitioning to aging

NOTE Confidence: 0.88865805

00:02:56.822 --> 00:02:59.958 research as well as the pool be sin.

NOTE Confidence: 0.88865805

00:02:59.960 --> 00:03:01.770 Urging leaders career Development Award.

NOTE Confidence: 0.88865805

00:03:01.770 --> 00:03:04.154 This is a K Award given by the

NOTE Confidence: 0.88865805

00:03:04.154 --> 00:03:06.668 NIH that really looks to identify

NOTE Confidence: 0.88865805

00:03:06.668 --> 00:03:08.963 and develop emerging leaders in

NOTE Confidence: 0.88865805

00:03:08.963 --> 00:03:11.339 the field of aging research.

NOTE Confidence: 0.8636372

00:03:11.340 --> 00:03:13.741 He has looked at sleep quality and

NOTE Confidence: 0.8636372

00:03:13.741 --> 00:03:16.244 amyloid beta kinetics and whether these

NOTE Confidence: 0.8636372

00:03:16.244 --> 00:03:18.599 can be modulated by pharmacological

NOTE Confidence: 0.8636372

00:03:18.599 --> 00:03:20.159 behavioral manipulation of sleep.

NOTE Confidence: 0.8636372

00:03:20.160 --> 00:03:22.736 He has looked at sleep and circadian

NOTE Confidence: 0.8636372

00:03:22.736 --> 00:03:25.663 biology and the fact of these on

NOTE Confidence: 0.8636372

00:03:25.663 --> 00:03:27.415 Alzheimer's disease and related

NOTE Confidence: 0.8636372

00:03:27.415 --> 00:03:29.897 disorders and he's also looked at

NOTE Confidence: 0.8636372

00:03:29.897 --> 00:03:31.807 whether we can manipulate sleep

NOTE Confidence: 0.8636372

00:03:31.807 --> 00:03:33.468 to prevent Alzheimer's disease.

NOTE Confidence: 0.8636372

00:03:33.468 --> 00:03:35.598 And on a personal note,

NOTE Confidence: 0.8636372

00:03:35.600 --> 00:03:38.127 I just want to acknowledge my relationship

NOTE Confidence: 0.8636372

00:03:38.127 --> 00:03:40.472 with doctor Lucy and what would a

NOTE Confidence: 0.8636372

00:03:40.472 --> 00:03:42.699 friend and colleague he has been to me.

NOTE Confidence: 0.8636372

00:03:42.700 --> 00:03:43.992 We've known each other

NOTE Confidence: 0.8636372

00:03:43.992 --> 00:03:45.607 for a couple years now.

NOTE Confidence: 0.8636372

00:03:45.610 --> 00:03:47.434 We started ouf cheering a paper

NOTE Confidence: 0.8636372

00:03:47.434 --> 00:03:49.480 session together at the sleep meeting,

NOTE Confidence: 0.8636372

00:03:49.480 --> 00:03:52.184 and since that time he is really been

NOTE Confidence: 0.8636372

00:03:52.184 --> 00:03:54.024 very generous in terms of reaching

NOTE Confidence: 0.8636372

00:03:54.024 --> 00:03:56.768 out to me to help me with my own

NOTE Confidence: 0.8636372

00:03:56.768 --> 00:03:58.850 research and the field of sleeping.

NOTE Confidence: 0.8636372

00:03:58.850 --> 00:04:00.788 Aging is a pretty small field,

NOTE Confidence: 0.8636372

00:04:00.790 --> 00:04:04.003 so it's it's nice to have a friend and.

NOTE Confidence: 0.8636372

00:04:04.010 --> 00:04:06.243 I really appreciate all the help that

NOTE Confidence: 0.8636372

00:04:06.243 --> 00:04:08.794 he's given me and I think it's really

NOTE Confidence: 0.8636372

00:04:08.794 --> 00:04:11.005 exciting to have him here today to

NOTE Confidence: 0.8636372

00:04:11.005 --> 00:04:13.147 talk about a topic that we haven't

NOTE Confidence: 0.8636372

00:04:13.147 --> 00:04:15.350 heard so much about in this session.

NOTE Confidence: 0.8636372

00:04:15.350 --> 00:04:17.627 And so he is going to be speaking today

NOTE Confidence: 0.8636372

00:04:17.627 --> 00:04:19.288 about the bidirectional relationship

NOTE Confidence: 0.8636372

00:04:19.288 --> 00:04:21.988 between sleep and Alzheimer's disease so.

NOTE Confidence: 0.8636372

00:04:21.990 --> 00:04:22.644 Doctor Lucy,

NOTE Confidence: 0.8636372

00:04:22.644 --> 00:04:24.933 thank you for coming and I will

NOTE Confidence: 0.8636372

00:04:24.933 --> 00:04:26.340 turn it over to you.

NOTE Confidence: 0.8252603

00:04:28.620 --> 00:04:31.470 Thank you very much, doctor minor.

NOTE Confidence: 0.8252603

00:04:31.470 --> 00:04:34.308 I'm honored to have the invitation

NOTE Confidence: 0.8252603

00:04:34.308 --> 00:04:37.620 to speak to you today about

NOTE Confidence: 0.8252603

00:04:37.620 --> 00:04:40.268 sleep and Alzheimer's disease.

NOTE Confidence: 0.8252603

00:04:40.270 --> 00:04:43.406 And the work that that I've been involved

NOTE Confidence: 0.8252603

00:04:43.406 --> 00:04:46.727 in and many others at Washington

NOTE Confidence: 0.8252603

00:04:46.727 --> 00:04:49.179 University and other institutions.

NOTE Confidence: 0.8252603

00:04:49.180 --> 00:04:51.370 These are my excuse me.

NOTE Confidence: 0.8252603

00:04:51.370 --> 00:04:53.590 My disclosures I've put asterisk

NOTE Confidence: 0.8252603

00:04:53.590 --> 00:04:55.366 with my active research

NOTE Confidence: 0.8252603

00:04:55.366 --> 00:04:57.479 support primarily from the NIH,

NOTE Confidence: 0.8252603

00:04:57.480 --> 00:04:59.755 as well as other research

NOTE Confidence: 0.8252603

00:04:59.755 --> 00:05:02.522 support that has funded some of

NOTE Confidence: 0.8252603

00:05:02.522 --> 00:05:04.910 the work that I'll be showing.

NOTE Confidence: 0.8252603

00:05:04.910 --> 00:05:07.192 I like to disclose that I consult

NOTE Confidence: 0.8252603

00:05:07.192 --> 00:05:09.322 for Merck and additional disclosure

NOTE Confidence: 0.8252603

00:05:09.322 --> 00:05:11.486 that's not directly relevant

NOTE Confidence: 0.8252603

00:05:11.486 --> 00:05:13.650 for my financial interests,

NOTE Confidence: 0.8252603

00:05:13.650 --> 00:05:15.394 but is that doctors,

NOTE Confidence: 0.8252603

00:05:15.394 --> 00:05:16.266 Randall Bateman,

NOTE Confidence: 0.8252603

00:05:16.270 --> 00:05:18.650 and David Holtzman as well

NOTE Confidence: 0.8252603

00:05:18.650 --> 00:05:20.078 as Washington University?

NOTE Confidence: 0.8252603

00:05:20.080 --> 00:05:21.628 Have a licensed intellectual

NOTE Confidence: 0.8252603

00:05:21.628 --> 00:05:23.563 property to a company called

NOTE Confidence: 0.8252603

00:05:23.563 --> 00:05:25.989 C2 N Diagnostics that they also

NOTE Confidence: 0.8252603

00:05:25.989 --> 00:05:27.565 a financial investment in.

NOTE Confidence: 0.8252603

00:05:27.570 --> 00:05:29.802 I do not unfortunately have a

NOTE Confidence: 0.8252603

00:05:29.802 --> 00:05:32.289 financial investment in C2 N Diagnostics.

NOTE Confidence: 0.77621853

00:05:35.690 --> 00:05:38.162 So the objectives today for our

NOTE Confidence: 0.77621853

00:05:38.162 --> 00:05:41.537 discussion is going to go over a brief

NOTE Confidence: 0.77621853

00:05:41.537 --> 00:05:44.009 Alzheimer's disease primmer kind of to

NOTE Confidence: 0.77621853

00:05:44.088 --> 00:05:46.545 get everybody on the same page about

NOTE Confidence: 0.77621853

00:05:46.545 --> 00:05:50.045 about a D when I present to anadi

NOTE Confidence: 0.77621853

00:05:50.045 --> 00:05:53.320 audience I always give asleep primmer.

NOTE Confidence: 0.77621853

00:05:53.320 --> 00:05:56.211 Then we'll go over the evidence for

NOTE Confidence: 0.77621853

00:05:56.211 --> 00:05:58.014 a bidirectional relationship between

NOTE Confidence: 0.77621853

00:05:58.014 --> 00:05:59.978 sleep and Alzheimer's disease,

NOTE Confidence: 0.77621853

00:05:59.980 --> 00:06:01.240 and then discuss.

NOTE Confidence: 0.77621853

00:06:01.240 --> 00:06:02.920 Discuss several potential mechanisms

NOTE Confidence: 0.77621853

00:06:02.920 --> 00:06:05.310 that may mediate that relationship,

NOTE Confidence: 0.77621853

00:06:05.310 --> 00:06:07.968 including a beta reduction and clearance,

NOTE Confidence: 0.77621853

00:06:07.970 --> 00:06:12.080 Cal Phosphorylation and the erection system.

NOTE Confidence: 0.77621853

00:06:12.080 --> 00:06:14.930 So Alzheimer's disease is progressive,

NOTE Confidence: 0.77621853

00:06:14.930 --> 00:06:16.110 neurodegenerative disease.

NOTE Confidence: 0.77621853

00:06:16.110 --> 00:06:19.060 It's characterized by the deposition

NOTE Confidence: 0.77621853

00:06:19.060 --> 00:06:21.770 of extracellular amyloid beta plaques.

NOTE Confidence: 0.77621853

00:06:21.770 --> 00:06:24.620 The deposition of amyloid plaque

NOTE Confidence: 0.77621853

00:06:24.620 --> 00:06:26.330 is concentration dependent,

NOTE Confidence: 0.77621853

00:06:26.330 --> 00:06:29.110 so the greater the concentration

NOTE Confidence: 0.77621853

00:06:29.110 --> 00:06:32.600 of amyloid beta in the brain,

NOTE Confidence: 0.77621853

00:06:32.600 --> 00:06:36.020 such as insoluble in the cerebral

NOTE Confidence: 0.77621853

00:06:36.020 --> 00:06:39.684 spinal fluid, the more likely you

NOTE Confidence: 0.77621853

00:06:39.684 --> 00:06:42.208 will have plaque formation.

NOTE Confidence: 0.77621853

00:06:42.210 --> 00:06:46.004 And different forms of amyloid beta are

NOTE Confidence: 0.77621853

00:06:46.004 --> 00:06:50.338 more likely to form analyte path plaques.

NOTE Confidence: 0.77621853

00:06:50.340 --> 00:06:51.488 For instance,

NOTE Confidence: 0.77621853

00:06:51.488 --> 00:06:54.932 amyloid beta 42 is most likely

NOTE Confidence: 0.77621853

00:06:54.932 --> 00:06:57.899 to aggregate as plaque inform,

NOTE Confidence: 0.77621853

00:06:57.900 --> 00:06:59.793 inform amyloid deposition.

NOTE Confidence: 0.77621853

00:06:59.793 --> 00:07:01.686 There's also neurofibrillary

NOTE Confidence: 0.77621853

00:07:01.686 --> 00:07:04.770 tangles of hyper phosphorylated Tau

NOTE Confidence: 0.77621853

00:07:04.770 --> 00:07:07.185 aggregates that form inside neurons.

NOTE Confidence: 0.77621853

00:07:07.190 --> 00:07:11.310 An results in neuronal death.

NOTE Confidence: 0.77621853

00:07:11.310 --> 00:07:12.918 Loss of synaptic,

NOTE Confidence: 0.77621853

00:07:12.918 --> 00:07:16.134 synaptic loss of neurons and synaptic

NOTE Confidence: 0.77621853

00:07:16.134 --> 00:07:19.490 to function lead to brain atrophy such

NOTE Confidence: 0.77621853

00:07:19.490 --> 00:07:23.526 as as seen in the figure on the left.

NOTE Confidence: 0.77621853

00:07:23.530 --> 00:07:26.140 Formation is also involved in

NOTE Confidence: 0.77621853

00:07:26.140 --> 00:07:27.706 eventually memory problems,

NOTE Confidence: 0.77621853

00:07:27.710 --> 00:07:30.330 other cognitive deficits and dementia.

NOTE Confidence: 0.85796946

00:07:38.380 --> 00:07:41.102 This slide shows some of the neuroimaging

NOTE Confidence: 0.85796946

00:07:41.102 --> 00:07:44.667 that can look at the changes in the brain

NOTE Confidence: 0.85796946

00:07:44.667 --> 00:07:47.270 that we see with Alzheimer's disease.

NOTE Confidence: 0.85796946

00:07:47.270 --> 00:07:49.610 In the left column are images

NOTE Confidence: 0.85796946

00:07:49.610 --> 00:07:51.170 taking from individuals with

NOTE Confidence: 0.85796946

00:07:51.240 --> 00:07:53.730 Alzheimer's disease and on the right,

NOTE Confidence: 0.85796946

00:07:53.730 --> 00:07:56.160 or individuals who are clinically normal.

NOTE Confidence: 0.85796946

00:07:56.160 --> 00:07:58.180 The first set of scans,

NOTE Confidence: 0.85796946

00:07:58.180 --> 00:07:59.389 A&BRFDG pet scans.

NOTE Confidence: 0.85796946

00:07:59.389 --> 00:08:00.598 Looking at metabolism,

NOTE Confidence: 0.85796946

00:08:00.600 --> 00:08:03.264 you can see that there's lower

NOTE Confidence: 0.85796946

00:08:03.264 --> 00:08:05.660 metabolism in the 80 brain.

NOTE Confidence: 0.85796946

00:08:05.660 --> 00:08:07.920 Looking at the MRI changes,

NOTE Confidence: 0.85796946

00:08:07.920 --> 00:08:09.744 there's significant atrophy that

NOTE Confidence: 0.85796946

00:08:09.744 --> 00:08:12.480 occlude occurs in those with Alzheimer's

NOTE Confidence: 0.85796946

00:08:12.552 --> 00:08:14.677 disease and Pittsburgh Compound B.

NOTE Confidence: 0.85796946

00:08:14.680 --> 00:08:17.010 Amyloid pet scans show significantly

NOTE Confidence: 0.85796946

00:08:17.010 --> 00:08:19.340 increased amyloid deposition and those

NOTE Confidence: 0.85796946

00:08:19.408 --> 00:08:21.124 with Alzheimer's disease compared

NOTE Confidence: 0.85796946

00:08:21.124 --> 00:08:23.698 to those who are clinically normal.

NOTE Confidence: 0.8187831

00:08:26.470 --> 00:08:29.060 In recent years we've also.

NOTE Confidence: 0.8187831

00:08:29.060 --> 00:08:33.196 There's also been a development of Tau pet,

NOTE Confidence: 0.8187831

00:08:33.200 --> 00:08:37.295 which allows for us to look at Tau Pathology
NOTE Confidence: 0.8187831
00:08:37.295 --> 00:08:41.104 in vivo and this figure from Keith
NOTE Confidence: 0.8187831
00:08:41.104 --> 00:08:45.119 Johnson's group that was published in 2016,
NOTE Confidence: 0.8187831
00:08:45.120 --> 00:08:48.816 and the annals of neurology shows that as
NOTE Confidence: 0.8187831
00:08:48.816 --> 00:08:52.887 the mini mental state exam score declines,
NOTE Confidence: 0.8187831
00:08:52.890 --> 00:08:55.086 there's increasing tab pathology.
NOTE Confidence: 0.8187831
00:08:55.086 --> 00:08:58.380 In the medial temporal regions that
NOTE Confidence: 0.8187831
00:08:58.461 --> 00:09:01.371 then spreads out through the temporal
NOTE Confidence: 0.8187831
00:09:01.371 --> 00:09:04.509 lobes and the remainder of the Cortex.
NOTE Confidence: 0.8187831
00:09:04.510 --> 00:09:06.885 And using neuroimaging and also
NOTE Confidence: 0.8187831
00:09:06.885 --> 00:09:09.260 measuring employed beta and Tau
NOTE Confidence: 0.8187831
00:09:09.335 --> 00:09:11.219 in cerebral spinal fluid,
NOTE Confidence: 0.8187831
00:09:11.220 --> 00:09:14.566 we've been able to, as a field,
NOTE Confidence: 0.8187831
00:09:14.570 --> 00:09:17.769 determine when we see changes in these
NOTE Confidence: 0.8187831
00:09:17.769 --> 00:09:20.320 different biomarkers across 80 pathogenesis.
NOTE Confidence: 0.8187831
00:09:20.320 --> 00:09:23.841 So this figure shows a typical what's

NOTE Confidence: 0.8187831

00:09:23.841 --> 00:09:26.340 sometimes called Jacks curves for

NOTE Confidence: 0.8187831

00:09:26.340 --> 00:09:29.052 Clifford Jack from the male clinic

NOTE Confidence: 0.8187831

00:09:29.052 --> 00:09:31.809 who have been the lead author.

NOTE Confidence: 0.8187831

00:09:31.810 --> 00:09:34.460 A number of papers describing

NOTE Confidence: 0.8187831

00:09:34.460 --> 00:09:36.050 this biomarker model.

NOTE Confidence: 0.8187831

00:09:36.050 --> 00:09:39.002 On the X axis we have the clinical

NOTE Confidence: 0.8187831

00:09:39.002 --> 00:09:41.552 disease stage of Alzheimer's disease

NOTE Confidence: 0.8187831

00:09:41.552 --> 00:09:44.437 from cognitively normal to mild

NOTE Confidence: 0.8187831

00:09:44.437 --> 00:09:46.615 cognitive impairment between the

NOTE Confidence: 0.8187831

00:09:46.615 --> 00:09:48.975 dashed lines and then dementia,

NOTE Confidence: 0.8187831

00:09:48.980 --> 00:09:52.179 and you can see that very early

NOTE Confidence: 0.8187831

00:09:52.179 --> 00:09:54.250 on amyloid deposition begins.

