WEBVTT

- NOTE duration:"00:56:38"
- NOTE recognizability:0.861
- NOTE language:en-us
- NOTE Confidence: 0.833060248
- 00:00:00.000 --> 00:00:02.905 My name is Andrea Zentrack and I'm
- NOTE Confidence: 0.833060248
- $00{:}00{:}02{.}905 \dashrightarrow 00{:}00{:}05{.}151$ an assistant professor at Yale
- NOTE Confidence: 0.833060248
- $00:00:05.151 \dashrightarrow 00:00:06.995$ University School of Medicine.
- NOTE Confidence: 0.833060248
- $00{:}00{:}07{.}000 \dashrightarrow 00{:}00{:}10{.}395$ And we lcome to yet another edition of
- NOTE Confidence: 0.833060248
- $00:00:10.395 \rightarrow 00:00:13.600$ the Joint Sleep Conference between
- NOTE Confidence: 0.833060248
- 00:00:13.600 00:00:15.220 our programs in the Northeast.
- NOTE Confidence: 0.833060248
- $00:00:15.220 \longrightarrow 00:00:18.100$ I think we've grown from 2.
- NOTE Confidence: 0.833060248
- 00:00:18.100 --> 00:00:22.178 Two programs to 6. And I don't know.
- NOTE Confidence: 0.833060248
- $00:00:22.178 \longrightarrow 00:00:23.900$ Just say that we have an
- NOTE Confidence: 0.833060248
- 00:00:23.971 --> 00:00:25.750 outstanding speaker today,
- NOTE Confidence: 0.833060248
- $00:00:25.750 \longrightarrow 00:00:27.675$ and so during the talk I'll ask
- NOTE Confidence: 0.833060248
- $00{:}00{:}27.675 \dashrightarrow 00{:}00{:}29.570$ you that you mute yourselves.
- NOTE Confidence: 0.833060248
- $00:00:29.570 \longrightarrow 00:00:32.291$ If you have a question or
- NOTE Confidence: 0.833060248

00:00:32.291 - > 00:00:33.546 wanted to make him comment,

NOTE Confidence: 0.833060248

 $00{:}00{:}33.550 \dashrightarrow 00{:}00{:}37.078$ please do so in the chat.

NOTE Confidence: 0.833060248

 $00{:}00{:}37.080 \dashrightarrow 00{:}00{:}40.002$ In the chat is where also

NOTE Confidence: 0.833060248

00:00:40.002 --> 00:00:41.950 instructions for obtaining CME

NOTE Confidence: 0.833060248

 $00:00:42.045 \rightarrow 00:00:45.177$ credit for today's talk will appear.

NOTE Confidence: 0.833060248

 $00:00:45.180 \longrightarrow 00:00:46.632$ And so if you are not

NOTE Confidence: 0.833060248

 $00:00:46.632 \rightarrow 00:00:47.600$ registered with the LCM,

NOTE Confidence: 0.833060248

 $00:00:47.600 \longrightarrow 00:00:50.029$ you would have to do that first.

NOTE Confidence: 0.833060248

 $00{:}00{:}50{.}030 \dashrightarrow 00{:}00{:}52{.}724$ And you can receive credit for

NOTE Confidence: 0.833060248

 $00{:}00{:}52.724 \dashrightarrow 00{:}00{:}55.047$ attending the session 15 minutes

NOTE Confidence: 0.833060248

 $00:00:55.047 \longrightarrow 00:00:56.960$ prior to the end or 15 minutes

NOTE Confidence: 0.833060248

 $00:00:56.960 \longrightarrow 00:00:58.450$ after the end of the session.

NOTE Confidence: 0.871507492

 $00:01:00.800 \longrightarrow 00:01:03.260$ And so, without further ado,

NOTE Confidence: 0.871507492

 $00:01:03.260 \longrightarrow 00:01:04.880$ I wanted to introduce the

NOTE Confidence: 0.871507492

 $00:01:04.880 \longrightarrow 00:01:06.176$ very special speaker today.

NOTE Confidence: 0.871604843333333

 $00:01:08.190 \longrightarrow 00:01:10.787$ A friend of mine and a colleague

- NOTE Confidence: 0.871604843333333
- 00:01:10.787 --> 00:01:12.865 of mine doctor Sabera Abbott,
- NOTE Confidence: 0.871604843333333
- $00{:}01{:}12.865 \dashrightarrow 00{:}01{:}15.535$ and so Doctor Abbott is an
- NOTE Confidence: 0.871604843333333
- 00:01:15.535 --> 00:01:17.769 assistant professor of neurology
- NOTE Confidence: 0.871604843333333
- $00{:}01{:}17.769 \dashrightarrow 00{:}01{:}20.049$ at the Northwestern Medicine.
- NOTE Confidence: 0.871604843333333
- 00:01:20.050 --> 00:01:22.948 And in Chicago, and I know Sabra,
- NOTE Confidence: 0.871604843333333
- $00:01:22.950 \rightarrow 00:01:25.698$ since our residency times and neurology
- NOTE Confidence: 0.871604843333333
- $00{:}01{:}25.698 \dashrightarrow 00{:}01{:}28.545$ back in Beth Israel Deaconess when
- NOTE Confidence: 0.871604843333333
- 00:01:28.545 --> 00:01:29.955 I did my detour through neurology
- NOTE Confidence: 0.871604843333333
- 00:01:29.955 --> 00:01:31.823 before I went to a pulmonary critical
- NOTE Confidence: 0.871604843333333
- $00:01:31.823 \rightarrow 00:01:33.208$ care and then eventually sleep,
- NOTE Confidence: 0.871604843333333
- $00:01:33.210 \longrightarrow 00:01:33.987$ and so little,
- NOTE Confidence: 0.871604843333333
- $00{:}01{:}33{.}987 \dashrightarrow 00{:}01{:}36{.}140$ did we know we started in the same
- NOTE Confidence: 0.871604843333333
- 00:01:36.140 --> 00:01:38.388 place and ended up in the same domain?
- NOTE Confidence: 0.871604843333333
- $00:01:38.390 \dashrightarrow 00:01:40.945$ And so I'm really excited to have
- NOTE Confidence: 0.871604843333333
- $00:01:40.945 \longrightarrow 00:01:43.226$ her talk to us today because
- NOTE Confidence: 0.871604843333333

 $00:01:43.226 \rightarrow 00:01:45.506$ she is an outstanding physician,

NOTE Confidence: 0.871604843333333

00:01:45.510 --> 00:01:46.380 incredible scientist,

NOTE Confidence: 0.871604843333333

 $00{:}01{:}46.380 \dashrightarrow 00{:}01{:}49.520$ and the and a a great clinician

NOTE Confidence: 0.871604843333333

 $00:01:49.520 \longrightarrow 00:01:52.170$ who cares about her patients.

NOTE Confidence: 0.871604843333333

 $00:01:52.170 \longrightarrow 00:01:53.918$ But aside from that,

NOTE Confidence: 0.871604843333333

00:01:53.918 --> 00:01:56.103 she started her academic career

NOTE Confidence: 0.871604843333333

00:01:56.103 --> 00:01:57.979 at Carleton College,

NOTE Confidence: 0.871604843333333

 $00:01:57.980 \longrightarrow 00:02:00.647$ where she received the BA in Psychology

NOTE Confidence: 0.871604843333333

 $00{:}02{:}00{.}650 \dashrightarrow 00{:}02{:}02{.}204$ and then moved on to University

NOTE Confidence: 0.871604843333333

00:02:02.204 --> 00:02:03.780 of Illinois at Urbana Champaign,

NOTE Confidence: 0.871604843333333

 $00:02:03.780 \longrightarrow 00:02:05.780$ where she got her masters,

NOTE Confidence: 0.871604843333333

 $00{:}02{:}05{.}780 \dashrightarrow 00{:}02{:}08{.}276$ followed by a PhD in Molecular

NOTE Confidence: 0.871604843333333

00:02:08.276 --> 00:02:09.524 and integrative Physiology,

NOTE Confidence: 0.871604843333333

 $00:02:09.530 \dashrightarrow 00:02:11.777$ and then got her MD there before

NOTE Confidence: 0.871604843333333

 $00{:}02{:}11.777 \dashrightarrow 00{:}02{:}14.309$ moving on to Beth Israel Deaconess

NOTE Confidence: 0.871604843333333

00:02:14.310 - > 00:02:16.278 Medical Center with Harvard,

- NOTE Confidence: 0.871604843333333
- $00:02:16.278 \longrightarrow 00:02:18.246$ where she got her.
- NOTE Confidence: 0.871604843333333
- 00:02:18.250 --> 00:02:18.898 Neurology residency,
- NOTE Confidence: 0.871604843333333
- $00:02:18.898 \rightarrow 00:02:21.166$ where she was also a chief resident,
- NOTE Confidence: 0.871604843333333
- $00{:}02{:}21{.}170 \dashrightarrow 00{:}02{:}21{.}751$ and.
- NOTE Confidence: 0.871604843333333
- 00:02:21.751 --> 00:02:24.656 Completed her clinical sleep fellowship
- NOTE Confidence: 0.871604843333333
- $00:02:24.656 \rightarrow 00:02:29.158$ back in Chicago at Northwestern and
- NOTE Confidence: 0.871604843333333
- $00{:}02{:}29{.}158 \dashrightarrow 00{:}02{:}35{.}026$ so Sabra is a prolific academician.
- NOTE Confidence: 0.871604843333333
- $00{:}02{:}35{.}030 \dashrightarrow 00{:}02{:}38{.}068$ She does research and has ROI and
- NOTE Confidence: 0.871604843333333
- 00:02:38.068 --> 00:02:40.929 program grants that she is a Co
- NOTE Confidence: 0.871604843333333
- $00:02:40.929 \longrightarrow 00:02:45.138$ investigator on and she's old so
- NOTE Confidence: 0.871604843333333
- $00:02:45.138 \rightarrow 00:02:49.473$ published dozens of papers and.
- NOTE Confidence: 0.871604843333333
- $00{:}02{:}49{.}480 \dashrightarrow 00{:}02{:}53{.}146$ Chapters that are read throughout the
- NOTE Confidence: 0.871604843333333
- $00:02:53.146 \longrightarrow 00:02:57.850$ world and are also appear in doctor
- NOTE Confidence: 0.871604843333333
- $00:02:57.850 \dashrightarrow 00:03:00.174$ Kriegers principles and practice,
- NOTE Confidence: 0.871604843333333
- 00:03:00.174 --> 00:03:00.950 Sleep Medicine,
- NOTE Confidence: 0.871604843333333

 $00:03:00.950 \rightarrow 00:03:03.830$ and so just looking at her first publication,

NOTE Confidence: 0.871604843333333

 $00:03:03.830 \longrightarrow 00:03:05.839$ it sort of gives it away of

NOTE Confidence: 0.871604843333333

 $00{:}03{:}05{.}839 \dashrightarrow 00{:}03{:}07{.}774$ what her passion is and her

NOTE Confidence: 0.871604843333333

00:03:07.774 --> 00:03:09.510 first publication back in 2003,

NOTE Confidence: 0.871604843333333

 $00{:}03{:}09{.}510 \dashrightarrow 00{:}03{:}11{.}070$ and journal Neuroscience is

NOTE Confidence: 0.871604843333333

00:03:11.070 --> 00:03:12.240 circadian clock controlled

NOTE Confidence: 0.871604843333333

 $00:03:12.240 \dashrightarrow 00:03:13.959$ regulation of cyclic GMP protein

NOTE Confidence: 0.871604843333333

00:03:13.959 - 00:03:15.717 kinase G in an external domain,

NOTE Confidence: 0.871604843333333

 $00{:}03{:}15{.}720 \dashrightarrow 00{:}03{:}19{.}140$ and so she is a.

NOTE Confidence: 0.81877606945

 $00:03:21.490 \longrightarrow 00:03:22.922$ Aficionado of circadian clock.

NOTE Confidence: 0.81877606945

 $00{:}03{:}22{.}922 \dashrightarrow 00{:}03{:}26{.}012$ And that's what she's going to talk to us

NOTE Confidence: 0.81877606945

 $00:03:26.012 \rightarrow 00:03:28.063$ today about keeping time in the clinic.

NOTE Confidence: 0.81877606945

 $00:03:28.070 \rightarrow 00:03:30.018$ Understanding and managing the

NOTE Confidence: 0.81877606945

 $00{:}03{:}30{.}018 \dashrightarrow 00{:}03{:}31{.}966$ circadian patient from bedside

NOTE Confidence: 0.81877606945

 $00:03:31.970 \longrightarrow 00:03:34.730$ to from bench to be dside. And so.

NOTE Confidence: 0.81877606945

 $00:03:34.730 \dashrightarrow 00:03:36.950$ I'm looking forward to the stock.

00:03:36.950 --> 00:03:38.868 Thank you so much for being with

NOTE Confidence: 0.81877606945

 $00{:}03{:}38{.}868 \dashrightarrow 00{:}03{:}40{.}727$ us Zebra and let's get to it.

NOTE Confidence: 0.875420375833334

 $00:03:41.750 \longrightarrow 00:03:43.850$ Great, well thank you Andre for

NOTE Confidence: 0.875420375833334

 $00:03:43.850 \rightarrow 00:03:45.726$ that very very kind introduction

NOTE Confidence: 0.875420375833334

 $00{:}03{:}45.726 \dashrightarrow 00{:}03{:}48.519$ and I too am very pleased that

NOTE Confidence: 0.875420375833334

 $00{:}03{:}48.519 \dashrightarrow 00{:}03{:}50.829$ despite losing you as a neurologist,

NOTE Confidence: 0.875420375833334

 $00:03:50.830 \dashrightarrow 00:03:55.694$ our paths continued across along the way so.

NOTE Confidence: 0.875420375833334

 $00{:}03{:}55{.}700 \dashrightarrow 00{:}03{:}57{.}564$ It was in one of our discussions that

NOTE Confidence: 0.875420375833334

 $00{:}03{:}57{.}564 \dashrightarrow 00{:}03{:}59{.}289$ Andre and I actually had about this

NOTE Confidence: 0.875420375833334

 $00:03:59.289 \dashrightarrow 00:04:01.123$ talk where he made what I thought

NOTE Confidence: 0.875420375833334

00:04:01.123 --> 00:04:02.538 was a very insightful comment.

NOTE Confidence: 0.875420375833334

00:04:02.540 --> 00:04:03.730 Which and I don't know if you

NOTE Confidence: 0.875420375833334

 $00:04:03.730 \longrightarrow 00:04:04.240$ even remember this,

NOTE Confidence: 0.875420375833334

 $00{:}04{:}04{.}240 \dashrightarrow 00{:}04{:}06{.}676$ but you said that circadian rhythms are

NOTE Confidence: 0.875420375833334

 $00{:}04{:}06.676 \dashrightarrow 00{:}04{:}08.860$ like the neurology of Sleep Medicine,

 $00:04:08.860 \longrightarrow 00:04:11.016$ and I think that is very true

NOTE Confidence: 0.875420375833334

 $00{:}04{:}11.016 \dashrightarrow 00{:}04{:}11.940$ in some respects.

NOTE Confidence: 0.875420375833334

 $00:04:11.940 \longrightarrow 00:04:13.806$ I think that circadian rhythms and

NOTE Confidence: 0.875420375833334

 $00:04:13.806 \rightarrow 00:04:16.240$ neurology are both a little intimidating.

NOTE Confidence: 0.875420375833334

 $00:04:16.240 \longrightarrow 00:04:17.584$ When you first experience

NOTE Confidence: 0.875420375833334

 $00{:}04{:}17.584 \dashrightarrow 00{:}04{:}19.264$ them and 1st approach them.

NOTE Confidence: 0.875420375833334

00:04:19.270 --> 00:04:20.920 But once you actually understand

NOTE Confidence: 0.875420375833334

 $00:04:20.920 \longrightarrow 00:04:22.240$ the logic behind them,

NOTE Confidence: 0.875420375833334

 $00:04:22.240 \rightarrow 00:04:24.410$ they can be incredibly gratifying.

NOTE Confidence: 0.875420375833334

 $00:04:24.410 \longrightarrow 00:04:26.986$ And really a great field to be in.

NOTE Confidence: 0.875420375833334

 $00:04:26.990 \longrightarrow 00:04:27.262$ Granted,

NOTE Confidence: 0.875420375833334

 $00{:}04{:}27{.}262 \dashrightarrow 00{:}04{:}29{.}710$ I have the bias that I am a neurologist

NOTE Confidence: 0.875420375833334

 $00:04:29.770 \longrightarrow 00:04:31.870$ who specializes in circadian rhythms,

NOTE Confidence: 0.875420375833334

 $00{:}04{:}31.870 \dashrightarrow 00{:}04{:}33.514$ so maybe I am taking that

NOTE Confidence: 0.875420375833334

 $00:04:33.514 \rightarrow 00:04:34.336$ a little personally,

NOTE Confidence: 0.875420375833334

 $00:04:34.340 \longrightarrow 00:04:36.032$ but my overall goal today is

 $00:04:36.032 \longrightarrow 00:04:38.056$ really to try to make circadian

NOTE Confidence: 0.875420375833334

 $00:04:38.056 \rightarrow 00:04:40.126$ biology a little less intimidating

NOTE Confidence: 0.875420375833334

 $00:04:40.126 \longrightarrow 00:04:42.250$ for every body in the audience,

NOTE Confidence: 0.875420375833334

 $00:04:42.250 \rightarrow 00:04:44.090$ and I know we've got a wide range

NOTE Confidence: 0.875420375833334

 $00:04:44.090 \longrightarrow 00:04:45.726$ of experience just based on some of NOTE Confidence: 0.875420375833334

 $00{:}04{:}45.726 \dashrightarrow 00{:}04{:}47.400$ the names that I've seen coming in

NOTE Confidence: 0.875420375833334

 $00:04:47.400 \rightarrow 00:04:48.894$ in terms of how comfortable people

NOTE Confidence: 0.875420375833334

 $00:04:48.894 \rightarrow 00:04:50.528$ may be with circadian biology,

NOTE Confidence: 0.875420375833334

 $00:04:50.528 \longrightarrow 00:04:52.032$ but hopefully everybody will

NOTE Confidence: 0.875420375833334

 $00:04:52.032 \longrightarrow 00:04:54.152$ walk away just feeling a little

NOTE Confidence: 0.875420375833334

 $00:04:54.152 \longrightarrow 00:04:55.697$ bit better about the topic.

NOTE Confidence: 0.875420375833334

00:04:55.700 --> 00:04:57.180 I'm gonna start off.

NOTE Confidence: 0.875420375833334

 $00{:}04{:}57.180 \dashrightarrow 00{:}04{:}59.030$ With just a general overview

NOTE Confidence: 0.875420375833334

 $00{:}04{:}59{.}030 \dashrightarrow 00{:}05{:}00{.}759$ of circadian rhythms,

NOTE Confidence: 0.875420375833334

 $00{:}05{:}00{.}760 \dashrightarrow 00{:}05{:}02{.}134$ just to make sure every body is

 $00:05:02.134 \rightarrow 00:05:03.780$ starting off on the same page and

NOTE Confidence: 0.875420375833334

 $00{:}05{:}03.780 \dashrightarrow 00{:}05{:}05.355$ then gonna walk through a couple of

NOTE Confidence: 0.875420375833334

 $00:05:05.405 \rightarrow 00:05:06.920$ case examples of patients who've

NOTE Confidence: 0.875420375833334

 $00:05:06.920 \rightarrow 00:05:08.435$ come through the circadian clinic

NOTE Confidence: 0.875420375833334

 $00{:}05{:}08{.}440 \dashrightarrow 00{:}05{:}10{.}760$ with me both going through them as an

NOTE Confidence: 0.875420375833334

 $00:05:10.760 \rightarrow 00:05:12.818$ illustration of sort of how to manage

NOTE Confidence: 0.875420375833334

 $00:05:12.818 \rightarrow 00:05:14.740$ the bread and butter circadian patient,

NOTE Confidence: 0.875420375833334

 $00{:}05{:}14.740 \dashrightarrow 00{:}05{:}16.707$ but also some tips and tricks that

NOTE Confidence: 0.875420375833334

 $00{:}05{:}16.707 \dashrightarrow 00{:}05{:}18.189$ we've taken from the research

NOTE Confidence: 0.875420375833334

 $00:05:18.189 \rightarrow 00:05:20.205$ domain to try to help manage them.

NOTE Confidence: 0.875420375833334

 $00:05:20.210 \longrightarrow 00:05:21.161$ And then lastly,

NOTE Confidence: 0.875420375833334

 $00{:}05{:}21{.}161 \dashrightarrow 00{:}05{:}23{.}380$ I'll wrap up with a summary of

NOTE Confidence: 0.875420375833334

 $00:05:23.452 \longrightarrow 00:05:25.542$ a research project we recently

NOTE Confidence: 0.875420375833334

 $00:05:25.542 \rightarrow 00:05:27.910$ completed that was really based on.

NOTE Confidence: 0.875420375833334

 $00{:}05{:}27{.}910 \dashrightarrow 00{:}05{:}29{.}320$ Some of the insights that we

NOTE Confidence: 0.875420375833334

 $00:05:29.320 \longrightarrow 00:05:30.730$ had from seeing these patients.

- NOTE Confidence: 0.875420375833334
- $00:05:30.730 \longrightarrow 00:05:33.718$ So without further ado.
- NOTE Confidence: 0.875420375833334
- $00:05:33.720 \longrightarrow 00:05:35.736$ First step is to get the slides to advance.
- NOTE Confidence: 0.875420375833334
- $00:05:35.740 \longrightarrow 00:05:38.980$ There we go, so I have no disclosures.
- NOTE Confidence: 0.875420375833334
- $00:05:38.980 \longrightarrow 00:05:40.160$ And as Andre said,
- NOTE Confidence: 0.875420375833334
- $00{:}05{:}40{.}160 \dashrightarrow 00{:}05{:}41{.}930$ the CME information is also gonna
- NOTE Confidence: 0.875420375833334
- $00:05:41.993 \longrightarrow 00:05:43.295$ be in the chat for you,
- NOTE Confidence: 0.875420375833334
- $00{:}05{:}43{.}300 \dashrightarrow 00{:}05{:}45{.}610$ but it's on the screen here.
- NOTE Confidence: 0.875420375833334
- 00:05:45.610 --> 00:05:47.386 So just to get things started,
- NOTE Confidence: 0.875420375833334
- 00:05:47.390 --> 00:05:49.086 I always want to make sure that we
- NOTE Confidence: 0.875420375833334
- $00:05:49.086 \rightarrow 00:05:50.593$ kind of talk through the general
- NOTE Confidence: 0.875420375833334
- $00:05:50.593 \dashrightarrow 00:05:52.507$ concept of what do we even mean
- NOTE Confidence: 0.875420375833334
- $00:05:52.507 \dashrightarrow 00:05:54.072$ when we're talking about circadian
- NOTE Confidence: 0.875420375833334
- $00:05:54.072 \longrightarrow 00:05:56.312$ rhythms and they're in general all NOTE Confidence: 0.875420375833334
- $00:05:56.312 \dashrightarrow 00:05:58.767$ of the physiological processes that NOTE Confidence: 0.875420375833334
- $00{:}05{:}58{.}767 \dashrightarrow 00{:}02{.}089$ we have that have a near 24 hour
- NOTE Confidence: 0.875420375833334

 $00:06:02.089 \longrightarrow 00:06:04.590$ or about a day property to them.

NOTE Confidence: 0.875420375833334

 $00{:}06{:}04.590 \dashrightarrow 00{:}06{:}06.886$ And I think it's easiest to understand

NOTE Confidence: 0.875420375833334

 $00{:}06{:}06{.}886 \dashrightarrow 00{:}06{:}09{.}203$ these if we think about them from

NOTE Confidence: 0.875420375833334

 $00{:}06{:}09{.}203 \dashrightarrow 00{:}06{:}11.690$ the idea of our sleep wake rhythms,

NOTE Confidence: 0.875420375833334

 $00:06:11.690 \longrightarrow 00:06:13.982$ because those definitely have a daily

NOTE Confidence: 0.875420375833334

 $00{:}06{:}13.982 \dashrightarrow 00{:}06{:}16.537$ occurrence to them, and so I've.

NOTE Confidence: 0.875420375833334

 $00:06:16.537 \rightarrow 00:06:19.820$ Plotted out here just a very idealized

NOTE Confidence: 0.875420375833334

00:06:19.919 --> 00:06:21.626 sleep wake schedule of somebody,

NOTE Confidence: 0.875420375833334

 $00:06:21.626 \rightarrow 00:06:23.460$ and so we've got daytime over here.

NOTE Confidence: 0.875420375833334

 $00:06:23.460 \longrightarrow 00:06:24.255$ On the left.

NOTE Confidence: 0.875420375833334

00:06:24.255 --> 00:06:25.580 We've got night time here,

NOTE Confidence: 0.864063417692308

 $00:06:25.580 \dashrightarrow 00:06:27.309$ and these black bars are the sleep

NOTE Confidence: 0.864063417692308

 $00:06:27.309 \longrightarrow 00:06:29.119$ periods for each of these individuals,

NOTE Confidence: 0.864063417692308

 $00:06:29.120 \longrightarrow 00:06:30.680$ or for this one individual.

NOTE Confidence: 0.864063417692308

 $00:06:30.680 \longrightarrow 00:06:33.560$ And you can see that in this 24 hour

NOTE Confidence: 0.864063417692308

 $00:06:33.560 \rightarrow 00:06:35.160$ environment every day they go to bed at

- NOTE Confidence: 0.864063417692308
- $00:06:35.207 \rightarrow 00:06:36.863$ the same time wake up at the same time,
- NOTE Confidence: 0.864063417692308
- $00:06:36.870 \rightarrow 00:06:39.110$ and they're generally sleeping when
- NOTE Confidence: 0.864063417692308
- $00:06:39.110 \longrightarrow 00:06:41.354$ it's dark out, but the question?
- NOTE Confidence: 0.864063417692308
- $00:06:41.354 \rightarrow 00:06:43.440$ The first one that comes up is,
- NOTE Confidence: 0.864063417692308
- $00:06:43.440 \longrightarrow 00:06:45.114$ is this something that is simply
- NOTE Confidence: 0.864063417692308
- $00:06:45.114 \longrightarrow 00:06:46.960$ a response to the environment?
- NOTE Confidence: 0.864063417692308
- $00:06:46.960 \longrightarrow 00:06:48.090$ So the sun goes down.
- NOTE Confidence: 0.864063417692308
- $00:06:48.090 \dashrightarrow 00:06:49.666$ So we decide maybe we'll go to sleep.
- NOTE Confidence: 0.864063417692308
- 00:06:49.670 -> 00:06:51.476 The sun comes up, we wake up.
- NOTE Confidence: 0.864063417692308
- $00:06:51.480 \longrightarrow 00:06:53.125$ Or is this something that's
- NOTE Confidence: 0.864063417692308
- 00:06:53.125 --> 00:06:54.770 actually intrinsic to your biology?
- NOTE Confidence: 0.864063417692308
- $00:06:54.770 \longrightarrow 00:06:56.890$ Is this something that would
- NOTE Confidence: 0.864063417692308
- $00:06:56.890 \longrightarrow 00:06:59.010$ happen even outside of that?
- NOTE Confidence: 0.864063417692308
- $00{:}06{:}59{.}010 \dashrightarrow 00{:}07{:}00{.}630$ Twenty that light,
- NOTE Confidence: 0.864063417692308
- 00:07:00.630 --> 00:07:01.710 dark environment,
- NOTE Confidence: 0.864063417692308

 $00{:}07{:}01.710 \dashrightarrow 00{:}07{:}03.726$ and so several researchers set out

NOTE Confidence: 0.864063417692308

 $00{:}07{:}03.726 \dashrightarrow 00{:}07{:}06.069$ to try to answer this question.

NOTE Confidence: 0.864063417692308

00:07:06.070 --> 00:07:08.324 One of them was the pair of

NOTE Confidence: 0.864063417692308

 $00:07:08.324 \longrightarrow 00:07:09.849$ Nathaniel Kleitman and his

NOTE Confidence: 0.864063417692308

 $00:07:09.849 \dashrightarrow 00:07:11.809$ graduate student Bruce Richardson.

