

Optimize & Control Your Brain Chemistry to Improve Health & Performance | Huberman Lab Podcast #80

In this episode, I explain the biological roles of the four major neuromodulators—dopamine, epinephrine (aka adrenaline), serotonin, and acetylcholine—and describe how these neuromodulators impact a wide variety of mental states and behaviors, including focus, creativity, motivation, drive, learning, alertness, mood, relationships, and feelings of well-being. Then, with that foundational understanding in mind, I describe a potent toolkit of science-supported behavioral, nutrition, and supplementation tools that can be used to increase baseline levels of individual neuromodulators and that can be modified for specific goals. This episode summarizes low-or-no-cost, actionable, science-based tools that can benefit anyone in order to enhance their levels of brain chemicals and improve mental health, physical health, and performance.

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- Welcome to the Huberman Lab Podcast, where we discuss science and science-based tools for everyday life. I'm Andrew Huberman, and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. Today, we are going to discuss your brain chemistry and how to control and optimize your brain chemistry for all aspects of mental health, physical health, and performance. Many times before on the Huberman Lab Podcast, and frankly, every time I'm a guest on another podcast, I get questions about science and science-based tools for things like enhancing sleep, enhancing focus, enhancing creativity, improving relationships, getting over grief and on and on, all of

which are valid questions and for which there are protocols that are based in science and that work the first time and every time. However far more important than knowing a protocol is understanding why a given protocol works. That's why I'm always hammering on mechanism and explaining the cells and circuits and chemicals, at least to some detail, so that people can understand not just what to do, but why it works and therefore, how to change a protocol as their life circumstances change, or as goals change. Now today we are going to go even a layer deeper. We're going to explore the foundations of your biology in your brain and body that allow any protocol to work because as it turns out, all of the protocols out there, whether or not it's a breathing protocol or a supplement or a prescription drug or an exercise routine, they all tap into and leverage a core set of just a few biological mechanisms. That's right, beneath everything you are able to do and feel and indeed beneath every protocol that allows you to change for the better and optimize your mental health, physical health, and performance, there's just a small subset of chemicals that you're leveraging toward that change. So today we are going to talk about the four major pillars of neurochemistry that allow you to, for instance, be focused when you want to focus, that allow you to relax when you need to relax and de-stress, that allow you to optimize your sleep, that allow you to optimize your exercise routine or to work through a pain point in relationship or in career or in your relationship to yourself. So what I can say for sure is that by the end of this episode, you will have a much richer understanding about how your brain and nervous system and indeed your entire body work. And you'll have a much firmer understanding as to which protocols and tools to reach for given your particular goals in the moment, in the day, across the week, across the month, across the year, and indeed across your entire lifespan. So what we're really going for today are principles, deeper understanding of why any given protocol works and we are also going to discuss specific protocols. Some of those protocols I've discussed on previous episodes of the Huberman Lab Podcast, but I must say, many of the protocols and tools that I will discuss are brand new and based on research that I have not discussed at all, simply because the research papers came out only recently, or these are papers that I only recently unearthed. In fact, I'm going to share with you two recent studies in a moment that are exceedingly important for optimizing your sleep and these are studies that, again, I've never discussed in any episode on sleep or on any other podcast. So by the end of today's episode, you're going to have far more knowledge about your biology and psychology than you did at the start and you'll be armed with many more tools and most importantly, principles so that

you can navigate not just the tools presented on this podcast,

00:03:40 Momentous Supplements

but in the vast landscape of tools that are out there for mental health, physical health and performance. The Huberman Lab Podcast is proud to announce that we've partnered with Momentous supplements. We've done that for several reasons. First of all, the quality of their supplements is exceedingly high. Second of all, we wanted to have a location where you could find all of the supplements discussed on the Huberman Lab Podcast in one easy to find place. You can now find that place at livemomentous.com/huberman. In addition, Momentous supplements ship internationally, something that a lot of other supplement companies simply do not do. So that's terrific whether or not you live in the US or you live abroad. Right now, not all of the supplements that we discuss on the Huberman Lab Podcast are listed, but that catalog of supplements is being expanded very rapidly and a good number of them that we've talked about, some of the more prominent ones for sleep and focus and other aspects of mental and physical health