NOTE Confidence: 0.8187831

00:09:54.250 --> 00:09:57.594 This can be 15 to 20 years before

NOTE Confidence: 0.8187831

00:09:57.594 --> 00:10:00.119 cognitive and cognitive symptom.

NOTE Confidence: 0.8187831

00:10:00.120 --> 00:10:02.880 Begin and by the time cognitive

NOTE Confidence: 0.8187831

00:10:02.880 --> 00:10:04.260 symptoms start employed,

NOTE Confidence: 0.8187831

00:10:04.260 --> 00:10:07.716 deposition is nearly at its peak.

NOTE Confidence: 0.8187831

00:10:07.720 --> 00:10:11.560 Towel lags behind that.

NOTE Confidence: 0.8187831

00:10:11.560 --> 00:10:15.053 About 5 to 7 years before clinical

NOTE Confidence: 0.8187831

00:10:15.053 --> 00:10:18.517 symptoms followed by changes in brain

NOTE Confidence: 0.8187831

00:10:18.517 --> 00:10:21.637 structure such as hippocampal atrophy,

NOTE Confidence: 0.8187831

00:10:21.640 --> 00:10:24.640 changes in memory and followed by

NOTE Confidence: 0.8187831

00:10:24.640 --> 00:10:26.640 clinical deterioration when the

NOTE Confidence: 0.8187831

00:10:26.726 --> 00:10:30.036 individual progressed toward full dementia.

NOTE Confidence: 0.82900655

00:10:32.840 --> 00:10:35.269 A major goal of the field for

NOTE Confidence: 0.82900655

00:10:35.269 --> 00:10:37.600 processing last 20 years has been

NOTE Confidence: 0.82900655

00:10:37.600 --> 00:10:39.625 to define these biomarker changes

NOTE Confidence: 0.82900655

00:10:39.625 --> 00:10:42.598 to both define who who is likely

NOTE Confidence: 0.82900655

00:10:42.598 --> 00:10:45.890 to get Alzheimer's disease, too.

NOTE Confidence: 0.82900655

00:10:45.890 --> 00:10:51.082 222 correctly. Attempted categorized

NOTE Confidence: 0.82900655

00:10:51.082 --> 00:10:54.486 individuals into the right.

NOTE Confidence: 0.82900655

00:10:54.490 --> 00:10:56.810 Disease processes there are other

NOTE Confidence: 0.82900655

00:10:56.810 --> 00:10:59.130 causes of dementia than Alzheimer's

NOTE Confidence: 0.82900655

00:10:59.203 --> 00:11:01.358 disease and potentially to guide

NOTE Confidence: 0.82900655

00:11:01.358 --> 00:11:04.012 intervention trials and to push the

NOTE Confidence: 0.82900655

00:11:04.012 --> 00:11:06.604 intervention period as early as possible,

NOTE Confidence: 0.82900655

00:11:06.610 --> 00:11:09.658 and some of that is coming to fruition

NOTE Confidence: 0.82900655

00:11:09.658 --> 00:11:12.074 with trials that are beginning

NOTE Confidence: 0.82900655

00:11:12.074 --> 00:11:14.694 during the clinically normal period.

NOTE Confidence: 0.82900655

00:11:14.700 --> 00:11:16.488 In some specialized groups.

NOTE Confidence: 0.86044985

00:11:19.620 --> 00:11:22.212 So I'd like to to to move on to

NOTE Confidence: 0.86044985

00:11:22.212 --> 00:11:25.254 some of the evidence that connects

NOTE Confidence: 0.86044985

00:11:25.254 --> 00:11:27.390 sleep and Alzheimer's disease.

NOTE Confidence: 0.86044985

00:11:27.390 --> 00:11:30.168 We've known for decades that individuals

NOTE Confidence: 0.86044985

00:11:30.168 --> 00:11:32.490 with dementia have disturbed sleep.

NOTE Confidence: 0.86044985

00:11:32.490 --> 00:11:35.050 But what's been increasingly recognized

NOTE Confidence: 0.86044985

00:11:35.050 --> 00:11:39.209 over proxy in the last 15 years is that

NOTE Confidence: 0.86044985

00:11:39.209 --> 00:11:42.499 changes in sleep may serve as a marker

NOTE Confidence: 0.86044985

00:11:42.499 --> 00:11:45.271 for risk of future cognitive impairment

NOTE Confidence: 0.86044985

00:11:45.271 --> 00:11:48.108 or risk of future Alzheimer's disease.

NOTE Confidence: 0.86044985

00:11:48.108 --> 00:11:51.830 Or a marker for the underlying pathology.

NOTE Confidence: 0.86044985

00:11:51.830 --> 00:11:54.550 So in a study in 2011 from Ricardo

NOTE Confidence: 0.86044985

00:11:54.550 --> 00:11:57.287 Osorio from NYU individuals who reported

NOTE Confidence: 0.86044985

00:11:57.287 --> 00:12:00.257 insomnia had a faster progression from

NOTE Confidence: 0.86044985

00:12:00.339 --> 00:12:03.135 normal cognition to dementia and in

NOTE Confidence: 0.86044985

00:12:03.135 --> 00:12:06.092 multiple other studies list some of them,

NOTE Confidence: 0.86044985

00:12:06.092 --> 00:12:09.222 many of them listed at the bottom of

NOTE Confidence: 0.86044985

00:12:09.222 --> 00:12:11.737 the slide have associated numerously

NOTE Confidence: 0.86044985

00:12:11.737 --> 00:12:14.698 parameters with either 80 pathology or

NOTE Confidence: 0.86044985

00:12:14.698 --> 00:12:17.296 risk or risk of cognitive impairment

NOTE Confidence: 0.86044985

00:12:17.296 --> 00:12:18.685 in the future.

NOTE Confidence: 0.86044985

00:12:18.685 --> 00:12:21.260 And so basically parameters include

NOTE Confidence: 0.86044985

00:12:21.260 --> 00:12:23.718 total sleep time, sleep efficiency,

NOTE Confidence: 0.86044985

00:12:23.718 --> 00:12:26.442 non ram, slide activity and sleep

NOTE Confidence: 0.86044985

00:12:26.442 --> 00:12:28.250 disorders like sleep apnea.

NOTE Confidence: 0.86214674

00:12:34.460 --> 00:12:36.348 Considering total sleep time

NOTE Confidence: 0.86214674

00:12:36.348 --> 00:12:38.708 and risk of impaired cognition,

NOTE Confidence: 0.86214674

00:12:38.710 --> 00:12:41.068 many studies have shown that both

NOTE Confidence: 0.86214674

00:12:41.068 --> 00:12:43.272 short and long sleep duration

NOTE Confidence: 0.86214674

00:12:43.272 --> 00:12:45.476 are associated with increased

NOTE Confidence: 0.86214674

00:12:45.476 --> 00:12:47.680 risk of cognitive impairment.

NOTE Confidence: 0.86214674

00:12:47.680 --> 00:12:51.448 So at the in this top bullet point,

NOTE Confidence: 0.86214674

00:12:51.450 --> 00:12:54.410 short sleep duration of less

NOTE Confidence: 0.86214674

00:12:54.410 --> 00:12:57.820 than equal to five hours in.

NOTE Confidence: 0.86214674

00:12:57.820 --> 00:13:01.523 Cohort of 18 / 1800 community dwelling

NOTE Confidence: 0.86214674

00:13:01.523 --> 00:13:05.229 older women had increased risk of

NOTE Confidence: 0.86214674

00:13:05.229 --> 00:13:08.594 cognitive impairment after two years.

NOTE Confidence: 0.86214674

00:13:08.600 --> 00:13:10.900 Another study of over 3000

NOTE Confidence: 0.86214674

00:13:10.900 --> 00:13:12.280 dwelling older men,

NOTE Confidence: 0.86214674

00:13:12.280 --> 00:13:14.645 those reporting greater than 9

NOTE Confidence: 0.86214674

00:13:14.645 --> 00:13:17.010 hours of sleep Cross Sectionally

NOTE Confidence: 0.86214674

00:13:17.094 --> 00:13:19.198 had increased cognitive impairment

NOTE Confidence: 0.86214674

00:13:19.198 --> 00:13:21.828 and there's many other studies

NOTE Confidence: 0.86214674

00:13:21.828 --> 00:13:24.235 that I could I could go over.

NOTE Confidence: 0.86214674

00:13:24.240 --> 00:13:26.898 Some show also showing short sleep

NOTE Confidence: 0.86214674

00:13:26.898 --> 00:13:29.215 duration being associated with cognitive

NOTE Confidence: 0.86214674

00:13:29.215 --> 00:13:31.600 problems or long sleep duration,

NOTE Confidence: 0.86214674

00:13:31.600 --> 00:13:32.480 or both,

NOTE Confidence: 0.86214674

00:13:32.480 --> 00:13:36.625 such as this figure on the right that that

NOTE Confidence: 0.86214674

00:13:36.625 --> 00:13:40.307 came out recently in JAMA Network Open.

NOTE Confidence: 0.86214674

00:13:40.310 --> 00:13:43.566 Journal this was a pooled study of two

NOTE Confidence: 0.86214674

00:13:43.566 --> 00:13:46.460 cohorts of over 20,000 individuals,

NOTE Confidence: 0.86214674

00:13:46.460 --> 00:13:50.128 and they found that the self reported

NOTE Confidence: 0.86214674

00:13:50.128 --> 00:13:53.557 sleep duration that was very low is

NOTE Confidence: 0.86214674

00:13:53.557 --> 00:13:56.203 probably less than five hours of

NOTE Confidence: 0.86214674

00:13:56.298 --> 00:13:59.698 sleep per night or on the higher end,

NOTE Confidence: 0.86214674

00:13:59.700 --> 00:14:03.484 say 7 1/2 hours of sleep per night.

NOTE Confidence: 0.86214674

00:14:03.490 --> 00:14:05.490 That was self reported.

NOTE Confidence: 0.86214674

00:14:05.490 --> 00:14:07.990 There was declines in cognitive

NOTE Confidence: 0.86214674

00:14:07.990 --> 00:14:10.659 performance on a cognitive composite of.

NOTE Confidence: 0.86214674

00:14:10.660 --> 00:14:11.662 Several tests.

NOTE Confidence: 0.86214674

00:14:11.662 --> 00:14:15.169 And so this suggests that potentially short,

NOTE Confidence: 0.86214674

00:14:15.170 --> 00:14:18.250 and I think it's very good evidence

NOTE Confidence: 0.86214674

00:14:18.250 --> 00:14:21.300 that short and long sleep duration

NOTE Confidence: 0.86214674

00:14:21.300 --> 00:14:24.576 could be a marker for cognitive

NOTE Confidence: 0.86214674

00:14:24.576 --> 00:14:27.588 impairment and also a predictor of it.

NOTE Confidence: 0.86214674

00:14:27.590 --> 00:14:30.406 I think that the I think the the

NOTE Confidence: 0.86214674

00:14:30.406 --> 00:14:32.933 reason why short sleep duration could

NOTE Confidence: 0.86214674

00:14:32.933 --> 00:14:36.280 be a risk factor is fairly evident.

NOTE Confidence: 0.86214674

00:14:36.280 --> 00:14:38.656 They're just not getting enough restorative

NOTE Confidence: 0.86214674

00:14:38.656 --> 00:14:40.840 sleep for longer sleep duration.

NOTE Confidence: 0.86214674

00:14:40.840 --> 00:14:42.910 I suspect that the quality

NOTE Confidence: 0.86214674

00:14:42.910 --> 00:14:44.980 of the sleep is poor,

NOTE Confidence: 0.86214674

00:14:44.980 --> 00:14:47.374 either due to an unrecognized sleep

NOTE Confidence: 0.86214674

00:14:47.374 --> 00:14:50.359 problem or other or other other issue.

NOTE Confidence: 0.8388676

00:14:52.730 --> 00:14:55.142 Obstructive sleep apnea has been associated

NOTE Confidence: 0.8388676

00:14:55.142 --> 00:14:57.360 with increased risk of dementia.

NOTE Confidence: 0.8388676

00:14:57.360 --> 00:15:00.055 This is work from Christine Ya Phase

NOTE Confidence: 0.8388676

00:15:00.055 --> 00:15:02.533 Group at UCSF that's published in

NOTE Confidence: 0.8388676

00:15:02.533 --> 00:15:05.969 JAMA nine years ago and this study of

NOTE Confidence: 0.8388676

00:15:05.969 --> 00:15:08.645 300 older women who are cognitively

NOTE Confidence: 0.8388676

00:15:08.645 --> 00:15:11.652 normal and followed for four years,

NOTE Confidence: 0.8388676

00:15:11.652 --> 00:15:14.976 oxygens de saturation index greater than

NOTE Confidence: 0.8388676

00:15:14.976 --> 00:15:18.295 equal to 15 was associated with 1.7.

NOTE Confidence: 0.8388676

00:15:18.300 --> 00:15:20.810 Your odds of getting cottonmouth,

NOTE Confidence: 0.8388676

00:15:20.810 --> 00:15:22.878 cotton impairment or dementia

NOTE Confidence: 0.8388676

00:15:22.878 --> 00:15:25.980 compared to those with less than

NOTE Confidence: 0.8388676

00:15:26.067 --> 00:15:28.815 15 de saturation events per hour,

NOTE Confidence: 0.8388676

00:15:28.820 --> 00:15:31.795 and this is after adjusting

NOTE Confidence: 0.8388676

00:15:31.795 --> 00:15:33.580 for multiple covariates.

NOTE Confidence: 0.8388676

00:15:33.580 --> 00:15:37.713 And if spending greater than 7% of

NOTE Confidence: 0.8388676

00:15:37.713 --> 00:15:40.971 the night in apnea hypocapnia had

NOTE Confidence: 0.8388676

00:15:40.971 --> 00:15:45.920 an odds ratio of two for having risk

NOTE Confidence: 0.8388676

00:15:45.920 --> 00:15:49.125 of cognitive impairment or dementia,

NOTE Confidence: 0.8388676

00:15:49.130 --> 00:15:52.115 again also adjusting for multiple

NOTE Confidence: 0.8388676

00:15:52.115 --> 00:15:53.309 potential confounders.

NOTE Confidence: 0.8204676

00:15:57.490 --> 00:16:00.322 Studies have also looked at cognitively

NOTE Confidence: 0.8204676

00:16:00.322 --> 00:16:03.024 normal individuals and whether or not

NOTE Confidence: 0.8204676

00:16:03.024 --> 00:16:05.621 their sleep is disturbed when they have

NOTE Confidence: 0.8204676

00:16:05.621 --> 00:16:08.290 evidence of Alzheimer's disease pathology.

NOTE Confidence: 0.8204676

00:16:08.290 --> 00:16:11.930 The figure on the left is from Adam Spira in

NOTE Confidence: 0.8204676

00:16:12.014 --> 00:16:15.488 the Baltimore longitudinal study of aging,

NOTE Confidence: 0.8204676

00:16:15.490 --> 00:16:17.402 or where Conley Normal,

NOTE Confidence: 0.8204676

00:16:17.402 --> 00:16:20.270 older adults who reported less than

NOTE Confidence: 0.8204676

00:16:20.360 --> 00:16:23.216 or equal to six hours of sleep per

NOTE Confidence: 0.8204676

00:16:23.216 --> 00:16:25.581 night had greater amyloid deposition

NOTE Confidence: 0.8204676

00:16:25.581 --> 00:16:28.719 on pet scans compared to those.

NOTE Confidence: 0.8204676

00:16:28.720 --> 00:16:32.017 Or reporting sleeping 6 to 7 hours

NOTE Confidence: 0.8204676

00:16:32.017 --> 00:16:35.228 or greater than 7 hours per night.

NOTE Confidence: 0.8204676

00:16:35.230 --> 00:16:36.631 From my institution.

NOTE Confidence: 0.8204676

00:16:36.631 --> 00:16:39.433 UL Joo measured sleep efficiency using

NOTE Confidence: 0.8204676

00:16:39.433 --> 00:16:41.684 actigraphy and cognitively normal older

NOTE Confidence: 0.8204676

00:16:41.684 --> 00:16:44.246 adults who also had cerebral spinal

NOTE Confidence: 0.8204676

00:16:44.320 --> 00:16:46.860 fluid for amyloid beta concentrations,

NOTE Confidence: 0.8204676

00:16:46.860 --> 00:16:49.821 so she was able to establish whether

NOTE Confidence: 0.8204676

00:16:49.821 --> 00:16:51.970 they were cognitively everything,

NOTE Confidence: 0.8204676

00:16:51.970 --> 00:16:53.830 whether they are employed

NOTE Confidence: 0.8204676

00:16:53.830 --> 00:16:55.225 negative or positive,

NOTE Confidence: 0.8204676

00:16:55.230 --> 00:16:57.274 based on the employee.

NOTE Confidence: 0.8204676

00:16:57.274 --> 00:16:58.807 Beta 42 concentrations.

NOTE Confidence: 0.8204676

00:16:58.810 --> 00:17:01.385 The concentration of amyloid beta

NOTE Confidence: 0.8204676

00:17:01.385 --> 00:17:03.960 decreases when your amyloid positive

NOTE Confidence: 0.8204676

00:17:04.038 --> 00:17:06.918 so less than or equal to 500 picograms

NOTE Confidence: 0.8204676

00:17:06.918 --> 00:17:09.664 fermil was consistent with being amyloid

NOTE Confidence: 0.8204676

00:17:09.664 --> 00:17:12.580 positive and a larger percentage of.

NOTE Confidence: 0.8145365

00:17:15.460 --> 00:17:18.603 Individuals who are kind of normal amyloid

NOTE Confidence: 0.8145365

00:17:18.603 --> 00:17:21.822 positive or more likely to have lower

NOTE Confidence: 0.8145365

00:17:21.822 --> 00:17:25.150 sleep efficiency compared to those who are

NOTE Confidence: 0.8145365

00:17:25.150 --> 00:17:27.940 cognitively normal but amyloid negative.

NOTE Confidence: 0.8145365

00:17:27.940 --> 00:17:31.900 So evidence that from these two studies that

NOTE Confidence: 0.8145365

00:17:31.900 --> 00:17:35.500 changes in sleep can reflect underlying

NOTE Confidence: 0.8145365

00:17:35.500 --> 00:17:38.650 changes in amyloid beta pathology.