NOTE Confidence: 0.864063417692308

00:07:11.810 --> 00:07:13.574 And they did an experiment where

NOTE Confidence: 0.864063417692308

 $00:07:13.574 \longrightarrow 00:07:15.464$ they went into Mammoth Cave in

NOTE Confidence: 0.864063417692308

 $00:07:15.464 \rightarrow 00:07:17.104$ Kentucky and monitored their sleep.

NOTE Confidence: 0.864063417692308

 $00:07:17.110 \longrightarrow 00:07:19.460$ Behaviors in the absence of

NOTE Confidence: 0.864063417692308

 $00:07:19.460 \longrightarrow 00:07:21.810$ those light dark time cues,

NOTE Confidence: 0.864063417692308

 $00:07:21.810 \longrightarrow 00:07:22.704$ and then similarly,

NOTE Confidence: 0.864063417692308

 $00:07:22.704 \longrightarrow 00:07:24.790$ you're going to ask off who is

NOTE Confidence: 0.864063417692308

 $00:07:24.852 \longrightarrow 00:07:26.757$ really considered kind of the

NOTE Confidence: 0.864063417692308

00:07:26.757 --> 00:07:28.662 father of human circadian biology,

NOTE Confidence: 0.864063417692308

 $00:07:28.670 \dashrightarrow 00:07:30.962$ underwent a series of bunker experiments

NOTE Confidence: 0.864063417692308

 $00:07:30.962 \rightarrow 00:07:33.221$ in Germany where he took subjects

 $00{:}07{:}33{.}221 \dashrightarrow 00{:}07{:}35{.}538$ and put them into this bunker here

NOTE Confidence: 0.864063417692308

 $00{:}07{:}35{.}538 \dashrightarrow 00{:}07{:}37{.}913$ and then monitored their behavior in

NOTE Confidence: 0.864063417692308

 $00:07:37.913 \rightarrow 00:07:40.526$ the absence of those external time cues,

NOTE Confidence: 0.864063417692308

00:07:40.526 --> 00:07:42.434 I encourage you to go read

NOTE Confidence: 0.864063417692308

 $00:07:42.434 \rightarrow 00:07:43.570$ these original papers,

NOTE Confidence: 0.864063417692308

 $00{:}07{:}43.570 \dashrightarrow 00{:}07{:}45.786$ but I just took a small excerpt from

NOTE Confidence: 0.864063417692308

 $00:07:45.786 \dashrightarrow 00:07:48.148$ them here and you can see he describes.

NOTE Confidence: 0.864063417692308

 $00{:}07{:}48.150 \dashrightarrow 00{:}07{:}50.246$ There's a locked double door at the entrance

NOTE Confidence: 0.864063417692308

 $00:07:50.246 \dashrightarrow 00:07:52.515$ in the small room between the two doors.

NOTE Confidence: 0.864063417692308

 $00{:}07{:}52.520 \dashrightarrow 00{:}07{:}55.121$ An ice box serves for a first storage of

NOTE Confidence: 0.864063417692308

 $00:07:55.121 \rightarrow 00:07:57.556$ urine samples through the same channel.

NOTE Confidence: 0.864063417692308

 $00{:}07{:}57{.}560 \dashrightarrow 00{:}07{:}59{.}552$ We supply the subject with fresh

NOTE Confidence: 0.864063417692308

 $00{:}07{:}59{.}552 \dashrightarrow 00{:}08{:}01{.}216$ food and other necessities such

NOTE Confidence: 0.864063417692308

 $00:08:01.216 \rightarrow 00:08:03.134$ as one bottle of endex beer daily.

NOTE Confidence: 0.864063417692308

 $00:08:03.140 \longrightarrow 00:08:05.100$ So remember that when you're

00:08:05.100 --> 00:08:07.060 writing your Irbs include beer.

NOTE Confidence: 0.864063417692308

00:08:07.060 --> 00:08:09.856 If you're doing German research studies,

NOTE Confidence: 0.864063417692308

00:08:09.860 --> 00:08:11.768 but what I thought was really

NOTE Confidence: 0.864063417692308

 $00:08:11.768 \longrightarrow 00:08:13.389$ insightful about this was that

NOTE Confidence: 0.864063417692308

 $00{:}08{:}13.389 \dashrightarrow 00{:}08{:}15.093$ he also participated in his own

NOTE Confidence: 0.864063417692308

 $00:08:15.093 \dashrightarrow 00:08:17.219$ studies as a research participant,

NOTE Confidence: 0.864063417692308

 $00:08:17.220 \rightarrow 00:08:20.020$ and so this is actually a plot of his own.

NOTE Confidence: 0.864063417692308

 $00:08:20.020 \dashrightarrow 00:08:22.610$ Sleep wake rhythms when he was in

NOTE Confidence: 0.864063417692308

 $00:08:22.610 \rightarrow 00:08:24.838$ that bunker and so you can see these

NOTE Confidence: 0.864063417692308

 $00{:}08{:}24.838 \dashrightarrow 00{:}08{:}26.598$ black lines here are when he was

NOTE Confidence: 0.864063417692308

 $00{:}08{:}26.598 \dashrightarrow 00{:}08{:}28.588$ going to bed and waking up each night

NOTE Confidence: 0.864063417692308

 $00:08:28.588 \rightarrow 00:08:30.513$ as well as plotting the rhythms of

NOTE Confidence: 0.864063417692308

 $00:08:30.513 \dashrightarrow 00:08:34.698$ his urine output during that time.

NOTE Confidence: 0.864063417692308

 $00:08:34.700 \longrightarrow 00:08:36.842$ He included in the paper this

NOTE Confidence: 0.864063417692308

 $00:08:36.842 \rightarrow 00:08:38.900$ comment that from the knowledge

NOTE Confidence: 0.864063417692308

00:08:38.900 - 00:08:40.580 of animal experiments,

00:08:40.580 --> 00:08:42.673 I was convinced that I had a

NOTE Confidence: 0.864063417692308

 $00:08:42.673 \rightarrow 00:08:44.200$ period shorter than 24 hours,

NOTE Confidence: 0.864063417692308

 $00:08:44.200 \longrightarrow 00:08:46.865$ which had previously been seen

NOTE Confidence: 0.864063417692308

00:08:46.865 --> 00:08:48.997 in many nocturnal animals,

NOTE Confidence: 0.864063417692308

 $00:08:49.000 \rightarrow 00:08:51.000$ such as mice for example.

NOTE Confidence: 0.864063417692308

 $00:08:51.000 \dashrightarrow 00:08:53.020$ But he said when I was released on day 10,

NOTE Confidence: 0.864063417692308

 $00:08:53.020 \rightarrow 00:08:54.791$ I was therefore highly surprised to be

NOTE Confidence: 0.864063417692308

00:08:54.791 --> 00:08:57.197 told that my last waking up time was 3:00 PM,

NOTE Confidence: 0.864063417692308

 $00:08:57.200 \longrightarrow 00:08:59.120$ and so again an example that even the

NOTE Confidence: 0.864063417692308

 $00:08:59.120 \longrightarrow 00:09:01.003$ best minds in the world sometimes are

NOTE Confidence: 0.864063417692308

 $00:09:01.003 \rightarrow 00:09:02.951$ hypothesis are wrong and we have to

NOTE Confidence: 0.864063417692308

 $00:09:02.951 \dashrightarrow 00:09:04.855$ sort of change our thinking about things.

NOTE Confidence: 0.864063417692308

00:09:04.860 --> 00:09:07.396 But I think also just a very interesting,

NOTE Confidence: 0.864063417692308

 $00:09:07.400 \rightarrow 00:09:09.630$ interesting description of these first

NOTE Confidence: 0.864063417692308

 $00:09:09.630 \rightarrow 00:09:11.860$ experiments trying to figure out

 $00:09:11.929 \rightarrow 00:09:13.654$ what actually happens to humans

NOTE Confidence: 0.913842297272727

 $00{:}09{:}13.654 \dashrightarrow 00{:}09{:}16.079$ in the absence of these time cues.

NOTE Confidence: 0.913842297272727

 $00:09:16.080 \longrightarrow 00:09:17.478$ So as you can see here,

NOTE Confidence: 0.913842297272727

00:09:17.480 -> 00:09:19.895 if we took our idealized human here,

NOTE Confidence: 0.913842297272727

 $00{:}09{:}19{.}900 \dashrightarrow 00{:}09{:}21{.}875$ put them in an environment

NOTE Confidence: 0.913842297272727

00:09:21.875 --> 00:09:24.240 devoid of time cues each day,

NOTE Confidence: 0.913842297272727

 $00:09:24.240 \longrightarrow 00:09:26.893$ most humans get a little bit later

NOTE Confidence: 0.913842297272727

 $00:09:26.893 \longrightarrow 00:09:29.648$ and a little bit later each day.

NOTE Confidence: 0.913842297272727

 $00{:}09{:}29.650 \dashrightarrow 00{:}09{:}32.020$ These behaviors are primarily regulated

NOTE Confidence: 0.913842297272727

 $00:09:32.020 \rightarrow 00:09:34.390$ by the Super cosmetic nucleus,

NOTE Confidence: 0.913842297272727

 $00{:}09{:}34{.}390 \dashrightarrow 00{:}09{:}36{.}318$ and so I have a cross section here.

NOTE Confidence: 0.913842297272727

 $00:09:36.320 \rightarrow 00:09:39.528$ This is a coronal section through a human

NOTE Confidence: 0.913842297272727

00:09:39.528 --> 00:09:42.267 hypothalamus and you can see basically here.

NOTE Confidence: 0.913842297272727

00:09:42.270 --> 00:09:44.010 We've got our optic chiasm,

NOTE Confidence: 0.913842297272727

 $00{:}09{:}44.010 \dashrightarrow 00{:}09{:}46.140$ the Super chias matic nucleus are these

NOTE Confidence: 0.913842297272727

 $00:09:46.140 \longrightarrow 00:09:48.449$ two little areas outlined in yellow here.

00:09:48.450 --> 00:09:50.345 They're directly above the optic

NOTE Confidence: 0.913842297272727

 $00:09:50.345 \rightarrow 00:09:52.240$ chiasm and within the hypothalamus,

NOTE Confidence: 0.913842297272727

 $00:09:52.240 \longrightarrow 00:09:54.045$ so they can receive light

NOTE Confidence: 0.913842297272727

 $00:09:54.045 \rightarrow 00:09:55.489$ information from the environment,

NOTE Confidence: 0.913842297272727

 $00:09:55.490 \longrightarrow 00:09:57.906$ and then they can also take that information

NOTE Confidence: 0.913842297272727

 $00:09:57.906 \rightarrow 00:10:00.168$ and send signals to the hypothalamus.

NOTE Confidence: 0.913842297272727

 $00:10:00.170 \rightarrow 00:10:01.780$ Where they can regulate things like sleep,

NOTE Confidence: 0.913842297272727

00:10:01.780 --> 00:10:03.940 wake behavior, feeding behavior,

NOTE Confidence: 0.913842297272727

 $00:10:03.940 \longrightarrow 00:10:05.560$ core body temperature,

NOTE Confidence: 0.913842297272727

00:10:05.560 --> 00:10:06.706 rhythmic hormone release,

NOTE Confidence: 0.913842297272727

 $00:10:06.706 \longrightarrow 00:10:08.234$ everything else that has

NOTE Confidence: 0.913842297272727

 $00{:}10{:}08{.}234 \dashrightarrow 00{:}10{:}09{.}780$ that daily rhythm to it.

NOTE Confidence: 0.913842297272727

 $00:10:09.780 \longrightarrow 00:10:12.790$ Now we know that it's not just the SCN it

NOTE Confidence: 0.913842297272727

 $00{:}10{:}12.870 \dashrightarrow 00{:}10{:}15.958$ seems to be sort of the primary pacemaker,

NOTE Confidence: 0.913842297272727

 $00{:}10{:}15{.}960 \dashrightarrow 00{:}10{:}17{.}784$ but every other cell and tissue

 $00:10:17.784 \longrightarrow 00:10:20.024$ in our body also has a clock in

NOTE Confidence: 0.913842297272727

 $00:10:20.024 \longrightarrow 00:10:21.883$ it and the SCN we think serves

NOTE Confidence: 0.913842297272727

00:10:21.883 --> 00:10:23.971 to help coordinate and keep those

NOTE Confidence: 0.913842297272727

 $00:10:23.971 \rightarrow 00:10:27.369$ clocks In Sync with each other.

NOTE Confidence: 0.913842297272727

 $00{:}10{:}27{.}370 \dashrightarrow 00{:}10{:}29{.}440$ So I think one of the things that I

NOTE Confidence: 0.913842297272727

 $00{:}10{:}29{.}440$ --> $00{:}10{:}31{.}114$ find most fascinating about circadian NOTE Confidence: 0.913842297272727

00:10:31.114 --> 00:10:34.077 biology is not only that we have this

NOTE Confidence: 0.913842297272727

00:10:34.077 --> 00:10:35.729 intrinsic time keeping mechanism,

NOTE Confidence: 0.913842297272727

00:10:35.730 --> 00:10:39.816 but it's also dynamic and it can be reset

NOTE Confidence: 0.913842297272727

 $00:10:39.816 \longrightarrow 00:10:43.724$ like a clock or a watch with time cues,

NOTE Confidence: 0.913842297272727

 $00{:}10{:}43.730 \dashrightarrow 00{:}10{:}46.568$ and that resetting is both stimulus

NOTE Confidence: 0.913842297272727

 $00:10:46.568 \rightarrow 00:10:49.649$ specific and time of day specific.

NOTE Confidence: 0.913842297272727

00:10:49.650 - 00:10:52.089 So if we go back to our human example,

NOTE Confidence: 0.913842297272727

 $00:10:52.090 \rightarrow 00:10:53.690$ so now we've put them in a cave,

NOTE Confidence: 0.913842297272727

 $00{:}10{:}53.690 \dashrightarrow 00{:}10{:}56.186$ they have no light, dark exposure.

NOTE Confidence: 0.913842297272727

 $00:10:56.190 \rightarrow 00:10:57.390$ Each day, they're going to bed.

 $00{:}10{:}57{.}390 \dashrightarrow 00{:}10{:}59{.}154$ A little bit later and a little bit later,

NOTE Confidence: 0.913842297272727

 $00:10:59.160 \longrightarrow 00:11:01.608$ and if we come in at some point

NOTE Confidence: 0.913842297272727

 $00:11:01.608 \dashrightarrow 00:11:03.620$ during their biological daytime,

NOTE Confidence: 0.913842297272727

 $00:11:03.620 \rightarrow 00:11:05.666$ the time when they'd normally be

NOTE Confidence: 0.913842297272727

 $00:11:05.666 \rightarrow 00:11:07.635$ awake normally be expecting to see

NOTE Confidence: 0.913842297272727

 $00:11:07.635 \rightarrow 00:11:09.255$ light and expose them to light.

NOTE Confidence: 0.913842297272727

 $00:11:09.260 \longrightarrow 00:11:10.639$ You can see that the following day,

NOTE Confidence: 0.913842297272727

 $00:11:10.640 \rightarrow 00:11:14.175$ it really doesn't change that daily rhythm,

NOTE Confidence: 0.913842297272727

 $00{:}11{:}14{.}180 \dashrightarrow 00{:}11{:}16{.}679$ but if instead we came in shortly

NOTE Confidence: 0.913842297272727

00:11:16.679 - 00:11:19.460 after the time that they fell asleep,

NOTE Confidence: 0.913842297272727

00:11:19.460 - 00:11:21.210 so during a time when they normally

NOTE Confidence: 0.913842297272727

 $00{:}11{:}21{.}210 \dashrightarrow 00{:}11{:}22.689$ wouldn't expect to be seen light

NOTE Confidence: 0.913842297272727

 $00{:}11{:}22.689 \dashrightarrow 00{:}11{:}23.819$ and expose them to light,

NOTE Confidence: 0.913842297272727

 $00{:}11{:}23.820 \dashrightarrow 00{:}11{:}25.976$ you can see that the following day

NOTE Confidence: 0.913842297272727

 $00:11:25.980 \longrightarrow 00:11:28.470$ that whole behavior gets later.

 $00:11:28.470 \longrightarrow 00:11:30.366$ And you can interpret that as

NOTE Confidence: 0.913842297272727

 $00{:}11{:}30{.}366 \dashrightarrow 00{:}11{:}31{.}630$ almost an error signal.

NOTE Confidence: 0.913842297272727

 $00:11:31.630 \longrightarrow 00:11:34.306$ So perhaps the signal that day

NOTE Confidence: 0.913842297272727

 $00:11:34.306 \rightarrow 00:11:36.950$ length is longer than expected,

NOTE Confidence: 0.913842297272727

 $00:11:36.950 \rightarrow 00:11:38.408$ so we should push everything later.

NOTE Confidence: 0.913842297272727

00:11:38.410 --> 00:11:39.030 So again,

NOTE Confidence: 0.913842297272727

 $00:11:39.030 \longrightarrow 00:11:40.580$ we're sleeping when it's dark

NOTE Confidence: 0.913842297272727

 $00:11:40.580 \rightarrow 00:11:42.149$ and we're awakening it's light.

NOTE Confidence: 0.913842297272727

 $00:11:42.150 \longrightarrow 00:11:44.310$ And then on the other end of the spectrum,

NOTE Confidence: 0.913842297272727

 $00:11:44.310 \longrightarrow 00:11:46.284$ if you take them and expose them

NOTE Confidence: 0.913842297272727

 $00:11:46.284 \rightarrow 00:11:48.348$ to light in the early morning.

NOTE Confidence: 0.913842297272727

 $00{:}11{:}48{.}350 \dashrightarrow 00{:}11{:}50{.}380$ So shortly before they were gonna wake

NOTE Confidence: 0.913842297272727

00:11:50.380 --> 00:11:52.647 up shortly before dawn would normally occur,

NOTE Confidence: 0.913842297272727

 $00:11:52.650 \longrightarrow 00:11:54.060$ you can see that the following

NOTE Confidence: 0.913842297272727

 $00:11:54.060 \rightarrow 00:11:55.410$ day they actually get earlier,

NOTE Confidence: 0.913842297272727

 $00{:}11{:}55{.}410 \dashrightarrow 00{:}11{:}57{.}531$ and so again a stimulus that daylight

- NOTE Confidence: 0.913842297272727
- $00:11:57.531 \rightarrow 00:11:59.810$ is showing up earlier than expected.
- NOTE Confidence: 0.913842297272727
- $00:11:59.810 \longrightarrow 00:12:01.190$ We should move everything earlier,
- NOTE Confidence: 0.913842297272727
- $00:12:01.190 \rightarrow 00:12:04.940$ so again, we're appropriately aligned.
- NOTE Confidence: 0.87452492
- $00:12:04.940 \longrightarrow 00:12:07.019$ In order to actually plot these results,
- NOTE Confidence: 0.87452492
- $00{:}12{:}07{.}020 \dashrightarrow 00{:}12{:}08{.}440$ we use something called a
- NOTE Confidence: 0.87452492
- $00:12:08.440 \longrightarrow 00:12:09.860$ phase response curve and we'll
- NOTE Confidence: 0.87452492
- $00:12:09.916 \longrightarrow 00:12:11.440$ show some more of these later.
- NOTE Confidence: 0.87452492
- $00:12:11.440 \longrightarrow 00:12:15.220$ But basically this is just a 24
- NOTE Confidence: 0.87452492
- $00{:}12{:}15{.}220 \dashrightarrow 00{:}12{:}18{.}072$ hour plot here and our stimulus
- NOTE Confidence: 0.87452492
- $00:12:18.072 \rightarrow 00:12:20.358$ during the daytime has no effect,
- NOTE Confidence: 0.87452492
- 00:12:20.360 --> 00:12:21.837 so it's not causing a phase shift,
- NOTE Confidence: 0.87452492
- $00:12:21.840 \longrightarrow 00:12:23.220$ whereas our early evening
- NOTE Confidence: 0.87452492
- $00:12:23.220 \rightarrow 00:12:24.945$ stimulus is causing a delay
- NOTE Confidence: 0.87452492
- $00{:}12{:}24{.}945 \dashrightarrow 00{:}12{:}27{.}019$ or a negative deflection here,
- NOTE Confidence: 0.87452492
- $00:12:27.020 \longrightarrow 00:12:28.595$ and our stimulus at the end of
- NOTE Confidence: 0.87452492

 $00:12:28.595 \longrightarrow 00:12:30.292$ the night is causing an advance

NOTE Confidence: 0.87452492

 $00:12:30.292 \longrightarrow 00:12:31.897$ or a positive deflection here.

NOTE Confidence: 0.87452492

 $00:12:31.900 \longrightarrow 00:12:33.080$ Now that was a cartoon.

NOTE Confidence: 0.87452492

 $00{:}12{:}33.080 \dashrightarrow 00{:}12{:}34.250$ This is what it actually looks

NOTE Confidence: 0.87452492

 $00{:}12{:}34{.}250 \dashrightarrow 00{:}12{:}35{.}030$ like in real life.

NOTE Confidence: 0.87452492

 $00{:}12{:}35{.}030 \dashrightarrow 00{:}12{:}37{.}534$ This is an example of a light phase

NOTE Confidence: 0.87452492

 $00{:}12{:}37{.}534 \dashrightarrow 00{:}12{:}39{.}260$ response curve obtained from humans

NOTE Confidence: 0.87452492

 $00:12:39.260 \longrightarrow 00:12:41.668$ and one of the important things to

NOTE Confidence: 0.87452492

00:12:41.740 --> 00:12:43.960 keep in mind when you're managing

NOTE Confidence: 0.87452492

 $00{:}12{:}43.960 \dashrightarrow 00{:}12{:}46.120$ circadian patients is the switch point,

NOTE Confidence: 0.87452492

 $00:12:46.120 \longrightarrow 00:12:46.800$ right here,

NOTE Confidence: 0.87452492

 $00{:}12{:}46.800 \dashrightarrow 00{:}12{:}49.319$ and so we know that this occurs

NOTE Confidence: 0.87452492

 $00:12:49.319 \longrightarrow 00:12:51.731$ about the point of the core

NOTE Confidence: 0.87452492

 $00:12:51.731 \rightarrow 00:12:52.937$ body temperature nature,

NOTE Confidence: 0.87452492

 $00:12:52.940 \longrightarrow 00:12:55.145$ which for most people occurs about 2

NOTE Confidence: 0.87452492

 $00:12:55.145 \rightarrow 00:12:57.178$ hours before their natural wait time.

00:12:57.180 --> 00:12:59.392 So if you're trying to time light

NOTE Confidence: 0.87452492

 $00{:}12{:}59{.}392 \dashrightarrow 00{:}13{:}01{.}008$ to appropriately shift a patient

NOTE Confidence: 0.87452492

 $00:13:01.008 \rightarrow 00:13:02.538$ in One Direction or another,

NOTE Confidence: 0.87452492

 $00:13:02.540 \longrightarrow 00:13:03.985$ it's really important that your

NOTE Confidence: 0.87452492

 $00:13:03.985 \longrightarrow 00:13:05.780$ timing that light based on their.

NOTE Confidence: 0.87452492

 $00{:}13{:}05{.}780 \dashrightarrow 00{:}13{:}07{.}650$ Biological time and not based

NOTE Confidence: 0.87452492

 $00:13:07.650 \longrightarrow 00:13:09.900$ on the external clock time just

NOTE Confidence: 0.87452492

 $00:13:09.900 \longrightarrow 00:13:11.455$ to give you an example,

NOTE Confidence: 0.87452492

 $00{:}13{:}11{.}460 \dashrightarrow 00{:}13{:}13{.}595$ many of my patients don't fall a sleep

NOTE Confidence: 0.87452492

 $00{:}13{:}13{.}595 \dashrightarrow 00{:}13{:}15{.}428$ till 345 in the morning and so if I

NOTE Confidence: 0.87452492

 $00:13:15.428 \longrightarrow 00:13:17.319$ were to give them light in the quote,

NOTE Confidence: 0.87452492

00:13:17.320 --> 00:13:18.166 UN quote morning,

NOTE Confidence: 0.87452492

 $00{:}13{:}18{.}166 \dashrightarrow 00{:}13{:}19{.}858$ so at 7:00 or 8:00 AM,

NOTE Confidence: 0.87452492

00:13:19.860 --> 00:13:21.210 I'd actually still be hitting

NOTE Confidence: 0.87452492

 $00{:}13{:}21{.}210 \dashrightarrow 00{:}13{:}22{.}924$ them on the spades delay portion

 $00:13:22.924 \rightarrow 00:13:24.784$ of the phase response curve and

NOTE Confidence: 0.87452492

 $00{:}13{:}24.784 \dashrightarrow 00{:}13{:}26.324$ could potentially make them even

NOTE Confidence: 0.87452492

 $00:13:26.324 \rightarrow 00:13:27.714$ worse by shifting them later.

NOTE Confidence: 0.87452492

 $00{:}13{:}27{.}720 \dashrightarrow 00{:}13{:}30{.}296$ So making sure that you keep this in

NOTE Confidence: 0.87452492

 $00:13:30.296 \rightarrow 00:13:32.745$ mind when you're trying to determine

NOTE Confidence: 0.87452492

 $00:13:32.745 \rightarrow 00:13:34.870$ treatment timing for your patients.

NOTE Confidence: 0.87452492

 $00:13:34.870 \longrightarrow 00:13:37.910$ Now one of the other.

NOTE Confidence: 0.87452492

 $00{:}13{:}37{.}910 \dashrightarrow 00{:}13{:}39{.}917$ Stimuli that we make use of in the clinic.

NOTE Confidence: 0.87452492

00:13:39.920 --> 00:13:41.114 Like I mentioned,

NOTE Confidence: 0.87452492

 $00:13:41.114 \longrightarrow 00:13:43.502$ each response is both time of

NOTE Confidence: 0.87452492

 $00:13:43.502 \longrightarrow 00:13:45.780$ day and stimulus dependent,

NOTE Confidence: 0.87452492

 $00:13:45.780 \longrightarrow 00:13:47.383$ and so one of the other tools

NOTE Confidence: 0.87452492

 $00:13:47.383 \rightarrow 00:13:48.720$ we use is melatonin,

NOTE Confidence: 0.87452492

 $00:13:48.720 \longrightarrow 00:13:52.380$ so our bodies naturally produce melatonin,

NOTE Confidence: 0.87452492

 $00:13:52.380 \rightarrow 00:13:54.648$ typically with levels rising a few hours

NOTE Confidence: 0.87452492

 $00:13:54.648 \rightarrow 00:13:56.798$ before you naturally fall asleep at night.