00:04:30 Sleep & Maintaining Healthy Metabolism

are already there. Again, you can find them at livemomentous.com/huberman. Every so often, I come across a study or set of studies that I get so excited about that I start telling everybody in my immediate life and I insist on also sharing it with you, the listeners of this podcast, because I find the information to be so incredibly interesting and actionable. The two studies that I'm going to discuss both relate to sleep and sleep states and how to access better sleep. The first one was published in the journal Cell Reports, Cell Press journal, excellent journal. And the title of this paper is "Rapid and Reversible Control of Human Metabolism "by Individual Sleep States". We will provide a link to this study in the show captions. The first author is Nora Nowak, N-O-W-A-K. And basically what they did is they measured the different forms of metabolism that occur while humans sleep. As far as I know, this is one of the first studies of this kind. There are many studies of metabolism. There are many studies of sleep. This study focused on how different states of sleep such as rapid eye movement sleep, which is associated with dreaming and high emotional content dreams versus slow wave sleep, which tends

to be more focused on physical repair of the body, more mundane dreams, how those different states of mind during sleep relate to different aspects of metabolism and what they found was absolutely fascinating. First of all, they found that sleep states regulate more than 50%, half of all the metabolite features detected in human breath. What does that mean? Well, it turns out that you can figure out what humans are metabolizing in particular, more lipids or more carbohydrate, whether or not they're relying more on glucose metabolism based on the contents of their breath. This is true during waking and during sleep. And this is what allowed them to do these incredible measurements of what's being metabolized during sleep. They measured close to 2000 metabolites in breath, every 10 seconds across the entire night's sleep. And what they found was that there are major pathways related to lipid metabolism, fat metabolism, or to carbohydrate metabolism or other forms of metabolism that are up or down regulated as human beings transition between slow wave sleep, rapid eye movement sleep and waking. And you might say waking? Well, yes, they also looked as people fell asleep and as they emerged from sleep. And believe it or not every so often during sleep, you wake up, you didn't know this, but you wake up in the middle of the night, you look around and you go back to sleep. You're not aware of it because you're still in a rather sleep like state, although you are awake. What they found was that sleep and the various states of sleep regulated individual metabolic pathways. They found for instance, that the switch from sleep to wakefulness reduces fatty acid oxidation. So that means while you're asleep, you're oxidating more fatty acids. And as you wake up, that becomes less the case. And there's a switch in slow wave sleep that increases fatty acid oxidation. And there's this transition from rapid eye movement sleep to other aspects of sleep that brings about things like the so-called TCA cycle. Some of you familiar with metabolism will be familiar with the TCA cycle, the so-called tricarboxylic acid cycle, intermediates, that's fancy nerd speak for specific aspects of metabolism being regulated during this rapid eye movement sleep transition. What does all this mean? And how is this actionable? Well, on many episodes of the Huberman Lab Podcast such as the master sleep episode and the episode that we're going into in further depth today, we're going to talk about sleep and how to optimize sleep. It's been thought of, but not really tamped down that quality and depth of sleep and duration of sleep is important for metabolism during the daytime. And indeed that's the case. If people are sleep deprived or they're not sleeping enough, things like glucose metabolism, et cetera, get really disrupted during the daytime. But what this current study shows is that the metabolism that you experience during sleep,

or to be more specific, the range of different types of metabolism that you experience during sleep may serve to tune up or to ensure that the specific aspects of metabolism that you require during wakefulness are working properly. In addition to that, this study clearly shows that getting enough sleep allows you to transition through all the various forms of metabolism and use all those different forms of metabolites during sleep in a way that's immensely beneficial for the systems of your brain and body. So the take home message here is that, as the author state, sleep and experiencing the different states of sleep, slow wave sleep early in the night, predominantly, plus rapid eye movement sleep toward the end of the night is extremely important for optimizing metabolic circuits for human performance and health. In other words, by not getting sufficient duration sleep, you're not allowing your body and brain to transition through all the different aspects of fuel utilization and you're not teaching your brain and body how to use similar types of fuels during wakefulness. So again, all of this points to the fact that we need to be getting sufficient quality and duration of sleep. So if you're sleep deprived, even by an hour or so, you're going to get far less rapid eye movement sleep because rapid eye movement sleep is what occurs toward the end of a sleep night. During the early part of the night, far more slow wave sleep. In getting less rapid eye movement sleep, we know it makes you more emotionally labile, but now we know it's also going to alter certain forms of glucose metabolism during the night