NOTE Confidence: 0.8145365

00:17:38.650 --> 00:17:43.326 Looking at non ram slow wave activity.

NOTE Confidence: 0.8145365

00:17:43.330 --> 00:17:46.386 This is also been a marker of great

NOTE Confidence: 0.8145365

00:17:46.386 --> 00:17:49.440 interest to our group and other groups.

NOTE Confidence: 0.8145365

00:17:49.440 --> 00:17:52.624 Figure on the left is from Matthew Walker's

NOTE Confidence: 0.8145365

00:17:52.624 --> 00:17:55.947 group at UC Berkeley and they studied 26.

NOTE Confidence: 0.8145365

00:17:55.950 --> 00:17:57.129 Can't be normal.

NOTE Confidence: 0.8145365

00:17:57.129 --> 00:17:59.880 Older adults and using pet scans looked

NOTE Confidence: 0.8145365

00:17:59.954 --> 00:18:02.480 at the medial prefrontal cortex and

NOTE Confidence: 0.8145365

00:18:02.480 --> 00:18:05.408 the Android Burden there and show that

NOTE Confidence: 0.8145365

00:18:05.408 --> 00:18:07.748 is amyloid increased in this region.

NOTE Confidence: 0.8145365

00:18:07.750 --> 00:18:11.789 There is a decrease in non REM

NOTE Confidence: 0.8145365

00:18:11.789 --> 00:18:12.943 slave activity.

NOTE Confidence: 0.8145365

00:18:12.950 --> 00:18:15.145 Here in Washington University we

NOTE Confidence: 0.8145365

00:18:15.145 --> 00:18:18.809 looked at a mix of Conley Normalan,

NOTE Confidence: 0.8145365

00:18:18.810 --> 00:18:20.758 mildly impaired older adults.

NOTE Confidence: 0.8145365

00:18:20.758 --> 00:18:23.193 There is total of 38.

NOTE Confidence: 0.8145365

00:18:23.200 --> 00:18:25.640 About 80% were cognitively normal,

NOTE Confidence: 0.8145365

00:18:25.640 --> 00:18:28.965 and we found that non REM sleep

NOTE Confidence: 0.8145365

00:18:28.965 --> 00:18:32.372 activity at both 1 to 4.5 Hertz and

NOTE Confidence: 0.8145365

00:18:32.372 --> 00:18:35.626 and also it was the most significant

NOTE Confidence: 0.8145365

00:18:35.626 --> 00:18:38.806 effect that wanted to herds,

NOTE Confidence: 0.8145365

00:18:38.810 --> 00:18:42.870 was was inversely associated with.

NOTE Confidence: 0.8145365

00:18:42.870 --> 00:18:45.260 Tau deposition on pet scans,

NOTE Confidence: 0.8145365

00:18:45.260 --> 00:18:48.606 where as the sort of activity decreased,

NOTE Confidence: 0.8145365

00:18:48.610 --> 00:18:51.532 there was an increase in the

NOTE Confidence: 0.8145365

00:18:51.532 --> 00:18:54.921 Tau deposition and this is after

NOTE Confidence: 0.8145365

00:18:54.921 --> 00:18:57.605 adjusting for multiple covariates.

NOTE Confidence: 0.8145365

00:18:57.610 --> 00:18:59.315 These figures show regional analysis

NOTE Confidence: 0.8145365

00:18:59.315 --> 00:19:01.440 where we use the same model,

NOTE Confidence: 0.8145365

00:19:01.440 --> 00:19:03.869 but instead of using the global composite,

NOTE Confidence: 0.8145365

00:19:03.870 --> 00:19:05.385 included each region separately and

NOTE Confidence: 0.8145365

00:19:05.385 --> 00:19:07.354 these are the regions that remain

NOTE Confidence: 0.8145365

00:19:07.354 --> 00:19:08.946 significant even after adjusting

NOTE Confidence: 0.8145365

00:19:08.946 --> 00:19:10.140 for multiple comparisons,

NOTE Confidence: 0.8145365

00:19:10.140 --> 00:19:12.506 so they were they were highly significant

NOTE Confidence: 0.8145365

00:19:12.506 --> 00:19:14.641 in terms of the relationship with

NOTE Confidence: 0.8145365

00:19:14.641 --> 00:19:17.098 with an on ramp slow of activity.

NOTE Confidence: 0.85056037

00:19:22.490 --> 00:19:24.614 So the two questions that really

NOTE Confidence: 0.85056037

00:19:24.614 --> 00:19:27.278 underlie my work are based on the

NOTE Confidence: 0.85056037

00:19:27.278 --> 00:19:29.248 idea that sleep dysfunction is

NOTE Confidence: 0.85056037

00:19:29.248 --> 00:19:32.003 associated with the risk of cognitive

NOTE Confidence: 0.85056037

00:19:32.003 --> 00:19:33.903 impairment and Alzheimer's disease,

NOTE Confidence: 0.85056037

00:19:33.910 --> 00:19:36.766 and there's a long lead time for

NOTE Confidence: 0.85056037

00:19:36.766 --> 00:19:37.990 Alzheimer disease pathogenesis.

NOTE Confidence: 0.85056037

00:19:37.990 --> 00:19:41.662 So we chicken in the egg question about this.

NOTE Confidence: 0.85056037

00:19:41.670 --> 00:19:43.262 About this bidirectional relationship.

NOTE Confidence: 0.85056037

00:19:43.262 --> 00:19:46.560 What is what is what is coming first?

NOTE Confidence: 0.85056037

00:19:46.560 --> 00:19:49.416 Or is it for? Is it possible?

NOTE Confidence: 0.85056037

00:19:49.420 --> 00:19:52.748 Is what I think that you could have.

NOTE Confidence: 0.85056037

00:19:52.750 --> 00:19:54.630 Sleep disturbances that are being

NOTE Confidence: 0.85056037

00:19:54.630 --> 00:19:56.510 caused by Alzheimer's disease pathology

NOTE Confidence: 0.85056037

00:19:56.568 --> 00:19:58.373 but also Alzheimer's disease with

NOTE Confidence: 0.85056037

00:19:58.373 --> 00:20:00.178 sleep disturbances can be promoting.

NOTE Confidence: 0.85056037

00:20:00.180 --> 00:20:03.498 Same resumes pathology.

NOTE Confidence: 0.85056037

00:20:03.500 --> 00:20:06.300 And in the remainder of the talk,

NOTE Confidence: 0.85056037

00:20:06.300 --> 00:20:08.916 I want to go through a few mechanisms

NOTE Confidence: 0.85056037

00:20:08.916 --> 00:20:11.499 that may explain this relationship.

NOTE Confidence: 0.8965814

00:20:17.500 --> 00:20:20.300 Actually, I before I get to the mechanisms

NOTE Confidence: 0.8965814

00:20:20.300 --> 00:20:23.262 I didn't want to make one point about

NOTE Confidence: 0.8965814

00:20:23.262 --> 00:20:25.619 the complexity of trying to sort out.

NOTE Confidence: 0.8409617

00:20:27.880 --> 00:20:29.074 What what, what,

NOTE Confidence: 0.8409617

00:20:29.074 --> 00:20:31.860 what changes are occurring and when in

NOTE Confidence: 0.8409617

00:20:31.941 --> 00:20:34.769 terms of sleep and 80 the pathogenesis,

NOTE Confidence: 0.8409617

00:20:34.770 --> 00:20:39.586 the factors that affect 80 risk and sleep.

NOTE Confidence: 0.8409617

00:20:39.590 --> 00:20:43.132 Are many so age, sex, physical activity,

NOTE Confidence: 0.8409617

00:20:43.132 --> 00:20:44.650 depression, vascular disease,

NOTE Confidence: 0.8409617

00:20:44.650 --> 00:20:47.000 health disparities could affect both

NOTE Confidence: 0.8409617

00:20:47.000 --> 00:20:50.537 sleep quality as well as the risk

NOTE Confidence: 0.8409617

00:20:50.537 --> 00:20:52.745 of developing Alzheimer's disease.

NOTE Confidence: 0.8409617

00:20:52.750 --> 00:20:55.786 And some of these factors may

NOTE Confidence: 0.8409617

00:20:55.786 --> 00:20:57.810 affect each each other.

NOTE Confidence: 0.8409617

00:20:57.810 --> 00:20:58.820 For instance,

NOTE Confidence: 0.8409617

00:20:58.820 --> 00:21:01.345 decreased physical activity with age,

NOTE Confidence: 0.8409617

00:21:01.350 --> 00:21:02.865 increased medical comorbidities

NOTE Confidence: 0.8409617

00:21:02.865 --> 00:21:05.895 such as vascular disease with age,

NOTE Confidence: 0.8409617

00:21:05.900 --> 00:21:08.490 and it's not understood how

NOTE Confidence: 0.8409617

00:21:08.490 --> 00:21:10.562 these factors may interact.

NOTE Confidence: 0.8409617

00:21:10.570 --> 00:21:12.515 Modify or mediate each other

NOTE Confidence: 0.8409617

00:21:12.515 --> 00:21:14.908 and it just illustrate that that

NOTE Confidence: 0.8409617

00:21:14.908 --> 00:21:17.158 point I'd like to highlight this

NOTE Confidence: 0.8409617

00:21:17.158 --> 00:21:19.329 paper from Carla Styles for go.

NOTE Confidence: 0.8409617

00:21:19.330 --> 00:21:21.283 So and Tom Gill at Yale that

NOTE Confidence: 0.8409617

00:21:21.283 --> 00:21:23.277 when I was putting together

NOTE Confidence: 0.8409617

00:21:23.277 --> 00:21:25.429 my career development award,

NOTE Confidence: 0.8409617

00:21:25.430 --> 00:21:25.815 really,

NOTE Confidence: 0.8409617

00:21:25.815 --> 00:21:28.125 really brought together a lot of

NOTE Confidence: 0.8409617

00:21:28.125 --> 00:21:30.927 things that I was reading and thinking

NOTE Confidence: 0.8409617

00:21:30.927 --> 00:21:33.279 about and was a nice framework

NOTE Confidence: 0.8409617

00:21:33.360 --> 00:21:35.460 for me and I think illustrates

NOTE Confidence: 0.8409617

00:21:35.460 --> 00:21:37.656 the effect of just age alone.

NOTE Confidence: 0.8409617

00:21:37.656 --> 00:21:40.840 On trying to get at the bottom of.

NOTE Confidence: 0.8409617

00:21:40.840 --> 00:21:42.600 Of the relationship between

NOTE Confidence: 0.8409617

00:21:42.600 --> 00:21:44.360 sleep and Alzheimer's disease.

NOTE Confidence: 0.8409617

00:21:44.360 --> 00:21:46.904 Now we know that there are

NOTE Confidence: 0.8409617

00:21:46.904 --> 00:21:49.200 multiple factors that a sleep,

NOTE Confidence: 0.8409617

00:21:49.200 --> 00:21:50.080 sleep, sleep,

NOTE Confidence: 0.8409617

00:21:50.080 --> 00:21:51.840 sleep factors that change

NOTE Confidence: 0.8409617

00:21:51.840 --> 00:21:53.160 during normal aging,

NOTE Confidence: 0.8409617

00:21:53.160 --> 00:21:55.800 such as decreased slow wave activity.

NOTE Confidence: 0.8409617

00:21:55.800 --> 00:21:58.260 And there can be sex differences

NOTE Confidence: 0.8409617

00:21:58.260 --> 00:22:00.640 for some of these factors.

NOTE Confidence: 0.8409617

00:22:00.640 --> 00:22:02.368 There's precipitating factors that

NOTE Confidence: 0.8409617

00:22:02.368 --> 00:22:04.960 occur with usual aging like increased

NOTE Confidence: 0.8409617

00:22:05.020 --> 00:22:07.240 incidence of primary sleep disorders,

NOTE Confidence: 0.8409617

00:22:07.240 --> 00:22:08.936 change in health status.

NOTE Confidence: 0.8409617

00:22:08.936 --> 00:22:11.056 There can be psychosocial factors

NOTE Confidence: 0.8409617

00:22:11.056 --> 00:22:13.768 like social isolation and bereavement.

NOTE Confidence: 0.8409617

00:22:13.770 --> 00:22:15.675 And these can interact together

NOTE Confidence: 0.8409617

00:22:15.675 --> 00:22:17.580 to affect sleep that could

NOTE Confidence: 0.8409617

00:22:17.654 --> 00:22:20.089 potentially lead to adverse outcomes,

NOTE Confidence: 0.8409617

00:22:20.090 --> 00:22:22.556 and these adverse outcomes in and

NOTE Confidence: 0.8409617

00:22:22.556 --> 00:22:24.200 of themselves could potentially

NOTE Confidence: 0.8409617

00:22:24.270 --> 00:22:25.978 feedback and impair asleep.

NOTE Confidence: 0.8409617

00:22:25.980 --> 00:22:28.927 And so I think that just underlies

NOTE Confidence: 0.8409617

00:22:28.927 --> 00:22:29.769 the complex.

NOTE Confidence: 0.8409617

00:22:29.770 --> 00:22:32.521 The complexity of the task to really

NOTE Confidence: 0.8409617

00:22:32.521 --> 00:22:34.230 establish the relationship between

NOTE Confidence: 0.8409617

00:22:34.230 --> 00:22:36.078 sleep in Alzheimer's disease,

NOTE Confidence: 0.8409617

00:22:36.080 --> 00:22:38.060 especially with the eye toward

NOTE Confidence: 0.8409617

00:22:38.060 --> 00:22:40.573 using it using a sleep intervention

NOTE Confidence: 0.8409617

00:22:40.573 --> 00:22:42.818 to prevent or delay AD.

NOTE Confidence: 0.86940813

00:22:46.790 --> 00:22:48.880 OK, now onto the mechanism.

NOTE Confidence: 0.86940813

00:22:48.880 --> 00:22:51.624 So first I want to talk about is

NOTE Confidence: 0.86940813

00:22:51.624 --> 00:22:54.300 amyloid beta production and clearance.

NOTE Confidence: 0.8335245

00:22:57.470 --> 00:22:59.810 We know that amyloid beta fluctuates

NOTE Confidence: 0.8335245

00:22:59.810 --> 00:23:01.860 with the sleep Wake Cycle.

NOTE Confidence: 0.8335245

00:23:01.860 --> 00:23:04.695 This has been shown in mice and

NOTE Confidence: 0.8335245

00:23:04.695 --> 00:23:07.447 the figure on the on the left,

NOTE Confidence: 0.8335245

00:23:07.450 --> 00:23:09.802 where the interstitial fluid

NOTE Confidence: 0.8335245

00:23:09.802 --> 00:23:12.154 concentration of amyloid beta.

NOTE Confidence: 0.8335245

00:23:12.160 --> 00:23:14.320 Oscillates with the minutes awake

NOTE Confidence: 0.8335245

00:23:14.320 --> 00:23:17.020 per hour when those are lower,

NOTE Confidence: 0.8335245

00:23:17.020 --> 00:23:20.188 their concentration is lower.

NOTE Confidence: 0.8335245

00:23:20.190 --> 00:23:23.256 And it's also been seen in humans.

NOTE Confidence: 0.8335245

00:23:23.260 --> 00:23:25.474 This is a study that was

NOTE Confidence: 0.8335245

00:23:25.474 --> 00:23:27.614 conducted by Randall Bateman at

NOTE Confidence: 0.8335245

00:23:27.614 --> 00:23:29.390 watching Washington University,

NOTE Confidence: 0.8335245

00:23:29.390 --> 00:23:33.338 where lumbar catheters or placed in CSF

NOTE Confidence: 0.8335245

00:23:33.338 --> 00:23:36.909 was sampled every hour for 36 hours.

NOTE Confidence: 0.8335245

00:23:36.910 --> 00:23:39.844 A beta 42 and a beta 40 were shown

NOTE Confidence: 0.8335245

00:23:39.844 --> 00:23:43.174 to oscillate over this 36 hour period

NOTE Confidence: 0.8335245

00:23:43.174 --> 00:23:46.618 and to be associated with with sleep,

NOTE Confidence: 0.8335245

00:23:46.620 --> 00:23:49.406 and so the triangles are the total

NOTE Confidence: 0.8335245

00:23:49.406 --> 00:23:52.098 sleep time in minutes per hour.

NOTE Confidence: 0.8335245

00:23:52.100 --> 00:23:55.444 You'll notice that there is a delay of

NOTE Confidence: 0.8335245

00:23:55.444 --> 00:23:57.613 approximately 5 hours between changes

NOTE Confidence: 0.8335245

00:23:57.613 --> 00:24:00.539 in a beta and changes and sleep,

NOTE Confidence: 0.8335245

00:24:00.540 --> 00:24:03.732 and this is due to the transit time

NOTE Confidence: 0.8335245

00:24:03.732 --> 00:24:07.250 from the brain to the lumbar catheter.

NOTE Confidence: 0.8335245

00:24:07.250 --> 00:24:09.718 In the lower back.

NOTE Confidence: 0.8715732

00:24:12.150 --> 00:24:14.950 One mechanism that that

NOTE Confidence: 0.8715732

00:24:14.950 --> 00:24:18.450 that has been proposed to.

NOTE Confidence: 0.8715732

00:24:18.450 --> 00:24:20.990 Mediate the changes in concentration

NOTE Confidence: 0.8715732

00:24:20.990 --> 00:24:23.022 with changes in sleep.

NOTE Confidence: 0.8715732

00:24:23.030 --> 00:24:25.580 Wake activity is neuronal activity.

NOTE Confidence: 0.8715732

00:24:25.580 --> 00:24:28.628 So neural activity decreases during sleep.

NOTE Confidence: 0.8715732

00:24:28.630 --> 00:24:32.186 In this study they had monitored sleep.

NOTE Confidence: 0.8715732

00:24:32.190 --> 00:24:36.271 You can see slow waves that were

NOTE Confidence: 0.8715732

00:24:36.271 --> 00:24:40.009 recorded and they correlated with.