- NOTE Confidence: 0.87452492
- $00:13:56.800 \longrightarrow 00:13:57.876$ As you can see,
- NOTE Confidence: 0.87452492
- 00:13:57.876 --> 00:13:59.490 indicated by the up arrow here
- NOTE Confidence: 0.87452492
- $00{:}13{:}59{.}552 \dashrightarrow 00{:}14{:}01{.}477$ and then dropping off as we fall
- NOTE Confidence: 0.87452492
- 00:14:01.477 --> 00:14:03.221 as
leep and the proposed sleep
- NOTE Confidence: 0.87452492
- $00:14:03.221 \rightarrow 00:14:04.937$ window is approximately here.
- NOTE Confidence: 0.87452492
- $00{:}14{:}04{.}940 \dashrightarrow 00{:}14{:}07{.}916$ With these, these upright lines here.
- NOTE Confidence: 0.87452492
- $00{:}14{:}07{.}920 \dashrightarrow 00{:}14{:}09{.}528$ And so with melaton in.
- NOTE Confidence: 0.87452492
- $00:14:09.528 \longrightarrow 00:14:11.890$ Again, think of it like an error signal.
- NOTE Confidence: 0.87452492
- $00{:}14{:}11{.}890 \dashrightarrow 00{:}14{:}15{.}026$ So if you give someone melaton in before
- NOTE Confidence: 0.87452492
- $00:14:15.026 \rightarrow 00:14:17.650$ they would naturally be producing it,
- NOTE Confidence: 0.87452492
- $00:14:17.650 \longrightarrow 00:14:19.650$ you end up pulling them
- NOTE Confidence: 0.87452492
- $00:14:19.650 \longrightarrow 00:14:21.250$ earlier or advancing them.
- NOTE Confidence: 0.87452492
- $00:14:21.250 \rightarrow 00:14:23.260$ Whereas if you give them melatonin
- NOTE Confidence: 0.87452492
- $00{:}14{:}23{.}260 \dashrightarrow 00{:}14{:}24{.}830$ after they stop producing it,
- NOTE Confidence: 0.87452492
- $00:14:24.830 \longrightarrow 00:14:26.160$ you end up delaying them
- NOTE Confidence: 0.87452492

- $00:14:26.160 \longrightarrow 00:14:27.224$ or pulling them later.
- NOTE Confidence: 0.87452492
- $00{:}14{:}27{.}230 \dashrightarrow 00{:}14{:}28{.}061$ And so again,
- NOTE Confidence: 0.87452492
- $00:14:28.061 \longrightarrow 00:14:30.633$ tools that we can make use of in the
- NOTE Confidence: 0.87452492
- $00:14:30.633 \rightarrow 00:14:32.614$ clinic to try to help shift people
- NOTE Confidence: 0.87452492
- $00{:}14{:}32{.}614 \dashrightarrow 00{:}14{:}34{.}709$ in One Direction or the other.
- NOTE Confidence: 0.87452492
- $00{:}14{:}34{.}710 \dashrightarrow 00{:}14{:}36{.}660$ But keeping in mind that if
- NOTE Confidence: 0.87452492
- 00:14:36.660 00:14:37.960 you give somebody melatonin.
- NOTE Confidence: 0.87452492
- $00{:}14{:}37{.}960 \dashrightarrow 00{:}14{:}39{.}958$ You want to make sure that if
- NOTE Confidence: 0.87452492
- 00:14:39.958 --> 00:14:41.310 you're giving them melaton
in
- NOTE Confidence: 0.87452492
- $00:14:41.310 \longrightarrow 00:14:43.360$ with the goal of advancing them,
- NOTE Confidence: 0.87452492
- 00:14:43.360 --> 00:14:45.592 you wanna make sure that you're
- NOTE Confidence: 0.87452492
- 00:14:45.592 --> 00:14:47.460 having the melaton
in present here,
- NOTE Confidence: 0.87452492
- 00:14:47.460 -> 00:14:49.840 but no longer having it present here,
- NOTE Confidence: 0.87452492
- $00:14:49.840 \longrightarrow 00:14:51.772$ which is why we care so much
- NOTE Confidence: 0.87452492
- $00{:}14{:}51.772 \dashrightarrow 00{:}14{:}52.600$ about dosing of
- NOTE Confidence: 0.923717357272727
- 00:14:52.671 -> 00:14:54.510 melatonin, because we want to make

- NOTE Confidence: 0.923717357272727
- $00:14:54.510 \longrightarrow 00:14:56.317$ sure we don't give them a really
- NOTE Confidence: 0.923717357272727
- 00:14:56.317 --> 00:14:57.677 high dose of melatonin here,
- NOTE Confidence: 0.923717357272727
- $00:14:57.680 \longrightarrow 00:15:00.180$ so it may help advance.
- NOTE Confidence: 0.923717357272727
- $00:15:00.180 \longrightarrow 00:15:01.480$ But then it's still sitting
- NOTE Confidence: 0.923717357272727
- $00:15:01.480 \longrightarrow 00:15:03.080$ around in the system out here,
- NOTE Confidence: 0.923717357272727
- $00:15:03.080 \longrightarrow 00:15:04.600$ where then it's delaying and
- NOTE Confidence: 0.923717357272727
- $00:15:04.600 \rightarrow 00:15:05.816$ then working against us.
- NOTE Confidence: 0.8799680766666667
- $00:15:10.490 \rightarrow 00:15:12.560$ So with that as the introduction,
- NOTE Confidence: 0.8799680766666667
- $00{:}15{:}12{.}560 \dashrightarrow 00{:}15{:}14{.}728$ I now want to move on to talking
- NOTE Confidence: 0.8799680766666667
- $00:15:14.728 \rightarrow 00:15:16.740$ about how we actually put this
- NOTE Confidence: 0.8799680766666667
- $00:15:16.740 \longrightarrow 00:15:18.495$ into practice in the clinic,
- NOTE Confidence: 0.8799680766666667
- $00{:}15{:}18{.}500 \dashrightarrow 00{:}15{:}21{.}932$ and we think of primarily these four main
- NOTE Confidence: 0.8799680766666667
- 00:15:21.932 --> 00:15:24.479 intrinsic circadian rhythm sleep disorders,
- NOTE Confidence: 0.8799680766666667
- $00:15:24.480 \longrightarrow 00:15:26.802$ advanced delayed non 24 in your
- NOTE Confidence: 0.8799680766666667
- $00{:}15{:}26.802 \dashrightarrow 00{:}15{:}29.040$ regular sleep wake rhythm disorder.
- NOTE Confidence: 0.8799680766666667

 $00:15:29.040 \longrightarrow 00:15:32.576$ We also do see some shift work disorder.

NOTE Confidence: 0.8799680766666667

 $00:15:32.580 \rightarrow 00:15:36.639$ Excuse me and then very rarely some jet lag.

NOTE Confidence: 0.8799680766666667

00:15:36.640 --> 00:15:37.650 Starting to come back now,

NOTE Confidence: 0.8799680766666667

 $00:15:37.650 \rightarrow 00:15:39.914$ but had a two year hiatus from that.

NOTE Confidence: 0.8799680766666667

 $00:15:39.920 \longrightarrow 00:15:42.770$ With the Payam pandemic certainly,

NOTE Confidence: 0.8799680766666667

 $00{:}15{:}42.770 \dashrightarrow 00{:}15{:}44.688$ but for today what I really wanna

NOTE Confidence: 0.8799680766666667

 $00{:}15{:}44.688 \dashrightarrow 00{:}15{:}46.415$ focus on are the two disorders

NOTE Confidence: 0.8799680766666667

 $00{:}15{:}46{.}415 \dashrightarrow 00{:}15{:}48{.}375$ I tend to see most in clinic.

NOTE Confidence: 0.8799680766666667

 $00{:}15{:}48{.}380 \dashrightarrow 00{:}15{:}49{.}865$ Specifically, delayed sleep,

NOTE Confidence: 0.8799680766666667

 $00{:}15{:}49.865 \dashrightarrow 00{:}15{:}53.034$ wake phase disorder and non 24 and

NOTE Confidence: 0.8799680766666667

 $00:15:53.034 \rightarrow 00:15:54.586$ we're going to start off with the case.

NOTE Confidence: 0.903201377894737

 $00:15:58.380 \longrightarrow 00:16:01.286$ So we have a patient who is a 34 year old

NOTE Confidence: 0.903201377894737

 $00:16:01.286 \rightarrow 00:16:03.990$ woman and she comes into clinic and says,

NOTE Confidence: 0.903201377894737

 $00:16:03.990 \longrightarrow 00:16:05.166$ you know I used to be a quote

NOTE Confidence: 0.903201377894737

00:16:05.166 --> 00:16:06.079 UN quote normal sleeper.

NOTE Confidence: 0.903201377894737

 $00:16:06.080 \longrightarrow 00:16:07.718$ I'd go to bed around 11.

 $00:16:07.720 \rightarrow 00:16:10.216$ I'd have no trouble falling asleep

NOTE Confidence: 0.903201377894737

 $00:16:10.220 \dashrightarrow 00:16:11.956$ sleep through the night. I was fine.

NOTE Confidence: 0.903201377894737

00:16:11.960 --> 00:16:13.538 She got into a car accident,

NOTE Confidence: 0.903201377894737

 $00:16:13.540 \longrightarrow 00:16:15.040$ had a whiplash injury.

NOTE Confidence: 0.903201377894737

00:16:15.040 --> 00:16:16.915 And really since that point,

NOTE Confidence: 0.903201377894737

 $00{:}16{:}16{.}920 \dashrightarrow 00{:}16{:}19{.}258$ her bedtime moved around to the point

NOTE Confidence: 0.903201377894737

 $00:16:19.258 \rightarrow 00:16:21.936$ where by the time she came to see me,

NOTE Confidence: 0.903201377894737

 $00:16:21.940 \longrightarrow 00:16:24.220$ she was often not falling asleep till 3:30.

NOTE Confidence: 0.903201377894737

 $00:16:24.220 \longrightarrow 00:16:25.380$ Sometimes as late as nine.

NOTE Confidence: 0.903201377894737

 $00:16:25.380 \longrightarrow 00:16:27.865$ AM. And so as a first step,

NOTE Confidence: 0.903201377894737

 $00:16:27.870 \longrightarrow 00:16:29.300$ when evaluating these patients really

NOTE Confidence: 0.903201377894737

 $00{:}16{:}29{.}300 \dashrightarrow 00{:}16{:}32{.}012$ what we want to do is get a sense of

NOTE Confidence: 0.903201377894737

 $00{:}16{:}32.012 \dashrightarrow 00{:}16{:}33.550$ what are their patterns really like,

NOTE Confidence: 0.903201377894737

 $00{:}16{:}33{.}550 \dashrightarrow 00{:}16{:}35{.}122$ and to do that,

NOTE Confidence: 0.903201377894737

 $00{:}16{:}35{.}122 \dashrightarrow 00{:}16{:}37{.}087$ we use something called actigraphy.

 $00:16:37.090 \rightarrow 00:16:39.151$ So this is just an example of one of

NOTE Confidence: 0.903201377894737

 $00:16:39.151 \rightarrow 00:16:41.508$ the actigraphy watches we use in clinic,

NOTE Confidence: 0.903201377894737

 $00:16:41.510 \longrightarrow 00:16:42.782$ and an example of what the

NOTE Confidence: 0.903201377894737

 $00:16:42.782 \longrightarrow 00:16:43.630$ data might look like.

NOTE Confidence: 0.903201377894737

 $00:16:43.630 \longrightarrow 00:16:45.310$ This is not from this patient,

NOTE Confidence: 0.903201377894737

 $00:16:45.310 \longrightarrow 00:16:47.710$ as you'll quickly figure out,

NOTE Confidence: 0.903201377894737

 $00{:}16{:}47.710 \dashrightarrow 00{:}16{:}49.902$ but basically general activity.

NOTE Confidence: 0.903201377894737

 $00:16:49.902 \longrightarrow 00:16:51.850$ Again, we plot in 24 hours,

NOTE Confidence: 0.903201377894737

 $00:16:51.850 \longrightarrow 00:16:54.286$ so we're going from noon to noon.

NOTE Confidence: 0.903201377894737

 $00:16:54.290 \longrightarrow 00:16:56.030$ Activity is indicated by

NOTE Confidence: 0.903201377894737

 $00{:}16{:}56{.}030 \dashrightarrow 00{:}16{:}57{.}770$ these black bars here.

NOTE Confidence: 0.903201377894737

 $00:16:57.770 \longrightarrow 00:16:59.640$ Light exposure by the yellow

NOTE Confidence: 0.903201377894737

 $00:16:59.640 \longrightarrow 00:17:01.136$ line that's running through

NOTE Confidence: 0.903201377894737

 $00:17:01.136 \longrightarrow 00:17:02.782$ here and then we've highlighted

NOTE Confidence: 0.903201377894737

 $00:17:02.782 \rightarrow 00:17:04.690$ the sleep window here in blue,

NOTE Confidence: 0.903201377894737

 $00:17:04.690 \dashrightarrow 00:17:06.748$ and so this is actually for myself.

- NOTE Confidence: 0.903201377894737
- $00{:}17{:}06.750 \dashrightarrow 00{:}17{:}07.842$ When I was testing.
- NOTE Confidence: 0.903201377894737
- $00:17:07.842 \rightarrow 00:17:08.934$ One of these watches,
- NOTE Confidence: 0.903201377894737
- 00:17:08.940 --> 00:17:11.005 and you'll see why I didn't use
- NOTE Confidence: 0.903201377894737
- 00:17:11.005 00:17:12.980 the patient as an example here,
- NOTE Confidence: 0.903201377894737
- $00:17:12.980 \longrightarrow 00:17:15.380$ because it gets much messier
- NOTE Confidence: 0.903201377894737
- $00:17:15.380 \longrightarrow 00:17:17.300$ in the clinical environment.
- NOTE Confidence: 0.903201377894737
- $00{:}17{:}17{.}300 \dashrightarrow 00{:}17{:}20{.}244$ And so these dark blue bars here are
- NOTE Confidence: 0.903201377894737
- $00:17:20.244 \rightarrow 00:17:23.337$ actually when the patient took the watch off.
- NOTE Confidence: 0.903201377894737
- $00{:}17{:}23.340 \dashrightarrow 00{:}17{:}25.540$ So you can see the first problem is
- NOTE Confidence: 0.903201377894737
- $00:17:25.540 \rightarrow 00:17:27.162$ simply getting patients to wear the
- NOTE Confidence: 0.903201377894737
- $00:17:27.162 \longrightarrow 00:17:29.616$ watch for the full one to two or three
- NOTE Confidence: 0.903201377894737
- $00:17:29.616 \rightarrow 00:17:31.660$ weeks that you're having them wear them.
- NOTE Confidence: 0.903201377894737
- $00:17:31.660 \longrightarrow 00:17:33.668$ But the other thing is that you can
- NOTE Confidence: 0.903201377894737
- $00{:}17{:}33.668 \dashrightarrow 00{:}17{:}35.540$ see from this recording are one.
- NOTE Confidence: 0.903201377894737
- $00:17:35.540 \rightarrow 00:17:36.900$ The overall activity thresholds
- NOTE Confidence: 0.903201377894737

 $00:17:36.900 \longrightarrow 00:17:39.283$ were sent the set the same on

NOTE Confidence: 0.903201377894737

 $00{:}17{:}39{.}283 \dashrightarrow 00{:}17{:}40{.}698$ both of those actor grams,

NOTE Confidence: 0.903201377894737

 $00:17:40.700 \longrightarrow 00:17:42.878$ but you can see this patient

NOTE Confidence: 0.903201377894737

 $00:17:42.878 \rightarrow 00:17:44.330$ is quite inactive overall.

NOTE Confidence: 0.903201377894737

 $00{:}17{:}44{.}330 \dashrightarrow 00{:}17{:}46{.}493$ And then you can also see overall

NOTE Confidence: 0.903201377894737

00:17:46.493 --> 00:17:48.112 her sleep patterns are quite

NOTE Confidence: 0.903201377894737

 $00:17:48.112 \longrightarrow 00:17:49.984$ irregular in terms of wait time.

NOTE Confidence: 0.903201377894737

 $00:17:49.990 \rightarrow 00:17:52.748$ Often this is set by other obligations,

NOTE Confidence: 0.903201377894737

 $00{:}17{:}52{.}750 \dashrightarrow 00{:}17{:}54{.}050$ for example like having to

NOTE Confidence: 0.903201377894737

 $00:17:54.050 \rightarrow 00:17:55.350$ get to work on time,

NOTE Confidence: 0.903201377894737

00:17:55.350 --> 00:17:57.090 but on average she's typically

NOTE Confidence: 0.903201377894737

 $00{:}17{:}57{.}090 \dashrightarrow 00{:}17{:}59{.}169$ falling a sleep somewhere on one to

NOTE Confidence: 0.903201377894737

 $00{:}17{:}59{.}169 \dashrightarrow 00{:}18{:}01{.}094$ two in the morning during this time

NOTE Confidence: 0.903201377894737

 $00:18:01.094 \rightarrow 00:18:03.610$ frame and getting up anywhere from

NOTE Confidence: 0.903201377894737

 $00:18:03.610 \longrightarrow 00:18:06.650$ 8 to noon depending on the day.

NOTE Confidence: 0.903201377894737

 $00:18:06.650 \longrightarrow 00:18:08.538$ So one of the other tools that we

- NOTE Confidence: 0.903201377894737
- $00:18:08.538 \longrightarrow 00:18:10.606$ can make use of to try to get a
- NOTE Confidence: 0.903201377894737
- $00:18:10.606 \rightarrow 00:18:12.543$ sense of whether a patient has a
- NOTE Confidence: 0.903201377894737
- $00{:}18{:}12.543 \dashrightarrow 00{:}18{:}14.652$ circadian disorder and what exactly it is,
- NOTE Confidence: 0.903201377894737
- $00:18:14.652 \longrightarrow 00:18:16.908$ is to get a sense of what time
- NOTE Confidence: 0.903201377894737
- $00:18:16.908 \rightarrow 00:18:18.610$ they're naturally producing.
- NOTE Confidence: 0.903201377894737
- 00:18:18.610 --> 00:18:18.967 Melatonin.
- NOTE Confidence: 0.903201377894737
- 00:18:18.967 --> 00:18:20.038 Like I said,
- NOTE Confidence: 0.903201377894737
- $00:18:20.038 \rightarrow 00:18:22.180$ for most people that typically starts
- NOTE Confidence: 0.903201377894737
- $00{:}18{:}22{.}244 \dashrightarrow 00{:}18{:}24{.}492$ an hour or about two to three hours
- NOTE Confidence: 0.903201377894737
- $00:18:24.492 \longrightarrow 00:18:26.229$ before their natural sleep time.
- NOTE Confidence: 0.903201377894737
- 00:18:26.230 --> 00:18:28.694 And so in clinic we've set up these
- NOTE Confidence: 0.903201377894737
- $00{:}18{:}28.694 \dashrightarrow 00{:}18{:}31.172$ kits where we can actually collect
- NOTE Confidence: 0.903201377894737
- $00{:}18{:}31{.}172 \dashrightarrow 00{:}18{:}33{.}407$ melaton in from an individual saliva.
- NOTE Confidence: 0.903201377894737
- $00{:}18{:}33{.}410 \dashrightarrow 00{:}18{:}35{.}167$ So over here we've got these tubes.
- NOTE Confidence: 0.903201377894737
- $00:18:35.170 \longrightarrow 00:18:37.106$ They have a little cotton swabs in them.
- NOTE Confidence: 0.866837005

 $00:18:37.110 \longrightarrow 00:18:39.174$ They can go through these in

NOTE Confidence: 0.866837005

 $00{:}18{:}39{.}174 \dashrightarrow 00{:}18{:}41{.}169$ order every half hour to hour.

NOTE Confidence: 0.866837005

 $00:18:41.170 \rightarrow 00:18:43.090$ During that time point before bedtime,

NOTE Confidence: 0.866837005

 $00:18:43.090 \rightarrow 00:18:45.127$ we have them wear these blue blocking

NOTE Confidence: 0.866837005

 $00:18:45.127 \rightarrow 00:18:46.869$ glasses and dim the lights during

NOTE Confidence: 0.866837005

 $00{:}18{:}46{.}869 \dashrightarrow 00{:}18{:}48{.}752$ that time and using that we can

NOTE Confidence: 0.866837005

 $00{:}18{:}48{.}813 \dashrightarrow 00{:}18{:}51{.}158$ then obtain a profile of what their

NOTE Confidence: 0.866837005

 $00:18:51.158 \rightarrow 00:18:52.882$ normal melatonin profiles look like.

NOTE Confidence: 0.866837005

00:18:52.882 --> 00:18:55.018 So in this particular patient you

NOTE Confidence: 0.866837005

00:18:55.018 --> 00:18:57.579 can see her saliva melatonin here,

NOTE Confidence: 0.866837005

 $00{:}18{:}57{.}580 \dashrightarrow 00{:}18{:}59{.}215$ so she started collecting around

NOTE Confidence: 0.866837005

00:18:59.215 --> 00:19:01.917 7:30 and you can see that the point

NOTE Confidence: 0.866837005

00:19:01.917 --> 00:19:03.582 at which your melatonin started

NOTE Confidence: 0.866837005

 $00:19:03.582 \longrightarrow 00:19:05.738$ to rise is just after midnight,

NOTE Confidence: 0.866837005

 $00:19:05.740 \rightarrow 00:19:07.988$ and so this fits with her report when

NOTE Confidence: 0.866837005

 $00:19:07.988 \longrightarrow 00:19:10.020$ she came in of often not falling

- NOTE Confidence: 0.866837005
- 00:19:10.020 --> 00:19:11.980 asleep till 2-3 in the morning,
- NOTE Confidence: 0.866837005
- $00{:}19{:}11{.}980 \dashrightarrow 00{:}19{:}14{.}969$ and so all of this data together.
- NOTE Confidence: 0.866837005
- $00:19:14.970 \longrightarrow 00:19:17.928$ Really supports the diagnosis of delayed
- NOTE Confidence: 0.866837005
- $00:19:17.928 \rightarrow 00:19:20.802$ sleep wake phase disorder and I've
- NOTE Confidence: 0.866837005
- $00{:}19{:}20.802 \dashrightarrow 00{:}19{:}23.268$ included here the ICCSD 3 criteria.
- NOTE Confidence: 0.866837005
- 00:19:23.270 --> 00:19:23.548 Basically,
- NOTE Confidence: 0.866837005
- $00:19:23.548 \rightarrow 00:19:25.494$ you need a significant delay in the
- NOTE Confidence: 0.866837005
- $00:19:25.494 \rightarrow 00:19:27.444$ phase of the major sleep episode in
- NOTE Confidence: 0.866837005
- $00:19:27.444 \longrightarrow 00:19:29.104$ relation to the desired or required
- NOTE Confidence: 0.866837005
- $00:19:29.104 \rightarrow 00:19:30.706$ sleep time and wake up time.
- NOTE Confidence: 0.866837005
- 00:19:30.710 -> 00:19:32.276 Symptoms have to be present for
- NOTE Confidence: 0.866837005
- $00:19:32.276 \longrightarrow 00:19:33.320$ at least three months,
- NOTE Confidence: 0.866837005
- $00:19:33.320 \longrightarrow 00:19:34.990$ but if they're allowed to
- NOTE Confidence: 0.866837005
- $00{:}19{:}34{.}990 \dashrightarrow 00{:}19{:}36{.}326$ choose their own schedule,
- NOTE Confidence: 0.866837005
- $00:19:36.330 \longrightarrow 00:19:39.110$ they actually sleep better.
- NOTE Confidence: 0.866837005

 $00:19:39.110 \longrightarrow 00:19:41.766$ It look like to diagnose this with either

NOTE Confidence: 0.866837005

 $00:19:41.766 \longrightarrow 00:19:44.735$ a sleep log or actigraphy for at least 7,

NOTE Confidence: 0.866837005

 $00:19:44.740 \longrightarrow 00:19:45.721$ preferably 14 days.

NOTE Confidence: 0.866837005

 $00:19:45.721 \longrightarrow 00:19:47.683$ To show this delay in the

NOTE Confidence: 0.866837005

 $00:19:47.683 \longrightarrow 00:19:49.459$ timing of their sleep period,

NOTE Confidence: 0.866837005

 $00:19:49.460 \longrightarrow 00:19:51.090$ and then obviously you want

NOTE Confidence: 0.866837005

 $00:19:51.090 \longrightarrow 00:19:53.584$ to make sure that you rule out

NOTE Confidence: 0.866837005

 $00{:}19{:}53{.}584 \dashrightarrow 00{:}19{:}55{.}579$ other sleep disorders that could

NOTE Confidence: 0.866837005

 $00{:}19{:}55{.}579 \dashrightarrow 00{:}19{:}57{.}310$ be explaining this better.

NOTE Confidence: 0.866837005

 $00{:}19{:}57{.}310 \dashrightarrow 00{:}19{:}59{.}074$ In terms of what causes delayed

NOTE Confidence: 0.866837005

00:19:59.074 --> 00:20:00.250 sleep wake phase disorder,

NOTE Confidence: 0.866837005

 $00{:}20{:}00{.}250 \dashrightarrow 00{:}20{:}02{.}310$ there are many potential theories,

NOTE Confidence: 0.866837005

 $00{:}20{:}02{.}310 \dashrightarrow 00{:}20{:}05{.}124$ so there are familial cases of this,

NOTE Confidence: 0.866837005

 $00{:}20{:}05{.}130 \dashrightarrow 00{:}20{:}06{.}942$ and so there's been a description

NOTE Confidence: 0.866837005

 $00:20:06.942 \longrightarrow 00:20:08.556$ of a cryptochrome 1 mutation

NOTE Confidence: 0.866837005

 $00:20:08.556 \longrightarrow 00:20:10.266$ in some families with this.

- NOTE Confidence: 0.866837005
- 00:20:10.270 --> 00:20:11.990 This is one of the core clock genes,
- NOTE Confidence: 0.866837005
- $00{:}20{:}11{.}990 \dashrightarrow 00{:}20{:}13{.}550$ and I didn't go into this
- NOTE Confidence: 0.866837005
- $00:20:13.550 \longrightarrow 00:20:14.330$ in the introduction,
- NOTE Confidence: 0.866837005
- $00:20:14.330 \longrightarrow 00:20:17.445$ but we have within each of ourselves
- NOTE Confidence: 0.866837005
- $00{:}20{:}17.450 \dashrightarrow 00{:}20{:}20{.}938$ a core set of clock genes and that
- NOTE Confidence: 0.866837005
- 00:20:20.938 --> 00:20:22.805 transcription translation feedback loop
- NOTE Confidence: 0.866837005
- 00:20:22.805 --> 00:20:26.025 typically takes about 24 hours to complete,
- NOTE Confidence: 0.866837005
- $00:20:26.030 \rightarrow 00:20:26.648$ but mutations?
- NOTE Confidence: 0.866837005
- $00:20:26.648 \longrightarrow 00:20:29.120$ Could be their speed that up or slow
- NOTE Confidence: 0.866837005
- $00{:}20{:}29{.}190 \dashrightarrow 00{:}20{:}31{.}311$ that down can either make you advanced
- NOTE Confidence: 0.866837005
- $00:20:31.311 \longrightarrow 00:20:33.534$ in the case of speeding it up or
- NOTE Confidence: 0.866837005
- $00{:}20{:}33{.}534 \dashrightarrow 00{:}20{:}35{.}752$ delay in the case of slowing it down.
- NOTE Confidence: 0.866837005
- $00:20:35.752 \rightarrow 00:20:38.020$ So you can think of these patients
- NOTE Confidence: 0.866837005
- $00:20:38.090 \rightarrow 00:20:40.155$ as simply just persistently running
- NOTE Confidence: 0.866837005
- $00:20:40.155 \rightarrow 00:20:42.610$ a little bit behind everybody else.
- NOTE Confidence: 0.866837005

 $00{:}20{:}42.610 \dashrightarrow 00{:}20{:}44.878$ And that goes along with demonstrations

NOTE Confidence: 0.866837005

 $00{:}20{:}44.878 \dashrightarrow 00{:}20{:}47.187$ from several labs that these patients

NOTE Confidence: 0.866837005

 $00{:}20{:}47.187 \dashrightarrow 00{:}20{:}49.749$ tend to have a longer circadian period.

NOTE Confidence: 0.866837005

 $00:20:49.750 \longrightarrow 00:20:52.039$ So left to their own devices they

NOTE Confidence: 0.866837005

 $00{:}20{:}52{.}039 \dashrightarrow 00{:}20{:}54{.}634$ get later and later each day much

NOTE Confidence: 0.866837005

 $00{:}20{:}54.634 \dashrightarrow 00{:}20{:}56.564$ later than the average person.

NOTE Confidence: 0.866837005

 $00{:}20{:}56{.}570 \dashrightarrow 00{:}20{:}58{.}412$ And there have been several reported

NOTE Confidence: 0.866837005

 $00:20:58.412 \rightarrow 00:21:00.450$ cases of people with head injuries,

NOTE Confidence: 0.866837005

 $00{:}21{:}00{.}450 \dashrightarrow 00{:}21{:}02{.}790$ and we think that this may be due to NOTE Confidence: 0.866837005

 $00{:}21{:}02{.}790 \dashrightarrow 00{:}21{:}05{.}354$ either a delay and or decrease in the NOTE Confidence: 0.866837005

00:21:05.354 --> 00:21:07.050 amplitude of melatonin production.

NOTE Confidence: 0.866837005

 $00:21:07.050 \longrightarrow 00:21:08.541$ And then we'll get into this a

NOTE Confidence: 0.866837005

00:21:08.541 -> 00:21:09.510 little bit more later,

NOTE Confidence: 0.866837005

 $00{:}21{:}09{.}510 \dashrightarrow 00{:}21{:}11{.}652$ but there does also seem to be a role

NOTE Confidence: 0.866837005

 $00{:}21{:}11.652 \dashrightarrow 00{:}21{:}14.000$ for both timing of exposure as well

NOTE Confidence: 0.866837005

 $00:21:14.000 \rightarrow 00:21:15.780$ as responsiveness to bright light.