00:09:52 Tools: How to Wake Up Earlier, Night Owls

and during wakefulness. So that all underscores the need to get sleep. But then the question is how to get enough sleep and how to make sure you get into all these different sleep states. And this is particularly important for you so-called night owls. There's a lot of controversy out there as to whether or not different so-called chronotypes exist, that is people who just naturally or genetically want to be an early bird, wake up early and go to bed early. So these people that wake up at 4:00 AM and would be most comfortable going to bed by seven or 8:00 PM or 9:00 PM. Then they are so called night owls, people that would feel best or tend to feel best when they go to sleep at 1:00 AM, 2:00 AM, even 3:00 AM, and like to wake up later 8:00, 9:00, 10:00, or even 11:00 AM or noon. And then of course, most people go to sleep somewhere between 10:00 PM and midnight and wake up somewhere between 5:00 AM and 7:00 AM, or I suppose more typically 6:00 AM and 8:00 AM. Now whether or not real chronotypes exist or whether or

not people simply select schedules for sleep and wakefulness that they like because of their social schedules or the activities they enjoy. For instance, some people like to really go out, they like to go out dancing or hear music, or spend time in venues that are only open late at night, and don't even open until noon or after. Other people like myself rarely go out at night but I like to get up early. I like to exercise. I like to see the sunrise, et cetera. So I don't know if I'm a morning person or an evening person. I just know the things I enjoy tend to happen in the early part of the day. And the things that I don't enjoy quite as much tend to happen late at night. Regardless of whether or not there are real genetic propensities to be a night owl or an early bird or a sort of typical person right there in the middle, it's very important that people have some control over their sleep schedule and even more important, that people are able to get sufficient amount of REM sleep and slow wave sleep, for many reasons, but including the reasons I discussed in the previous study related to metabolism. I'm very excited, therefore, about a study that came out in sleep medicine. This was a few years ago, but somehow I missed this one. It was published in 2019. And the title of this article is "Resetting the Late Timing of 'Night Owls' "Has a Positive Impact on Mental Health, "Physical Health and Performance". This is a study done in humans, focusing specifically on people that like to stay up late and sleep in, but who desire to be able to get up and feel alert in order to go to work or study and they want to go to sleep a bit earlier. And so there are a lot of questions embedded in this study in particular, whether or not people can actually shift their schedule by a few hours or more. Some people out there contend that if you're a night owl, that's just going to be impossible or very, very challenging to do. Turns out it's not impossible and it's not even that challenging to do provided you do the right things. Just a brief overview of the study and then I'll give you the key takeaways. It was a randomized control trial. It involved a number of different people, both male and female. And what they did was they used non-pharmacological, practical interventions in a real world setting, here I'm paraphrasing. They used targeted light exposure. They used consistent sleep, wake times. They used fixed meal times, caffeine intake and exercise. And this is one of the reasons I love this study so much because I've done episodes where I've talked about temperature, exercise, feeding, and most importantly, light exposure as a way to control and shift your sleep wake cycles, your so-called circadian timing and entrainment. What did they find? Well, they found "Significant improvements "in terms of mood so far less depression and stress", subjectively measured, "as well as improved cognitive performance", that was objectively measured. So improved reaction

times, improved physical grip strength, which is actually a measure not just of strength per se, but also of nervous system function and a number of things that people could do in order to optimize their morning hours, even though they were night owls previously. What did they have people do? Well, I'm going to just going to list this off sort of rapid fire succession. Then we'll provide a link to the study if you want to learn more. First of all, they told participants to try and wake up two to three hours before their typical wake up time, two to three hours. That seems brutal to me and probably seems brutal to you if you're somebody who typically wakes up at 10:00 AM to try and get up at eight or even 7:00 AM consistently, but they were also asked to maximize outdoor light exposure during the mornings for reasons that if you've listened to this podcast before, if you've heard me talk about before, you know, that I'm constantly talking about, I'll probably go into the grave shouting, please get as much light exposure from sunlight early in the day as possible because it sets in motion a huge number of things that are beneficial for your mental health and physical health, including dopamine production, timing melatonin production correctly, reducing cortisol peaks late in the day, et cetera, et cetera. So they asked them to get a lot of outdoor light exposure. They didn't give them a specific amount. What they said, maximize outdoor light exposure during the mornings, the time before noon. And again, they had them waking up two to three hours before their habitual wake up time. They were also told, and this is very important if you're going to shift your schedule earlier, to try and keep sleep wake times fixed between their work days and their weekends. So not sleeping in on the weekends or not having any sleep in days, regardless of how well they slept the night before. How fixed? Within 15 to 30 minutes of their pre-designated time. So if they were waking up at seven o'clock one day, they set their alarm and they made sure they got out of bed at seven o'clock every day plus or minus 30 minutes, but never later than 7:30, never earlier than 6:30. Participants were also asked to try and go to sleep two to three hours before their habitual bedtime. So again, these are people that want to stay up late, like 11:00 PM, perhaps, but even as late as 1:00 AM or 2:00 AM. And now they are asked to go to sleep two to three hours before their habitual bedtime and to wake up two to three hours earlier, as I mentioned earlier. They were also told, and I love this because it fits with many of the things we've talked about on this podcast before, to try and limit light exposure during the evenings, dim the lights or limit altogether artificial lights. Lot of reasons for that, I covered that in the Master Sleep episode, I covered that in the Optimized Health Using Light episode. You can find those at HubermanLab.com.