NOTE Confidence: 0.8715732

00:24:40.010 --> 00:24:42.674 Metabolic activity on a pet scan

NOTE Confidence: 0.8715732

00:24:42.674 --> 00:24:45.637 showed that as the slave activity

NOTE Confidence: 0.8715732

00:24:45.637 --> 00:24:48.377 increased that there was a

NOTE Confidence: 0.8715732

00:24:48.377 --> 00:24:51.075 decrease in metabolic activity in

NOTE Confidence: 0.8715732

00:24:51.075 --> 00:24:53.949 the regions that they looked at.

NOTE Confidence: 0.8715732

00:24:53.950 --> 00:24:56.560 More.

NOTE Confidence: 0.8715732

00:24:56.560 --> 00:25:00.355 Controlled experiments in animal models

NOTE Confidence: 0.8715732

00:25:00.355 --> 00:25:04.150 have shown that stimulating pathway

NOTE Confidence: 0.8715732

00:25:04.257 --> 00:25:07.657 electrical stimulation has increased

NOTE Confidence: 0.8715732

00:25:07.657 --> 00:25:11.907 amyloid beta concentrations in the

NOTE Confidence: 0.8715732

00:25:11.907 --> 00:25:14.789 interstitial fluid and blocking.

NOTE Confidence: 0.8715732

00:25:14.790 --> 00:25:17.598 Oral activity has decreased them and

NOTE Confidence: 0.8715732

00:25:17.598 --> 00:25:20.034 other proteins that are released

NOTE Confidence: 0.8715732

00:25:20.034 --> 00:25:22.932 with neural activity such as Tau

NOTE Confidence: 0.8715732

00:25:22.932 --> 00:25:24.381 and Alpha Synuclein,

NOTE Confidence: 0.8715732

00:25:24.390 --> 00:25:27.750 have shown the same effect in mice,

NOTE Confidence: 0.8715732

00:25:27.750 --> 00:25:29.190 where stimulation increases,

NOTE Confidence: 0.8715732

00:25:29.190 --> 00:25:31.110 the concentration of both.

NOTE Confidence: 0.818451100000001

00:25:34.030 --> 00:25:36.732 On the foot on the opposite side

NOTE Confidence: 0.818451100000001

00:25:36.732 --> 00:25:39.056 of production we have clearance

NOTE Confidence: 0.818451100000001

00:25:39.056 --> 00:25:41.771 and there's a clearance mechanism

NOTE Confidence: 0.818451100000001

00:25:41.771 --> 00:25:44.844 that's been proposed to to control

NOTE Confidence: 0.818451100000001

00:25:44.844 --> 00:25:47.109 the oscillation of amyloid beta.

NOTE Confidence: 0.818451100000001

00:25:47.110 --> 00:25:50.164 This is the glymphatic system where

NOTE Confidence: 0.818451100000001

00:25:50.164 --> 00:25:53.818 convective bulk flow of fluid from the

NOTE Confidence: 0.818451100000001

00:25:53.818 --> 00:25:56.872 arterial system to the venous system

NOTE Confidence: 0.818451100000001

00:25:56.872 --> 00:26:00.580 removes solid waste products from the brain.

NOTE Confidence: 0.818451100000001

00:26:00.580 --> 00:26:04.258 First described in.

NOTE Confidence: 0.818451100000001

00:26:04.260 --> 00:26:07.403 If it's Association with sleep in this

NOTE Confidence: 0.818451100000001

00:26:07.403 --> 00:26:10.201 landmark paper from making it regards

NOTE Confidence: 0.818451100000001

00:26:10.201 --> 00:26:12.937 lab at the University of Rochester,

NOTE Confidence: 0.818451100000001

00:26:12.940 --> 00:26:16.139 where dye injected on the cortical surface.

NOTE Confidence: 0.818451100000001

00:26:16.140 --> 00:26:19.796 In this case, the green died during sleep,

NOTE Confidence: 0.818451100000001

00:26:19.800 --> 00:26:22.085 penetrates into the prank comma

NOTE Confidence: 0.818451100000001

00:26:22.085 --> 00:26:24.370 much more deeply than that.

NOTE Confidence: 0.818451100000001

00:26:24.370 --> 00:26:27.100 The red dye injected during during

NOTE Confidence: 0.818451100000001

00:26:27.100 --> 00:26:29.899 wakefulness and the proposed mechanism is

NOTE Confidence: 0.818451100000001

00:26:29.899 --> 00:26:33.049 that when we're when individual is younger,

NOTE Confidence: 0.818451100000001

00:26:33.050 --> 00:26:34.448 this flow is.

NOTE Confidence: 0.818451100000001

00:26:34.448 --> 00:26:36.778 Very efficient at removing waste

NOTE Confidence: 0.818451100000001

00:26:36.778 --> 00:26:39.029 products such as amyloid beta,

NOTE Confidence: 0.818451100000001

00:26:39.030 --> 00:26:41.305 but becomes disrupted with age

NOTE Confidence: 0.818451100000001

00:26:41.305 --> 00:26:43.580 leading to those we didn't.

NOTE Confidence: 0.818451100000001

00:26:43.580 --> 00:26:45.400 Emily beta accumulating in

NOTE Confidence: 0.818451100000001

00:26:45.400 --> 00:26:47.220 the brain forming pathology,

NOTE Confidence: 0.818451100000001

00:26:47.220 --> 00:26:49.752 further disrupting it and acting as

NOTE Confidence: 0.818451100000001

00:26:49.752 --> 00:26:52.230 a especially a feedback mechanism.

NOTE Confidence: 0.8068333

00:26:54.410 --> 00:26:56.340 I think that's you know,

NOTE Confidence: 0.8068333

00:26:56.340 --> 00:26:58.650 since since a beta of fluctuates,

NOTE Confidence: 0.8068333

00:26:58.650 --> 00:27:00.206 a sleep wake activity,

NOTE Confidence: 0.8068333

00:27:00.206 --> 00:27:02.151 it immediately raises the question

NOTE Confidence: 0.8068333

00:27:02.151 --> 00:27:04.420 of if you can manipulate sleep,

NOTE Confidence: 0.8068333

00:27:04.420 --> 00:27:06.952 can you manipulate amyloid beta and

NOTE Confidence: 0.8068333

00:27:06.952 --> 00:27:09.805 studies in mice have shown that

NOTE Confidence: 0.8068333

00:27:09.805 --> 00:27:11.969 sleep deprivation does increase.

NOTE Confidence: 0.8068333

00:27:11.970 --> 00:27:14.958 Soluble amyloid beta concentrations

NOTE Confidence: 0.8068333

00:27:14.958 --> 00:27:20.110 in this very elegant study from Ulju.

NOTE Confidence: 0.8068333

00:27:20.110 --> 00:27:22.435 Slow wave sleep was selectively

NOTE Confidence: 0.8068333

00:27:22.435 --> 00:27:24.760 disrupted using tones while participants

NOTE Confidence: 0.8068333

00:27:24.831 --> 00:27:27.134 were sleeping and they had a lumbar

NOTE Confidence: 0.8068333

00:27:27.134 --> 00:27:29.377 puncture in the morning following the

NOTE Confidence: 0.8068333

00:27:29.377 --> 00:27:31.741 intervention and also did it twice

NOTE Confidence: 0.8068333

00:27:31.741 --> 00:27:34.330 with a sham procedure where slowed

NOTE Confidence: 0.8068333

00:27:34.330 --> 00:27:36.924 sleep was not being disrupted and

NOTE Confidence: 0.8068333

00:27:36.924 --> 00:27:39.532 what she had shown was that great of

NOTE Confidence: 0.8068333

00:27:39.532 --> 00:27:42.166 the disruption in slow wave sleep.

NOTE Confidence: 0.8068333

00:27:42.170 --> 00:27:44.366 The greater the increase in slave

NOTE Confidence: 0.8068333

00:27:44.366 --> 00:27:46.335 activity between the two interventions

NOTE Confidence: 0.8068333

00:27:46.335 --> 00:27:49.373 and was really elegant about this method,

NOTE Confidence: 0.8068333

00:27:49.380 --> 00:27:52.020 is it isolated.

NOTE Confidence: 0.8068333

00:27:52.020 --> 00:27:54.860 Non REM slow wave sleep and did not

NOTE Confidence: 0.8068333

00:27:54.860 --> 00:27:56.961 actually result in differences in

NOTE Confidence: 0.8068333

00:27:56.961 --> 00:27:59.595 the total sleep time between the

NOTE Confidence: 0.8068333

00:27:59.595 --> 00:28:01.669 participants and there was no difference

NOTE Confidence: 0.8068333

00:28:01.669 --> 00:28:04.419 in a beta for any changes in total

NOTE Confidence: 0.8068333

00:28:04.419 --> 00:28:07.762 sleep time and I thought it was very

NOTE Confidence: 0.8068333

00:28:07.762 --> 00:28:10.287 elegant and well executed study.

NOTE Confidence: 0.8068333

00:28:10.290 --> 00:28:14.945 My lab has been very interested in.

NOTE Confidence: 0.8068333

00:28:14.950 --> 00:28:18.128 Translating the findings from mice to humans,

NOTE Confidence: 0.8068333

00:28:18.130 --> 00:28:19.478 and to do this,

NOTE Confidence: 0.8068333

00:28:19.478 --> 00:28:23.357 we we brought in 30 to 60 year old

NOTE Confidence: 0.8068333

00:28:23.357 --> 00:28:26.297 cognitively normal participants in place.

NOTE Confidence: 0.8068333

00:28:26.300 --> 00:28:29.499 Lumbar catheters at 7:00 in the morning

NOTE Confidence: 0.8068333

00:28:29.499 --> 00:28:31.693 and sampled cerebral spinal fluid

NOTE Confidence: 0.8068333

00:28:31.693 --> 00:28:34.677 every two hours for 36 hours and had

NOTE Confidence: 0.8068333

00:28:34.755 --> 00:28:37.650 them under different sleep conditions.

NOTE Confidence: 0.8068333

00:28:37.650 --> 00:28:40.828 In this study there was eight participants,

NOTE Confidence: 0.8068333

00:28:40.830 --> 00:28:43.656 but they all came back and

NOTE Confidence: 0.8068333

00:28:43.656 --> 00:28:45.540 repeated the study so.

NOTE Confidence: 0.8068333

00:28:45.540 --> 00:28:46.532 Four of the participants

NOTE Confidence: 0.8068333

00:28:46.532 --> 00:28:48.020 did all three of the arms.

NOTE Confidence: 0.8068333

00:28:48.020 --> 00:28:51.008 They did the control group, which is in blue.

NOTE Confidence: 0.8068333

00:28:51.008 --> 00:28:52.319 They did sleep.

NOTE Confidence: 0.8068333

00:28:52.320 --> 00:28:54.528 The sleep deprived group in red

NOTE Confidence: 0.8068333

00:28:54.528 --> 00:28:57.320 and the green drug group where they

NOTE Confidence: 0.8068333

00:28:57.320 --> 00:28:59.798 received sodium oxybate and the goal

NOTE Confidence: 0.8068333

00:28:59.798 --> 00:29:02.495 of sodium oxybate was to increase

NOTE Confidence: 0.8068333

00:29:02.495 --> 00:29:04.705 slow wave sleep and hopefully

NOTE Confidence: 0.8068333

00:29:04.710 --> 00:29:06.775 decrease the concentration of amyloid

NOTE Confidence: 0.8068333

00:29:06.775 --> 00:29:08.840 beta and cerebral spinal fluid.

NOTE Confidence: 0.8068333

00:29:08.840 --> 00:29:10.488 The other four participants

NOTE Confidence: 0.8068333

00:29:10.488 --> 00:29:12.136 repeated the study twice,

NOTE Confidence: 0.8068333

00:29:12.140 --> 00:29:15.095 so there's twenty time courses

NOTE Confidence: 0.8068333

00:29:15.095 --> 00:29:18.050 that went into this data.

NOTE Confidence: 0.8068333

00:29:18.050 --> 00:29:20.228 Because the participants were all kept

NOTE Confidence: 0.8068333

00:29:20.228 --> 00:29:23.118 awake for the first 12 hours of the study,

NOTE Confidence: 0.8068333

00:29:23.120 --> 00:29:25.528 we normalized all of the time points

NOTE Confidence: 0.8068333

00:29:25.528 --> 00:29:28.190 to the average of that first 12 hours.

NOTE Confidence: 0.8068333

00:29:28.190 --> 00:29:30.218 That's why the curves line up,

NOTE Confidence: 0.8068333

00:29:30.220 --> 00:29:32.586 and then at 9:00 PM at the

NOTE Confidence: 0.8068333

00:29:32.586 --> 00:29:33.600 vertical dashed line,

NOTE Confidence: 0.8068333

00:29:33.600 --> 00:29:34.948 the control participants were

NOTE Confidence: 0.8068333

00:29:34.948 --> 00:29:37.320 allowed to sleep as they were able.

NOTE Confidence: 0.8068333

00:29:37.320 --> 00:29:39.468 The drug group got their first

NOTE Confidence: 0.8068333

00:29:39.468 --> 00:29:41.890 dose of sodium oxybate and a second

NOTE Confidence: 0.8068333

00:29:41.890 --> 00:29:43.732 dose at 1:00 in the morning,

NOTE Confidence: 0.8068333

00:29:43.740 --> 00:29:45.710 and then the sleep deprived

NOTE Confidence: 0.8068333

00:29:45.710 --> 00:29:47.286 group was permitted to.

NOTE Confidence: 0.8068333

00:29:47.290 --> 00:29:49.130 They just stay with that.

NOTE Confidence: 0.8068333

00:29:49.130 --> 00:29:50.542 They just stayed awake.

NOTE Confidence: 0.8068333

00:29:50.542 --> 00:29:51.954 They were behaviorally kept

NOTE Confidence: 0.8068333

00:29:51.954 --> 00:29:53.529 awake without any stimulants.

NOTE Confidence: 0.8068333

00:29:53.530 --> 00:29:56.099 The shaded area is the overnight period,

NOTE Confidence: 0.8068333

00:29:56.100 --> 00:29:58.005 accounting for the transit time

NOTE Confidence: 0.8068333

00:29:58.005 --> 00:30:00.300 from the brain and captures this.

NOTE Confidence: 0.8068333

00:30:00.300 --> 00:30:02.700 Period for all the participants

NOTE Confidence: 0.8068333

00:30:02.700 --> 00:30:06.099 and we found that a beta 3840

NOTE Confidence: 0.8068333

00:30:06.099 --> 00:30:09.249 and 42 is was increased about 30%

NOTE Confidence: 0.8068333

00:30:09.250 --> 00:30:13.070 compared to the control group.

NOTE Confidence: 0.8068333

00:30:13.070 --> 00:30:14.980 As far as these isoforms,

NOTE Confidence: 0.8068333

00:30:14.980 --> 00:30:17.266 we've talked about a beta 42.

NOTE Confidence: 0.8068333

00:30:17.270 --> 00:30:20.007 This is the one most likely to

NOTE Confidence: 0.8068333

00:30:20.007 --> 00:30:22.239 aggregate into plaque in the brain.

NOTE Confidence: 0.8068333

00:30:22.240 --> 00:30:25.384 Abeta 40 is the most abundant

NOTE Confidence: 0.8068333

00:30:25.384 --> 00:30:27.480 form of amyloid beta.

NOTE Confidence: 0.86718524

00:30:27.480 --> 00:30:29.890 Followed by a beta 38.

NOTE Confidence: 0.79840666

00:30:33.230 --> 00:30:35.540 We've looked at in these samples at

NOTE Confidence: 0.79840666

00:30:35.540 --> 00:30:37.634 other proteins that are released with

NOTE Confidence: 0.79840666

00:30:37.634 --> 00:30:39.722 synaptic activity that some one of

NOTE Confidence: 0.79840666

00:30:39.722 --> 00:30:42.110 which you've looked at Alpha Synuclein,

NOTE Confidence: 0.79840666

00:30:42.110 --> 00:30:44.740 which in the sweet ride

NOTE Confidence: 0.79840666

00:30:44.740 --> 00:30:46.318 participants also increases.

NOTE Confidence: 0.79840666

00:30:46.320 --> 00:30:48.660 Significantly, and this is unpublished

NOTE Confidence: 0.79840666

00:30:48.660 --> 00:30:51.625 data that was done in collaboration

NOTE Confidence: 0.79840666

00:30:51.625 --> 00:30:54.901 with Paul Worley's lab at Johns

NOTE Confidence: 0.79840666

00:30:54.901 --> 00:30:56.930 Hopkins Neural Pentraxin two,

NOTE Confidence: 0.79840666

00:30:56.930 --> 00:30:58.950 which also is increased.

NOTE Confidence: 0.8143345

00:31:02.530 --> 00:31:05.130 Finally, in this experiment we

NOTE Confidence: 0.8143345

00:31:05.130 --> 00:31:07.210 infused all the participants

NOTE Confidence: 0.8143345

00:31:07.210 --> 00:31:09.928 with carbon 13 labeled leucine.

NOTE Confidence: 0.8143345

00:31:09.930 --> 00:31:11.740 This is for stable isotope

NOTE Confidence: 0.8143345

00:31:11.740 --> 00:31:13.188 labeling kinetics to measure

NOTE Confidence: 0.8143345

00:31:13.188 --> 00:31:14.709 production and clearance rates.

NOTE Confidence: 0.8143345

00:31:14.710 --> 00:31:17.390 They were infused at 9:00 PM and you

NOTE Confidence: 0.8143345

00:31:17.390 --> 00:31:20.151 can see the delay before you start

NOTE Confidence: 0.8143345

00:31:20.151 --> 00:31:22.948 to see any labeled Amyloid Beta and

NOTE Confidence: 0.8143345

00:31:22.948 --> 00:31:25.398 the labeling curve at the rise in

NOTE Confidence: 0.8143345

00:31:25.398 --> 00:31:28.260 the percent labeled Peak and then

NOTE Confidence: 0.8143345

00:31:28.260 --> 00:31:31.740 it starts to starts to drop and.

NOTE Confidence: 0.8143345

00:31:31.740 --> 00:31:33.750 Based on the kinetic modeling,

NOTE Confidence: 0.8143345

00:31:33.750 --> 00:31:36.242 the changes in concentration that we we

NOTE Confidence: 0.8143345

00:31:36.242 --> 00:31:38.958 found were due primarily to production.