- NOTE Confidence: 0.93661724
- $00:21:18.070 \rightarrow 00:21:20.350$ So we've made the diagnosis.
- NOTE Confidence: 0.93661724
- $00{:}21{:}20{.}350 \dashrightarrow 00{:}21{:}22{.}254$ Now what do we do as far
- NOTE Confidence: 0.93661724
- $00:21:22.254 \rightarrow 00:21:23.670$ as treating this patient?
- NOTE Confidence: 0.93661724
- $00:21:23.670 \longrightarrow 00:21:25.980$ And I've put up two things.
- NOTE Confidence: 0.93661724
- $00:21:25.980 \longrightarrow 00:21:27.186$ We'll get to the next one,
- NOTE Confidence: 0.93661724
- $00{:}21{:}27{.}190 \dashrightarrow 00{:}21{:}29{.}062$ so I've included here.
- NOTE Confidence: 0.93661724
- $00:21:29.062 \longrightarrow 00:21:30.934$ The current published 2015
- NOTE Confidence: 0.93661724
- 00:21:30.934 --> 00:21:32.770 ASM treatment guidelines,
- NOTE Confidence: 0.93661724
- $00{:}21{:}32{.}770 \dashrightarrow 00{:}21{:}34{.}455$ which basically say that in
- NOTE Confidence: 0.93661724
- 00:21:34.455 --> 00:21:35.803 both adults and children,
- NOTE Confidence: 0.93661724
- $00:21:35.810 \longrightarrow 00:21:37.988$ we recommend using
- NOTE Confidence: 0.93661724
- $00{:}21{:}37{.}988 \dashrightarrow 00{:}21{:}40{.}166$ strategically timed melaton in.
- NOTE Confidence: 0.93661724
- 00:21:40.170 --> 00:21:42.266 Now I will say that I don't actually
- NOTE Confidence: 0.93661724
- $00{:}21{:}42.266 \dashrightarrow 00{:}21{:}44.317$ follow what's currently in the guidelines,
- NOTE Confidence: 0.93661724
- $00{:}21{:}44{.}320 \dashrightarrow 00{:}21{:}46{.}896$ so the one reference that they cite
- NOTE Confidence: 0.93661724

 $00:21:46.896 \longrightarrow 00:21:49.663$ actually was a study that used 5

NOTE Confidence: 0.93661724

 $00:21:49.663 \rightarrow 00:21:52.045$ milligrams between 7:00 and 9:00 PM.

NOTE Confidence: 0.93661724

 $00{:}21{:}52{.}050 \dashrightarrow 00{:}21{:}53{.}922$ And So what I've put here is actually NOTE Confidence: 0.93661724

00:21:53.922 --> 00:21:55.620 what I tend to do clinically,

NOTE Confidence: 0.93661724

 $00{:}21{:}55{.}620 \dashrightarrow 00{:}21{:}57{.}438$ and we're starting to work together

NOTE Confidence: 0.93661724

 $00{:}21{:}57{.}438$ --> $00{:}21{:}59{.}055$ with several other circadian clinics NOTE Confidence: 0.93661724

00:21:59.055 --> 00:22:00.459 on some consensus guidelines.

NOTE Confidence: 0.93661724

 $00:22:00.460 \rightarrow 00:22:02.672$ And I think we're all in agreement

NOTE Confidence: 0.93661724

 $00{:}22{:}02{.}672 \dashrightarrow 00{:}22{:}05{.}148$ that we typically now tend to go lower NOTE Confidence: 0.93661724

 $00{:}22{:}05{.}148 \dashrightarrow 00{:}22{:}07{.}220$ and have changed the timing slightly.

NOTE Confidence: 0.93661724

 $00{:}22{:}07{.}220 \dashrightarrow 00{:}22{:}09{.}558$ So if I'm managing a patient with

NOTE Confidence: 0.93661724

 $00:22:09.558 \rightarrow 00:22:11.600$ delayed sleep wake phase disorder.

NOTE Confidence: 0.93661724

 $00:22:11.600 \rightarrow 00:22:13.370$ I will typically give them

NOTE Confidence: 0.93661724

 $00{:}22{:}13{.}370 \dashrightarrow 00{:}22{:}15{.}140$ half a milligram of melatonin.

NOTE Confidence: 0.93661724

 $00{:}22{:}15.140 \dashrightarrow 00{:}22{:}15.423$ Again,

NOTE Confidence: 0.93661724

 $00:22:15.423 \longrightarrow 00:22:17.121$ with that idea of keeping that

- NOTE Confidence: 0.93661724
- $00:22:17.121 \longrightarrow 00:22:18.986$ dose low so it's that strategic

00:22:18.986 --> 00:22:20.576 pulse that's there when you

NOTE Confidence: 0.93661724

 $00:22:20.576 \rightarrow 00:22:22.657$ need it and gone when you don't.

NOTE Confidence: 0.93661724

 $00:22:22.660 \rightarrow 00:22:24.052$ And based on that phase response

NOTE Confidence: 0.93661724

 $00{:}22{:}24.052 \dashrightarrow 00{:}22{:}25.559$ curve that I showed you earlier,

NOTE Confidence: 0.93661724

 $00{:}22{:}25{.}560 \dashrightarrow 00{:}22{:}27{.}215$ it's about five hours prior

NOTE Confidence: 0.93661724

 $00:22:27.215 \longrightarrow 00:22:28.539$ to their current bedtime,

NOTE Confidence: 0.93661724

 $00:22:28.540 \rightarrow 00:22:31.246$ so if they biologically were allowed

NOTE Confidence: 0.93661724

 $00:22:31.246 \longrightarrow 00:22:33.959$ to sleep when they prefer to,

NOTE Confidence: 0.93661724

 $00:22:33.960 \longrightarrow 00:22:35.976$ or if they're not that delayed,

NOTE Confidence: 0.93661724

 $00:22:35.980 \longrightarrow 00:22:36.930$ we're just trying to shift

NOTE Confidence: 0.93661724

 $00{:}22{:}36{.}930 \dashrightarrow 00{:}22{:}37{.}880$ them an hour or two.

NOTE Confidence: 0.93661724

 $00{:}22{:}37{.}880 \dashrightarrow 00{:}22{:}39{.}651$ I will sometimes just give it an

NOTE Confidence: 0.93661724

00:22:39.651 --> 00:22:41.680 hour prior to their desired bedtime,

NOTE Confidence: 0.93661724

 $00{:}22{:}41.680 \dashrightarrow 00{:}22{:}42.919$ and we'll go through some of that.

 $00:22:42.920 \longrightarrow 00:22:46.007$ Data for that in the next slide.

NOTE Confidence: 0.93661724

 $00{:}22{:}46.010 \dashrightarrow 00{:}22{:}48.074$ It's key for all of these patients to

NOTE Confidence: 0.93661724

00:22:48.074 --> 00:22:49.827 avoid bright light prior to bedtime,

NOTE Confidence: 0.93661724

 $00:22:49.830 \longrightarrow 00:22:51.804$ we'll talk about some of the

NOTE Confidence: 0.93661724

 $00:22:51.804 \longrightarrow 00:22:53.120$ data supporting that later.

NOTE Confidence: 0.93661724

 $00{:}22{:}53{.}120 \dashrightarrow 00{:}22{:}55{.}528$ And then we also make sure that they

NOTE Confidence: 0.93661724

 $00:22:55.528 \rightarrow 00:22:57.531$ get bright light after their wake

NOTE Confidence: 0.93661724

 $00:22:57.531 \rightarrow 00:23:00.224$ time and that can be anywhere from 30

NOTE Confidence: 0.93661724

 $00{:}23{:}00{.}224 \dashrightarrow 00{:}23{:}02{.}415$ minutes to two hours of light total.

NOTE Confidence: 0.93661724

 $00:23:02.420 \longrightarrow 00:23:03.860$ I usually spread that out over

NOTE Confidence: 0.93661724

00:23:03.860 --> 00:23:04.820 4 hours and again,

NOTE Confidence: 0.93661724

 $00{:}23{:}04{.}820 \dashrightarrow 00{:}23{:}07{.}004$ like I emphasized if they're having to

NOTE Confidence: 0.93661724

 $00:23:07.004 \rightarrow 00:23:09.538$ get up earlier than they naturally would,

NOTE Confidence: 0.93661724

 $00:23:09.540 \longrightarrow 00:23:11.130$ I actually have them wear dark

NOTE Confidence: 0.93661724

 $00{:}23{:}11{.}130 \dashrightarrow 00{:}23{:}12{.}808$ glasses until that time when they

NOTE Confidence: 0.93661724

 $00:23:12.808 \rightarrow 00:23:14.768$ would be waking up so they're not

00:23:14.768 --> 00:23:15.959 inadvertently getting bright light

NOTE Confidence: 0.93661724

 $00{:}23{:}15{.}959 \dashrightarrow 00{:}23{:}17{.}954$ during the phase delay portion of the

NOTE Confidence: 0.93661724

 $00:23:17.960 \rightarrow 00:23:19.586$ phase response curve instead of the

NOTE Confidence: 0.93661724

 $00:23:19.586 \rightarrow 00:23:21.179$ phase advanced portion where we want it.

NOTE Confidence: 0.89183024

 $00{:}23{:}23{.}230 \dashrightarrow 00{:}23{:}25{.}624$ So I told you I'd go through the rationale NOTE Confidence: 0.89183024

 $00{:}23{:}25{.}624 \dashrightarrow 00{:}23{:}28{.}154$ for the one hour prior to desired bed time.

NOTE Confidence: 0.89183024

 $00{:}23{:}28{.}160 \dashrightarrow 00{:}23{:}29{.}972$ So after the ASM guidelines came

NOTE Confidence: 0.89183024

 $00{:}23{:}29{.}972 \dashrightarrow 00{:}23{:}32{.}059$ out this this study was published,

NOTE Confidence: 0.89183024

 $00{:}23{:}32{.}060 \dashrightarrow 00{:}23{:}35{.}282$ which basically was looking at the

NOTE Confidence: 0.89183024

 $00{:}23{:}35{.}282 \dashrightarrow 00{:}23{:}38{.}020$ use of melaton in the treatment of

NOTE Confidence: 0.89183024

 $00:23:38.020 \rightarrow 00:23:39.420$ delayed sleep wake phase disorder.

NOTE Confidence: 0.89183024

 $00{:}23{:}39{.}420 \dashrightarrow 00{:}23{:}41{.}500$ They took 116 participants with

NOTE Confidence: 0.89183024

 $00{:}23{:}41{.}500 \dashrightarrow 00{:}23{:}43{.}580$ delayed sleep wake phase disorder.

NOTE Confidence: 0.89183024

 $00{:}23{:}43{.}580 \dashrightarrow 00{:}23{:}46{.}073$ They define that as the delmo had to either NOTE Confidence: 0.89183024

 $00{:}23{:}46.073 \dashrightarrow 00{:}23{:}48.394$ occur less than 30 minutes before or at

 $00:23:48.394 \rightarrow 00:23:50.548$ some point after their desired bedtime.

NOTE Confidence: 0.89183024

 $00{:}23{:}50{.}550 \dashrightarrow 00{:}23{:}52{.}460$ So there was a mismatch

NOTE Confidence: 0.89183024

 $00:23:52.460 \longrightarrow 00:23:53.606$ between their biological.

NOTE Confidence: 0.89183024

 $00:23:53.610 \rightarrow 00:23:56.718$ Timing and when they wanted to sleep.

NOTE Confidence: 0.89183024

 $00:23:56.720 \longrightarrow 00:23:58.780$ In, on average, these patients

NOTE Confidence: 0.89183024

 $00{:}23{:}58{.}780 \dashrightarrow 00{:}24{:}01{.}820$ had a sleep onset of about 1:30.

NOTE Confidence: 0.89183024

 $00:24:01.820 \longrightarrow 00:24:05.084$ Their sleep offset was at about 9:00 AM.

NOTE Confidence: 0.89183024

 $00:24:05.090 \longrightarrow 00:24:06.956$ And they were randomized to either

NOTE Confidence: 0.89183024

 $00{:}24{:}06{.}956 \dashrightarrow 00{:}24{:}08{.}875$ four weeks of place bo or half

NOTE Confidence: 0.89183024

 $00{:}24{:}08.875 \dashrightarrow 00{:}24{:}10.099$ a milligram of melaton in,

NOTE Confidence: 0.89183024

00:24:10.100 --> 00:24:11.964 and they were told to take it one

NOTE Confidence: 0.89183024

00:24:11.964 --> 00:24:13.521 hour prior to their desired bed
time

NOTE Confidence: 0.89183024

 $00{:}24{:}13{.}521 \dashrightarrow 00{:}24{:}15{.}684$ and then to get into bed at that

NOTE Confidence: 0.89183024

00:24:15.684 --> 00:24:17.334 desired bed
time and on average for

NOTE Confidence: 0.89183024

 $00{:}24{:}17{.}334 \dashrightarrow 00{:}24{:}18{.}655$ the study population they wanted

NOTE Confidence: 0.89183024

 $00:24:18.655 \longrightarrow 00:24:20.440$ to go to bed at about 10:30.

 $00:24:22.930 \longrightarrow 00:24:24.070$ After that four weeks,

NOTE Confidence: 0.823465209130435

 $00{:}24{:}24{.}070 \dashrightarrow 00{:}24{:}25{.}780$ they found that the melaton in group

NOTE Confidence: 0.823465209130435

 $00{:}24{:}25{.}838 \dashrightarrow 00{:}24{:}27{.}595$ had an onset sleep onset time that

NOTE Confidence: 0.823465209130435

 $00:24:27.595 \longrightarrow 00:24:29.190$ moved about half an hour earlier.

NOTE Confidence: 0.823465209130435

 $00:24:29.190 \rightarrow 00:24:31.310$ Their sleep efficiency also improved.

NOTE Confidence: 0.823465209130435

00:24:31.310 --> 00:24:33.290 They did do a subgroup analysis

NOTE Confidence: 0.823465209130435

 $00:24:33.290 \longrightarrow 00:24:34.995$ where they didn't actually find

NOTE Confidence: 0.823465209130435

00:24:34.995 --> 00:24:36.610 a significant change in Dino,

NOTE Confidence: 0.823465209130435

 $00{:}24{:}36{.}610 \dashrightarrow 00{:}24{:}38{.}570$ and to go back to the point

NOTE Confidence: 0.823465209130435

00:24:38.570 --> 00:24:41.156 that I made earlier that I do

NOTE Confidence: 0.823465209130435

 $00:24:41.156 \rightarrow 00:24:43.241$ differentiate between the milder and

NOTE Confidence: 0.823465209130435

 $00:24:43.241 \rightarrow 00:24:45.817$ the more severe delayed patients.

NOTE Confidence: 0.823465209130435

00:24:45.820 --> 00:24:47.428 This tends to work pretty well,

NOTE Confidence: 0.823465209130435

 $00:24:47.430 \longrightarrow 00:24:49.686$ for example, if it's a patient

NOTE Confidence: 0.823465209130435

 $00:24:49.686 \rightarrow 00:24:51.696$ who's falling asleep at 12:31.

00:24:51.696 --> 00:24:55.238 They wanna fall asleep at 1111 thirty.

NOTE Confidence: 0.823465209130435

 $00:24:55.240 \rightarrow 00:24:57.337$ It tends to help them shift at that point,

NOTE Confidence: 0.823465209130435

 $00{:}24{:}57{.}340$ --> $00{:}24{:}59{.}626$ and they're not spending a tremendous NOTE Confidence: 0.823465209130435

 $00:24:59.626 \rightarrow 00:25:02.749$ amount of time in bed not able to sleep.

NOTE Confidence: 0.823465209130435

 $00{:}25{:}02{.}750 \dashrightarrow 00{:}25{:}04{.}973$ But take for example if I have one of

NOTE Confidence: 0.823465209130435

 $00:25:04.973 \rightarrow 00:25:06.892$ my patients who doesn't fall asleep

NOTE Confidence: 0.823465209130435

00:25:06.892 --> 00:25:09.309 till 3-4 or five in the morning,

NOTE Confidence: 0.823465209130435

 $00:25:09.310 \longrightarrow 00:25:11.726$ but they'd like to fall asleep at 11.

NOTE Confidence: 0.823465209130435

 $00:25:11.730 \longrightarrow 00:25:13.938$ Now I'm telling them take this

NOTE Confidence: 0.823465209130435

 $00:25:13.938 \rightarrow 00:25:17.282$ melatonin at 10:00 PM. Get into bed 11.

NOTE Confidence: 0.823465209130435

 $00:25:17.282 \longrightarrow 00:25:20.090$ And lay there for five hours.

NOTE Confidence: 0.823465209130435

 $00:25:20.090 \rightarrow 00:25:22.010$ Obviously that's just going to feed

NOTE Confidence: 0.823465209130435

 $00{:}25{:}22.010 \dashrightarrow 00{:}25{:}23.716$ into some of their frustrations

NOTE Confidence: 0.823465209130435

 $00:25:23.716 \rightarrow 00:25:25.888$ that they've been dealing with for

NOTE Confidence: 0.823465209130435

 $00:25:25.888 \rightarrow 00:25:28.774$ most of their life, and we do see.

NOTE Confidence: 0.823465209130435

 $00:25:28.774 \rightarrow 00:25:32.259$ A lot of comorbid insomnia in these patients,

 $00:25:32.260 \rightarrow 00:25:34.227$ and so that's why if we're trying

NOTE Confidence: 0.823465209130435

 $00:25:34.227 \rightarrow 00:25:35.480$ to make larger moves,

NOTE Confidence: 0.823465209130435

 $00{:}25{:}35{.}480 \dashrightarrow 00{:}25{:}36{.}468$ there's a larger mismatch.

NOTE Confidence: 0.823465209130435

 $00:25:36.468 \rightarrow 00:25:38.341$ We tend to do this more targeted

NOTE Confidence: 0.823465209130435

00:25:38.341 - > 00:25:40.046 treatment where we really inch

NOTE Confidence: 0.823465209130435

 $00:25:40.046 \rightarrow 00:25:41.410$ their rhythm earlier instead.

NOTE Confidence: 0.8523694

 $00{:}25{:}43.510 \dashrightarrow 00{:}25{:}45.841$ So going back to case one so we treated

NOTE Confidence: 0.8523694

 $00{:}25{:}45{.}841 \dashrightarrow 00{:}25{:}48{.}458$ her with that timed melaton in timed light.

NOTE Confidence: 0.8523694

 $00{:}25{:}48{.}460 \dashrightarrow 00{:}25{:}49{.}905$ She responded really well and

NOTE Confidence: 0.8523694

00:25:49.905 --> 00:25:51.678 she actually was able to shift

NOTE Confidence: 0.8523694

 $00:25:51.678 \rightarrow 00:25:53.328$ her bedtime to about 10:00 PM.

NOTE Confidence: 0.8523694

 $00{:}25{:}53{.}330 \dashrightarrow 00{:}25{:}55{.}626$ Her sleep latency decreased about 10 minutes,

NOTE Confidence: 0.8523694

 $00{:}25{:}55{.}630 \dashrightarrow 00{:}25{:}57{.}508$ which was great and she actually

NOTE Confidence: 0.8523694

 $00{:}25{:}57{.}508 \dashrightarrow 00{:}25{:}59{.}788$ did really well for about two years.

NOTE Confidence: 0.8523694

 $00{:}25{:}59{.}790 \dashrightarrow 00{:}26{:}01{.}764$ But then she started having several

 $00{:}26{:}01{.}764 \dashrightarrow 00{:}26{:}04{.}148$ days per week where she started drifting

NOTE Confidence: 0.8523694

 $00{:}26{:}04{.}148 \dashrightarrow 00{:}26{:}06{.}493$ later so she was falling a sleep and

NOTE Confidence: 0.8523694

 $00:26:06.556 \rightarrow 00:26:08.756$ waking up later and ended up having to

NOTE Confidence: 0.8523694

 $00:26:08.756 \rightarrow 00:26:11.389$ miss or be late to several days of work.

NOTE Confidence: 0.8523694

 $00:26:11.390 \longrightarrow 00:26:13.270$ She was at the point where she was about to.

NOTE Confidence: 0.8523694

 $00{:}26{:}13.270 \dashrightarrow 00{:}26{:}14.494$ Trust or sick days.

NOTE Confidence: 0.8523694

00:26:14.494 --> 00:26:16.024 She was potentially gonna lose

NOTE Confidence: 0.8523694

 $00:26:16.024 \rightarrow 00:26:18.413$ her job and so we really needed to

NOTE Confidence: 0.8523694

 $00{:}26{:}18{.}413 \dashrightarrow 00{:}26{:}19{.}680$ figure out something to do.

NOTE Confidence: 0.8523694

00:26:19.680 --> 00:26:21.808 And it was actually right around this

NOTE Confidence: 0.8523694

 $00:26:21.808 \rightarrow 00:26:23.833$ time that Ken writes group published

NOTE Confidence: 0.8523694

 $00{:}26{:}23.833 \dashrightarrow 00{:}26{:}25.939$ this study and so another one.

NOTE Confidence: 0.8523694

 $00:26:25.940 \longrightarrow 00:26:26.820$ If you haven't read it,

NOTE Confidence: 0.8523694

 $00:26:26.820 \longrightarrow 00:26:28.098$ definitely take a look at this,

NOTE Confidence: 0.8523694

 $00{:}26{:}28{.}100 \dashrightarrow 00{:}26{:}30{.}977$ but this was his infamous camping study

NOTE Confidence: 0.8523694

 $00:26:30.980 \rightarrow 00:26:33.255$ where he took a group of individuals

- NOTE Confidence: 0.8523694
- $00:26:33.255 \rightarrow 00:26:36.292$ and you could see indicated over here

 $00{:}26{:}36{.}292 \dashrightarrow 00{:}26{:}38{.}280$ under electrical lighting conditions.

NOTE Confidence: 0.8523694

 $00:26:38.280 \longrightarrow 00:26:40.140$ Their melaton in onset was

NOTE Confidence: 0.8523694

 $00:26:40.140 \longrightarrow 00:26:42.000$ occurring sometime after sunset.

NOTE Confidence: 0.8523694

00:26:42.000 --> 00:26:43.364 They're offset was occurring.

NOTE Confidence: 0.8523694

00:26:43.364 --> 00:26:44.046 After sunrise,

NOTE Confidence: 0.8523694

 $00:26:44.050 \longrightarrow 00:26:46.180$ so they were delayed with

NOTE Confidence: 0.8523694

 $00:26:46.180 \longrightarrow 00:26:47.884$ respect to the environment.

NOTE Confidence: 0.8523694

 $00{:}26{:}47.890 \dashrightarrow 00{:}26{:}49.858$ He took them camping in Colorado

NOTE Confidence: 0.8523694

 $00:26:49.858 \longrightarrow 00:26:52.545$ for a week and with that natural

NOTE Confidence: 0.8523694

 $00{:}26{:}52.545 \dashrightarrow 00{:}26{:}55.143$ light exposure he managed to shift

NOTE Confidence: 0.8523694

 $00{:}26{:}55{.}143 \dashrightarrow 00{:}26{:}57{.}188$ every body earlier and better in,

NOTE Confidence: 0.8523694

 $00{:}26{:}57{.}190 \dashrightarrow 00{:}26{:}59{.}280$ train them with the environment.

NOTE Confidence: 0.8523694

00:26:59.280 --> 00:27:01.860 You can see melaton
in onset and

NOTE Confidence: 0.8523694

 $00{:}27{:}01{.}860 \dashrightarrow 00{:}27{:}04{.}499$ offset are now better matched with

 $00:27:04.499 \longrightarrow 00:27:06.983$ sunset and sunrise and so this

NOTE Confidence: 0.8523694

 $00{:}27{:}06{.}983 \dashrightarrow 00{:}27{:}09{.}847$ made it into the general public.

NOTE Confidence: 0.8523694

00:27:09.850 --> 00:27:11.740 News had a lot of publicity

NOTE Confidence: 0.8523694

 $00:27:11.740 \longrightarrow 00:27:13.860$ around it and so my patient.

NOTE Confidence: 0.8523694

 $00{:}27{:}13.860 \dashrightarrow 00{:}27{:}16.308$ All this and her question for me at

NOTE Confidence: 0.8523694

00:27:16.308 --> 00:27:18.585 first was should I go to Colorado

NOTE Confidence: 0.8523694

 $00{:}27{:}18.585 \dashrightarrow 00{:}27{:}21.615$ and go camping and it turns out that

NOTE Confidence: 0.8523694

 $00:27:21.615 \rightarrow 00:27:23.945$ she is somebody who likes to camp.

NOTE Confidence: 0.8523694

 $00{:}27{:}23.945 \dashrightarrow 00{:}27{:}25.590$ She will often go camping in the

NOTE Confidence: 0.8523694

 $00{:}27{:}25.647 \dashrightarrow 00{:}27{:}26.947$ area in Illinois and Wisconsin

NOTE Confidence: 0.8523694

 $00{:}27{:}26{.}947 \dashrightarrow 00{:}27{:}28{.}956$ and we sort of talked through the

NOTE Confidence: 0.8523694

 $00:27:28.956 \longrightarrow 00:27:30.260$ rationale behind the study.

NOTE Confidence: 0.8523694

 $00:27:30.260 \longrightarrow 00:27:32.150$ And so there's really nothing magical

NOTE Confidence: 0.8523694

 $00{:}27{:}32{.}150 \dashrightarrow 00{:}27{:}34{.}277$ about the Rockies as far as we know.

NOTE Confidence: 0.8523694

 $00:27:34.280 \rightarrow 00:27:36.434$ It's really just that elimination of

NOTE Confidence: 0.8523694

 $00:27:36.434 \rightarrow 00:27:38.740$ electrical lighting that made the difference,

- NOTE Confidence: 0.8523694
- $00:27:38.740 \longrightarrow 00:27:40.210$ and so she actually was able to
- NOTE Confidence: 0.8523694
- $00:27:40.210 \longrightarrow 00:27:42.000$ set up a tent in her backyard.
- NOTE Confidence: 0.8523694
- $00:27:42.000 \longrightarrow 00:27:43.460$ This is not her tent,
- NOTE Confidence: 0.8523694
- $00:27:43.460 \longrightarrow 00:27:45.188$ it's a Google image of tent.
- NOTE Confidence: 0.8523694
- $00:27:45.190 \longrightarrow 00:27:45.521$ Backyard,
- NOTE Confidence: 0.8523694
- 00:27:45.521 --> 00:27:48.169 but she was able to set up a
- NOTE Confidence: 0.8523694
- $00:27:48.169 \longrightarrow 00:27:49.808$ tent in her backyard.
- NOTE Confidence: 0.8523694
- $00:27:49.810 \longrightarrow 00:27:51.986$ Really could follow that schedule for a week.
- NOTE Confidence: 0.8523694
- $00{:}27{:}51{.}990 \dashrightarrow 00{:}27{:}53{.}886$ She turned off all electrical lights,
- NOTE Confidence: 0.8523694
- $00:27:53.890 \longrightarrow 00:27:56.170$ all lights in her yard.
- NOTE Confidence: 0.8523694
- $00:27:56.170 \longrightarrow 00:27:57.878$ The only thing that kind of failed
- NOTE Confidence: 0.8523694
- $00:27:57.878 \rightarrow 00:27:59.803$ us along the way is one night a
- NOTE Confidence: 0.8523694
- 00:27:59.803 --> 00:28:01.260 skunk did come in sprayer tent,
- NOTE Confidence: 0.8523694
- $00{:}28{:}01{.}260 \dashrightarrow 00{:}28{:}02{.}875$ but because we had talked
- NOTE Confidence: 0.8523694
- $00:28:02.875 \rightarrow 00:28:04.490$ through what the principle was,
- NOTE Confidence: 0.8523694

 $00:28:04.490 \longrightarrow 00:28:06.050$ that one night she went into her house

NOTE Confidence: 0.8523694

 $00{:}28{:}06{.}050 \dashrightarrow 00{:}28{:}07{.}470$ trying to make sure she turned on.