They're asking them to do that here. And they asked participants to keep a regular schedule for their daily meals, not eating on the hour consistently, you know, at 9:00 AM, noon, 3:00 PM, exactly. But within again, about 15 to 30 minutes, they're always eating at the same times. That was also important. And again, that's because we have these so-called food in trained circadian clocks. When you eat, tells your body when to be alert and when you're not eating, when to be asleep. And they were told to not drink any caffeine after 3:00 PM in the afternoon. Another theme that we've talked about on this podcast. They were also told not to take naps after 4:00 PM. Naps are an interesting feature of the sleep wake cycle. To be very brief about this and to pull from the episode that I did with world sleep expert from the University of California Berkeley, Matt Walker, naps are great for many people, but don't nap if it interferes with your nighttime sleep. And in this study, they told them don't nap after 4:00 PM. And if you are a napper, don't nap for more than 90 minutes. 10 minute naps are fine. 20 minute naps are fine. Zero minute naps are fine, but don't nap for more than 90 minutes. And don't nap after 4:00 PM. And to exercise during the morning. Now this one can be a bit controversial because I know a lot of the PTs out there and a lot of the online, you know, gym rats and people who, and runners too, for that matter, will say, well according to body temperature and research, it's best to exercise in the afternoon. Look, it's better to exercise sometime as opposed to no time, but if you're focused on how to shift your schedule earlier, meaning get up earlier and go to sleep earlier, this study had people exercise in the early part of the day, certainly before 2:00 PM and ideally before noon. So again, this is a really important study because it combines a lot of different variables to arrive at this very impressive shift where people can get up two to three hours earlier and then pretty consistently and reflexively start going to bed two to three hours earlier, feeling more alert during the day, again, improvements in cognitive performance, mood and physical performance, grip, strength, et cetera. Very few studies are able to or are willing to tackle so many variables and combine them in one study. This paper, I think, does a marvelous job of doing this and is incorporating things that individually, each have some support for them in animal studies and previous human studies. But as far as I know, this is one of the few studies that really combines all these different features in one place, eating times, keeping those consistent, getting maximal sunlight exposure earlier in the day, getting up at a consistent time, going to sleep at a consistent time and on and on. It's a really marvelous study for that reason. And I think for any of you that are night owls and any of you that want to reinforce your early waking and early to bed

times, and I think for most all of you who fall into that general middle category of tend to go to sleep somewhere between 10:00 PM and midnight, 'cause that's most people and tend to wake up sometime between 6:00 AM and 8:00 AM, well, maybe you want to become more of an early riser or maybe you're going to travel or the seasons are changing and you want to shift your time or you have a new job, et cetera, or something that's actually very common in terms of relationship struggle. You want to match your wake sleep times, or maybe you want to offset your wake sleep times from a significant other, these sorts of approaches that I described here and that are supported by the data in this paper are absolutely powerful and science supported. And I'm certain that if you were to apply them, that you would see essentially the same effects

00:19:32 AG1 (Athletic Greens), Thesis, InsideTracker

that were observed here. Before we begin, I'd like to emphasize that this podcast is separate from my teaching and research roles at Stanford. It is however, part of my desire and effort to bring zero cost to consumer information about science and science related tools to the general public. In keeping with that theme, I'd like to thank the sponsors of today's podcast. Our first sponsor is Athletic Greens now called AG1. AG1 is an all-in-one vitamin mineral probiotic drink that also includes adaptogens and digestive enzymes for health. Now the probiotics are particularly important to me because there is now a wealth of data showing that our gut microbiome, that is trillions of little microbacteria that are good for us, impact our immune system, our hormones, and the so-called gut brain access, the connections between our gut and our brain that go in both directions, gut to brain and brain to gut, that control things like our mood, our ability to think clearly and focus and overall brain health. And with AG1, I'm able to optimize that gut brain access through the probiotics and the vitamins, minerals, adaptogens and digestive enzymes, support a number of other things that relate to immediate and long-term health. In fact, anytime people ask me, what's the one supplement they should take, I say AG1 Athletic Greens, because it's going to cover all of your bases to the greatest degree. If you'd like to try Athletic Greens, you can go to athleticgreens.com/huberman to claim a special offer. They'll give you five free travel packs that make it easy to mix up AG1 while you're on the road. And they'll give you a year supply of vitamin D3 K2. Vitamin D3 and K2 are important for cardiovascular function and calcium regulation, and a number of other important aspects of health.