NOTE Confidence: 0.8143345

00:31:38.960 --> 00:31:41.508 That seemed to be the really the

NOTE Confidence: 0.8143345

00:31:41.508 --> 00:31:43.983 necessary and critical factor that was

NOTE Confidence: 0.8143345

00:31:43.983 --> 00:31:46.173 driving the changes in concentration,

NOTE Confidence: 0.8143345

00:31:46.180 --> 00:31:49.486 and the reason sort of just

NOTE Confidence: 0.8143345

00:31:49.486 --> 00:31:51.690 the simple reason too.

NOTE Confidence: 0.8143345

00:31:51.690 --> 00:31:53.778 That when you look at the curves to

NOTE Confidence: 0.8143345

00:31:53.778 --> 00:31:56.095 tell it there's there's not a difference

NOTE Confidence: 0.8143345

00:31:56.095 --> 00:31:58.649 in clearance is that the curves are

NOTE Confidence: 0.8143345

00:31:58.649 --> 00:32:00.923 superimposable in terms of the upslope,

NOTE Confidence: 0.8143345

00:32:00.930 --> 00:32:03.900 their peak time and the down the down slope.

NOTE Confidence: 0.8143345

00:32:03.900 --> 00:32:06.609 The fact that there's a little bit

NOTE Confidence: 0.8143345

00:32:06.609 --> 00:32:09.794 of it's a little bit lower here for

NOTE Confidence: 0.8143345

00:32:09.794 --> 00:32:13.050 the for the in the control group.

NOTE Confidence: 0.8143345

00:32:13.050 --> 00:32:15.661 Is not a significant part of the

NOTE Confidence: 0.8143345

00:32:15.661 --> 00:32:17.991 modeling help explain that I just

NOTE Confidence: 0.8143345

00:32:17.991 --> 00:32:19.891 want to show this sensitivity

NOTE Confidence: 0.8143345

00:32:19.891 --> 00:32:22.342 analysis that was done as part of

NOTE Confidence: 0.8143345

00:32:22.342 --> 00:32:24.343 the paper we published this result.

NOTE Confidence: 0.8143345

00:32:24.343 --> 00:32:27.327 Here we change the production rate plus or

NOTE Confidence: 0.8143345

00:32:27.327 --> 00:32:30.518 minus 99% and you can only see the black.

NOTE Confidence: 0.8143345

00:32:30.520 --> 00:32:33.096 The black set of baseline line because

NOTE Confidence: 0.8143345

00:32:33.096 --> 00:32:35.620 there's no difference in the labeling curve.

NOTE Confidence: 0.8143345

00:32:35.620 --> 00:32:38.602 But as you change the fractional

NOTE Confidence: 0.8143345

00:32:38.602 --> 00:32:42.338 turnover rate to plus or minus 5 to 20%.

NOTE Confidence: 0.8143345

00:32:42.340 --> 00:32:44.538 You begin to see that the curve

NOTE Confidence: 0.8143345

00:32:44.538 --> 00:32:46.357 separate or the faster turnover

NOTE Confidence: 0.8143345

00:32:46.357 --> 00:32:48.763 and green has a steeper upslope,

NOTE Confidence: 0.8143345

00:32:48.770 --> 00:32:51.182 earlier peak time and then drops

NOTE Confidence: 0.8143345

00:32:51.182 --> 00:32:53.279 faster with the opposite being

NOTE Confidence: 0.8143345

00:32:53.279 --> 00:32:55.339 true for the slower turnover.

NOTE Confidence: 0.8143345

00:32:55.340 --> 00:33:00.479 And in a real world example of these changes,

NOTE Confidence: 0.8143345

00:33:00.480 --> 00:33:03.335 is looking at different individuals

NOTE Confidence: 0.8143345

00:33:03.335 --> 00:33:05.619 with different amyloids status.

NOTE Confidence: 0.8143345

00:33:05.620 --> 00:33:11.038 So this is a study of 101 older older

NOTE Confidence: 0.8143345

00:33:11.038 --> 00:33:15.750 adults who had the labeling infused.

NOTE Confidence: 0.8143345

00:33:15.750 --> 00:33:18.950 And our zero and then were sampled for

NOTE Confidence: 0.8143345

00:33:18.950 --> 00:33:22.479 36 hours and the amyloid negative group.

NOTE Confidence: 0.8143345

00:33:22.480 --> 00:33:24.430 Medic changes of a beta 3840

NOTE Confidence: 0.8143345

00:33:24.430 --> 00:33:26.720 and 42 are all overlapping.

NOTE Confidence: 0.8143345

00:33:26.720 --> 00:33:30.410 You don't see any differences, but an animal.

NOTE Confidence: 0.8143345

00:33:30.410 --> 00:33:32.180 A positive individuals.

NOTE Confidence: 0.8143345

00:33:32.180 --> 00:33:33.006 Data 42,

NOTE Confidence: 0.8143345

00:33:33.006 --> 00:33:35.897 which is more likely to aggregate into

NOTE Confidence: 0.8143345

00:33:35.897 --> 00:33:39.065 plaque as a steeper rise and earlier peak,

NOTE Confidence: 0.8143345

00:33:39.070 --> 00:33:41.737 and then it drops faster on the

NOTE Confidence: 0.8143345

00:33:41.737 --> 00:33:44.743 tail and the reason why you see

NOTE Confidence: 0.8143345

00:33:44.743 --> 00:33:47.395 this faster turnover is that the

NOTE Confidence: 0.8143345

00:33:47.488 --> 00:33:50.099 A Beta 42 is being retained in

NOTE Confidence: 0.8143345

00:33:50.099 --> 00:33:53.420 the brain as insoluble plaque.

NOTE Confidence: 0.8143345

00:33:53.420 --> 00:33:54.888 And essentially functionally from

NOTE Confidence: 0.8143345

00:33:54.888 --> 00:33:57.730 the point of view of the catheter,

NOTE Confidence: 0.8143345

00:33:57.730 --> 00:34:01.349 which is in the lower back essentially

NOTE Confidence: 0.8143345

00:34:01.349 --> 00:34:04.178 being cleared from the from the.

NOTE Confidence: 0.8143345

00:34:04.180 --> 00:34:04.740 Fluid.

NOTE Confidence: 0.8191028

00:34:06.790 --> 00:34:09.844 I think that the stabilized and

NOTE Confidence: 0.8191028

00:34:09.844 --> 00:34:11.880 labeling the stabilized labeling

NOTE Confidence: 0.8191028

00:34:11.963 --> 00:34:14.910 kinetics is a very powerful method to

NOTE Confidence: 0.8191028

00:34:14.910 --> 00:34:17.881 look at protein kinetics in vivo and

NOTE Confidence: 0.8191028

00:34:17.881 --> 00:34:20.772 a number of proteins have been looked

NOTE Confidence: 0.8191028

00:34:20.772 --> 00:34:22.580 at for neurodegenerative diseases,

NOTE Confidence: 0.8191028

00:34:22.580 --> 00:34:25.093 and I just if there's more if

NOTE Confidence: 0.8191028

00:34:25.093 --> 00:34:27.390 you'd like more information to

NOTE Confidence: 0.8191028

00:34:27.390 --> 00:34:30.240 review this very complicated topic,

NOTE Confidence: 0.8191028

00:34:30.240 --> 00:34:33.280 there is this review article

NOTE Confidence: 0.8191028

00:34:33.280 --> 00:34:36.320 that came out last year.

NOTE Confidence: 0.8191028

00:34:36.320 --> 00:34:38.768 I just want to point out as well

NOTE Confidence: 0.8191028

00:34:38.768 --> 00:34:41.129 that not all proteins that we've

NOTE Confidence: 0.8191028

00:34:41.129 --> 00:34:43.637 looked at are affected by sleep.

NOTE Confidence: 0.8191028

00:34:43.640 --> 00:34:45.901 When we looked at proteins that are

NOTE Confidence: 0.8191028

00:34:45.901 --> 00:34:48.030 not released with synaptic activity,

NOTE Confidence: 0.8191028

00:34:48.030 --> 00:34:50.226 we don't see any changes with

NOTE Confidence: 0.8191028

00:34:50.226 --> 00:34:50.958 sleep deprivation,

NOTE Confidence: 0.8191028

00:34:50.960 --> 00:34:52.368 so neurofilament light chain,

NOTE Confidence: 0.8191028

00:34:52.368 --> 00:34:54.990 which is a marker for Alzheimer's disease,

NOTE Confidence: 0.8191028

00:34:54.990 --> 00:34:58.212 is not increased sleep duration and

NOTE Confidence: 0.8191028

00:34:58.212 --> 00:35:02.017 the same is true with for GF AP.

NOTE Confidence: 0.8191028

00:35:02.020 --> 00:35:04.428 And what happens if you sleep deprived?

NOTE Confidence: 0.8191028

00:35:04.430 --> 00:35:06.150 If you're sleep deprived for

NOTE Confidence: 0.8191028

00:35:06.150 --> 00:35:07.870 a long period of time,

NOTE Confidence: 0.8191028

00:35:07.870 --> 00:35:09.985 chronic sleep deprivation that's been

NOTE Confidence: 0.8191028

00:35:09.985 --> 00:35:12.990 tested in mice and sleep deprivation.

NOTE Confidence: 0.8191028

00:35:12.990 --> 00:35:17.034 21 days resulted in increased amyloid

NOTE Confidence: 0.8191028

00:35:17.034 --> 00:35:19.730 deposition in multiple regions

NOTE Confidence: 0.8191028

00:35:19.836 --> 00:35:23.106 compared to compared to controls.

NOTE Confidence: 0.8191028

00:35:23.110 --> 00:35:26.603 Suggesting that this could this could be

NOTE Confidence: 0.8191028

00:35:26.603 --> 00:35:30.179 a mechanism whereby sleep sleep disturbance,

NOTE Confidence: 0.8191028

00:35:30.180 --> 00:35:32.900 increasing wakefulness during sleep increases

NOTE Confidence: 0.8191028

00:35:32.900 --> 00:35:35.620 the concentration which overtime promotes.

NOTE Confidence: 0.8191028

00:35:35.620 --> 00:35:39.850 The deposition of amyloid plaque.

NOTE Confidence: 0.8191028

00:35:39.850 --> 00:35:41.884 A second mechanism I'd like to

NOTE Confidence: 0.8191028

00:35:41.884 --> 00:35:44.530 go over is Tau phosphorylation.

NOTE Confidence: 0.8191028

00:35:44.530 --> 00:35:46.650 I didn't mention Tau previously,

NOTE Confidence: 0.8191028

00:35:46.650 --> 00:35:49.200 but we have looked at Tao,

NOTE Confidence: 0.8191028

00:35:49.200 --> 00:35:52.175 which is also released with neural activity,

NOTE Confidence: 0.8191028

00:35:52.180 --> 00:35:55.580 and we see that it is increased 30

NOTE Confidence: 0.8191028

00:35:55.580 --> 00:35:58.565 to 40% compared to control for a

NOTE Confidence: 0.8191028

00:35:58.565 --> 00:36:01.100 number of different forms of Tao.

NOTE Confidence: 0.8191028

00:36:01.100 --> 00:36:02.375 This is 381,

NOTE Confidence: 0.8191028

00:36:02.375 --> 00:36:04.500 eighty one or two 181,

NOTE Confidence: 0.8191028

00:36:04.500 --> 00:36:07.050 Syrian 202 or 202, and three.

NOTE Confidence: 0.8191028

00:36:07.050 --> 00:36:09.870 I mean 217 or T 217.

NOTE Confidence: 0.8191028

00:36:09.870 --> 00:36:12.418 This is the same.

NOTE Confidence: 0.8191028

00:36:12.420 --> 00:36:15.500 Data from using the samples from the

NOTE Confidence: 0.8191028

00:36:15.500 --> 00:36:18.371 study have already been discussing with

NOTE Confidence: 0.8191028

00:36:18.371 --> 00:36:21.787 the same normalization and it looks very

NOTE Confidence: 0.8191028

00:36:21.875 --> 00:36:25.075 similar to the to the amyloid beta data,

NOTE Confidence: 0.8191028

00:36:25.080 --> 00:36:27.618 so that sleep duration is increasing

NOTE Confidence: 0.8191028

00:36:27.618 --> 00:36:30.821 Tau soluble forms of Tau and human

NOTE Confidence: 0.8191028

00:36:30.821 --> 00:36:33.677 cerebral spinal fluid and prolonged sleep

NOTE Confidence: 0.8191028

00:36:33.677 --> 00:36:36.825 duration and mice can promote Tau pathology.

NOTE Confidence: 0.8191028

00:36:36.830 --> 00:36:37.744 This paper,

NOTE Confidence: 0.8191028

00:36:37.744 --> 00:36:40.029 published last year and science

NOTE Confidence: 0.8191028

00:36:40.029 --> 00:36:42.460 involved seeds of Tau injected.

NOTE Confidence: 0.8191028

00:36:42.460 --> 00:36:44.782 The Locusts Arulius and those animals

NOTE Confidence: 0.8191028

00:36:44.782 --> 00:36:46.735 that were chronically sleep deprived

NOTE Confidence: 0.8191028

00:36:46.735 --> 00:36:48.460 had increased Tau pathology on

NOTE Confidence: 0.8191028

00:36:48.460 --> 00:36:50.995 the same side that the seeds were

NOTE Confidence: 0.8191028

00:36:50.995 --> 00:36:52.815 injected compared to the controls.

NOTE Confidence: 0.8481379

00:36:56.880 --> 00:36:58.728 One very interesting and

NOTE Confidence: 0.8481379

00:36:58.728 --> 00:37:01.038 unexpected finding was that when

NOTE Confidence: 0.8481379

00:37:01.038 --> 00:37:03.820 we looked at phosphorylated Tau,

NOTE Confidence: 0.8481379

00:37:03.820 --> 00:37:06.300 we saw differences depending on

NOTE Confidence: 0.8481379

00:37:06.300 --> 00:37:08.780 the site that was phosphorylated.

NOTE Confidence: 0.8481379

00:37:08.780 --> 00:37:11.944 So looking at phosphorylated T 181 very

NOTE Confidence: 0.8481379

00:37:11.944 --> 00:37:15.729 similar to the unphosphorylated form but P.

NOTE Confidence: 0.8481379

00:37:15.730 --> 00:37:19.370 202 was I think it's pretty clear

NOTE Confidence: 0.8481379

00:37:19.370 --> 00:37:22.445 the sleep duration is much lower

NOTE Confidence: 0.8481379

00:37:22.445 --> 00:37:25.735 and it's the same as the control.

NOTE Confidence: 0.8481379

00:37:25.740 --> 00:37:28.668 It's slightly above the drug group,

NOTE Confidence: 0.8481379

00:37:28.670 --> 00:37:30.134 whereas phosphorylate 217

NOTE Confidence: 0.8481379

00:37:30.134 --> 00:37:31.598 was actually increased.

NOTE Confidence: 0.8481379

00:37:31.600 --> 00:37:35.496 Instead of being 30 to 40% increase its

NOTE Confidence: 0.8481379

00:37:35.496 --> 00:37:39.528 65 to 80% increased above controls.

NOTE Confidence: 0.8481379

00:37:39.530 --> 00:37:43.370 And another way to look at this is the ratio,

NOTE Confidence: 0.8481379

00:37:43.370 --> 00:37:45.285 which gives a measure of

NOTE Confidence: 0.8481379

00:37:45.285 --> 00:37:46.434 the phosphorylation rate,

NOTE Confidence: 0.8481379

00:37:46.440 --> 00:37:49.472 and here during the sleep period and it

NOTE Confidence: 0.8481379

00:37:49.472 --> 00:37:51.819 actually across the whole time course,

NOTE Confidence: 0.8481379

00:37:51.820 --> 00:37:53.735 the all of the intervention

NOTE Confidence: 0.8481379

00:37:53.735 --> 00:37:54.884 groups are overlapping,

NOTE Confidence: 0.8481379

00:37:54.890 --> 00:37:57.422 whereas there's a decline in the

NOTE Confidence: 0.8481379

00:37:57.422 --> 00:37:58.688 phosphorus phosphorylation ratio

NOTE Confidence: 0.8481379

00:37:58.688 --> 00:38:01.120 for 202 where the secret group is

NOTE Confidence: 0.8481379

00:38:01.120 --> 00:38:03.339 actually lower than the control group.

NOTE Confidence: 0.8481379

00:38:03.340 --> 00:38:06.404 And in here we can see the 202.

NOTE Confidence: 0.8481379

00:38:06.410 --> 00:38:07.712 Seventeen is phosphorylated

NOTE Confidence: 0.8481379

00:38:07.712 --> 00:38:09.448 at a greater rate.

NOTE Confidence: 0.8481379

00:38:09.450 --> 00:38:13.182 In the in the secret group

NOTE Confidence: 0.8481379

00:38:13.182 --> 00:38:15.048 compared to control.

NOTE Confidence: 0.8481379

00:38:15.050 --> 00:38:18.690 I think the phosphorylated T 217 is

NOTE Confidence: 0.8481379

00:38:18.690 --> 00:38:22.428 very interesting form of touted to be

NOTE Confidence: 0.8481379

00:38:22.428 --> 00:38:25.028 increased 'cause it's recently been

NOTE Confidence: 0.8481379

00:38:25.028 --> 00:38:28.567 shown to be a marker for the early AD.

NOTE Confidence: 0.8481379

00:38:28.570 --> 00:38:31.454 This is a paper that was published

NOTE Confidence: 0.8481379

00:38:31.454 --> 00:38:33.867 in nature medicine earlier this

NOTE Confidence: 0.8481379

00:38:33.867 --> 00:38:36.592 year from the Domeli inherited

NOTE Confidence: 0.8481379

00:38:36.592 --> 00:38:38.227 Alzheimer Disease Network.

NOTE Confidence: 0.8481379

00:38:38.230 --> 00:38:40.226 Looking at individual mutations

NOTE Confidence: 0.8481379

00:38:40.226 --> 00:38:42.222 that Predispose Domani inherited

NOTE Confidence: 0.8481379

00:38:42.222 --> 00:38:45.060 for AD and phosphorylated T 217.

NOTE Confidence: 0.8481379

00:38:45.060 --> 00:38:47.652 Increases earlier even than 181 and

NOTE Confidence: 0.8481379

00:38:47.652 --> 00:38:51.667 appears to be a marker for amyloid plaque.