NOTE Confidence: 0.8523694

00:28:07.470 --> 00:28:08.042 No lights,

NOTE Confidence: 0.8523694

 $00:28:08.042 \rightarrow 00:28:10.044$ washed her tent the next day and

NOTE Confidence: 0.8523694

00:28:10.044 --> 00:28:11.719 went back to it and it actually

NOTE Confidence: 0.8523694

 $00:28:11.719 \longrightarrow 00:28:12.448$ worked really well.

NOTE Confidence: 0.8523694

00:28:12.450 --> 00:28:14.526 So after a week of camping

NOTE Confidence: 0.8523694

 $00:28:14.530 \longrightarrow 00:28:15.710$ we got our schedule.

NOTE Confidence: 0.8523694

 $00{:}28{:}15{.}710 \dashrightarrow 00{:}28{:}17{.}480$ Advanced and then she will sometimes

NOTE Confidence: 0.8523694

 $00{:}28{:}17{.}541 \dashrightarrow 00{:}28{:}19{.}781$ now go back and re entrain with these

NOTE Confidence: 0.8523694

 $00{:}28{:}19.781 \dashrightarrow 00{:}28{:}21.242$ electricity free weekends to kind

NOTE Confidence: 0.8523694

 $00:28:21.242 \longrightarrow 00:28:22.934$ of get herself back on schedule.

NOTE Confidence: 0.854828793888889

 $00{:}28{:}22{.}940 \dashrightarrow 00{:}28{:}24{.}896$ And I think from a logistics

NOTE Confidence: 0.854828793888889

 $00{:}28{:}24.896 \dashrightarrow 00{:}28{:}26.544$ standpoint probably the thing I'm

NOTE Confidence: 0.854828793888889

 $00:28:26.544 \rightarrow 00:28:28.560$ most satisfied about is we could get.

NOTE Confidence: 0.854828793888889

 $00:28:28.560 \longrightarrow 00:28:31.192$ We got her a week of short term

 $00:28:31.192 \rightarrow 00:28:33.680$ disability to do this camping as well.

NOTE Confidence: 0.854828793888889

00:28:33.680 --> 00:28:35.542 So we got our employer to cover

NOTE Confidence: 0.854828793888889

 $00:28:35.542 \longrightarrow 00:28:37.480$ it as part of her treatment.

NOTE Confidence: 0.854828793888889

 $00:28:37.480 \longrightarrow 00:28:39.440$ So that was just a nice insight

NOTE Confidence: 0.854828793888889

 $00:28:39.440 \longrightarrow 00:28:41.659$ into both how to manage the basic

NOTE Confidence: 0.854828793888889

 $00:28:41.659 \longrightarrow 00:28:43.304$ circadian disorder as well as

NOTE Confidence: 0.854828793888889

 $00{:}28{:}43{.}304 \dashrightarrow 00{:}28{:}45{.}789$ how we make use of some of the

NOTE Confidence: 0.854828793888889

 $00:28:45.789 \longrightarrow 00:28:47.350$ published data that's out there.

NOTE Confidence: 0.854828793888889

00:28:47.350 --> 00:28:50.456 And now I'd like to move on to my

NOTE Confidence: 0.854828793888889

 $00:28:50.456 \rightarrow 00:28:53.064$ second case so this is another one of

NOTE Confidence: 0.854828793888889

 $00:28:53.064 \rightarrow 00:28:55.102$ my favorite patients who I've been

NOTE Confidence: 0.854828793888889

 $00:28:55.102 \rightarrow 00:28:57.692$ following pretty much from the bright after.

NOTE Confidence: 0.854828793888889

00:28:57.700 --> 00:28:59.340 I think he may have been one of the first

NOTE Confidence: 0.854828793888889

00:28:59.380 --> 00:29:00.980 patients I had as a brand new attending,

NOTE Confidence: 0.854828793888889

 $00:29:00.980 \rightarrow 00:29:03.339$ and I've been following him ever since.

 $00:29:03.340 \longrightarrow 00:29:05.538$ At the time I first saw him,

NOTE Confidence: 0.854828793888889

 $00{:}29{:}05{.}540 \dashrightarrow 00{:}29{:}06{.}515$ he was 35.

NOTE Confidence: 0.854828793888889

 $00{:}29{:}06{.}515 \dashrightarrow 00{:}29{:}09{.}779$ He was somebody who like many of my patients,

NOTE Confidence: 0.854828793888889

00:29:09.780 --> 00:29:11.565 said he's always been a night owl,

NOTE Confidence: 0.854828793888889

 $00{:}29{:}11{.}570 \dashrightarrow 00{:}29{:}13{.}954$ but he came in because at some point

NOTE Confidence: 0.854828793888889

 $00:29:13.954 \rightarrow 00:29:16.044$ things got worse and he could no

NOTE Confidence: 0.854828793888889

 $00:29:16.044 \longrightarrow 00:29:18.050$ longer follow a 24 hour schedule

NOTE Confidence: 0.854828793888889

 $00{:}29{:}18.050 \dashrightarrow 00{:}29{:}19.352$ I've dubbed in the Martian because

NOTE Confidence: 0.854828793888889

 $00{:}29{:}19{.}352 \dashrightarrow 00{:}29{:}21{.}122$ a lot of my patients with this

NOTE Confidence: 0.854828793888889

 $00{:}29{:}21.122 \dashrightarrow 00{:}29{:}22.537$ disorder will refer to themselves

NOTE Confidence: 0.854828793888889

 $00{:}29{:}22{.}537 \dashrightarrow 00{:}29{:}24{.}521$ as that because the Mars day is a

NOTE Confidence: 0.854828793888889

 $00:29:24.521 \rightarrow 00:29:27.629$ little bit longer than the Earth Day.

NOTE Confidence: 0.854828793888889

 $00:29:27.630 \longrightarrow 00:29:29.730$ So, like many of my patients,

NOTE Confidence: 0.854828793888889

 $00:29:29.730 \longrightarrow 00:29:31.595$ he had kept meticulously blogs

NOTE Confidence: 0.854828793888889

00:29:31.595 - 00:29:33.750 before he came to see me,

NOTE Confidence: 0.854828793888889

 $00:29:33.750 \longrightarrow 00:29:36.095$ and this is just an example of

- NOTE Confidence: 0.854828793888889
- 00:29:36.095 00:29:38.467 what his sleep looked like before
- NOTE Confidence: 0.854828793888889
- $00{:}29{:}38.467 \dashrightarrow 00{:}29{:}41.047$ things started to get even worse.
- NOTE Confidence: 0.854828793888889
- $00:29:41.050 \rightarrow 00:29:43.010$ What I have here is a double plot,
- NOTE Confidence: 0.854828793888889
- $00:29:43.010 \rightarrow 00:29:45.327$ and so we've got this sleep period.
- NOTE Confidence: 0.854828793888889
- $00:29:45.330 \longrightarrow 00:29:47.148$ Up here is replatted down here.
- NOTE Confidence: 0.854828793888889
- 00:29:47.150 --> 00:29:48.790 This is 48 hours and you'll see why
- NOTE Confidence: 0.854828793888889
- $00{:}29{:}48.790 \dashrightarrow 00{:}29{:}50.513$ in the next slides it's a little
- NOTE Confidence: 0.854828793888889
- $00:29:50.513 \rightarrow 00:29:52.030$ easier to plot things this way,
- NOTE Confidence: 0.854828793888889
- 00:29:52.030 --> 00:29:53.353 but if you wanted to just focus
- NOTE Confidence: 0.854828793888889
- $00:29:53.353 \rightarrow 00:29:54.787$ on the right side to begin with.
- NOTE Confidence: 0.854828793888889
- $00:29:54.790 \longrightarrow 00:29:56.494$ What we have is kind of what we
- NOTE Confidence: 0.854828793888889
- $00:29:56.494 \rightarrow 00:29:57.870$ typically see with these delayed.
- NOTE Confidence: 0.854828793888889
- $00:29:57.870 \longrightarrow 00:30:00.072$ Emotions that they sort of force
- NOTE Confidence: 0.854828793888889
- $00{:}30{:}00{.}072 \dashrightarrow 00{:}30{:}02{.}576$ themselves into a midnight to $8{:}00$ AM
- NOTE Confidence: 0.854828793888889
- $00:30:02.576 \rightarrow 00:30:04.514$ scheduled during the week they delayed
- NOTE Confidence: 0.854828793888889

 $00:30:04.514 \rightarrow 00:30:07.398$ to their preferred schedule on the weekend,

NOTE Confidence: 0.854828793888889

 $00:30:07.400 \longrightarrow 00:30:08.918$ and then they go back and

NOTE Confidence: 0.854828793888889

 $00{:}30{:}08{.}918 \dashrightarrow 00{:}30{:}10{.}340$ forth and back and forth.

NOTE Confidence: 0.854828793888889

 $00:30:10.340 \longrightarrow 00:30:14.480$ It's not great, but they can live with it.

NOTE Confidence: 0.854828793888889

00:30:14.480 --> 00:30:16.503 He saw a very well meaning sleep

NOTE Confidence: 0.854828793888889

 $00{:}30{:}16{.}503 \dashrightarrow 00{:}30{:}18{.}412$ provider who was trying to treat

NOTE Confidence: 0.854828793888889

 $00:30:18.412 \rightarrow 00:30:20.362$ him initially by giving him some

NOTE Confidence: 0.854828793888889

00:30:20.362 --> 00:30:21.988 bright light in the morning,

NOTE Confidence: 0.854828793888889

 $00:30:21.990 \rightarrow 00:30:25.370$ which you can see here and then he was

NOTE Confidence: 0.854828793888889

 $00:30:25.370 \rightarrow 00:30:27.110$ instructed to follow Chronotherapy.

NOTE Confidence: 0.854828793888889

 $00:30:27.110 \longrightarrow 00:30:29.282$ So that idea of gradually delaying

NOTE Confidence: 0.854828793888889

00:30:29.282 --> 00:30:31.809 your sleep wake period until you reach

NOTE Confidence: 0.854828793888889

 $00:30:31.809 \rightarrow 00:30:34.168$ the point where you're going to sleep

NOTE Confidence: 0.854828793888889

 $00:30:34.231 \rightarrow 00:30:36.248$ and waking up when you prefer to.

NOTE Confidence: 0.854828793888889

 $00:30:36.248 \dashrightarrow 00:30:38.102$ And at that point you're supposed

NOTE Confidence: 0.854828793888889

 $00:30:38.102 \longrightarrow 00:30:40.380$ to try to put the brakes on it

- NOTE Confidence: 0.854828793888889
- $00:30:40.380 \dashrightarrow 00:30:42.060$ and keep things from delaying.
- NOTE Confidence: 0.854828793888889
- $00:30:42.060 \longrightarrow 00:30:43.836$ And with that he was supposed
- NOTE Confidence: 0.854828793888889
- $00:30:43.836 \longrightarrow 00:30:45.020$ to start taking melatonin.
- NOTE Confidence: 0.854828793888889
- $00{:}30{:}45{.}020 \dashrightarrow 00{:}30{:}49{.}260$ As indicated in green and using bright light.
- NOTE Confidence: 0.854828793888889
- 00:30:49.260 --> 00:30:49.870 Unfortunately,
- NOTE Confidence: 0.854828793888889
- $00:30:49.870 \rightarrow 00:30:54.140$ he started drifting and just kept going,
- NOTE Confidence: 0.854828793888889
- $00:30:54.140 \longrightarrow 00:30:55.344$ and so by the time he came
- NOTE Confidence: 0.854828793888889
- $00:30:55.344 \longrightarrow 00:30:56.579$ to see me in the office,
- NOTE Confidence: 0.854828793888889
- $00{:}30{:}56{.}580 \dashrightarrow 00{:}30{:}58{.}918$ this is what his actigraphy looked like,
- NOTE Confidence: 0.854828793888889
- $00:30:58.920 \rightarrow 00:31:02.016$ and you can barely make out his activity.
- NOTE Confidence: 0.919239327777778
- $00:31:02.020 \rightarrow 00:31:04.148$ He overall tends to be a fairly
- NOTE Confidence: 0.91923932777778
- $00{:}31{:}04{.}148 \dashrightarrow 00{:}31{:}05{.}760$ inactive person, but if you kind
- NOTE Confidence: 0.919239327777778
- $00{:}31{:}05{.}760 \dashrightarrow 00{:}31{:}07{.}750$ of lean back and squint a little,
- NOTE Confidence: 0.919239327777778
- $00{:}31{:}07{.}750 \dashrightarrow 00{:}31{:}09{.}862$ you can see that his onset of activity
- NOTE Confidence: 0.919239327777778
- $00:31:09.862 \longrightarrow 00:31:11.791$ every day gets a little later and
- NOTE Confidence: 0.91923932777778

 $00:31:11.791 \longrightarrow 00:31:13.688$ a little later, and a little later.

NOTE Confidence: 0.919239327777778

 $00:31:13.688 \rightarrow 00:31:15.320$ This is an outlier here because

NOTE Confidence: 0.919239327777778

00:31:15.378 --> 00:31:16.978 he had a doctor's appointment.

NOTE Confidence: 0.919239327777778

 $00:31:16.980 \rightarrow 00:31:18.786$ The other thing that's noteworthy about him,

NOTE Confidence: 0.91923932777778

 $00:31:18.790 \longrightarrow 00:31:20.980$ and we'll get to this later.

NOTE Confidence: 0.91923932777778

 $00{:}31{:}20{.}980 \dashrightarrow 00{:}31{:}23{.}348$ He really doesn't have a lot of light

NOTE Confidence: 0.91923932777778

 $00{:}31{:}23{.}348 \dashrightarrow 00{:}31{:}25{.}596$ exposure and so you can see that that

NOTE Confidence: 0.91923932777778

 $00{:}31{:}25{.}596 \dashrightarrow 00{:}31{:}27{.}486$ yellow line here has very low amplitude

NOTE Confidence: 0.91923932777778

 $00{:}31{:}27{.}486 \dashrightarrow 00{:}31{:}30{.}206$ to it and if you talk to him about this,

NOTE Confidence: 0.919239327777778

00:31:30.206 --> 00:31:31.766 he really prefers to spend

NOTE Confidence: 0.919239327777778

 $00:31:31.766 \longrightarrow 00:31:33.620$ his time in dimly lit rooms.

NOTE Confidence: 0.919239327777778

 $00:31:33.620 \longrightarrow 00:31:35.540$ He finds bright light,

NOTE Confidence: 0.919239327777778

 $00{:}31{:}35{.}540 \dashrightarrow 00{:}31{:}37{.}940$ kind of irritating and just

NOTE Confidence: 0.91923932777778

 $00:31:37.940 \longrightarrow 00:31:39.858$ really doesn't like it.

NOTE Confidence: 0.919239327777778

 $00{:}31{:}39{.}860 \dashrightarrow 00{:}31{:}41{.}756$ So he fits the criteria for non 24

NOTE Confidence: 0.919239327777778

 $00:31:41.756 \rightarrow 00:31:43.206$ hour sleep break rhythm disorder

00:31:43.206 --> 00:31:45.348 and if I didn't mention this before,

NOTE Confidence: 0.919239327777778

 $00:31:45.350 \rightarrow 00:31:47.394$ he does have normal image forming vision.

NOTE Confidence: 0.919239327777778

 $00:31:47.400 \longrightarrow 00:31:50.550$ So this is not a blind patient.

NOTE Confidence: 0.919239327777778

 $00:31:50.550 \longrightarrow 00:31:52.622$ So for non 24 they can come in

NOTE Confidence: 0.919239327777778

 $00:31:52.622 \dashrightarrow 00:31:54.769$ with lots of different complaints.

NOTE Confidence: 0.91923932777778

00:31:54.770 - 00:31:56.950 They can either have insomnia,

NOTE Confidence: 0.919239327777778

 $00:31:56.950 \rightarrow 00:31:58.685$ excessive daytime sleepiness or maybe

NOTE Confidence: 0.91923932777778

 $00:31:58.685 \rightarrow 00:32:01.088$ both depending on where you hit them

NOTE Confidence: 0.919239327777778

 $00{:}32{:}01.088 \dashrightarrow 00{:}32{:}02.930$ within that constant delay and cycle.

NOTE Confidence: 0.919239327777778

 $00{:}32{:}02{.}930 \dashrightarrow 00{:}32{:}04{.}298$ Some of them have figured out

NOTE Confidence: 0.919239327777778

 $00:32:04.298 \longrightarrow 00:32:04.982$ what's going on,

NOTE Confidence: 0.91923932777778

 $00{:}32{:}04{.}990 \dashrightarrow 00{:}32{:}06{.}488$ but it's something to keep in mind

NOTE Confidence: 0.919239327777778

 $00{:}32{:}06{.}488 \dashrightarrow 00{:}32{:}08{.}331$ if you have some body who just cannot

NOTE Confidence: 0.919239327777778

 $00{:}32{:}08{.}331 \dashrightarrow 00{:}32{:}10{.}300$ describe their sleep wake schedule to you.

NOTE Confidence: 0.919239327777778

 $00:32:10.300 \longrightarrow 00:32:11.492$ Investigating a little bit

 $00:32:11.492 \longrightarrow 00:32:12.684$ further with that trigger.

NOTE Confidence: 0.91923932777778

 $00{:}32{:}12.690 \dashrightarrow 00{:}32{:}15.687$ Fear sleep logs to really get a sense of

NOTE Confidence: 0.919239327777778

 $00:32:15.687 \rightarrow 00:32:18.700$ what the pattern is can be very helpful.

NOTE Confidence: 0.91923932777778

 $00:32:18.700 \rightarrow 00:32:20.218$ In terms of what causes this,

NOTE Confidence: 0.91923932777778

 $00{:}32{:}20{.}220 \dashrightarrow 00{:}32{:}22{.}220$ so this was first described

NOTE Confidence: 0.919239327777778

 $00{:}32{:}22{.}220 \dashrightarrow 00{:}32{:}23{.}420$ in blind individuals.

NOTE Confidence: 0.91923932777778

 $00:32:23.420 \longrightarrow 00:32:24.500$ We're going to get into this

NOTE Confidence: 0.91923932777778

 $00:32:24.500 \longrightarrow 00:32:25.500$ a little bit more later,

NOTE Confidence: 0.91923932777778

 $00{:}32{:}25{.}500 \dashrightarrow 00{:}32{:}27{.}642$ but really it makes sense if

NOTE Confidence: 0.919239327777778

 $00:32:27.642 \rightarrow 00:32:29.580$ you lose that photic input.

NOTE Confidence: 0.919239327777778

 $00:32:29.580 \longrightarrow 00:32:32.415$ If you lose that light signal to the SDN,

NOTE Confidence: 0.91923932777778

 $00:32:32.420 \longrightarrow 00:32:34.160$ telling the SDN when it's

NOTE Confidence: 0.91923932777778

00:32:34.160 - 00:32:35.900 night and when it's daytime,

NOTE Confidence: 0.919239327777778

 $00{:}32{:}35{.}900 \dashrightarrow 00{:}32{:}37{.}682$ you're then going to follow that

NOTE Confidence: 0.91923932777778

 $00:32:37.682 \rightarrow 00:32:39.497$ intrinsic rhythm and get later and

NOTE Confidence: 0.919239327777778

 $00:32:39.497 \rightarrow 00:32:41.213$ later and so in blind individuals.

00:32:41.220 --> 00:32:42.740 This has been previously described,

NOTE Confidence: 0.919239327777778

 $00:32:42.740 \longrightarrow 00:32:43.988$ although not everybody who's

NOTE Confidence: 0.919239327777778

 $00:32:43.988 \longrightarrow 00:32:45.236$ blind has this disorder.

NOTE Confidence: 0.919239327777778

 $00:32:45.240 \longrightarrow 00:32:46.940$ To keep that in mind.

NOTE Confidence: 0.919239327777778

 $00{:}32{:}46{.}940 \dashrightarrow 00{:}32{:}49{.}190$ And then in our patient here we do see

NOTE Confidence: 0.91923932777778

 $00:32:49.190 \longrightarrow 00:32:51.575$ a lot of these in sighted patients.

NOTE Confidence: 0.919239327777778

00:32:51.580 --> 00:32:52.978 It's likely multifactorial.

NOTE Confidence: 0.91923932777778

00:32:52.978 --> 00:32:55.774 A combination of minimal social cues,

NOTE Confidence: 0.91923932777778

00:32:55.780 --> 00:32:57.259 potentially a prolonged

NOTE Confidence: 0.919239327777778

00:32:57.259 --> 00:32:58.738 intrinsic circadian period,

NOTE Confidence: 0.919239327777778

 $00{:}32{:}58{.}740 \dashrightarrow 00{:}33{:}01{.}348$ and what I most often see is that

NOTE Confidence: 0.91923932777778

 $00{:}33{:}01{.}348 \dashrightarrow 00{:}33{:}03{.}240$ these individuals will start as what

NOTE Confidence: 0.919239327777778

 $00:33:03.240 \rightarrow 00:33:05.580$ we call sort of the extreme delayed,

NOTE Confidence: 0.919239327777778

 $00:33:05.580 \rightarrow 00:33:07.116$ and then eventually they just sort

NOTE Confidence: 0.919239327777778

 $00:33:07.116 \longrightarrow 00:33:08.918$ of fall off and become non 24,

 $00:33:08.920 \longrightarrow 00:33:11.678$ and they may alternate and go back

NOTE Confidence: 0.91923932777778

 $00{:}33{:}11.678 \dashrightarrow 00{:}33{:}14.131$ and forth between the semi stable

NOTE Confidence: 0.919239327777778

 $00:33:14.131 \rightarrow 00:33:16.507$ and trainment and being non 24.

NOTE Confidence: 0.919239327777778

 $00:33:16.510 \longrightarrow 00:33:18.634$ So going through the task force

NOTE Confidence: 0.919239327777778

 $00{:}33{:}18.634 \dashrightarrow 00{:}33{:}20.050$ guidelines on basically there

NOTE Confidence: 0.919239327777778

 $00{:}33{:}20.109 \dashrightarrow 00{:}33{:}22.083$ is a recommendation for the use

NOTE Confidence: 0.91923932777778

 $00:33:22.083 \longrightarrow 00:33:23.070$ of timed melatonin.

NOTE Confidence: 0.919239327777778

00:33:23.070 - 00:33:26.002 Clinically, what we tend to do in blind,

NOTE Confidence: 0.91923932777778

 $00:33:26.002 \longrightarrow 00:33:27.186$ we'll still follow that,

NOTE Confidence: 0.919239327777778

 $00:33:27.190 \longrightarrow 00:33:29.365$ so typically using half a

NOTE Confidence: 0.919239327777778

00:33:29.365 --> 00:33:31.105 milligram to 3 milligrams,

NOTE Confidence: 0.919239327777778

 $00:33:31.110 \dashrightarrow 00:33:33.270$ taking an hour before desired bedtime,

NOTE Confidence: 0.91923932777778

 $00:33:33.270 \longrightarrow 00:33:35.240$ they're also is the approved

NOTE Confidence: 0.91923932777778

 $00:33:35.240 \longrightarrow 00:33:36.028$ medication tasimelteon,

NOTE Confidence: 0.91923932777778

 $00:33:36.030 \rightarrow 00:33:38.550$ which we'll talk about in the next slide.

NOTE Confidence: 0.919239327777778

00:33:38.550 --> 00:33:39.378 In sighted individuals,

 $00:33:39.378 \longrightarrow 00:33:41.990$ it tends to get a little more complicated,

NOTE Confidence: 0.91923932777778

 $00{:}33{:}41{.}990 \dashrightarrow 00{:}33{:}44{.}748$ and so we have a number of

NOTE Confidence: 0.919239327777778

 $00:33:44.748 \longrightarrow 00:33:45.930$ different protocols we've

NOTE Confidence: 0.878777485

 $00:33:46.010 \rightarrow 00:33:49.302$ been trying. We will often do half a

NOTE Confidence: 0.878777485

 $00:33:49.302 \dashrightarrow 00:33:51.556$ milligram of melatonin, about five

NOTE Confidence: 0.878777485

 $00:33:51.556 \rightarrow 00:33:54.196$ hours before their desired bedtime,

NOTE Confidence: 0.878777485

 $00:33:54.200 \rightarrow 00:33:56.538$ as more of the phase shifting dose,

NOTE Confidence: 0.878777485

 $00{:}33{:}56{.}540 \dashrightarrow 00{:}33{:}58{.}563$ and then an additional 1 milligram of

NOTE Confidence: 0.878777485

 $00:33:58.563 \dashrightarrow 00:34:00.375$ melatonin an hour before their desired NOTE Confidence: 0.878777485

 $00:34:00.375 \rightarrow 00:34:02.440$ bedtime is more of a hypnotic dose.

NOTE Confidence: 0.878777485

 $00:34:02.440 \rightarrow 00:34:04.336$ Once they're close to their desired

NOTE Confidence: 0.878777485

 $00{:}34{:}04{.}336 \dashrightarrow 00{:}34{:}06{.}739$ bed time to try to anchor them there,

NOTE Confidence: 0.878777485

00:34:06.740 --> 00:34:08.960 we'll use very strict sleep schedules,

NOTE Confidence: 0.878777485

 $00{:}34{:}08{.}960 \dashrightarrow 00{:}34{:}11{.}060$ timed light exposure when they wake up,

NOTE Confidence: 0.878777485

 $00{:}34{:}11.060 \dashrightarrow 00{:}34{:}13.068$ and then we'll talk a little bit more

 $00:34:13.068 \rightarrow 00:34:15.090$ about some of these other things we've

NOTE Confidence: 0.878777485

 $00{:}34{:}15.090 \dashrightarrow 00{:}34{:}16.870$ used feeding and activity as well.

NOTE Confidence: 0.878777485

00:34:16.870 --> 00:34:19.229 Just to go through has a meltdown,

NOTE Confidence: 0.878777485

 $00:34:19.230 \longrightarrow 00:34:21.246$ so this is a melatonin agonist.

NOTE Confidence: 0.878777485

 $00{:}34{:}21.250 \dashrightarrow 00{:}34{:}23.635$ This is the data from the set and reset

NOTE Confidence: 0.878777485

 $00{:}34{:}23.635 \dashrightarrow 00{:}34{:}25.668$ trial indicating its effectiveness,

NOTE Confidence: 0.878777485

 $00:34:25.670 \longrightarrow 00:34:27.637$ and in this trial they were just

NOTE Confidence: 0.878777485

 $00:34:27.637 \rightarrow 00:34:29.615$ looking at blind individuals and they

NOTE Confidence: 0.878777485

00:34:29.615 --> 00:34:32.412 found that 20% of the patients in the

NOTE Confidence: 0.878777485

00:34:32.412 --> 00:34:33.962 ta
simelteon group met their criteria

NOTE Confidence: 0.878777485

 $00{:}34{:}33{.}962 \dashrightarrow 00{:}34{:}35{.}950$ for in treatment at one month compared

NOTE Confidence: 0.878777485

 $00:34:36.001 \rightarrow 00:34:38.212$ to only 3% in the placebo group.

NOTE Confidence: 0.878777485

 $00:34:38.212 \longrightarrow 00:34:39.924$ So this is approved.

NOTE Confidence: 0.878777485

 $00:34:39.930 \longrightarrow 00:34:40.364$ Technically,

NOTE Confidence: 0.878777485

 $00{:}34{:}40{.}364 \dashrightarrow 00{:}34{:}42{.}968$ the FDA indications do not specify

NOTE Confidence: 0.878777485

 $00:34:42.968 \rightarrow 00:34:45.990$ that you have to be blind or sighted,

- NOTE Confidence: 0.878777485
- $00:34:45.990 \longrightarrow 00:34:47.206$ just that you're not.
- NOTE Confidence: 0.878777485
- 00:34:47.206 --> 00:34:48.726 24 although sometimes you will
- NOTE Confidence: 0.878777485
- $00:34:48.726 \rightarrow 00:34:50.548$ run into issues with insurance,
- NOTE Confidence: 0.878777485
- $00:34:50.550 \rightarrow 00:34:52.061$ trying to say that oh, they're not blind,
- NOTE Confidence: 0.878777485
- $00:34:52.061 \longrightarrow 00:34:53.146$ we're not gonna cover this.
- NOTE Confidence: 0.878777485
- $00{:}34{:}53.150 \dashrightarrow 00{:}34{:}54.670$ U sually that can be addressed
- NOTE Confidence: 0.878777485
- $00:34:54.670 \longrightarrow 00:34:56.190$ in a peer to peer.
- NOTE Confidence: 0.878777485
- 00:34:56.190 --> 00:34:58.188 The main reason I don't use this more though,
- NOTE Confidence: 0.878777485
- $00:34:58.190 \longrightarrow 00:34:59.968$ is that if you look down here,
- NOTE Confidence: 0.878777485
- $00:34:59.970 \longrightarrow 00:35:02.980$ the price of one month supply of
- NOTE Confidence: 0.878777485
- $00:35:02.980 \longrightarrow 00:35:05.692$ tasimelteon is about \$23,000 compared to
- NOTE Confidence: 0.878777485
- $00:35:05.692 \longrightarrow 00:35:09.010$ \$3.00 for one month supply of melatonin.
- NOTE Confidence: 0.878777485
- $00:35:09.010 \rightarrow 00:35:10.610$ I don't have anything personally
- NOTE Confidence: 0.878777485
- 00:35:10.610 --> 00:35:11.570 against hazing Melton.
- NOTE Confidence: 0.878777485
- $00{:}35{:}11.570 \dashrightarrow 00{:}35{:}12.872$ I think I've gotten a reputation
- NOTE Confidence: 0.878777485

 $00:35:12.872 \rightarrow 00:35:14.090$ as somebody who doesn't like it.