NOTE Confidence: 0.8481379

00:38:51.670 --> 00:38:53.955 There's also been extremely promising

NOTE Confidence: 0.8481379

00:38:53.955 --> 00:38:56.860 data came out over the summer,

NOTE Confidence: 0.8481379

00:38:56.860 --> 00:39:00.058 showing that in the blood phosphorylated

NOTE Confidence: 0.8481379

00:39:00.058 --> 00:39:05.020 T 217 as a marker for amyloid plaque.

NOTE Confidence: 0.8481379

00:39:05.020 --> 00:39:07.547 And so I think the implications of

NOTE Confidence: 0.8481379

00:39:07.547 --> 00:39:10.464 the relation of our finding with sleep

NOTE Confidence: 0.8481379

00:39:10.464 --> 00:39:13.104 deprivation increasing this form of of

NOTE Confidence: 0.8481379

00:39:13.182 --> 00:39:15.708 tower not not yet fully understood,

NOTE Confidence: 0.8481379

00:39:15.710 --> 00:39:17.770 but certainly suggests that we're

NOTE Confidence: 0.8481379

00:39:17.770 --> 00:39:20.408 increasing the risk at the very

NOTE Confidence: 0.8481379

00:39:20.408 --> 00:39:22.928 earliest stages of Alzheimer's disease.

NOTE Confidence: 0.8481379

00:39:22.930 --> 00:39:24.850 I don't have an explanation for

NOTE Confidence: 0.8481379

00:39:24.850 --> 00:39:26.765 how sleep is potentially affecting

NOTE Confidence: 0.8481379

00:39:26.765 --> 00:39:27.909 Tau phosphorylation,

NOTE Confidence: 0.8481379

00:39:27.910 --> 00:39:31.740 but I'm going to give my best thoughts on it.

NOTE Confidence: 0.8481379

00:39:31.740 --> 00:39:33.436 Tell phosphorylation is complex.

NOTE Confidence: 0.8481379

00:39:33.436 --> 00:39:36.719 I showed this slide nearly to state that

NOTE Confidence: 0.8481379

00:39:36.719 --> 00:39:39.399 to show that this shows that the town,

NOTE Confidence: 0.8481379

00:39:39.400 --> 00:39:40.615 the Tau protein,

NOTE Confidence: 0.8481379

00:39:40.615 --> 00:39:42.640 and the different regions that

NOTE Confidence: 0.8481379

00:39:42.640 --> 00:39:44.757 are have been known to be.

NOTE Confidence: 0.8481379

00:39:44.760 --> 00:39:47.148 I've been found to be phosphorylated

NOTE Confidence: 0.8481379

00:39:47.148 --> 00:39:49.479 and the enzymes involved and you

NOTE Confidence: 0.8481379

00:39:49.479 --> 00:39:51.477 can see that there are numerous

NOTE Confidence: 0.8481379

00:39:51.477 --> 00:39:52.800 enzymes and numerous.

NOTE Confidence: 0.7997596

00:39:55.080 --> 00:39:57.700 Sites that are phosphorylated and

NOTE Confidence: 0.7997596

00:39:57.700 --> 00:40:00.320 a potential mechanism that makes.

NOTE Confidence: 0.7997596

00:40:00.320 --> 00:40:02.820 Lane this is that.

NOTE Confidence: 0.7997596

00:40:02.820 --> 00:40:05.745 Work in Mysore last two years that is shown

NOTE Confidence: 0.7997596

00:40:05.745 --> 00:40:08.705 that changes in sleep wake activity effect,

NOTE Confidence: 0.7997596

00:40:08.710 --> 00:40:12.265 protein phosphorylation. In the brain.

NOTE Confidence: 0.7997596

00:40:12.265 --> 00:40:14.815 So in this 2018 nature paper,

NOTE Confidence: 0.7997596

00:40:14.820 --> 00:40:17.692 mice were sleep deprived for one to six

NOTE Confidence: 0.7997596

00:40:17.692 --> 00:40:21.313 days and over that time the amount of

NOTE Confidence: 0.7997596

00:40:21.313 --> 00:40:23.707 phosphoproteome increased at every every

NOTE Confidence: 0.7997596

00:40:23.707 --> 00:40:26.717 time point that they that they measured,

NOTE Confidence: 0.7997596

00:40:26.720 --> 00:40:30.365 and one of the one of the proteins that

NOTE Confidence: 0.7997596

00:40:30.365 --> 00:40:34.364 they had found was was affected was Mark 2,

NOTE Confidence: 0.7997596

00:40:34.370 --> 00:40:37.930 which is a kinase that has been shown

NOTE Confidence: 0.7997596

00:40:37.930 --> 00:40:41.698 to have one of many that has a role.

NOTE Confidence: 0.7997596

00:40:41.700 --> 00:40:43.470 Intel phosphorylation.

NOTE Confidence: 0.773841

00:40:45.770 --> 00:40:49.242 And then a paper last year published

NOTE Confidence: 0.773841

00:40:49.242 --> 00:40:52.023 in science showed that that

NOTE Confidence: 0.773841

00:40:52.023 --> 00:40:55.008 phosphorylation of proteins at synapses

NOTE Confidence: 0.773841

00:40:55.008 --> 00:40:58.739 cycles with the sleep wake activity.

NOTE Confidence: 0.773841

00:40:58.740 --> 00:41:02.030 And here in a they found 2200

NOTE Confidence: 0.773841

00:41:02.030 --> 00:41:04.693 proteins that that fossil peptides

NOTE Confidence: 0.773841

00:41:04.693 --> 00:41:07.578 that cycled across the day

NOTE Confidence: 0.773841

00:41:07.578 --> 00:41:10.590 and during sleep deprivation.

NOTE Confidence: 0.773841

00:41:10.590 --> 00:41:12.324 That number drops.

NOTE Confidence: 0.773841

00:41:12.324 --> 00:41:16.370 So there was only two point 3%.

NOTE Confidence: 0.773841

00:41:16.370 --> 00:41:19.520 Of the proteins that they measured.

NOTE Confidence: 0.773841

00:41:19.520 --> 00:41:22.220 We were cycling during the

NOTE Confidence: 0.773841

00:41:22.220 --> 00:41:23.840 sleep deprivation period.

NOTE Confidence: 0.8687948

00:41:26.540 --> 00:41:30.590 And there are previous examples of

NOTE Confidence: 0.8687948

00:41:30.590 --> 00:41:33.290 behavioral or environmental intervention

NOTE Confidence: 0.8687948

00:41:33.380 --> 00:41:35.990 changing Tau phosphorylation.

NOTE Confidence: 0.8687948

00:41:35.990 --> 00:41:41.278 Is 2001 JJVC paper three days of starvation?

NOTE Confidence: 0.8687948

00:41:41.280 --> 00:41:43.924 Increase the activity of

NOTE Confidence: 0.8687948

00:41:43.924 --> 00:41:45.907 protein phosphatase 2A,

NOTE Confidence: 0.8687948

00:41:45.910 --> 00:41:50.530 which is another enzyme involved in town.

NOTE Confidence: 0.8687948

00:41:50.530 --> 00:41:53.942 Phosphorylation and another study.

NOTE Confidence: 0.8687948

00:41:53.942 --> 00:41:59.060 Prolonged starvation in mice also increased.

NOTE Confidence: 0.8687948

00:41:59.060 --> 00:42:02.848 Fast forward T 217.

NOTE Confidence: 0.8687948

00:42:02.850 --> 00:42:03.939 Over that time,

NOTE Confidence: 0.8687948

00:42:03.939 --> 00:42:07.029 and this is one of the models that

NOTE Confidence: 0.8687948

00:42:07.029 --> 00:42:09.789 was proposed to explain how starvation

NOTE Confidence: 0.8687948

00:42:09.789 --> 00:42:13.358 could lead to Tao hyper phosphorylation.

NOTE Confidence: 0.8687948

00:42:13.360 --> 00:42:14.796 As you can see,

NOTE Confidence: 0.8687948

00:42:14.796 --> 00:42:16.591 it's quite it's quite complicated

NOTE Confidence: 0.8687948

00:42:16.591 --> 00:42:18.178 with phosphorylation potentially

NOTE Confidence: 0.8687948

00:42:18.178 --> 00:42:21.073 changing the activity of different

NOTE Confidence: 0.8687948

00:42:21.073 --> 00:42:23.296 kinases and phosphatases with

NOTE Confidence: 0.8687948

00:42:23.296 --> 00:42:25.810 the end result of altering Tau

NOTE Confidence: 0.8687948

00:42:25.810 --> 00:42:28.140 phosphorylation and leading to Tau.

NOTE Confidence: 0.8687948

00:42:28.140 --> 00:42:28.675 Hyperphosphorylation,

NOTE Confidence: 0.8687948

00:42:28.675 --> 00:42:31.350 and I think something potentially

NOTE Confidence: 0.8687948

00:42:31.350 --> 00:42:33.677 similar could be going on with.

NOTE Confidence: 0.8687948

00:42:33.680 --> 00:42:35.730 Sleep on the on phosphopeptides,

NOTE Confidence: 0.8687948

00:42:35.730 --> 00:42:38.962 but I think a lot more work is

NOTE Confidence: 0.8687948

00:42:38.962 --> 00:42:41.059 really needed in this area.

NOTE Confidence: 0.8169042

00:42:43.210 --> 00:42:46.015 Last time we talked about

NOTE Confidence: 0.8169042

00:42:46.015 --> 00:42:47.698 the erection system,

NOTE Confidence: 0.8169042

00:42:47.700 --> 00:42:51.102 so inducing sleep with dual orexin

NOTE Confidence: 0.8169042

00:42:51.102 --> 00:42:53.997 receptor antagonists decreases the soluble

NOTE Confidence: 0.8169042

00:42:53.997 --> 00:42:57.237 concentration of amyloid beta in mice.

NOTE Confidence: 0.8169042

00:42:57.240 --> 00:43:00.992 This is Elmer Accent and given across

NOTE Confidence: 0.8169042

00:43:00.992 --> 00:43:05.001 these light dark periods and keeps the

NOTE Confidence: 0.8169042

00:43:05.001 --> 00:43:08.451 amount of interstitial fluid a beta.

NOTE Confidence: 0.8169042

00:43:08.460 --> 00:43:11.320 The concentration very very steady

NOTE Confidence: 0.8169042

00:43:11.320 --> 00:43:13.036 and prolonged administration.

NOTE Confidence: 0.8169042

00:43:13.040 --> 00:43:15.674 Of Alma Rex and decreased amyloid

NOTE Confidence: 0.8169042

00:43:15.674 --> 00:43:18.120 plaque in multiple brain regions,

NOTE Confidence: 0.8169042

00:43:18.120 --> 00:43:19.503 including Intercel Cortex,

NOTE Confidence: 0.8169042

00:43:19.503 --> 00:43:20.886 the pyriform cortex.

NOTE Confidence: 0.73230743

00:43:23.080 --> 00:43:26.128 And an APP, PS1 transgenic mice

NOTE Confidence: 0.73230743

00:43:26.128 --> 00:43:28.160 that develop amyloid deposition.

NOTE Confidence: 0.73230743

00:43:28.160 --> 00:43:31.208 As you can see in this,

NOTE Confidence: 0.73230743

00:43:31.210 --> 00:43:34.381 this micrograph in a knocking out the

NOTE Confidence: 0.73230743

00:43:34.381 --> 00:43:37.490 rexon gene leads to decreased amyloid

NOTE Confidence: 0.73230743

00:43:37.490 --> 00:43:41.368 deposition and these are age matched animals,

NOTE Confidence: 0.73230743

00:43:41.370 --> 00:43:44.088 strongly suggesting a role for for

NOTE Confidence: 0.73230743

00:43:44.088 --> 00:43:47.076 the rexon system in developing mcloyd

NOTE Confidence: 0.73230743

00:43:47.076 --> 00:43:50.346 pathology there is some evidence in

NOTE Confidence: 0.73230743

00:43:50.346 --> 00:43:53.788 humans that directs and efficiency can.

NOTE Confidence: 0.73230743

00:43:53.790 --> 00:43:55.995 Can can alter amyloid deposition

NOTE Confidence: 0.73230743

00:43:55.995 --> 00:43:59.458 is a study from the University of

NOTE Confidence: 0.73230743

00:43:59.458 --> 00:44:02.383 Montpellier looking at narcolepsy type

NOTE Confidence: 0.73230743

00:44:02.383 --> 00:44:06.008 one subjects who had amyloid pet scan?

NOTE Confidence: 0.73230743

00:44:06.010 --> 00:44:08.817 And then age and sex matched controls

NOTE Confidence: 0.73230743

00:44:08.817 --> 00:44:12.029 from the Admin Cohort and Mattie Cohort.

NOTE Confidence: 0.73230743

00:44:12.030 --> 00:44:14.935 And they found that there was decreased

NOTE Confidence: 0.73230743

00:44:14.935 --> 00:44:17.567 amyloid pathology on these pet scans

NOTE Confidence: 0.73230743

00:44:17.567 --> 00:44:20.195 compared to their their matched controls.

NOTE Confidence: 0.73230743

00:44:20.200 --> 00:44:23.860 So some suggestive evidence that the

NOTE Confidence: 0.73230743

00:44:23.860 --> 00:44:26.670 direction deficiency may lead to.

NOTE Confidence: 0.73230743

00:44:26.670 --> 00:44:30.279 Altered amyloid pathology.

NOTE Confidence: 0.73230743

00:44:30.280 --> 00:44:32.935 And so putting this bidirectional

NOTE Confidence: 0.73230743

00:44:32.935 --> 00:44:33.997 relationship altogether,

NOTE Confidence: 0.73230743

00:44:34.000 --> 00:44:36.660 you know we have processes

NOTE Confidence: 0.73230743

00:44:36.660 --> 00:44:39.320 that can decrease sleep time.

NOTE Confidence: 0.73230743

00:44:39.320 --> 00:44:43.016 It could be from aging, sleep disorders,

NOTE Confidence: 0.73230743

00:44:43.016 --> 00:44:45.606 or multiple other factors that

NOTE Confidence: 0.73230743

00:44:45.606 --> 00:44:48.369 are known to impact sleep,

NOTE Confidence: 0.73230743

00:44:48.370 --> 00:44:49.966 social, environmental, mental,

NOTE Confidence: 0.73230743

00:44:49.966 --> 00:44:52.222 physical activity, medical comorbidities,

NOTE Confidence: 0.73230743

00:44:52.222 --> 00:44:55.202 and this increased wakefulness at

NOTE Confidence: 0.73230743

00:44:55.202 --> 00:44:58.025 night impacts the production and

NOTE Confidence: 0.73230743

00:44:58.025 --> 00:45:00.863 release of amyloid beta and Tau.

NOTE Confidence: 0.73230743

00:45:00.870 --> 00:45:03.243 The clearance of amyloid beta and Tau

NOTE Confidence: 0.73230743

00:45:03.243 --> 00:45:06.594 and the end result is you have higher

NOTE Confidence: 0.73230743

00:45:06.594 --> 00:45:08.406 concentrations of those proteins.

NOTE Confidence: 0.73230743

00:45:08.410 --> 00:45:09.998 Phosphorylation of Tau appears

NOTE Confidence: 0.73230743

00:45:09.998 --> 00:45:11.983 to be affected as well,

NOTE Confidence: 0.73230743

00:45:11.990 --> 00:45:13.970 and that promotes the formation

NOTE Confidence: 0.73230743

00:45:13.970 --> 00:45:15.554 of Alzheimer disease pathology,

NOTE Confidence: 0.73230743

00:45:15.560 --> 00:45:15.957 neurodegeneration,

NOTE Confidence: 0.73230743

00:45:15.957 --> 00:45:18.339 which then feeds back through synaptic.

NOTE Confidence: 0.73230743

00:45:18.340 --> 00:45:20.320 Internal dysfunction to disrupt sleep.

NOTE Confidence: 0.70218706

00:45:22.630 --> 00:45:26.726 And in numerous these factors such as aging,

NOTE Confidence: 0.70218706

00:45:26.730 --> 00:45:29.796 erexin and these other factors here,

NOTE Confidence: 0.70218706

00:45:29.800 --> 00:45:32.360 such as social and environmental,

NOTE Confidence: 0.70218706

00:45:32.360 --> 00:45:36.350 also can have effects on.

NOTE Confidence: 0.70218706

00:45:36.350 --> 00:45:39.665 No degeneration, and I think

NOTE Confidence: 0.70218706

00:45:39.665 --> 00:45:42.317 that this provides multiple.

NOTE Confidence: 0.89008534

00:45:45.510 --> 00:45:47.940 Areas for us to investigate potential

NOTE Confidence: 0.89008534

00:45:47.940 --> 00:45:50.973 changes that we may see in sleep

NOTE Confidence: 0.89008534

00:45:50.973 --> 00:45:52.761 wake activity during different

NOTE Confidence: 0.89008534

00:45:52.761 --> 00:45:54.750 stages of Alzheimer disease,

NOTE Confidence: 0.89008534

00:45:54.750 --> 00:45:56.988 as well as the potential for

NOTE Confidence: 0.89008534

00:45:56.988 --> 00:45:59.633 interventions to try to change the

NOTE Confidence: 0.89008534

00:45:59.633 --> 00:46:01.785 trajectory of Alzheimer's disease.

NOTE Confidence: 0.89008534

00:46:01.790 --> 00:46:05.408 To show that there is some

NOTE Confidence: 0.89008534

00:46:05.408 --> 00:46:07.820 evidence that you can.

NOTE Confidence: 0.89008534

00:46:07.820 --> 00:46:10.736 Do a sleep intervention and change

NOTE Confidence: 0.89008534

00:46:10.736 --> 00:46:13.924 the directory of some of these

NOTE Confidence: 0.89008534

00:46:13.924 --> 00:46:16.236 proteins we've been discussing.

NOTE Confidence: 0.89008534

00:46:16.240 --> 00:46:18.991 I'd just like to highlight this work

NOTE Confidence: 0.89008534

00:46:18.991 --> 00:46:21.978 again from UL joo published in 2019.

NOTE Confidence: 0.89008534

00:46:21.980 --> 00:46:23.306 Annals of neurology,

NOTE Confidence: 0.89008534

00:46:23.306 --> 00:46:25.074 where individuals with obstructive

NOTE Confidence: 0.89008534

00:46:25.074 --> 00:46:27.609 sleep apnea at a baseline study

NOTE Confidence: 0.89008534

00:46:27.609 --> 00:46:29.883 had a lumbar puncture and measured

NOTE Confidence: 0.89008534

00:46:29.883 --> 00:46:32.227 cerebral spinal fluid for amyloid beta.

NOTE Confidence: 0.89008534

00:46:32.230 --> 00:46:34.280 This is 40 and 42,

NOTE Confidence: 0.89008534

00:46:34.280 --> 00:46:37.150 as well as Tau and total protein,

NOTE Confidence: 0.89008534

00:46:37.150 --> 00:46:41.406 and then they were treated with C Pap.

NOTE Confidence: 0.89008534

00:46:41.410 --> 00:46:43.630 And then they return for another

NOTE Confidence: 0.89008534

00:46:43.630 --> 00:46:46.972 sleep study on C Pap told by another

NOTE Confidence: 0.89008534

00:46:46.972 --> 00:46:49.197 lumbar puncture the next morning,

NOTE Confidence: 0.89008534

00:46:49.200 --> 00:46:52.196 and what she found what doctors you

NOTE Confidence: 0.89008534

00:46:52.196 --> 00:46:55.216 found was that the greater the change

NOTE Confidence: 0.89008534

00:46:55.216 --> 00:46:58.628 in the nature of the drop in the hi,

NOTE Confidence: 0.89008534

00:46:58.630 --> 00:47:00.258 more of the decrease.

NOTE Confidence: 0.89008534

00:47:00.258 --> 00:47:03.140 In Emma Lloyd beta 42 and Tao,

NOTE Confidence: 0.89008534

00:47:03.140 --> 00:47:05.600 suggesting that this is just over.

NOTE Confidence: 0.89008534

00:47:05.600 --> 00:47:08.680 I believe it was.

NOTE Confidence: 0.89008534

00:47:08.680 --> 00:47:10.905 Relatively short period of time

NOTE Confidence: 0.89008534

00:47:10.905 --> 00:47:13.130 of three months, but it's.

NOTE Confidence: 0.847264

00:47:15.380 --> 00:47:16.276 Extrapolating forward,

NOTE Confidence: 0.847264

00:47:16.276 --> 00:47:18.964 it certainly provides evidence that if

NOTE Confidence: 0.847264

00:47:18.964 --> 00:47:21.936 we were to do this on an ongoing basis,

NOTE Confidence: 0.847264

00:47:21.940 --> 00:47:25.090 we might decrease the formation of amyloid

NOTE Confidence: 0.847264

00:47:25.090 --> 00:47:28.647 plaques or the spreading of tab mythology.

NOTE Confidence: 0.847264

00:47:28.650 --> 00:47:32.180 And I I think I, I think that as we get

NOTE Confidence: 0.847264

00:47:32.180 --> 00:47:34.940 more evidence that we can affect the.

NOTE Confidence: 0.847264

00:47:34.940 --> 00:47:36.292 These these critical proteins,

NOTE Confidence: 0.847264

00:47:36.292 --> 00:47:37.982 these proteins that are critical

NOTE Confidence: 0.847264

00:47:37.982 --> 00:47:39.379 for Alzheimer's disease.

NOTE Confidence: 0.847264

00:47:39.380 --> 00:47:43.884 We really need to know when to target.

NOTE Confidence: 0.847264

00:47:43.890 --> 00:47:45.105 A sleep intervention.

NOTE Confidence: 0.847264

00:47:45.105 --> 00:47:47.130 So should we do it?

NOTE Confidence: 0.847264

00:47:47.130 --> 00:47:49.250 You know, after before amyloid

NOTE Confidence: 0.847264

00:47:49.250 --> 00:47:52.398 plaque is begin to form or or after,

NOTE Confidence: 0.847264

00:47:52.400 --> 00:47:54.855 but before there's significant cow

NOTE Confidence: 0.847264

00:47:54.855 --> 00:47:58.299 pathology and I think that that's the

NOTE Confidence: 0.847264

00:47:58.299 --> 00:48:01.907 timing of when an intervention will occur is.

NOTE Confidence: 0.847264

00:48:01.910 --> 00:48:03.730 To be really critical here,

NOTE Confidence: 0.847264

00:48:03.730 --> 00:48:06.222 as well as what is the intervention

NOTE Confidence: 0.847264

00:48:06.222 --> 00:48:09.190 which I think as I've been alluding to,

NOTE Confidence: 0.847264

00:48:09.190 --> 00:48:10.646 could be incredibly complicated

NOTE Confidence: 0.847264

00:48:10.646 --> 00:48:12.466 depending on the underlying sleep,

NOTE Confidence: 0.847264

00:48:12.470 --> 00:48:13.918 disorder and other characteristics

NOTE Confidence: 0.847264

00:48:13.918 --> 00:48:15.004 of the participants.

NOTE Confidence: 0.847264

00:48:15.010 --> 00:48:17.290 But the ultimate goal is to

NOTE Confidence: 0.847264

00:48:17.290 --> 00:48:18.810 administer a sleep intervention

NOTE Confidence: 0.847264

00:48:18.879 --> 00:48:21.196 that would move them from high risk,

NOTE Confidence: 0.847264

00:48:21.200 --> 00:48:24.770 potentially down to the lower risk.

NOTE Confidence: 0.847264

00:48:24.770 --> 00:48:30.170 For developing cognitive symptoms from AD.

NOTE Confidence: 0.847264

00:48:30.170 --> 00:48:32.006 So just to conclude,

NOTE Confidence: 0.847264

00:48:32.006 --> 00:48:34.760 we discussed some of the evidence

NOTE Confidence: 0.847264

00:48:34.845 --> 00:48:37.601 for the bidirectional relationship

NOTE Confidence: 0.847264

00:48:37.601 --> 00:48:41.046 between sleep and Alzheimer's disease.

NOTE Confidence: 0.847264

00:48:41.050 --> 00:48:44.245 Sleep may be a potential marker of a D,

NOTE Confidence: 0.847264

00:48:44.250 --> 00:48:46.530 but I think additional work needs

NOTE Confidence: 0.847264

00:48:46.530 --> 00:48:49.272 to be done to define exactly

NOTE Confidence: 0.847264

00:48:49.272 --> 00:48:51.540 what sleep parameter might.

NOTE Confidence: 0.847264

00:48:51.540 --> 00:48:54.468 Be most efficient in terms of

NOTE Confidence: 0.847264

00:48:54.468 --> 00:48:57.235 being something that we could

NOTE Confidence: 0.847264

00:48:57.235 --> 00:48:59.377 follow relatively easily,

NOTE Confidence: 0.847264

00:48:59.380 --> 00:49:03.650 either to assess clinical risk.

NOTE Confidence: 0.847264

00:49:03.650 --> 00:49:07.511 Or or to follow in a drug trial and

NOTE Confidence: 0.847264

00:49:07.511 --> 00:49:09.923 understanding how other factors such

NOTE Confidence: 0.847264

00:49:09.923 --> 00:49:12.761 as age or sex physical activity

NOTE Confidence: 0.847264

00:49:12.851 --> 00:49:15.479 affect the use of that marker.

NOTE Confidence: 0.847264

00:49:15.480 --> 00:49:17.566 I think using sleep as an intervention

NOTE Confidence: 0.847264

00:49:17.566 --> 00:49:19.560 to prevent or delay Alzheimer's.

NOTE Confidence: 0.847264

00:49:19.560 --> 00:49:21.348 These are really need to narrow

NOTE Confidence: 0.847264

00:49:21.348 --> 00:49:23.405 down more and what the mechanism

NOTE Confidence: 0.847264

00:49:23.405 --> 00:49:24.997 is exactly that's working.

NOTE Confidence: 0.847264

00:49:25.000 --> 00:49:27.136 Is it changes in amyloid beta

NOTE Confidence: 0.847264

00:49:27.136 --> 00:49:28.987 production and clearance or the

NOTE Confidence: 0.847264

00:49:28.987 --> 00:49:31.521 release of proteins like Tao or the

NOTE Confidence: 0.847264

00:49:31.521 --> 00:49:33.498 phosphorylation of Tau or all of them,

NOTE Confidence: 0.847264

00:49:33.500 --> 00:49:36.398 and you know is there a special

NOTE Confidence: 0.847264

00:49:36.398 --> 00:49:39.708 role for the erection system here.

NOTE Confidence: 0.847264

00:49:39.710 --> 00:49:42.706 And I've already talked briefly about the,

NOTE Confidence: 0.847264

00:49:42.710 --> 00:49:44.955 you know what intervention might

NOTE Confidence: 0.847264

00:49:44.955 --> 00:49:47.200 be appropriate depending on what

NOTE Confidence: 0.847264

00:49:47.269 --> 00:49:48.717 the sleep problem is,

NOTE Confidence: 0.847264

00:49:48.720 --> 00:49:50.432 it could drastically change

NOTE Confidence: 0.847264

00:49:50.432 --> 00:49:52.144 what would be selected.

NOTE Confidence: 0.847264

00:49:52.150 --> 00:49:54.300 I think that longitudinal intervention,

NOTE Confidence: 0.847264

00:49:54.300 --> 00:49:54.792 interventional,

NOTE Confidence: 0.847264

00:49:54.792 --> 00:49:57.252 and implementation studies are really

NOTE Confidence: 0.847264

00:49:57.252 --> 00:50:00.399 critically needed in order to to address the.

NOTE Confidence: 0.847264

00:50:00.400 --> 00:50:03.748 These these questions.

NOTE Confidence: 0.847264

00:50:03.750 --> 00:50:06.235 I'd like to thank you all for

NOTE Confidence: 0.847264

00:50:06.235 --> 00:50:08.224 your attention like to thank

NOTE Confidence: 0.847264

00:50:08.224 --> 00:50:10.344 the participants for their time.

NOTE Confidence: 0.847264

00:50:10.350 --> 00:50:11.766 As you can imagine,

NOTE Confidence: 0.847264

00:50:11.766 --> 00:50:13.890 the catheter studies that I lead

NOTE Confidence: 0.847264

00:50:13.958 --> 00:50:16.652 are very intensive and I appreciate

NOTE Confidence: 0.847264

00:50:16.652 --> 00:50:18.448 their willingness to undertake

NOTE Confidence: 0.847264

00:50:18.518 --> 00:50:20.947 them and I'd like to thank everyone

NOTE Confidence: 0.847264

00:50:20.947 --> 00:50:23.304 listed here and in the picture,

NOTE Confidence: 0.847264

00:50:23.304 --> 00:50:25.932 which is the Alzheimer's disease research

NOTE Confidence: 0.847264

00:50:25.932 --> 00:50:28.409 community here at Washington University.

NOTE Confidence: 0.847264

00:50:28.410 --> 00:50:28.930 Thank you.

NOTE Confidence: 0.87911785

00:50:35.560 --> 00:50:37.440 Alright, thank you doctor Lucy,

NOTE Confidence: 0.87911785

00:50:37.440 --> 00:50:39.701 that was quite a tour through pretty

NOTE Confidence: 0.87911785

00:50:39.701 --> 00:50:42.431 much all of a nice primer on everything

NOTE Confidence: 0.87911785

00:50:42.431 --> 00:50:45.630 you need to know about sleep and its

NOTE Confidence: 0.87911785

00:50:45.630 --> 00:50:47.554 connection with Alzheimer's disease.

NOTE Confidence: 0.87911785

00:50:47.560 --> 00:50:50.296 So we do have a question and at

NOTE Confidence: 0.87911785

00:50:50.296 --> 00:50:53.185 this point I do want to welcome

NOTE Confidence: 0.87911785

00:50:53.185 --> 00:50:55.728 people to unmute themselves and ask

NOTE Confidence: 0.87911785

00:50:55.728 --> 00:50:58.464 a question or to put a question in

NOTE Confidence: 0.87911785

00:50:58.464 --> 00:51:01.060 the chat and so we'll start with

NOTE Confidence: 0.87911785

00:51:01.060 --> 00:51:03.309 the first question in the chat,

NOTE Confidence: 0.87911785

00:51:03.310 --> 00:51:05.697 which is will the need of seeing

NOTE Confidence: 0.87911785

00:51:05.697 --> 00:51:08.249 the full scope of sleep disruption.

NOTE Confidence: 0.87911785

00:51:08.250 --> 00:51:10.705 Forced the usage of full

NOTE Confidence: 0.87911785

00:51:10.705 --> 00:51:12.669 polysomnographers fee versus just

NOTE Confidence: 0.87911785

00:51:12.669 --> 00:51:14.966 screening for OSA with home sleep.

NOTE Confidence: 0.87911785

00:51:14.970 --> 00:51:15.990 Apnea testing

NOTE Confidence: 0.9068349

00:51:20.790 --> 00:51:24.258 so I think that.

NOTE Confidence: 0.9068349

00:51:24.260 --> 00:51:27.540 I think that it would depend on what.

NOTE Confidence: 0.9068349

00:51:27.540 --> 00:51:30.354 What what you're looking to to measure.

NOTE Confidence: 0.9068349

00:51:30.360 --> 00:51:32.778 So the home sleep apnea test.

NOTE Confidence: 0.9068349

00:51:32.780 --> 00:51:36.407 If you were, if you were looking to target.

NOTE Confidence: 0.87275124

00:51:38.900 --> 00:51:41.288 Sleep apnea and to treat that

NOTE Confidence: 0.87275124

00:51:41.288 --> 00:51:43.944 and try to prevent or delay

NOTE Confidence: 0.87275124

00:51:43.944 --> 00:51:46.374 Alzheimer's disease than a home.

NOTE Confidence: 0.87275124

00:51:46.380 --> 00:51:49.020 Sleep apnea test may be appropriate.

NOTE Confidence: 0.87275124

00:51:49.020 --> 00:51:51.235 I think that otherwise it's

NOTE Confidence: 0.87275124

00:51:51.235 --> 00:51:53.860 likely not going to provide any.

NOTE Confidence: 0.8001033

00:51:55.950 --> 00:51:58.265 Helpful information I do think

NOTE Confidence: 0.8001033

00:51:58.265 --> 00:52:00.580 home monitoring in general though

NOTE Confidence: 0.8001033

00:52:00.652 --> 00:52:02.747 could play an important role.

NOTE Confidence: 0.8001033

00:52:02.750 --> 00:52:05.336 So the study that I showed

NOTE Confidence: 0.8001033

00:52:05.336 --> 00:52:08.095 where we looked at non ram

NOTE Confidence: 0.8001033

00:52:08.095 --> 00:52:10.897 slow of activity at our center.

NOTE Confidence: 0.8001033

00:52:10.900 --> 00:52:14.260 We use a device that's worn on the

NOTE Confidence: 0.8001033

00:52:14.260 --> 00:52:16.790 forehead called the sleep profiler.

NOTE Confidence: 0.8001033

00:52:16.790 --> 00:52:20.798 It records a single EG from the forehead

NOTE Confidence: 0.8001033

00:52:20.798 --> 00:52:24.897 and we do that for multiple nights.

NOTE Confidence: 0.8001033

00:52:24.900 --> 00:52:27.040 And and that allows that.

NOTE Confidence: 0.8001033

00:52:27.040 --> 00:52:29.175 We've shown how that relates

NOTE Confidence: 0.8001033

00:52:29.175 --> 00:52:30.456 to Poly Sonography,

NOTE Confidence: 0.8001033

00:52:30.460 --> 00:52:33.997 and I think that you know that sort of

NOTE Confidence: 0.8001033

00:52:33.997 --> 00:52:35.820 monitoring or actigraphy monitoring

NOTE Confidence: 0.8001033

00:52:35.820 --> 00:52:39.450 would be feasable to be done at home.

NOTE Confidence: 0.8001033

00:52:39.450 --> 00:52:41.700 Another possibility that's that's in

NOTE Confidence: 0.8001033

00:52:41.700 --> 00:52:44.589 the paper that we published in 2019,

NOTE Confidence: 0.8001033

00:52:44.590 --> 00:52:46.730 is that if we could,

NOTE Confidence: 0.8001033

00:52:46.730 --> 00:52:48.865 we could look at different

NOTE Confidence: 0.8001033

00:52:48.865 --> 00:52:50.146 different sleep measures.

NOTE Confidence: 0.8525315

00:52:52.840 --> 00:52:54.404 Collected by different different

NOTE Confidence: 0.8525315

00:52:54.404 --> 00:52:56.750 methods and show how they relate

NOTE Confidence: 0.8525315

00:52:56.814 --> 00:52:58.500 in the same the same models.

NOTE Confidence: 0.8525315

00:52:58.500 --> 00:53:01.252 We might be able to to identify a

NOTE Confidence: 0.8525315

00:53:01.252 --> 00:53:03.912 similar question or set of questions or

NOTE Confidence: 0.8525315

00:53:03.912 --> 00:53:06.527 similar monitoring that we could do as

NOTE Confidence: 0.8525315

00:53:06.527 --> 00:53:08.795 an example in those 38 subjects where

NOTE Confidence: 0.8525315

00:53:08.795 --> 00:53:13.187 you found that non ram slow of activity.

NOTE Confidence: 0.8525315

00:53:13.190 --> 00:53:14.561 When it decreases,

NOTE Confidence: 0.8525315

00:53:14.561 --> 00:53:16.846 we have increased choupette signal.

NOTE Confidence: 0.8525315

00:53:16.850 --> 00:53:20.114 We also we also found that the Minutes

NOTE Confidence: 0.8525315

00:53:20.114 --> 00:53:22.425 reported napping was was positively

NOTE Confidence: 0.8525315

00:53:22.425 --> 00:53:24.790 associated with Tau pet signals,

NOTE Confidence: 0.8525315

00:53:24.790 --> 00:53:26.995 so that the longer they

NOTE Confidence: 0.8525315

00:53:26.995 --> 00:53:29.200 reported napping during the day,

NOTE Confidence: 0.8525315

00:53:29.200 --> 00:53:31.708 the greater the evidence of Tauopathy

NOTE Confidence: 0.8525315

00:53:31.708 --> 00:53:35.223 on pet that was in the same participants

NOTE Confidence: 0.8525315

00:53:35.223 --> 00:53:38.900 using the dissolver cord on the same nights.