NOTE Confidence: 0.878777485

 $00{:}35{:}14.090 \dashrightarrow 00{:}35{:}14.867$ It does work.

NOTE Confidence: 0.878777485

00:35:14.867 - 00:35:17.160 I just like to try the cheaper option.

NOTE Confidence: 0.878777485

 $00:35:17.160 \dashrightarrow 00:35:18.810$ 1st and then move to tasimelteon.

NOTE Confidence: 0.878777485

 $00{:}35{:}18.810 \dashrightarrow 00{:}35{:}23.108$ If I can't reach success with melaton in.

NOTE Confidence: 0.878777485

 $00:35:23.110 \dashrightarrow 00:35:25.258$ So we started treating that individual NOTE Confidence: 0.878777485

 $00:35:25.258 \dashrightarrow 00:35:28.549$ and he got back to me after we got his

NOTE Confidence: 0.878777485

 $00:35:28.549 \rightarrow 00:35:31.007$ sleep wake schedule on track and he said,

NOTE Confidence: 0.878777485

 $00{:}35{:}31{.}010 \dashrightarrow 00{:}35{:}31{.}264$ well.

NOTE Confidence: 0.878777485

00:35:31.264 --> 00:35:32.788 I'm going to bed and waking

NOTE Confidence: 0.878777485

 $00{:}35{:}32{.}788 \dashrightarrow 00{:}35{:}34{.}090$ up when I want to,

NOTE Confidence: 0.878777485

 $00:35:34.090 \longrightarrow 00:35:35.623$ but now it really feels like my

NOTE Confidence: 0.878777485

 $00:35:35.623 \rightarrow 00:35:37.280$ body has three different schedules.

NOTE Confidence: 0.878777485

 $00:35:37.280 \longrightarrow 00:35:38.954$ My physical self now seems to

NOTE Confidence: 0.878777485

 $00{:}35{:}38{.}954 \dashrightarrow 00{:}35{:}40{.}630$ follow a more normal schedule.

NOTE Confidence: 0.878777485

 $00:35:40.630 \rightarrow 00:35:42.814$ My mental self seems to be highly

 $00:35:42.814 \rightarrow 00:35:44.559$ nocturnal and my metabolism has

NOTE Confidence: 0.878777485

 $00{:}35{:}44{.}559 \dashrightarrow 00{:}35{:}47{.}142$ changed to require only one small meal

NOTE Confidence: 0.878777485

00:35:47.142 --> 00:35:49.387 every 24 hours instead of 12 hours.

NOTE Confidence: 0.878777485

 $00:35:49.390 \rightarrow 00:35:51.982$ And for me this was really

NOTE Confidence: 0.878777485

 $00{:}35{:}51{.}982 \dashrightarrow 00{:}35{:}54{.}263$ interesting because this to me

NOTE Confidence: 0.878777485

 $00:35:54.263 \dashrightarrow 00:35:56.598$ said we have desynchronized him,

NOTE Confidence: 0.878777485

 $00{:}35{:}56.600 \dashrightarrow 00{:}35{:}58.707$ so I mentioned that we have clocks

NOTE Confidence: 0.878777485

 $00{:}35{:}58.707 \dashrightarrow 00{:}36{:}00.750$ throughout our all throughout our body

NOTE Confidence: 0.878777485

 $00{:}36{:}00{.}750 \dashrightarrow 00{:}36{:}02{.}717$ and it seemed like we had gotten.

NOTE Confidence: 0.878777485

00:36:02.720 --> 00:36:05.320 Sleep wake schedule on track.

NOTE Confidence: 0.878777485

 $00:36:05.320 \rightarrow 00:36:07.660$ But for example, his peripheral clocks.

NOTE Confidence: 0.878777485

 $00{:}36{:}07.660 \dashrightarrow 00{:}36{:}10.796$ His metabolism was not in line with that,

NOTE Confidence: 0.878777485

 $00{:}36{:}10.800 \dashrightarrow 00{:}36{:}12.944$ so we got some sleep or some food

NOTE Confidence: 0.878777485

00:36:12.944 --> 00:36:15.273 logs from him and you can see just

NOTE Confidence: 0.878777485

 $00{:}36{:}15{.}273 \dashrightarrow 00{:}36{:}17{.}789$ listed here his meals and I did some

 $00:36:17.789 \longrightarrow 00:36:19.414$ estimated calories and it really

NOTE Confidence: 0.878777485

00:36:19.414 --> 00:36:21.610 like you said he's just eating

NOTE Confidence: 0.878777485

 $00:36:21.610 \rightarrow 00:36:23.873$ one meal encompassing most of his

NOTE Confidence: 0.878777485

 $00:36:23.873 \longrightarrow 00:36:26.078$ calories for the day at one time.

NOTE Confidence: 0.878777485

 $00{:}36{:}26.080 \dashrightarrow 00{:}36{:}28.768$ And so we started to do some additional

NOTE Confidence: 0.878777485

00:36:28.768 --> 00:36:31.116 work with him on adjusting food timing. NOTE Confidence: 0.878777485

 $00:36:31.116 \rightarrow 00:36:33.210$ Really coming up with the skeleton.

NOTE Confidence: 0.847453348181818

 $00{:}36{:}33{.}210 \dashrightarrow 00{:}36{.}36{.}050$ Eating period to be in alignment with his

NOTE Confidence: 0.847453348181818

 $00:36:36.050 \rightarrow 00:36:38.460$ sleep wake timing and we managed to get NOTE Confidence: 0.847453348181818

 $00:36:38.460 \longrightarrow 00:36:40.598$ him in trained and so now here he is.

NOTE Confidence: 0.847453348181818

 $00{:}36{:}40{.}600 \dashrightarrow 00{:}36{:}42{.}904$ He's still diligently and if this is now

NOTE Confidence: 0.847453348181818

 $00:36:42.904 \rightarrow 00:36:45.311$ 10 years later I think almost he continues

NOTE Confidence: 0.847453348181818

 $00:36:45.311 \longrightarrow 00:36:47.454$ to send me these monthly sleep Diaries

NOTE Confidence: 0.847453348181818

 $00:36:47.454 \rightarrow 00:36:49.904$ just to show me he's still on track.

NOTE Confidence: 0.847453348181818

 $00:36:49.904 \rightarrow 00:36:51.280$ He's still in trained.

NOTE Confidence: 0.847453348181818

 $00:36:51.280 \longrightarrow 00:36:52.927$ We were able to get him back to work.

 $00{:}36{:}52{.}930 \dashrightarrow 00{:}36{:}55{.}082$ He's on a flexible schedule now so he

NOTE Confidence: 0.847453348181818

 $00:36:55.082 \rightarrow 00:36:57.257$ works more of like a second shift hour,

NOTE Confidence: 0.847453348181818

 $00:36:57.260 \longrightarrow 00:36:59.703$ but he's going to work everyday and

NOTE Confidence: 0.847453348181818

 $00:36:59.703 \dashrightarrow 00:37:02.048$ is pretty happy with the schedule.

NOTE Confidence: 0.847453348181818

 $00:37:02.050 \longrightarrow 00:37:04.150$ So that leads to the final question,

NOTE Confidence: 0.847453348181818

00:37:04.150 -> 00:37:06.340 which is why do patients develop

NOTE Confidence: 0.847453348181818

00:37:06.340 --> 00:37:08.240 delayed sleep, wake phase disorder,

NOTE Confidence: 0.847453348181818

 $00:37:08.240 \longrightarrow 00:37:09.410$ and more importantly,

NOTE Confidence: 0.847453348181818

 $00{:}37{:}09{.}410 \dashrightarrow 00{:}37{:}11{.}880$ why do sighted patients develop

NOTE Confidence: 0.847453348181818

 $00{:}37{:}11{.}880 \dashrightarrow 00{:}37{:}14{.}510$ non 24 and we think about this

NOTE Confidence: 0.847453348181818

00:37:14.510 --> 00:37:16.850 first in terms of light exposure.

NOTE Confidence: 0.847453348181818

 $00{:}37{:}16.850 \dashrightarrow 00{:}37{:}18.810$ So if we go back to that idea

NOTE Confidence: 0.847453348181818

 $00{:}37{:}18.810 \dashrightarrow 00{:}37{:}20.070$ of in treatment,

NOTE Confidence: 0.847453348181818

 $00{:}37{:}20.070 \dashrightarrow 00{:}37{:}23.750$ so how do the rest of us without

NOTE Confidence: 0.847453348181818

 $00{:}37{:}23.750 \dashrightarrow 00{:}37{:}25.615$ circulating disorders sleep when it's

 $00:37:25.615 \rightarrow 00:37:27.820$ dark and be awake during the daytime?

NOTE Confidence: 0.847453348181818

 $00{:}37{:}27.820 \dashrightarrow 00{:}37{:}30.025$ And we think a lot of that comes from

NOTE Confidence: 0.847453348181818

00:37:30.025 - 00:37:31.908 that daily exposure to sunshine.

NOTE Confidence: 0.847453348181818

 $00:37:31.910 \rightarrow 00:37:34.235$ Giving us that morning advancing

NOTE Confidence: 0.847453348181818

 $00:37:34.235 \longrightarrow 00:37:36.513$ signal to keep us in line so that

NOTE Confidence: 0.847453348181818

00:37:36.513 --> 00:37:37.939 we're asleep when it's dark.

NOTE Confidence: 0.847453348181818

 $00:37:37.940 \longrightarrow 00:37:39.668$ So one theory for delayed sleep,

NOTE Confidence: 0.847453348181818

 $00:37:39.670 \longrightarrow 00:37:40.519$ wake phase disorders.

NOTE Confidence: 0.847453348181818

 $00{:}37{:}40.519 \dashrightarrow 00{:}37{:}42.500$ Oh these are people who are just

NOTE Confidence: 0.847453348181818

00:37:42.557 --> 00:37:44.496 staying up later and waking up later,

NOTE Confidence: 0.847453348181818

 $00{:}37{:}44.500 \dashrightarrow 00{:}37{:}45.982$ so may be they're getting too much

NOTE Confidence: 0.847453348181818

 $00:37:45.982 \longrightarrow 00:37:47.553$ light at night and it's pushing

NOTE Confidence: 0.847453348181818

 $00{:}37{:}47{.}553 \dashrightarrow 00{:}37{:}49{.}149$ them even later and they're getting

NOTE Confidence: 0.847453348181818

 $00:37:49.149 \longrightarrow 00:37:50.350$ less of that morning.

NOTE Confidence: 0.847453348181818

 $00:37:50.350 \dashrightarrow 00:37:51.778$ Advancing signal because they're

NOTE Confidence: 0.847453348181818

 $00:37:51.778 \longrightarrow 00:37:53.920$ just not waking up in time.

 $00:37:53.920 \rightarrow 00:37:55.750$ So we did one study trying to look at that,

NOTE Confidence: 0.847453348181818

 $00{:}37{:}55{.}750 \dashrightarrow 00{:}37{:}57{.}298$ and there are several of these

NOTE Confidence: 0.847453348181818

 $00:37:57.298 \longrightarrow 00:37:58.072$ out there published,

NOTE Confidence: 0.847453348181818

 $00:37:58.080 \longrightarrow 00:38:00.460$ and certainly if you look on the

NOTE Confidence: 0.847453348181818

 $00:38:00.460 \longrightarrow 00:38:02.746$ left hand panel here at light

NOTE Confidence: 0.847453348181818

00:38:02.746 --> 00:38:04.736 exposure related to clock time,

NOTE Confidence: 0.847453348181818

 $00:38:04.740 \longrightarrow 00:38:06.672$ our delayed patients are here in blue

NOTE Confidence: 0.847453348181818

 $00:38:06.672 \dashrightarrow 00:38:08.852$ and you can see that midnight is over

NOTE Confidence: 0.847453348181818

 $00:38:08.852 \rightarrow 00:38:10.800$ here on the left and really anywhere

NOTE Confidence: 0.847453348181818

 $00:38:10.800 \longrightarrow 00:38:13.184$ from about 10:00 PM to about 4:00 AM.

NOTE Confidence: 0.847453348181818

00:38:13.190 --> 00:38:14.590 They're definitely getting more

NOTE Confidence: 0.847453348181818

 $00{:}38{:}14.590 \dashrightarrow 00{:}38{:}16.340$ light exposure than our controls,

NOTE Confidence: 0.847453348181818

 $00:38:16.340 \rightarrow 00:38:18.254$ getting much less light first thing

NOTE Confidence: 0.847453348181818

 $00:38:18.254 \dashrightarrow 00:38:20.618$ in the morning up until about noon.

NOTE Confidence: 0.847453348181818

 $00:38:20.620 \rightarrow 00:38:21.424$ But interestingly,

 $00:38:21.424 \longrightarrow 00:38:24.238$ if you align that based on their.

NOTE Confidence: 0.847453348181818

 $00{:}38{:}24{.}240 \dashrightarrow 00{:}38{:}26{.}328$ Clock time so their internal time,

NOTE Confidence: 0.847453348181818

 $00:38:26.330 \dashrightarrow 00:38:29.000$ so using dim light melaton in onset

NOTE Confidence: 0.847453348181818

 $00:38:29.000 \rightarrow 00:38:32.707$ you can see that actually on this end.

NOTE Confidence: 0.847453348181818

 $00:38:32.710 \longrightarrow 00:38:35.391$ So in that region of fades delay

NOTE Confidence: 0.847453348181818

 $00{:}38{:}35{.}391 \dashrightarrow 00{:}38{:}37{.}630$ there's really no difference in

NOTE Confidence: 0.847453348181818

 $00:38:37.630 \longrightarrow 00:38:40.150$ that first early morning region.

NOTE Confidence: 0.847453348181818

00:38:40.150 --> 00:38:41.390 There's really no difference.

NOTE Confidence: 0.847453348181818

 $00:38:41.390 \longrightarrow 00:38:43.623$ We're only seeing a bit of a

NOTE Confidence: 0.847453348181818

 $00:38:43.623 \rightarrow 00:38:45.198$ difference in what we're terming

NOTE Confidence: 0.847453348181818

 $00:38:45.198 \longrightarrow 00:38:46.910$ the late phase advance window,

NOTE Confidence: 0.847453348181818

 $00:38:46.910 \longrightarrow 00:38:49.829$ so sort of later in the morning.

NOTE Confidence: 0.847453348181818

 $00:38:49.830 \dashrightarrow 00:38:52.080$ The delayed are getting a little

NOTE Confidence: 0.847453348181818

 $00:38:52.080 \longrightarrow 00:38:54.260$ bit less light exposure than the.

NOTE Confidence: 0.847453348181818

 $00:38:54.260 \longrightarrow 00:38:55.022$ Controls are getting,

NOTE Confidence: 0.847453348181818

 $00:38:55.022 \rightarrow 00:38:57.100$ and so we think they may be missing

 $00:38:57.100 \longrightarrow 00:38:59.036$ out on a little bit of that phase.

NOTE Confidence: 0.847453348181818

00:38:59.040 --> 00:38:59.996 Advancing signal,

NOTE Confidence: 0.847453348181818

 $00:38:59.996 \rightarrow 00:39:02.386$ but maybe not necessarily enough

NOTE Confidence: 0.847453348181818

 $00:39:02.386 \longrightarrow 00:39:04.809$ to fully explain the phenotype

NOTE Confidence: 0.847453348181818

 $00{:}39{:}04.809 \dashrightarrow 00{:}39{:}06.180$ that we're seeing.

NOTE Confidence: 0.847453348181818

 $00:39:06.180 \longrightarrow 00:39:08.217$ And So what are some other theories?

NOTE Confidence: 0.847453348181818

00:39:08.220 --> 00:39:08.574 So,

NOTE Confidence: 0.847453348181818

 $00:39:08.574 \longrightarrow 00:39:10.698$ another idea is that you get

NOTE Confidence: 0.847453348181818

00:39:10.698 - 00:39:12.520 the same light exposure,

NOTE Confidence: 0.847453348181818

 $00:39:12.520 \rightarrow 00:39:15.049$ but you have more of a response to it,

NOTE Confidence: 0.847453348181818

 $00:39:15.050 \rightarrow 00:39:17.180$ so maybe you're overly sensitive

NOTE Confidence: 0.847453348181818

 $00:39:17.180 \longrightarrow 00:39:19.310$ to evening light or under

NOTE Confidence: 0.859899833571429

 $00:39{:}19.386 \dashrightarrow 00{:}39{:}21.370$ sensitive to morning light.

NOTE Confidence: 0.859899833571429

00:39:21.370 --> 00:39:24.072 Sean Kane's group in Australia has done

NOTE Confidence: 0.859899833571429

 $00{:}39{:}24.072$ --> $00{:}39{:}26.827$ some work looking at this and they did

 $00:39:26.827 \rightarrow 00:39:29.165$ find that with the exact same light

NOTE Confidence: 0.859899833571429

 $00:39:29.165 \rightarrow 00:39:31.769$ pulse patients who were delayed had a

NOTE Confidence: 0.859899833571429

 $00:39:31.769 \rightarrow 00:39:33.836$ larger phase delay and I don't like

NOTE Confidence: 0.859899833571429

 $00:39:33.836 \rightarrow 00:39:36.632$ how this graph is because the delay is

NOTE Confidence: 0.859899833571429

 $00:39:36.632 \rightarrow 00:39:38.637$ actually positive instead of negative,

NOTE Confidence: 0.859899833571429

 $00:39:38.640 \rightarrow 00:39:41.733$ but they have a larger fades delay as NOTE Confidence: 0.859899833571429

 $00{:}39{:}41.733 \dashrightarrow 00{:}39{:}43.911$ well as greater suppression of melaton in

NOTE Confidence: 0.859899833571429

 $00:39:43.911 \rightarrow 00:39:46.508$ in response to an evening light pulse.

NOTE Confidence: 0.859899833571429

 $00:39{:}46.510 \dashrightarrow 00{:}39{:}48.726$ So there does seem to be some excess

NOTE Confidence: 0.859899833571429

 $00:39:48.726 \rightarrow 00:39:50.749$ sensitivity in some of these individuals.

NOTE Confidence: 0.859899833571429

 $00:39:50.750 \longrightarrow 00:39:51.830$ But then what?

NOTE Confidence: 0.859899833571429

 $00:39:51.830 \longrightarrow 00:39:53.270$ About the other question,

NOTE Confidence: 0.859899833571429

 $00:39:53.270 \rightarrow 00:39:56.648$ what about this morning light sensitivity?

NOTE Confidence: 0.859899833571429

 $00:39:56.650 \rightarrow 00:39:59.306$ So getting back to what I was touching

NOTE Confidence: 0.859899833571429

 $00:39:59.306 \rightarrow 00:40:01.987$ on before our eyes do a lot of things.

NOTE Confidence: 0.859899833571429

 $00:40:01.990 \rightarrow 00:40:03.814$ We have what we most commonly

- NOTE Confidence: 0.859899833571429
- $00:40:03.814 \longrightarrow 00:40:05.030$ think about this image,
- NOTE Confidence: 0.859899833571429
- $00{:}40{:}05{.}030 \dashrightarrow 00{:}40{:}06{.}830$ forming visions that we look at an apple.
- NOTE Confidence: 0.859899833571429
- $00{:}40{:}06{.}830 \dashrightarrow 00{:}40{:}08{.}390$ We see an apple,
- NOTE Confidence: 0.859899833571429
- $00{:}40{:}08{.}390 \dashrightarrow 00{:}40{:}11{.}350$ but there's also non image forming vision.
- NOTE Confidence: 0.859899833571429
- $00:40:11.350 \longrightarrow 00:40:13.474$ So these are things like these
- NOTE Confidence: 0.859899833571429
- $00:40:13.474 \longrightarrow 00:40:14.536$ circadian light response.
- NOTE Confidence: 0.859899833571429
- $00:40:14.540 \longrightarrow 00:40:15.885$ The alerting effects of light
- NOTE Confidence: 0.859899833571429
- $00:40:15.885 \longrightarrow 00:40:17.230$ and that sort of thing.
- NOTE Confidence: 0.859899833571429
- $00:40:17.230 \longrightarrow 00:40:18.680$ So the image forming vision.
- NOTE Confidence: 0.859899833571429
- $00:40:18.680 \longrightarrow 00:40:21.320$ This is a an image of the retina
- NOTE Confidence: 0.859899833571429
- $00:40:21.320 \rightarrow 00:40:23.487$ here image forming visions mediated
- NOTE Confidence: 0.859899833571429
- $00:40:23.487 \rightarrow 00:40:26.819$ primarily by our rods and cones here.
- NOTE Confidence: 0.859899833571429
- $00{:}40{:}26.820 \dashrightarrow 00{:}40{:}28.555$ That non image forming vision
- NOTE Confidence: 0.859899833571429
- $00{:}40{:}28.555 \dashrightarrow 00{:}40{:}30.290$ is primarily mediated by these
- NOTE Confidence: 0.859899833571429
- $00:40:30.349 \rightarrow 00:40:32.119$ intrinsically photosensitive retinal
- NOTE Confidence: 0.859899833571429

 $00:40:32.119 \longrightarrow 00:40:34.533$ ganglion cells that contain a

NOTE Confidence: 0.859899833571429

 $00:40:34.533 \rightarrow 00:40:36.177$ photo pigment called melanopsin,

NOTE Confidence: 0.859899833571429

 $00:40:36.180 \longrightarrow 00:40:38.568$ and the nice thing about these

NOTE Confidence: 0.859899833571429

 $00:40:38.568 \longrightarrow 00:40:41.471$ cells is that they not only project

NOTE Confidence: 0.859899833571429

 $00{:}40{:}41{.}471 \dashrightarrow 00{:}40{.}44{.}320$ to the SCN where they can mediate

NOTE Confidence: 0.859899833571429

 $00:40:44.402 \rightarrow 00:40:46.645$ the circadian signal of light,

NOTE Confidence: 0.859899833571429

 $00{:}40{:}46.645 \dashrightarrow 00{:}40{:}49.015$ but there's also a projection from

NOTE Confidence: 0.859899833571429

 $00:40:49.015 \longrightarrow 00:40:51.710$ these cells into the brainstem to

NOTE Confidence: 0.859899833571429

 $00:40:51.710 \longrightarrow 00:40:53.494$ the olivary pretectal nucleus,

NOTE Confidence: 0.859899833571429

 $00:40:53.500 \rightarrow 00:40:55.708$ which goes to the Edinger Westphal

NOTE Confidence: 0.859899833571429

 $00:40:55.708 \longrightarrow 00:40:57.180$ nucleus which controls pupil.

NOTE Confidence: 0.859899833571429

 $00:40:57.180 \longrightarrow 00:40:59.427$ Diameter so we can use that pathway

NOTE Confidence: 0.859899833571429

00:40:59.427 --> 00:41:02.283 as a way of measuring how well

NOTE Confidence: 0.859899833571429

 $00:41:02.283 \rightarrow 00:41:04.103$ these cells are functioning.

NOTE Confidence: 0.859899833571429

 $00:41:04.110 \longrightarrow 00:41:06.366$ We can do that in the clinic using

NOTE Confidence: 0.859899833571429

 $00:41:06.366 \rightarrow 00:41:07.625$ something called a pupillometer

- NOTE Confidence: 0.859899833571429
- $00:41:07.625 \rightarrow 00:41:09.205$ as we have pictured here,
- NOTE Confidence: 0.859899833571429
- $00{:}41{:}09{.}210 \dashrightarrow 00{:}41{:}11{.}037$ so there's a set of binoculars that
- NOTE Confidence: 0.859899833571429
- $00:41:11.037 \rightarrow 00:41:12.869$ the subject is going to look into,
- NOTE Confidence: 0.859899833571429
- $00{:}41{:}12.870 \dashrightarrow 00{:}41{:}15.204$ and then there's an infrared camera
- NOTE Confidence: 0.859899833571429
- $00:41:15.204 \rightarrow 00:41:17.171$ that actually outlines the pupil
- NOTE Confidence: 0.859899833571429
- 00:41:17.171 $\operatorname{-->}$ 00:41:20.026 diameter as seen here and then you can
- NOTE Confidence: 0.859899833571429
- $00:41:20.026 \rightarrow 00:41:21.896$ provide different light stimuli and
- NOTE Confidence: 0.859899833571429
- $00:41:21.896 \rightarrow 00:41:24.695$ then measure the pupil response to light.
- NOTE Confidence: 0.859899833571429
- 00:41:24.700 00:41:26.640 When we're looking at melanopsin,
- NOTE Confidence: 0.859899833571429
- $00:41:26.640 \rightarrow 00:41:30.056$ these cells really give you a sense of
- NOTE Confidence: 0.859899833571429
- $00:41:30.056 \rightarrow 00:41:33.557$ the overall light tone of the environment,
- NOTE Confidence: 0.859899833571429
- $00:41:33.560 \rightarrow 00:41:36.208$ and so rather than being a second by
- NOTE Confidence: 0.859899833571429
- $00:41:36.208 \rightarrow 00:41:38.596$ second response to the light that's there,
- NOTE Confidence: 0.859899833571429
- $00{:}41{:}38.600 \dashrightarrow 00{:}41{:}41.015$ they hold sort of a static response,
- NOTE Confidence: 0.859899833571429
- $00:41:41.020 \rightarrow 00:41:42.520$ and this is illustrated here.
- NOTE Confidence: 0.859899833571429

00:41:42.520 --> 00:41:44.296 If you look at the dotted blue line,

NOTE Confidence: 0.859899833571429

00:41:44.300 --> 00:41:46.568 so we've got pupil diameter here.

NOTE Confidence: 0.859899833571429

00:41:46.570 --> 00:41:48.908 If you provide a blue light stimulus,

NOTE Confidence: 0.859899833571429

 $00:41:48.910 \longrightarrow 00:41:50.158$ the people constrict.

NOTE Confidence: 0.859899833571429

 $00:41:50.158 \longrightarrow 00:41:52.238$ You turn off the stimulus,

NOTE Confidence: 0.859899833571429

 $00{:}41{:}52{.}240 \dashrightarrow 00{:}41{:}54{.}160$ and if those melanops in cells are

NOTE Confidence: 0.859899833571429

 $00:41:54.160 \rightarrow 00:41:56.129$ functioning the way they're supposed to.

NOTE Confidence: 0.859899833571429

 $00:41:56.130 \rightarrow 00:41:58.734$ That pupil will read dilate but not

NOTE Confidence: 0.859899833571429

 $00:41:58.734 \rightarrow 00:42:01.747$ fully back to the baseline right away.

NOTE Confidence: 0.859899833571429

 $00{:}42{:}01{.}750 \dashrightarrow 00{:}42{:}04{.}486$ Compare that to some body who doesn't

NOTE Confidence: 0.859899833571429

 $00{:}42{:}04{.}486 \dashrightarrow 00{:}42{:}06{.}780$ have well functioning melanops in cells.