NOTE Confidence: 0.8525315

00:53:38.900 --> 00:53:41.110 And I mean, 38 participants.

NOTE Confidence: 0.8525315

00:53:41.110 --> 00:53:41.984 I wouldn't.

NOTE Confidence: 0.8525315

00:53:41.984 --> 00:53:46.014 I wouldn't put a lot of a lot of

NOTE Confidence: 0.8525315

00:53:46.014 --> 00:53:48.923 my cards on that, but it certainly.

NOTE Confidence: 0.8525315

00:53:48.923 --> 00:53:51.730 Suggest that if you could do more

NOTE Confidence: 0.8525315

00:53:51.810 --> 00:53:54.636 studies or more participants at with

NOTE Confidence: 0.8525315

00:53:54.636 --> 00:53:57.748 other groups and really validate that

NOTE Confidence: 0.8525315

00:53:57.748 --> 00:54:01.168 that question gives you similar information,

NOTE Confidence: 0.8525315

00:54:01.170 --> 00:54:03.150 you could potentially imagine

NOTE Confidence: 0.8525315

00:54:03.150 --> 00:54:06.120 using something like that to screen

NOTE Confidence: 0.8525315

00:54:06.202 --> 00:54:08.257 for evidence of towel risk,

NOTE Confidence: 0.8525315

00:54:08.260 --> 00:54:10.148 risk of tap ethnology.

NOTE Confidence: 0.8852378

00:54:12.940 --> 00:54:16.290 So as a follow up comment, the comment is.

NOTE Confidence: 0.8852378

00:54:16.290 --> 00:54:19.319 It would be nice of the sleep if the

NOTE Confidence: 0.8852378

00:54:19.319 --> 00:54:21.811 sleep fields could come to agreement on

NOTE Confidence: 0.8852378

00:54:21.811 --> 00:54:24.766 the automated identification of slow slow

NOTE Confidence: 0.8852378

00:54:24.766 --> 00:54:27.700 wave activity versus Delta versus M3.

NOTE Confidence: 0.9022557

00:54:31.050 --> 00:54:32.651 And I, you know,

NOTE Confidence: 0.9022557

00:54:32.651 --> 00:54:35.273 I think related to that point.

NOTE Confidence: 0.9022557

00:54:35.280 --> 00:54:37.616 You know, sleep disturbance

NOTE Confidence: 0.9022557

00:54:37.616 --> 00:54:40.536 sleep complaints come in in

NOTE Confidence: 0.9022557

00:54:40.536 --> 00:54:43.539 so many different flavors.

NOTE Confidence: 0.9022557

00:54:43.540 --> 00:54:47.617 And so I'm sort of wondering is is it?

NOTE Confidence: 0.9022557

00:54:47.620 --> 00:54:51.400 Should we really just be focusing on?

NOTE Confidence: 0.9022557

00:54:51.400 --> 00:54:52.600 Slow wave activity?

NOTE Confidence: 0.9022557

00:54:52.600 --> 00:54:55.000 Or is it? Is that premature?

NOTE Confidence: 0.8203879

00:54:57.750 --> 00:55:00.990 I I don't I I don't think I would

NOTE Confidence: 0.8203879

00:55:00.990 --> 00:55:04.219 focus exclusively on slave activity.

NOTE Confidence: 0.8203879

00:55:04.220 --> 00:55:08.840 I there are a number of like I had discussed.

NOTE Confidence: 0.8203879

00:55:08.840 --> 00:55:11.445 There's there are multiple sleep

NOTE Confidence: 0.8203879

00:55:11.445 --> 00:55:15.181 parameters that have been found to be

NOTE Confidence: 0.8203879

00:55:15.181 --> 00:55:17.786 associated or associated with risk

NOTE Confidence: 0.8203879

00:55:17.786 --> 00:55:20.743 of cognitive impairment or risk of or

NOTE Confidence: 0.8203879

00:55:20.743 --> 00:55:24.740 evident risk of having a D pathology.

NOTE Confidence: 0.8203879

00:55:24.740 --> 00:55:28.288 And I think it.

NOTE Confidence: 0.8203879

00:55:28.290 --> 00:55:30.271 I think what I think about using

NOTE Confidence: 0.8203879

00:55:30.271 --> 00:55:32.938 sleep as a marker is that the rise

NOTE Confidence: 0.8203879

00:55:32.938 --> 00:55:34.683 of these blood based markers,

NOTE Confidence: 0.8203879

00:55:34.690 --> 00:55:36.526 which is really just come in

NOTE Confidence: 0.8203879

00:55:36.526 --> 00:55:38.210 the last couple of years.

NOTE Confidence: 0.8203879

00:55:38.210 --> 00:55:40.121 I think changes a little bit the

NOTE Confidence: 0.8203879

00:55:40.121 --> 00:55:42.114 way that I've been thinking about

NOTE Confidence: 0.8203879

00:55:42.114 --> 00:55:43.969 using sleep changes across AD.

NOTE Confidence: 0.8203879

00:55:43.970 --> 00:55:46.252 The original thought when we when I

NOTE Confidence: 0.8203879

00:55:46.252 --> 00:55:48.370 started on this work eight years ago

NOTE Confidence: 0.8203879

00:55:48.370 --> 00:55:50.402 is that it would be a noninvasive

NOTE Confidence: 0.8203879

00:55:50.402 --> 00:55:52.866 measure that could be used in the

NOTE Confidence: 0.8203879

00:55:52.866 --> 00:55:54.850 clinic to assess for risk along

NOTE Confidence: 0.8203879

00:55:54.850 --> 00:55:55.810 with other factors.

NOTE Confidence: 0.8203879

00:55:55.810 --> 00:55:58.006 I really don't think it will

NOTE Confidence: 0.8203879

00:55:58.006 --> 00:55:59.104 ever replace and.

NOTE Confidence: 0.8203879

00:55:59.110 --> 00:56:02.070 Amyloid pet scan or a Tau pet scan

NOTE Confidence: 0.8203879

00:56:02.070 --> 00:56:05.517 or CSF measures for amyloid and Tau,

NOTE Confidence: 0.8203879

00:56:05.520 --> 00:56:08.138 but something that could be a non

NOTE Confidence: 0.8203879

00:56:08.138 --> 00:56:09.832 invasively screened and potentially

NOTE Confidence: 0.8203879

00:56:09.832 --> 00:56:12.347 followed in an intervention trial.

NOTE Confidence: 0.8203879

00:56:12.350 --> 00:56:15.241 With the rise of these blood markers

NOTE Confidence: 0.8203879

00:56:15.241 --> 00:56:18.711 which are seem to be very robust in

NOTE Confidence: 0.8203879

00:56:18.711 --> 00:56:21.365 terms of identifying people with 80

NOTE Confidence: 0.8203879

00:56:21.365 --> 00:56:24.312 pathology and are going to be more

NOTE Confidence: 0.8203879

00:56:24.312 --> 00:56:26.438 less expensive and probably better

NOTE Confidence: 0.8203879

00:56:26.438 --> 00:56:28.568 tolerated by participants in patients,

NOTE Confidence: 0.8203879

00:56:28.570 --> 00:56:31.396 I think that defining how sleep

NOTE Confidence: 0.8203879

00:56:31.396 --> 00:56:33.280 changes across 80 pathogenesis.

NOTE Confidence: 0.8203879

00:56:33.280 --> 00:56:34.548 Could be critically important,

NOTE Confidence: 0.8203879

00:56:34.548 --> 00:56:36.133 maybe not as a marker,

NOTE Confidence: 0.8203879

00:56:36.140 --> 00:56:39.032 but for defining when you would

NOTE Confidence: 0.8203879

00:56:39.032 --> 00:56:40.478 want to intervene.

NOTE Confidence: 0.8203879

00:56:40.480 --> 00:56:43.390 That what that intervention with

NOTE Confidence: 0.8203879

00:56:43.390 --> 00:56:45.718 that intervention would be.

NOTE Confidence: 0.8203879

00:56:45.720 --> 00:56:49.440 I think to to use it as a screening method.

NOTE Confidence: 0.8203879

00:56:49.440 --> 00:56:52.037 I think we need to do PSG's.

NOTE Confidence: 0.8203879

00:56:52.040 --> 00:56:54.588 That could be a real challenge given

NOTE Confidence: 0.8203879

00:56:54.588 --> 00:56:56.810 just the numbers of individuals that

NOTE Confidence: 0.8203879

00:56:56.810 --> 00:56:59.730 we're talking about as we as we go

NOTE Confidence: 0.8203879

00:56:59.730 --> 00:57:02.088 forward from what the models project,

NOTE Confidence: 0.8203879

00:57:02.090 --> 00:57:04.184 the many millions that will be

NOTE Confidence: 0.8203879

00:57:04.184 --> 00:57:06.180 at risk of Alzheimer's disease.

NOTE Confidence: 0.8203879

00:57:06.180 --> 00:57:10.320 But if we can, you know.

NOTE Confidence: 0.8203879

00:57:10.320 --> 00:57:13.040 Use some of these.

NOTE Confidence: 0.8203879

00:57:13.040 --> 00:57:16.376 EG based and another sleep parameters

NOTE Confidence: 0.8203879

00:57:16.376 --> 00:57:19.211 to validate more easily deployable

NOTE Confidence: 0.8203879

00:57:19.211 --> 00:57:22.844 methods that I think would be very

NOTE Confidence: 0.8203879

00:57:22.844 --> 00:57:25.528 powerful as a screening tool.

NOTE Confidence: 0.827884

00:57:27.260 --> 00:57:28.916 So another question is what is

NOTE Confidence: 0.827884

00:57:28.916 --> 00:57:30.355 your thought about why sodium

NOTE Confidence: 0.827884

00:57:30.355 --> 00:57:31.760 oxybate did not decrease amyloid

NOTE Confidence: 0.827884

00:57:31.760 --> 00:57:34.010 or Tau in your experiments or in

NOTE Confidence: 0.827884

00:57:34.010 --> 00:57:35.438 the experiments you mentioned?

NOTE Confidence: 0.9076933

00:57:36.480 --> 00:57:39.348 That's a great question.

NOTE Confidence: 0.9076933

00:57:39.350 --> 00:57:44.618 I think there's two potential explanations.

NOTE Confidence: 0.9076933

00:57:44.620 --> 00:57:48.100 One is that we did have a wide

NOTE Confidence: 0.9076933

00:57:48.100 --> 00:57:50.486 wide variability in the effect

NOTE Confidence: 0.9076933

00:57:50.486 --> 00:57:52.856 of sodium oxybate on sleep,

NOTE Confidence: 0.9076933

00:57:52.860 --> 00:57:55.555 meaning that although we had

NOTE Confidence: 0.9076933

00:57:55.555 --> 00:57:57.172 statistically significant differences

NOTE Confidence: 0.9076933

00:57:57.172 --> 00:57:59.810 and all the sleep measures we

NOTE Confidence: 0.9076933

00:57:59.810 --> 00:58:02.480 looked at such as total sleep time,

NOTE Confidence: 0.9076933

00:58:02.480 --> 00:58:06.686 sleep efficiency, other other things for.

NOTE Confidence: 0.9076933

00:58:06.690 --> 00:58:07.980 Sleep deprivation group

NOTE Confidence: 0.9076933

00:58:07.980 --> 00:58:10.130 compared to control and drug.

NOTE Confidence: 0.9076933

00:58:10.130 --> 00:58:12.420 We did not have statistically

NOTE Confidence: 0.9076933

00:58:12.420 --> 00:58:13.794 significant differences between

NOTE Confidence: 0.9076933

00:58:13.794 --> 00:58:15.720 the control and drug group,

NOTE Confidence: 0.9076933

00:58:15.720 --> 00:58:19.444 so it may be that we didn't

NOTE Confidence: 0.9076933

00:58:19.444 --> 00:58:22.379 have an adequate effect on.

NOTE Confidence: 0.9076933

00:58:22.380 --> 00:58:23.294 On sleep,

NOTE Confidence: 0.9076933

00:58:23.294 --> 00:58:26.036 in order to change the concentrations,

NOTE Confidence: 0.9076933

00:58:26.040 --> 00:58:28.800 the other is that you know the slow

NOTE Confidence: 0.9076933

00:58:28.800 --> 00:58:30.604 waves that are pharmacologically

NOTE Confidence: 0.9076933

00:58:30.604 --> 00:58:33.712 induced by sodium oxybate may be

NOTE Confidence: 0.9076933

00:58:33.712 --> 00:58:36.548 different than physiologic slow waves,

NOTE Confidence: 0.9076933

00:58:36.550 --> 00:58:40.512 in which case methods such as closed

NOTE Confidence: 0.9076933

00:58:40.512 --> 00:58:43.223 loop acoustic stimulation to increase

NOTE Confidence: 0.9076933

00:58:43.223 --> 00:58:46.879 low waves may be a better approach to.

NOTE Confidence: 0.9076933

00:58:46.880 --> 00:58:49.460 To increase flow waves and

NOTE Confidence: 0.9076933

00:58:49.460 --> 00:58:51.524 decrease the concentrations of.

NOTE Confidence: 0.9076933

00:58:51.530 --> 00:58:52.799 Amyloid and Tau.

NOTE Confidence: 0.8710914

00:58:55.130 --> 00:58:58.460 Alright, well we are at the top of the hour.

NOTE Confidence: 0.8710914

00:58:58.460 --> 00:59:00.665 Want to thank our speaker again for

NOTE Confidence: 0.8710914

00:59:00.665 --> 00:59:02.961 this this great tour and then Lauren

NOTE Confidence: 0.8710914

00:59:02.961 --> 00:59:04.887 I think you had an announcement

NOTE Confidence: 0.8710914

00:59:04.955 --> 00:59:07.115 for everybody before they peel off.

NOTE Confidence: 0.8710914

00:59:07.120 --> 00:59:08.092 Yeah thanks everybody.

NOTE Confidence: 0.8710914

00:59:08.092 --> 00:59:10.937 Just wanted to let you know that we do

NOTE Confidence: 0.8710914

00:59:10.937 --> 00:59:13.521 not have a talk next week because it's the

NOTE Confidence: 0.8710914

00:59:13.521 --> 00:59:15.776 American College of Physicians Conference.

NOTE Confidence: 0.8710914

00:59:15.780 --> 00:59:18.292 But we will resume on October 28 with

NOTE Confidence: 0.8710914

00:59:18.292 --> 00:59:20.768 the talk by Frank sheer at Harvard.

NOTE Confidence: 0.8710914

00:59:20.770 --> 00:59:22.672 Who's going to be speaking about

NOTE Confidence: 0.8710914

00:59:22.672 --> 00:59:24.735 night work and disease in the

NOTE Confidence: 0.8710914

00:59:24.735 --> 00:59:26.195 role of circadian misalignment?

NOTE Confidence: 0.8710914

00:59:26.200 --> 00:59:28.992 So look forward to seeing you all then

NOTE Confidence: 0.8710914

00:59:28.992 --> 00:59:31.765 thanks so much. Thank you alright.

NOTE Confidence: 0.8710914

00:59:31.765 --> 00:59:33.400 Thanks again, Brendan.

NOTE Confidence: 0.8710914

00:59:33.400 --> 00:59:37.590 Thank you friend, thank you.

NOTE Confidence: 0.8710914

00:59:37.590 --> 00:59:40.047 I you know it is worth noting,

NOTE Confidence: 0.8710914

00:59:40.050 --> 00:59:42.834 I think at peak we were we had

NOTE Confidence: 0.8710914

00:59:42.834 --> 00:59:45.049 about 85 participants so.

NOTE Confidence: 0.8710914

00:59:45.050 --> 00:59:45.899 Oh, that's great.

NOTE Confidence: 0.8710914

00:59:45.900 --> 00:59:46.466 I think.

NOTE Confidence: 0.8710914

00:59:46.466 --> 00:59:48.447 Yeah, I think it was hard to

NOTE Confidence: 0.84200066

00:59:48.450 --> 00:59:50.445 tell. I would see the pings coming

NOTE Confidence: 0.84200066

00:59:50.445 --> 00:59:52.188 would cost like the screen would

NOTE Confidence: 0.84200066

00:59:52.188 --> 00:59:54.106 be like so and so's entered the

NOTE Confidence: 0.84200066

00:59:54.110 --> 00:59:55.796 waiting room. So yeah. Yeah yeah.

NOTE Confidence: 0.84200066

00:59:55.800 --> 00:59:57.788 So there was. There was a lot

NOTE Confidence: 0.84200066

00:59:57.790 --> 01:00:00.466 of activity, so good that's great.

NOTE Confidence: 0.84200066

01:00:00.470 --> 01:00:02.336 Alright, well thank you so

NOTE Confidence: 0.84200066

01:00:02.336 --> 01:00:04.196 much for the invitation and

NOTE Confidence: 0.8906467

01:00:04.200 --> 01:00:06.438 for the thank you for coming

NOTE Confidence: 0.8906467

01:00:06.438 --> 01:00:08.680 virtually and I'll be in touch.

NOTE Confidence: 0.80393

01:00:13.340 --> 01:00:15.560 Some reason I muted myself somehow,

NOTE Confidence: 0.80393

01:00:15.560 --> 01:00:18.104 but I also want to say that the

NOTE Confidence: 0.80393

01:00:18.104 --> 01:00:20.369 paper was just accepted today.

NOTE Confidence: 0.80393

01:00:20.370 --> 01:00:22.960 Oh good, the one you sent me.

NOTE Confidence: 0.80393

01:00:22.960 --> 01:00:26.290 OK, yeah, so I'm sure by the time so.

NOTE Confidence: 0.80393

01:00:26.290 --> 01:00:29.250 So if you were going to use anything

NOTE Confidence: 0.80393

01:00:29.250 --> 01:00:31.840 in an application, you'll be able to

NOTE Confidence: 0.80393

01:00:31.840 --> 01:00:34.060 decide as impressed. Yeah, OK, good,

NOTE Confidence: 0.80393

01:00:34.060 --> 01:00:37.219 alright? Alright, Thanks again. Take

NOTE Confidence: 0.78336304

01:00:37.220 --> 01:00:40.286 care bye bye.