NOTE Confidence: 0.859899833571429

 $00:42:06.780 \longrightarrow 00:42:08.658$ You can see the pupil diameter

NOTE Confidence: 0.859899833571429

 $00{:}42{:}08.658 \dashrightarrow 00{:}42{:}10.629$ here in the solid blue line,

NOTE Confidence: 0.859899833571429

 $00:42:10.630 \longrightarrow 00:42:11.416$ they constrict,

NOTE Confidence: 0.859899833571429

 $00:42:11.416 \rightarrow 00:42:13.381$ and then they radiate essentially

NOTE Confidence: 0.859899833571429

 $00:42:13.381 \longrightarrow 00:42:15.690$ back to where they were before,

 $00{:}42{:}15.690 \dashrightarrow 00{:}42{:}17.958$ and so we can use a measurement

NOTE Confidence: 0.859899833571429

 $00:42:17.958 \longrightarrow 00:42:18.972$ called the PIPR,

NOTE Confidence: 0.859899833571429

 $00:42:18.972 \longrightarrow 00:42:20.782$ which is literally just that

NOTE Confidence: 0.859899833571429

 $00:42:20.782 \longrightarrow 00:42:22.230$ difference between the post

NOTE Confidence: 0.8411176266666667

 $00:42:22.288 \longrightarrow 00:42:24.388$ stimulation and the pre stimulation.

NOTE Confidence: 0.8411176266666667

 $00:42:24.390 \longrightarrow 00:42:26.050$ So the larger that is.

NOTE Confidence: 0.8411176266666667

 $00:42:26.050 \longrightarrow 00:42:27.740$ The better the melanopsin cells

NOTE Confidence: 0.841117626666667

 $00:42:27.740 \rightarrow 00:42:30.040$ are functioning, the smaller it is,

NOTE Confidence: 0.8411176266666667

 $00{:}42{:}30{.}040 \dashrightarrow 00{:}42{:}31{.}660$ the worse they're functioning.

NOTE Confidence: 0.8411176266666667

00:42:31.660 --> 00:42:33.760 So our simple question was,

NOTE Confidence: 0.8411176266666667

 $00:42:33.760 \longrightarrow 00:42:36.084$ is the PIR impaired in patients with

NOTE Confidence: 0.8411176266666667

 $00{:}42{:}36.084 \dashrightarrow 00{:}42{:}37.732$ delayed sleep wake phase disorder

NOTE Confidence: 0.8411176266666667

 $00{:}42{:}37{.}732 \dashrightarrow 00{:}42{:}40{.}092$ non 24 and part of this comes back

NOTE Confidence: 0.8411176266666667

 $00{:}42{:}40{.}161 \dashrightarrow 00{:}42{:}41{.}967$ to I mentioned before that patient

NOTE Confidence: 0.8411176266666667

 $00:42:41.967 \longrightarrow 00:42:43.930$ with non 24 had minimal light

 $00:42:43.930 \longrightarrow 00:42:46.555$ exposure that tends to be a common

NOTE Confidence: 0.8411176266666667

 $00:42:46.555 \rightarrow 00:42:48.127$ phenotype with these individuals

NOTE Confidence: 0.8411176266666667

 $00:42:48.127 \longrightarrow 00:42:50.320$ they tend to not like bright light.

NOTE Confidence: 0.8411176266666667

 $00{:}42{:}50{.}320 \dashrightarrow 00{:}42{:}51{.}910$ They've kind of like your migraine

NOTE Confidence: 0.8411176266666667

 $00:42:51.956 \longrightarrow 00:42:53.186$ or they've turned down the

NOTE Confidence: 0.8411176266666667

 $00:42:53.186 \longrightarrow 00:42:54.416$ lights in the clinic room.

NOTE Confidence: 0.8411176266666667

 $00:42:54.420 \longrightarrow 00:42:56.499$ If they have the option to they

NOTE Confidence: 0.8411176266666667

 $00:42:56.499 \rightarrow 00:42:58.943$ tend to spend more time in dimly

NOTE Confidence: 0.8411176266666667

 $00:42:58.943 \longrightarrow 00:43:00.423$ lit environments because the

NOTE Confidence: 0.8411176266666667

 $00:43:00.423 \rightarrow 00:43:02.490$ light is irritating to them.

NOTE Confidence: 0.8411176266666667

 $00{:}43{:}02{.}490 \dashrightarrow 00{:}43{:}04{.}410$ So these are our study participants.

NOTE Confidence: 0.8411176266666667

 $00{:}43{:}04{.}410 \dashrightarrow 00{:}43{:}06{.}610$ We broke this down so we have our

NOTE Confidence: 0.8411176266666667

 $00:43:06.610 \longrightarrow 00:43:08.155$ control individuals here and then

NOTE Confidence: 0.8411176266666667

 $00:43:08.155 \longrightarrow 00:43:09.403$ within our clinical population

NOTE Confidence: 0.8411176266666667

 $00{:}43{:}09{.}403 \dashrightarrow 00{:}43{:}11{.}239$ we had patients who came in

NOTE Confidence: 0.8411176266666667

 $00:43:11.239 \rightarrow 00:43:12.367$ with purely delayed sleep,

- NOTE Confidence: 0.8411176266666667
- $00:43:12.370 \longrightarrow 00:43:13.240$ wake phase disorder,
- NOTE Confidence: 0.8411176266666667
- $00:43:13.240 \longrightarrow 00:43:15.652$ and I say that they just had a
- NOTE Confidence: 0.8411176266666667
- 00:43:15.652 --> 00:43:17.850 problem based on ICSD 3 criteria that
- NOTE Confidence: 0.8411176266666667
- 00:43:17.850 -> 00:43:19.787 they're sleep like timing was late,
- NOTE Confidence: 0.8411176266666667
- $00{:}43{:}19.790 \dashrightarrow 00{:}43{:}21.428$ but they never had a time period
- NOTE Confidence: 0.8411176266666667
- $00:43:21.428 \longrightarrow 00:43:22.894$ where it actually got later and
- NOTE Confidence: 0.8411176266666667
- $00:43:22.894 \rightarrow 00:43:24.328$ later and went around the clock.
- NOTE Confidence: 0.8411176266666667
- $00{:}43{:}24{.}330 \dashrightarrow 00{:}43{:}27{.}250$ We had twelve of those and then we had 12
- NOTE Confidence: 0.8411176266666667
- $00:43:27.329 \rightarrow 00:43:30.395$ patients who had symptoms of delayed sleep,
- NOTE Confidence: 0.8411176266666667
- $00:43:30.400 \rightarrow 00:43:31.033$ wake phase disorder.
- NOTE Confidence: 0.8411176266666667
- $00:43:31.033 \longrightarrow 00:43:32.299$ But if you asked them that.
- NOTE Confidence: 0.8411176266666667
- 00:43:32.300 --> 00:43:32.555 Question,
- NOTE Confidence: 0.8411176266666667
- $00{:}43{:}32{.}555 \dashrightarrow 00{:}43{:}34{.}340$ have you ever actually gotten so late
- NOTE Confidence: 0.8411176266666667
- $00:43:34.340 \longrightarrow 00:43:35.850$ that you've gone around the clock?
- NOTE Confidence: 0.8411176266666667
- 00:43:35.850 --> 00:43:37.290 Do you go back and forth
- NOTE Confidence: 0.8411176266666667

 $00:43:37.290 \longrightarrow 00:43:38.250$ between those two states?

NOTE Confidence: 0.8411176266666667

 $00:43:38.250 \rightarrow 00:43:41.746$ We had 17 patients who had that phenotype.

NOTE Confidence: 0.8411176266666667

 $00:43:41.750 \longrightarrow 00:43:43.256$ Overall, similar age.

NOTE Confidence: 0.8411176266666667

 $00:43:43.256 \rightarrow 00:43:45.766$ Obviously lower scores on the

NOTE Confidence: 0.8411176266666667

 $00:43:45.766 \rightarrow 00:43:48.207$ Horn osberg indicating more

NOTE Confidence: 0.8411176266666667

 $00:43:48.207 \longrightarrow 00:43:50.915$ eveningness within this population.

NOTE Confidence: 0.8411176266666667

00:43:50.920 --> 00:43:52.436 Worst scores on PSQI,

NOTE Confidence: 0.8411176266666667

 $00:43:52.436 \longrightarrow 00:43:53.952$ which is previously been

NOTE Confidence: 0.8411176266666667

 $00:43:53.952 \rightarrow 00:43:55.679$ described in DSPD patients,

NOTE Confidence: 0.8411176266666667

 $00:43:55.680 \rightarrow 00:43:58.837$ but not any sleepier than our controls,

NOTE Confidence: 0.8411176266666667

 $00{:}43{:}58{.}840 \dashrightarrow 00{:}44{:}00{.}580$ and then the average sleep onset,

NOTE Confidence: 0.8411176266666667

 $00:44:00.580 \longrightarrow 00:44:02.384$ offset and sleep midpoint,

NOTE Confidence: 0.8411176266666667

 $00:44:02.384 \rightarrow 00:44:05.495$ was significantly later in our delayed and

NOTE Confidence: 0.8411176266666667

00:44:05.495 --> 00:44:08.143 even later in our non 24 overlap group,

NOTE Confidence: 0.8411176266666667

 $00{:}44{:}08.150 \dashrightarrow 00{:}44{:}10.313$ but total sleep time was the same

NOTE Confidence: 0.8411176266666667

 $00:44:10.313 \rightarrow 00:44:12.404$ across all groups and then lastly

 $00:44:12.404 \longrightarrow 00:44:15.120$ the people on the tree testing in

NOTE Confidence: 0.8411176266666667

 $00{:}44{:}15{.}206 \dashrightarrow 00{:}44{:}18{.}258$ relation to time since they woke up

NOTE Confidence: 0.8411176266666667

 $00{:}44{:}18.258 \dashrightarrow 00{:}44{:}20.678$ was slightly closer to wake time.

NOTE Confidence: 0.8411176266666667

 $00:44:20.680 \longrightarrow 00:44:22.750$ And our delayed and non 24

NOTE Confidence: 0.8411176266666667

 $00:44:22.750 \longrightarrow 00:44:24.830$ overlap compared to our controls.

NOTE Confidence: 0.841117626666667

 $00{:}44{:}24{.}830 \dashrightarrow 00{:}44{:}26{.}990$ But we know that from previously

NOTE Confidence: 0.8411176266666667

 $00:44:26.990 \rightarrow 00:44:29.105$ published studies the PIPR only tends

NOTE Confidence: 0.841117626666667

00:44:29.105 - 00:44:31.545 to change around the time of dim light,

NOTE Confidence: 0.8411176266666667

 $00{:}44{:}31{.}550 \dashrightarrow 00{:}44{:}33{.}440$ melaton in onset and otherwise remains

NOTE Confidence: 0.8411176266666667

 $00:44:33.440 \rightarrow 00:44:35.330$ fairly stable throughout the day,

NOTE Confidence: 0.8411176266666667

 $00{:}44{:}35{.}330 \dashrightarrow 00{:}44{:}38{.}264$ and so we were well away from the Duomo

NOTE Confidence: 0.841117626666667

 $00{:}44{:}38{.}264 \dashrightarrow 00{:}44{:}40{.}718$ window for all of these individuals.

NOTE Confidence: 0.8411176266666667

 $00{:}44{:}40.720 \dashrightarrow 00{:}44{:}42.964$ This is data from one control

NOTE Confidence: 0.8411176266666667

 $00{:}44{:}42{.}964 \dashrightarrow 00{:}44{:}44{.}460$ and one delayed subject.

NOTE Confidence: 0.8411176266666667

 $00{:}44{:}44{.}460 \dashrightarrow 00{:}44{:}46{.}819$ Just showing an example of the tracing.

- 00:44:46.820 --> 00:44:48.926 And as you can see here,
- NOTE Confidence: 0.8411176266666667
- $00{:}44{:}48{.}930 \dashrightarrow 00{:}44{:}53{.}088$ our delayed patient in the solid blue,
- NOTE Confidence: 0.8411176266666667
- $00:44:53.090 \longrightarrow 00:44:54.322$ there's their pupil diameter.
- NOTE Confidence: 0.8411176266666667
- 00:44:54.322 --> 00:44:55.862 You provide the light stimulus,
- NOTE Confidence: 0.8411176266666667
- $00{:}44{:}55{.}870 \dashrightarrow 00{:}44{:}57{.}073$ the pupil constricts.
- NOTE Confidence: 0.8411176266666667
- $00{:}44{:}57.073 \dashrightarrow 00{:}44{:}59.078$ They radiate almost to exactly
- NOTE Confidence: 0.8411176266666667
- 00:44:59.078 --> 00:45:01.098 where they were pre stimulus
- NOTE Confidence: 0.8411176266666667
- $00:45:01.098 \rightarrow 00:45:02.626$ compared to our control,
- NOTE Confidence: 0.8411176266666667
- $00{:}45{:}02.630 \dashrightarrow 00{:}45{:}05.400$ who constricts and then maintains
- NOTE Confidence: 0.8411176266666667
- $00{:}45{:}05{.}400 \dashrightarrow 00{:}45{:}08{.}714$ that constriction post stimulus so you
- NOTE Confidence: 0.8411176266666667
- 00:45:08.714 --> 00:45:11.906 can see smaller pipr in our delayed
- NOTE Confidence: 0.8411176266666667
- $00:45:11.906 \rightarrow 00:45:14.128$ patient compared to our control.
- NOTE Confidence: 0.8411176266666667
- $00:45:14.130 \longrightarrow 00:45:15.924$ This is just quantifying it here
- NOTE Confidence: 0.8411176266666667
- $00:45:15.924 \longrightarrow 00:45:18.009$ and so you can see controls.
- NOTE Confidence: 0.8411176266666667
- $00{:}45{:}18.010 \dashrightarrow 00{:}45{:}20.764$ Overall have a larger Pi PR
- NOTE Confidence: 0.8411176266666667
- $00:45:20.764 \rightarrow 00:45:22.600$ significantly greater than the

- NOTE Confidence: 0.845463685
- 00:45:22.685 --> 00:45:24.269 non 24 hour overlap,
- NOTE Confidence: 0.845463685
- $00{:}45{:}24{.}270 \dashrightarrow 00{:}45{:}26{.}542$ and then there's kind of a range within
- NOTE Confidence: 0.845463685
- $00:45:26.542 \rightarrow 00:45:28.643$ that just delayed group which we think
- NOTE Confidence: 0.845463685
- $00:45:28.643 \rightarrow 00:45:30.978$ may come from the fact that there
- NOTE Confidence: 0.845463685
- $00:45:30.978 \rightarrow 00:45:33.366$ are several different phenotypes of delayed.
- NOTE Confidence: 0.845463685
- $00{:}45{:}33{.}370 \dashrightarrow 00{:}45{:}34{.}578$ There's sort of this.
- NOTE Confidence: 0.845463685
- 00:45:34.578 --> 00:45:36.088 We're still working on terminology,
- NOTE Confidence: 0.845463685
- $00{:}45{:}36{.}090 \dashrightarrow 00{:}45{:}38{.}282$ but some of them have a mismatch between
- NOTE Confidence: 0.845463685
- $00:45:38.282 \rightarrow 00:45:40.708$ their demo timing and their preferred timing,
- NOTE Confidence: 0.845463685
- $00{:}45{:}40.710 \dashrightarrow 00{:}45{:}42.383$ and some of them are both their
- NOTE Confidence: 0.845463685
- $00:45:42.383 \rightarrow 00:45:43.729$ demo and their sleep wake.
- NOTE Confidence: 0.845463685
- 00:45:43.730 --> 00:45:44.766 I mean it's delayed,
- NOTE Confidence: 0.845463685
- $00{:}45{:}44.766 \dashrightarrow 00{:}45{:}46.878$ so I think that we're capturing that with
- NOTE Confidence: 0.845463685
- $00{:}45{:}46.878 \dashrightarrow 00{:}45{:}48.910$ some of the variability that we see here.
- NOTE Confidence: 0.845463685
- $00{:}45{:}48{.}910 \dashrightarrow 00{:}45{:}51{.}164$ But essentially this is a first pass,
- NOTE Confidence: 0.845463685

 $00{:}45{:}51{.}170 \dashrightarrow 00{:}45{:}53{.}480$ telling us that we think that we

NOTE Confidence: 0.845463685

 $00:45:53.480 \rightarrow 00:45:55.345$ may have found a subpopulation

NOTE Confidence: 0.845463685

 $00{:}45{:}55{.}345 \dashrightarrow 00{:}45{:}57{.}745$ of individuals who have at least

NOTE Confidence: 0.845463685

 $00{:}45{:}57.745 \dashrightarrow 00{:}46{:}00.307$ based on bedside and office exam,

NOTE Confidence: 0.845463685

 $00{:}46{:}00{.}310 \dashrightarrow 00{:}46{:}02{.}490$ have normal image forming vision,

NOTE Confidence: 0.845463685

 $00:46:02.490 \longrightarrow 00:46:04.030$ but they're non image forming.

NOTE Confidence: 0.845463685

 $00{:}46{:}04{.}030$ --> $00{:}46{:}05{.}920$ Vision may have some impairment and

NOTE Confidence: 0.845463685

 $00{:}46{:}05{.}920 \dashrightarrow 00{:}46{:}08{.}824$ this may be part of why they end up

NOTE Confidence: 0.845463685

 $00{:}46{:}08.824 \dashrightarrow 00{:}46{:}10.820$ either delayed or developing this non NOTE Confidence: 0.845463685

 $00{:}46{:}10.820$ --> $00{:}46{:}12.932$ 24 hour phenotype because they're just NOTE Confidence: 0.845463685

 $00{:}46{:}12{.}932$ --> $00{:}46{:}16{.}098$ simply not able to respond normally to NOTE Confidence: 0.845463685

 $00:46:16.098 \rightarrow 00:46:18.733$ that morning advancing light signal.

NOTE Confidence: 0.845463685

 $00{:}46{:}18.740 \dashrightarrow 00{:}46{:}19.624$ And so with that,

NOTE Confidence: 0.845463685

 $00{:}46{:}19.624 \dashrightarrow 00{:}46{:}21.247$ I'd just like to acknowledge the people

NOTE Confidence: 0.845463685

 $00{:}46{:}21.247 \dashrightarrow 00{:}46{:}22.983$ who helped me out with this project

NOTE Confidence: 0.845463685

 $00:46:22.983 \longrightarrow 00:46:24.318$ and elsewhere within the clinic.

- NOTE Confidence: 0.845463685
- 00:46:24.320 --> 00:46:25.880 Uh, the funding sources for this,
- NOTE Confidence: 0.845463685
- $00:46:25.880 \longrightarrow 00:46:27.368$ as well as their clinical staff
- NOTE Confidence: 0.845463685
- $00{:}46{:}27{.}368 \dashrightarrow 00{:}46{:}28{.}931$ who conducted some of the people
- NOTE Confidence: 0.845463685
- $00{:}46{:}28{.}931 \dashrightarrow 00{:}46{:}30{.}765$ on the tree measures and have been
- NOTE Confidence: 0.845463685
- 00:46:30.765 --> 00:46:32.193 phenomenal at helping to manage
- NOTE Confidence: 0.845463685
- $00{:}46{:}32.193 \dashrightarrow 00{:}46{:}33.593$ these circadian patients as well.
- NOTE Confidence: 0.845463685
- $00:46:33.600 \rightarrow 00:46:34.395$ And with that,
- NOTE Confidence: 0.845463685
- 00:46:34.395 --> 00:46:35.985 I believe I did allow some
- NOTE Confidence: 0.845463685
- $00:46:35.985 \longrightarrow 00:46:37.379$ extra time for questions.
- NOTE Confidence: 0.89194022
- $00:46:41.390 \longrightarrow 00:46:43.226$ Fantastic thank you.
- NOTE Confidence: 0.89194022
- 00:46:43.226 --> 00:46:46.286 Thank you very much Sabra.
- NOTE Confidence: 0.89194022
- $00{:}46{:}46{.}290 \dashrightarrow 00{:}46{:}49{.}258$ A great great journey from the basics to
- NOTE Confidence: 0.89194022
- $00{:}46{:}49.258 \dashrightarrow 00{:}46{:}52.260$ clinic and over to the field of research.
- NOTE Confidence: 0.89194022
- $00:46:52.260 \longrightarrow 00:46:55.286$ And so the question the the
- NOTE Confidence: 0.89194022
- $00:46:55.286 \rightarrow 00:46:58.800$ pupil is a amazing thing.
- NOTE Confidence: 0.89194022

 $00:46:58.800 \longrightarrow 00:47:02.335$ And So what happens to the people

NOTE Confidence: 0.89194022

 $00:47:02.335 \longrightarrow 00:47:07.830$ and people who may not have sort of?

NOTE Confidence: 0.89194022

 $00:47:07.830 \longrightarrow 00:47:09.210$ May not be healthy otherwise,

NOTE Confidence: 0.89194022

 $00{:}47{:}09{.}210 \dashrightarrow 00{:}47{:}11{.}592$ so like it is our comorbidities

NOTE Confidence: 0.89194022

 $00{:}47{:}11.592 \dashrightarrow 00{:}47{:}13.878$ such as you know, diabetes,

NOTE Confidence: 0.89194022

00:47:13.878 --> 00:47:14.870 hypertension, etcetera.

NOTE Confidence: 0.89194022

00:47:14.870 --> 00:47:16.370 Obesity, for example,

NOTE Confidence: 0.89194022

 $00:47:16.370 \longrightarrow 00:47:18.870$ affect people that are responses.

NOTE Confidence: 0.865773047368421

00:47:19.730 --> 00:47:22.354 Absolutely. And So what I left out in

NOTE Confidence: 0.865773047368421

 $00:47:22.354 \rightarrow 00:47:25.105$ the abbreviated summary is that we took

NOTE Confidence: 0.865773047368421

 $00:47:25.105 \longrightarrow 00:47:26.729$ very otherwise healthy individuals,

NOTE Confidence: 0.865773047368421

 $00:47:26.730 \longrightarrow 00:47:30.027$ and so the pupil does so many

NOTE Confidence: 0.865773047368421

00:47:30.027 --> 00:47:32.250 different things. It gives you an

NOTE Confidence: 0.865773047368421

 $00:47:32.250 \rightarrow 00:47:33.530$ insight into autonomic function,

NOTE Confidence: 0.865773047368421

 $00{:}47{:}33{.}530 \dashrightarrow 00{:}47{:}34{.}994$ and so that's often where we

NOTE Confidence: 0.865773047368421

 $00:47:34.994 \longrightarrow 00:47:35.970$ tend to use pupillometry,

 $00:47:35.970 \longrightarrow 00:47:37.454$ particularly in the ICU,

NOTE Confidence: 0.865773047368421

 $00:47:37.454 \longrightarrow 00:47:38.938$ in the diabetes realm.

NOTE Confidence: 0.865773047368421

 $00:47:38.940 \longrightarrow 00:47:41.469$ And so it can give you a sense of

NOTE Confidence: 0.865773047368421

 $00:47:41.469 \rightarrow 00:47:42.952$ parasympathetic sympathetic balance that

NOTE Confidence: 0.865773047368421

 $00{:}47{:}42.952 \dashrightarrow 00{:}47{:}45.605$ tends to be that more immediate response.

NOTE Confidence: 0.865773047368421

 $00{:}47{:}45.610 \dashrightarrow 00{:}47{:}47.882$ And we do see some differences in these

NOTE Confidence: 0.865773047368421

 $00:47:47.882 \rightarrow 00:47:49.679$ patients in that autonomic realm.

NOTE Confidence: 0.865773047368421

 $00{:}47{:}49{.}680 \dashrightarrow 00{:}47{:}53{.}586$ As well, and then the PIPR that we were

NOTE Confidence: 0.865773047368421

 $00:47:53.586 \longrightarrow 00:47:56.062$ looking at tends to do more of that

NOTE Confidence: 0.865773047368421

 $00:47:56.062 \rightarrow 00:47:57.710$ retinal ganglion cell measurement,

NOTE Confidence: 0.865773047368421

 $00:47:57.710 \longrightarrow 00:47:59.398$ but you can see a loss of those

NOTE Confidence: 0.865773047368421

 $00{:}47{:}59{.}398 \dashrightarrow 00{:}48{:}01{.}597$ and lots of other disorders besides

NOTE Confidence: 0.865773047368421

 $00{:}48{:}01{.}597 \dashrightarrow 00{:}48{:}02{.}887$ delayed supplicates disorders,

NOTE Confidence: 0.865773047368421

 $00{:}48{:}02{.}890 \dashrightarrow 00{:}48{:}05{.}110$ so it's been reported there's been

NOTE Confidence: 0.865773047368421

 $00{:}48{:}05{.}110$ --> $00{:}48{:}07{.}150$ impairment in seasonal affective disorder.

00:48:07.150 - 00:48:08.598 We think that there may be some drop

NOTE Confidence: 0.865773047368421

00:48:08.598 --> 00:48:10.436 out of this in patients with Parkinson's,

NOTE Confidence: 0.865773047368421

 $00:48:10.440 \rightarrow 00:48:11.571$ and so absolutely,

NOTE Confidence: 0.865773047368421

 $00:48:11.571 \rightarrow 00:48:13.833$ I think you just examining the

NOTE Confidence: 0.865773047368421

 $00{:}48{:}13.833 \dashrightarrow 00{:}48{:}16.299$ people alone could find you know

NOTE Confidence: 0.865773047368421

 $00{:}48{:}16.299 \dashrightarrow 00{:}48{:}18.319$ problems in almost every disorder.

NOTE Confidence: 0.78916932

 $00:48:19.650 \rightarrow 00:48:25.060$ Cool well if you into the soul all right.

NOTE Confidence: 0.78916932

00:48:25.060 - 00:48:26.444 All right, so so we have some other

NOTE Confidence: 0.78916932

 $00:48:26.444 \rightarrow 00:48:27.568$ questions and I have a couple more, NOTE Confidence: 0.78916932

00:48:27.570 --> 00:48:29.146 but I want to make sure I address

NOTE Confidence: 0.78916932

 $00{:}48{:}29{.}146 \dashrightarrow 00{:}48{:}30{.}750$ the the folks in the Chancellor.

NOTE Confidence: 0.78916932

00:48:30.750 --> 00:48:32.415 Doctor Cohen is asking does

NOTE Confidence: 0.78916932

 $00:48:32.415 \longrightarrow 00:48:34.080$ the use of chronic exogenous

NOTE Confidence: 0.78916932

 $00:48:34.144 \rightarrow 00:48:38.034$ melatonin have any impact on ones

NOTE Confidence: 0.78916932

 $00:48:38.034 \rightarrow 00:48:39.036$ endogenous melatonin secretion?

NOTE Confidence: 0.78916932

 $00:48:39.036 \longrightarrow 00:48:40.706$ So does it suppress it?

00:48:42.170 --> 00:48:43.766 As we know, and certainly not

NOTE Confidence: 0.85292671777778

 $00:48:43.766 \longrightarrow 00:48:45.781$ at the doses that we tend to

NOTE Confidence: 0.85292671777778

00:48:45.781 --> 00:48:47.266 use for our circadian patients,

NOTE Confidence: 0.85292671777778

 $00:48:47.270 \dashrightarrow 00:48:49.583$ and so I will see a lot of patients

NOTE Confidence: 0.85292671777778

 $00:48:49.583 \longrightarrow 00:48:52.012$ who show up in clinic, and I think

NOTE Confidence: 0.85292671777778

 $00:48:52.012 \rightarrow 00:48:53.836$ our typical response is always well.

NOTE Confidence: 0.85292671777778

00:48:53.840 --> 00:48:54.716 If something doesn't work,

NOTE Confidence: 0.85292671777778

 $00{:}48{:}54.716 \dashrightarrow 00{:}48{:}56.916$ let me take more of it and so I think

NOTE Confidence: 0.85292671777778

 $00{:}48{:}56{.}916 \dashrightarrow 00{:}48{:}58{.}400$ the record I've seen is somebody who

NOTE Confidence: 0.85292671777778

 $00:48:58.400 \rightarrow 00:49:00.316$ came in by the time they came to see me.

NOTE Confidence: 0.85292671777778

00:49:00.316 --> 00:49:01.846 They were taking 80 milligrams

NOTE Confidence: 0.85292671777778

 $00{:}49{:}01{.}846 \dashrightarrow 00{:}49{:}03{.}070$ of melaton in at night.

NOTE Confidence: 0.85292671777778

 $00:49:03.070 \rightarrow 00:49:04.680$ I was surprised that they were actually

NOTE Confidence: 0.85292671777778

 $00{:}49{:}04.680 \dashrightarrow 00{:}49{:}06.570$ still awake in time for their appointment,

NOTE Confidence: 0.85292671777778

 $00{:}49{:}06{.}570 \dashrightarrow 00{:}49{:}10{.}634$ but in those doses I might be

 $00:49:10.634 \longrightarrow 00:49:12.330$ more concerned about this.

NOTE Confidence: 0.85292671777778

00:49:12.330 --> 00:49:13.860 But using half a milligram,

NOTE Confidence: 0.85292671777778

 $00:49:13.860 \rightarrow 00:49:15.876$ just trying to mimic physiological doses.

NOTE Confidence: 0.85292671777778

 $00:49:15.880 \longrightarrow 00:49:17.444$ We haven't noticed any.

NOTE Confidence: 0.85292671777778

 $00:49:17.444 \rightarrow 00:49:19.790$ Inability to produce your own melatonin.

NOTE Confidence: 0.85292671777778

00:49:19.790 --> 00:49:21.410 Know sort of negative feedback loop.

NOTE Confidence: 0.85292671777778

 $00:49:21.410 \longrightarrow 00:49:22.259$ Anything like that,

NOTE Confidence: 0.761386507777778

00:49:22.550 --> 00:49:24.320 right? Cool? Yeah, because I think

NOTE Confidence: 0.761386507777778

00:49:24.320 --> 00:49:26.619 you know a lot of people use

NOTE Confidence: 0.761386507777778

 $00:49:26.619 \rightarrow 00:49:28.384$ melatonin for induction of sleep,

NOTE Confidence: 0.761386507777778

 $00:49:28.390 \longrightarrow 00:49:29.470$ and some of them go up,

NOTE Confidence: 0.761386507777778

 $00{:}49{:}29{.}470 \dashrightarrow 00{:}49{:}32{.}356$ you know, 1012 etcetera and so,

NOTE Confidence: 0.761386507777778

 $00:49:32.360 \dashrightarrow 00:49:35.088$ and so that that always that's the cross.

NOTE Confidence: 0.761386507777778

 $00:49:35.088 \longrightarrow 00:49:36.810$ Our mind as we think about this.

NOTE Confidence: 0.761386507777778

 $00:49:36.810 \longrightarrow 00:49:38.630$ And so, doctor Ahn says,

NOTE Confidence: 0.761386507777778

00:49:38.630 - 00:49:41.534 and have you found that there are any

- NOTE Confidence: 0.761386507777778
- $00:49:41.534 \rightarrow 00:49:43.768$ dietary effects on melatonin testing?
- NOTE Confidence: 0.761386507777778
- 00:49:43.770 --> 00:49:47.070 So I have read that nuts,
- NOTE Confidence: 0.761386507777778
- 00:49:47.070 --> 00:49:47.938 fruits, alcohol?
- NOTE Confidence: 0.761386507777778
- 00:49:47.938 --> 00:49:50.108 Rice can increase melatonin levels,
- NOTE Confidence: 0.761386507777778
- $00{:}49{:}50{.}110 \dashrightarrow 00{:}49{:}51{.}664$ and you instruct patients to avoid
- NOTE Confidence: 0.761386507777778
- $00{:}49{:}51{.}664 \dashrightarrow 00{:}49{:}53{.}259$ these substances and the night when
- NOTE Confidence: 0.761386507777778
- $00:49:53.259 \rightarrow 00:49:54.777$ they do their military and testing.
- NOTE Confidence: 0.8047696925
- $00:49:55.290 \longrightarrow 00:49:56.837$ So we have a whole set of
- NOTE Confidence: 0.8047696925
- $00:49:56.837 \rightarrow 00:49:58.229$ instructions that we give patients,
- NOTE Confidence: 0.8047696925
- $00:49:58.230 \longrightarrow 00:49:59.946$ so there's a bunch of things
- NOTE Confidence: 0.8047696925
- $00:49:59.946 \longrightarrow 00:50:01.090$ that can affect melatonin.
- NOTE Confidence: 0.8047696925
- $00{:}50{:}01{.}090 \dashrightarrow 00{:}50{:}03{.}322$ I think one of the most important things
- NOTE Confidence: 0.8047696925
- $00:50:03.322 \rightarrow 00:50:06.384$ to keep in mind is beta blockers actually
- NOTE Confidence: 0.8047696925
- $00{:}50{:}06{.}384 \dashrightarrow 00{:}50{:}09{.}590$ inhibit melaton in production, so.
- NOTE Confidence: 0.8047696925
- $00:50:09.590 \longrightarrow 00:50:11.378$ Keeping that in mind when you're
- NOTE Confidence: 0.8047696925

 $00:50:11.378 \rightarrow 00:50:12.815$ testing your patients bananas,

NOTE Confidence: 0.8047696925

 $00:50:12.815 \rightarrow 00:50:16.560$ ibuprofen other things can also influence it,

NOTE Confidence: 0.8047696925

 $00{:}50{:}16.560 \dashrightarrow 00{:}50{:}19.472$ and so we in general instruct

NOTE Confidence: 0.8047696925

00:50:19.472 --> 00:50:21.404 patients do as much as possible,

NOTE Confidence: 0.8047696925

 $00:50:21.410 \longrightarrow 00:50:24.074$ don't eat anything within 15 minutes

NOTE Confidence: 0.8047696925

 $00:50:24.074 \dashrightarrow 00:50:27.200$ of doing the saliva testing as well.

NOTE Confidence: 0.8047696925

 $00:50:27.200 \longrightarrow 00:50:29.657$ But yeah, there's lots of things that

NOTE Confidence: 0.8047696925

 $00:50:29.657 \rightarrow 00:50:31.400$ can influence melatonin production,

NOTE Confidence: 0.8047696925

00:50:31.400 - 00:50:33.269 so we do try to instruct subjects

NOTE Confidence: 0.8047696925

 $00:50:33.269 \longrightarrow 00:50:34.699$ to be careful with them.

NOTE Confidence: 0.839260074

 $00{:}50{:}37{.}190 \dashrightarrow 00{:}50{:}40{.}900$ So from a practical standpoint.

NOTE Confidence: 0.839260074

 $00:50:40.900 \rightarrow 00:50:43.798$ How do you order the milestone testing?

NOTE Confidence: 0.839260074

 $00:50:43.800 \longrightarrow 00:50:45.780$ Who passed for it? Is that a pocket?

NOTE Confidence: 0.839260074

 $00:50:45.780 \longrightarrow 00:50:48.052$ Because I I want to do it with

NOTE Confidence: 0.839260074

 $00:50:48.052 \rightarrow 00:50:49.380$ my patience and so how do I?

NOTE Confidence: 0.839260074

00:50:49.380 --> 00:50:50.796 How do I? How do I do that?

 $00{:}50{:}50{.}800 \dashrightarrow 00{:}50{:}51{.}736$ I mean, I've done it before,

NOTE Confidence: 0.839260074

 $00:50:51.740 \longrightarrow 00:50:53.620$ but it was, you know,

NOTE Confidence: 0.839260074

 $00:50:53.620 \longrightarrow 00:50:54.910$ it took a little legwork

NOTE Confidence: 0.682369663333333

00:50:55.300 --> 00:50:57.556 right now. Our kids are homegrown,

NOTE Confidence: 0.682369663333333

 $00:50:57.560 \rightarrow 00:50:59.303$ so we put them together ourselves and

NOTE Confidence: 0.682369663333333

 $00{:}50{:}59{.}303 \dashrightarrow 00{:}51{:}01{.}487$ had to go through a whole process of

NOTE Confidence: 0.682369663333333

 $00:51:01.487 \rightarrow 00:51:03.472$ making our own epic order and everything

NOTE Confidence: 0.682369663333333

 $00{:}51{:}03{.}472 \dashrightarrow 00{:}51{:}05{.}404$ else to be able to implement and

NOTE Confidence: 0.682369663333333

 $00{:}51{:}05{.}404 \dashrightarrow 00{:}51{:}08{.}640$ them implement them in the clinic.

NOTE Confidence: 0.682369663333333

 $00{:}51{:}08.640 \dashrightarrow 00{:}51{:}10.985$ There is at least one commercial testing

NOTE Confidence: 0.682369663333333

 $00:51:10.985 \rightarrow 00:51:13.150$ group available that I've seen out there.

NOTE Confidence: 0.682369663333333

 $00:51:13.150 \rightarrow 00:51:16.327$ Their prices tended to be a little bit higher

NOTE Confidence: 0.682369663333333

00:51:16.330 --> 00:51:21.209 and I would interpret the data yourself.

NOTE Confidence: 0.682369663333333

 $00{:}51{:}21{.}210 \dashrightarrow 00{:}51{:}24{.}586$ But the right now I think the biggest

NOTE Confidence: 0.682369663333333

 $00{:}51{:}24.586 \dashrightarrow 00{:}51{:}27.164$ downside to melaton in testing is

 $00:51:27.164 \rightarrow 00:51:29.909$ it's not covered by insurance.

NOTE Confidence: 0.682369663333333

 $00:51:29.910 \longrightarrow 00:51:32.126$ We are working as a sort of consortium

NOTE Confidence: 0.682369663333333

 $00:51:32.126 \rightarrow 00:51:33.801$ of people interested in circulating

NOTE Confidence: 0.682369663333333

 $00:51:33.801 \rightarrow 00:51:36.265$ disorders on putting out a paper on

NOTE Confidence: 0.682369663333333

 $00{:}51{:}36{.}332 \dashrightarrow 00{:}51{:}38{.}306$ melaton in testing and sort of the

NOTE Confidence: 0.682369663333333

 $00{:}51{:}38{.}306 \dashrightarrow 00{:}51{:}40{.}198$ clinical benefits of it and continuing

NOTE Confidence: 0.682369663333333

 $00:51:40.198 \longrightarrow 00:51:42.186$ to work to try to get insurance

NOTE Confidence: 0.682369663333333

 $00:51:42.186 \rightarrow 00:51:43.420$ companies to routinely reimburse

NOTE Confidence: 0.682369663333333

 $00{:}51{:}43{.}420 \dashrightarrow 00{:}51{:}45{.}513$ for both demo testing and you didn't

NOTE Confidence: 0.682369663333333

 $00:51:45.569 \longrightarrow 00:51:46.985$ open the other can of worms,

NOTE Confidence: 0.682369663333333

 $00:51:46.990 \longrightarrow 00:51:48.458$ which is getting reimbursed

NOTE Confidence: 0.682369663333333

 $00{:}51{:}48.458 \dashrightarrow 00{:}51{:}49.559$ for actigraphy testing,

NOTE Confidence: 0.682369663333333

 $00:51:49.560 \longrightarrow 00:51:50.740$ which we're also working on.

NOTE Confidence: 0.807889908

 $00:51:52.080 \rightarrow 00:51:53.620$ Well, thank you and I'm

NOTE Confidence: 0.807889908

 $00:51:53.620 \longrightarrow 00:51:55.160$ doing it on both sides.

NOTE Confidence: 0.807889908

 $00:51:55.160 \rightarrow 00:51:56.918$ That doctor Hilbert has a question.

- NOTE Confidence: 0.807889908
- $00:51:56.920 \longrightarrow 00:51:59.005$ Given the variability and over

 $00{:}51{:}59{.}005 \dashrightarrow 00{:}52{:}00{.}948$ the counter melaton in branch of

NOTE Confidence: 0.807889908

 $00:52:00.948 \longrightarrow 00:52:03.356$ brand or locked a lot even what

NOTE Confidence: 0.807889908

 $00:52:03.356 \rightarrow 00:52:06.049$ do you recommend from melatonin

NOTE Confidence: 0.807889908

 $00:52:06.049 \rightarrow 00:52:08.317$ prescription or or purchases?

NOTE Confidence: 0.807889908

 $00:52:08.320 \longrightarrow 00:52:10.224$ It has to be USB grade or.

NOTE Confidence: 0.70069379375

 $00{:}52{:}11{.}270 \dashrightarrow 00{:}52{:}13{.}950$ So I I wear two hats on this.

NOTE Confidence: 0.70069379375

 $00:52:13.950 \rightarrow 00:52:16.713$ UM, my clinical hat is really what I care

NOTE Confidence: 0.70069379375

 $00{:}52{:}16.713 \dashrightarrow 00{:}52{:}19.444$ about more is that they get a low dose

NOTE Confidence: 0.70069379375

 $00:52:19.444 \rightarrow 00:52:21.868$ and whatever they're able to track down,

NOTE Confidence: 0.70069379375

 $00:52:21.870 \longrightarrow 00:52:23.809$ as long as it's half a milligram.

NOTE Confidence: 0.70069379375

 $00{:}52{:}23.810 \dashrightarrow 00{:}52{:}25.420$ I'm actually fine with that.

NOTE Confidence: 0.70069379375

 $00{:}52{:}25{.}420 \dashrightarrow 00{:}52{:}27{.}891$ We do have some specific melaton in that

NOTE Confidence: 0.70069379375

00:52:27.891 --> 00:52:31.266 we use for research studies and tend to be

NOTE Confidence: 0.70069379375

 $00{:}52{:}31{.}266 \dashrightarrow 00{:}52{:}33{.}290$ a little bit more consistent with that,

 $00:52:33.290 \longrightarrow 00:52:35.804$ but it's you know it's the

NOTE Confidence: 0.70069379375

00:52:35.804 --> 00:52:37.954 practicalities and medicine of trying

NOTE Confidence: 0.70069379375

 $00:52:37.954 \longrightarrow 00:52:40.348$ to get patients what they need.

NOTE Confidence: 0.70069379375

 $00:52:40.350 \longrightarrow 00:52:41.426$ One of my odd.

NOTE Confidence: 0.70069379375

00:52:41.426 --> 00:52:43.040 Of odd hobbies Prepandemic was I

NOTE Confidence: 0.70069379375

 $00{:}52{:}43.102 \dashrightarrow 00{:}52{:}44.920$ would wander around drug stores in NOTE Confidence: 0.70069379375

 $00{:}52{:}44{.}920 \dashrightarrow 00{:}52{:}47{.}092$ the area and start looking at their

NOTE Confidence: 0.70069379375

 $00{:}52{:}47.092 \dashrightarrow 00{:}52{:}49.178$ melaton in Isles and I would sort of

NOTE Confidence: 0.70069379375

 $00{:}52{:}49{.}180 \dashrightarrow 00{:}52{:}50{.}888$ keep my running list of where within

NOTE Confidence: 0.70069379375

 $00{:}52{:}50{.}888 \dashrightarrow 00{:}52{:}52{.}762$ walking area of the hospital you could

NOTE Confidence: 0.70069379375

 $00{:}52{:}52{.}762 \dashrightarrow 00{:}52{:}54{.}394$ actually find low dose melaton in so

NOTE Confidence: 0.70069379375

 $00{:}52{:}54{.}450 \dashrightarrow 00{:}52{:}56{.}046$ I could direct patients there too.

NOTE Confidence: 0.8079725166666667

 $00{:}52{:}57{.}480 \dashrightarrow 00{:}53{:}01{.}410$ Nice OK great. And and

NOTE Confidence: 0.8079725166666667

 $00{:}53{:}01{.}410 \dashrightarrow 00{:}53{:}03{.}760$ so I I think so. So the.

NOTE Confidence: 0.819050285

 $00:53:06.090 \rightarrow 00:53:09.280$ I guess one of the other questions I had was.

NOTE Confidence: 0.96429574125

 $00:53:11.670 \rightarrow 00:53:16.118$ Do you use any other technology other than?

 $00:53:16.120 \rightarrow 00:53:18.586$ Actigraphy is there anything else out

NOTE Confidence: 0.96429574125

 $00{:}53{:}18.586 \dashrightarrow 00{:}53{:}22.603$ there that is close enough to actigraphy to

NOTE Confidence: 0.96429574125

 $00:53:22.603 \rightarrow 00:53:26.329$ be used to understand activity patterns?

NOTE Confidence: 0.90176903111111

 $00{:}53{:}27{.}360 \dashrightarrow 00{:}53{:}29{.}583$ So, are you referring to things like like a NOTE Confidence: 0.5177398325

00:53:29.600 --> 00:53:32.248 wearable personal wearables? Yeah,

NOTE Confidence: 0.849884599764706

00:53:32.300 --> 00:53:34.372 I will take whatever data I can get

NOTE Confidence: 0.849884599764706

 $00{:}53{:}34{.}372 \dashrightarrow 00{:}53{:}36{.}979$ and I don't want to mess up my camera,

NOTE Confidence: 0.849884599764706

 $00{:}53{:}36{.}980 \dashrightarrow 00{:}53{:}39{.}381$ but the bullet in board that I have

NOTE Confidence: 0.849884599764706

 $00:53:39.381 \rightarrow 00:53:42.043$ right behind me in my office here

NOTE Confidence: 0.849884599764706

 $00:53:42.043 \rightarrow 00:53:44.389$ actually has examples of many different

NOTE Confidence: 0.849884599764706

 $00:53:44.458 \rightarrow 00:53:46.762$ types of sleep logs and reportable

NOTE Confidence: 0.849884599764706

 $00{:}53{:}46.762 \dashrightarrow 00{:}53{:}49.176$ data that I've gotten from patients.

NOTE Confidence: 0.849884599764706

 $00{:}53{:}49{.}176 \dashrightarrow 00{:}53{:}51{.}790$ Like I said, they tend to track

NOTE Confidence: 0.849884599764706

 $00{:}53{:}51{.}790 \dashrightarrow 00{:}53{:}53{.}740$ their data before they come in,

NOTE Confidence: 0.849884599764706

 $00{:}53{:}53{.}740 \dashrightarrow 00{:}53{:}55{.}452$ and so if all you have access to

 $00:53:55.452 \rightarrow 00:53:57.518$ and I think we also got much more.

NOTE Confidence: 0.849884599764706

 $00:53:57.520 \rightarrow 00:53:59.140$ Creative with this in the pandemic

NOTE Confidence: 0.849884599764706

 $00:53:59.140 \longrightarrow 00:54:01.268$ when we had times where we couldn't

NOTE Confidence: 0.849884599764706

00:54:01.268 --> 00:54:02.255 send out actigraphy,

NOTE Confidence: 0.849884599764706

 $00:54:02.260 \longrightarrow 00:54:03.898$ we couldn't get all the data on

NOTE Confidence: 0.849884599764706

 $00:54:03.898 \rightarrow 00:54:05.510$ the way that we normally did.

NOTE Confidence: 0.849884599764706

 $00{:}54{:}05{.}510 \dashrightarrow 00{:}54{:}07{.}934$ If they wanna send me Fitbit data with

NOTE Confidence: 0.849884599764706

 $00:54:07.934 \rightarrow 00:54:10.716$ all the caveats of how accurate that is,

NOTE Confidence: 0.849884599764706

 $00{:}54{:}10.720 \dashrightarrow 00{:}54{:}12.025$ whatever data they have available

NOTE Confidence: 0.849884599764706

 $00:54:12.025 \rightarrow 00:54:14.030$ and can send me, that's great.

NOTE Confidence: 0.849884599764706

 $00:54:14.030 \longrightarrow 00:54:15.950$ The downside to those,

NOTE Confidence: 0.849884599764706

 $00{:}54{:}15{.}950 \dashrightarrow 00{:}54{:}17{.}854$ and where I can get some insight

NOTE Confidence: 0.849884599764706

 $00{:}54{:}17.854 \dashrightarrow 00{:}54{:}19.767$ with that tiger fee that I can't

NOTE Confidence: 0.849884599764706

00:54:19.767 - > 00:54:21.327 get from some of the consumer

NOTE Confidence: 0.849884599764706

 $00:54:21.390 \rightarrow 00:54:23.124$ wearables is light exposure data and

NOTE Confidence: 0.849884599764706

 $00:54:23.124 \rightarrow 00:54:25.312$ that is a tool that we often use,

- NOTE Confidence: 0.849884599764706
- $00:54:25.312 \rightarrow 00:54:26.602$ and so we'll often find,
- NOTE Confidence: 0.849884599764706
- $00:54:26.610 \rightarrow 00:54:27.960$ for example, in these delayed.
- NOTE Confidence: 0.849884599764706
- $00{:}54{:}27{.}960 \dashrightarrow 00{:}54{:}29{.}616$ Since we can get a sense of ohh
- NOTE Confidence: 0.849884599764706
- $00:54:29.616 \longrightarrow 00:54:31.162$ you actually get a ton of light
- NOTE Confidence: 0.849884599764706
- $00:54:31.162 \longrightarrow 00:54:32.576$ right before bedtime or you have
- NOTE Confidence: 0.849884599764706
- $00:54:32.576 \rightarrow 00:54:33.966$ horrible curtains in your bedroom
- NOTE Confidence: 0.849884599764706
- 00:54:33.966 --> 00:54:35.776 and you're getting a bunch of morning
- NOTE Confidence: 0.849884599764706
- 00:54:35.776 --> 00:54:36.936 light before you're waking up.
- NOTE Confidence: 0.849884599764706
- $00{:}54{:}36{.}940 \dashrightarrow 00{:}54{:}39{.}356$ And so that's some insight that I can't
- NOTE Confidence: 0.849884599764706
- $00:54:39.356 \rightarrow 00:54:41.560$ necessarily get from the consumer wearables.
- NOTE Confidence: 0.849884599764706
- $00{:}54{:}41{.}560 \dashrightarrow 00{:}54{:}43{.}426$ But if we're just getting a
- NOTE Confidence: 0.849884599764706
- 00:54:43.426 --> 00:54:44.670 sense of overall patterns,
- NOTE Confidence: 0.849884599764706
- $00:54:44.670 \longrightarrow 00:54:46.314$ we're trying to get a sense
- NOTE Confidence: 0.849884599764706
- $00:54:46.314 \longrightarrow 00:54:47.136$ of treatment response.
- NOTE Confidence: 0.849884599764706
- $00{:}54{:}47{.}140 \dashrightarrow 00{:}54{:}48{.}946$ They're great and we've been trying to
- NOTE Confidence: 0.849884599764706

 $00:54:48.946 \rightarrow 00:54:51.100$ find ways to more easily get that data.

NOTE Confidence: 0.728532820833333

 $00:54:52.480 \longrightarrow 00:54:53.992$ Like not knowing the ends when

NOTE Confidence: 0.728532820833333

00:54:53.992 --> 00:54:57.380 you need to know the house, right?

NOTE Confidence: 0.728532820833333

 $00:54:57.380 \rightarrow 00:54:58.876$ You gotta have both sides of the equation.

NOTE Confidence: 0.728532820833333

 $00{:}54{:}58{.}880 \dashrightarrow 00{:}55{:}01{.}460$ OK wonderful, so so Sabra.

NOTE Confidence: 0.728532820833333

 $00:55:01.460 \dashrightarrow 00:55:03.972$ This is really great and so if you

NOTE Confidence: 0.728532820833333

 $00:55:03.972 \rightarrow 00:55:06.812$ were to give you know two bullets

NOTE Confidence: 0.728532820833333

 $00:55:06.812 \longrightarrow 00:55:09.560$ of advice for some body who is

NOTE Confidence: 0.728532820833333

 $00{:}55{:}09{.}655 \dashrightarrow 00{:}55{:}12{.}680$ managing a delayed phase patient,

NOTE Confidence: 0.728532820833333

 $00:55:12.680 \rightarrow 00:55:15.150$ what would be the one thing you have to do?

NOTE Confidence: 0.728532820833333

 $00{:}55{:}15{.}150 \dashrightarrow 00{:}55{:}16.690$ And one thing you should never do.

NOTE Confidence: 0.7680442225

 $00{:}55{:}18{.}180 \dashrightarrow 00{:}55{:}21{.}740$ Never give light at 8:00 AM unless that's

NOTE Confidence: 0.7680442225

 $00{:}55{:}21.740 \dashrightarrow 00{:}55{:}24.679$ their natural wake time and you have

NOTE Confidence: 0.6736409773

 $00:55:24.690 \rightarrow 00:55:26.820$ to. Why is that? Why don't you give let Adam

NOTE Confidence: 0.74570581125

 $00:55:26.830 \rightarrow 00:55:28.230$ why don't you give light at 8:00 AM?

NOTE Confidence: 0.74570581125

 $00:55:28.230 \rightarrow 00:55:29.765$ Because at that point you're

00:55:29.765 --> 00:55:31.300 probably gonna end up delaying

NOTE Confidence: 0.74570581125

 $00{:}55{:}31{.}358 \dashrightarrow 00{:}55{:}33{.}044$ them and making them even worse

NOTE Confidence: 0.74570581125

 $00:55:33.044 \rightarrow 00:55:34.590$ instead of making them better.

NOTE Confidence: 0.74570581125

 $00:55:34.590 \rightarrow 00:55:36.599$ And the one thing you should do

NOTE Confidence: 0.74570581125

 $00{:}55{:}36{.}599 \dashrightarrow 00{:}55{:}38{.}768$ is keep that melaton in dose low.

NOTE Confidence: 0.74570581125

00:55:38.770 --> 00:55:40.930 So like I said, typically half

NOTE Confidence: 0.74570581125

 $00:55:40.930 \longrightarrow 00:55:43.356$ a milligram no more than half a

NOTE Confidence: 0.74570581125

 $00{:}55{:}43.356 \dashrightarrow 00{:}55{:}44.896$ milligram to 3 milligrams don't

NOTE Confidence: 0.74570581125

 $00{:}55{:}44.896 \dashrightarrow 00{:}55{:}47.119$ get up into ten 2080 milligrams,

NOTE Confidence: 0.74769282

00:55:47.670 --> 00:55:49.434 OK? Perfect excellent,

NOTE Confidence: 0.74769282

 $00:55:49.434 \rightarrow 00:55:53.306$ so early and low and then late

NOTE Confidence: 0.74769282

 $00{:}55{:}53{.}306 \dashrightarrow 00{:}55{:}57{.}090$ and bright I guess is the.

NOTE Confidence: 0.74769282

 $00{:}55{:}57{.}090 \dashrightarrow 00{:}55{:}58{.}342$ Cool a wesome well great.

NOTE Confidence: 0.74769282

00:55:58.342 --> 00:55:59.594 Thank you very much.

NOTE Confidence: 0.74769282

 $00:55:59.600 \dashrightarrow 00:56:01.784$ And so if any body else has any other

 $00:56:01.784 \rightarrow 00:56:03.499$ questions we could probably well.

NOTE Confidence: 0.74769282

 $00:56:03.500 \rightarrow 00:56:05.698$ Actually, it's 259 so we're we're just

NOTE Confidence: 0.74769282

 $00{:}56{:}05{.}698 \dashrightarrow 00{:}56{:}08{.}227$ out of time and so thank you so much, Sabra.

NOTE Confidence: 0.74769282

 $00{:}56{:}08{.}227 \dashrightarrow 00{:}56{:}09{.}762$ This was wonderful and thank

NOTE Confidence: 0.74769282

 $00{:}56{:}09{.}762 \dashrightarrow 00{:}56{:}11{.}352$ you everyone for attending yet

NOTE Confidence: 0.74769282

 $00{:}56{:}11.352 \dashrightarrow 00{:}56{:}12.916$ another edition of our conference.

NOTE Confidence: 0.74769282

 $00{:}56{:}12.916 \dashrightarrow 00{:}56{:}15.100$ Please if you wanted to have your

NOTE Confidence: 0.74769282

 $00:56:15.160 \rightarrow 00:56:17.380$ credit for attending this conference,

NOTE Confidence: 0.74769282

 $00{:}56{:}17{.}380 \dashrightarrow 00{:}56{:}19{.}540$ you can go ahead and use the CME

NOTE Confidence: 0.74769282

 $00{:}56{:}19{.}540 \dashrightarrow 00{:}56{:}21{.}770$ code and we will see you guys in

NOTE Confidence: 0.74769282

 $00{:}56{:}21.770 \dashrightarrow 00{:}56{:}24.038$ May in the second Wednesday of May.

NOTE Confidence: 0.74769282

00:56:24.040 --> 00:56:25.190 Thank you so much everybody.

NOTE Confidence: 0.64021515

 $00:56:28.220 \longrightarrow 00:56:28.850$ My favorite.

NOTE Confidence: 0.7726614466666667

 $00{:}56{:}30{.}400 \dashrightarrow 00{:}56{:}31{.}198$ For having me.