Again, go to athleticgreens.com/huberman to claim that special offer of the five free travel packs and the year supply of vitamin D3 K2. Today's episode is also brought to us by Thesis. Thesis makes custom nootropics. And frankly, I'm not a big fan of the word nootropics. I've said that on various podcasts and on social media posts and the reason I'm not a fan of the word nootropics is it means smart drugs, but as a neuroscientist, I know that we don't have circuits in the brain or chemicals in the brain for being smart. We have circuits in the brain for focus and for task switching and for creativity. And oftentimes, those circuits differ from one another, although they collaborate to create things that we think of as intelligence or focus or creativity, et cetera. Thesis understands this and for that reason has developed custom nootropics that are matched to your particular goals and to your particular biology. They give you the opportunity to try several different blends over the course of a month and discover which ones work best for you and which ones don't. In addition to that personalization,

00:22:05 Nervous System Overview

they take it a step further by offering free consultations with a coach to help you optimize your experience and dial in your perfect formulas. I've been using Thesis for about eight months now and I can confidently say that their nootropics are the best that I've ever used. My go-to formula is the Clarity formula or the Motivation formula when I'm going to work or work out, meaning I'm going to do focus cognitive work, or I'm going to exercise. I also like their Energy formula prior to exercise. To get your own personalized nootropic starter kit, go online to takethesis.com/huberman. You can take a three minute quiz that will help match you to the best custom nootropics to start with. And Thesis will send you four different formulas to try in that first month. Again, that's takethesis.com/huberman and use the code Huberman at checkout to get 10% off your first order. Today's episode is also brought to us by InsideTracker. InsideTracker is a personalized nutrition platform that analyzes data from your blood and your DNA to help you better understand your body and help you reach your health goals. I've long been a believer in getting regular blood work done for the simple reason that many of the things that impact your immediate and long-term health can only be measured from a quality blood test. And nowadays with the advent of modern DNA test, you can also get insight into, for instance, what is your biological age and how does that compare to your chronological age? And of course, your biological age is really the one that matters. With

InsideTracker, there's an additional advantage over other blood tests and DNA tests. And that is with many blood tests and DNA tests out there, you get information back about hormones, lipids, et cetera, but you don't know what to do with that information. With InsideTracker, they have a very simple, easy to use personalized platform that tells you what sorts of changes to make in your nutrition, possible changes to supplementation, behavioral changes, et cetera, that will allow you to bring the numbers related to your hormones and your lipids, et cetera, into the ranges that are optimal for your mental health, physical health and performance goals. If you'd like to try InsideTracker you can go to insidetracker.com/huberman to get 20% off any of InsideTracker's plans. That's insidetracker.com/huberman to get 20% off. Let's talk about how to optimize and indeed how to control your brain chemistry for a sake of health and performance. Now in order to do that, we all need to be on the same page about some basic facts. Some of those basic facts involve learning some basic biology. And I promise that even if you don't have a biology or chemistry background, everything I'm about to say should be accessible and clear to you. The important thing to know is that your brain and your spinal cord and the rest of your so-called nervous system control all the organs of your body and that all the organs of your body feed back, meaning they communicate through chemicals and other means, to your nervous system. Now your nervous system plays a particularly important role in generating everything from sleep to wakefulness, creativity, stress, calm, et cetera, by way of a particular type of cell-cell interaction. And that's called synaptic communication. What is synaptic communication? Well, in order to understand that let's dial back a little bit further and try and understand for a moment what makes up your nervous system. In its simplest form, your nervous system is made of nerve cells that we call neurons. Neurons communicate with one another through chemicals. They release certain chemicals that make other neurons more or less likely to be electrically active. What do we mean by electrically active? We mean, as it sounds, electricity passing down through cells and then literally causing electricity in other cells. The simplest way to think about this is maybe when you were a kid or maybe even still now, you would wear socks and you'd shuffle along the floor to generate some static electricity, and then you'd touch someone [playful whirring] and you'd shock them with your finger. I'm a younger brother so I'd occasionally do that to my sister. I had friends, we would do that to one another. I know it's kind of silly and childish, yet, it illustrates the principle that we can generate electricity and pass electricity to other beings or in the case of neurons, from one neuron to the next. The way neurons do that,

is that in between the neurons, they're little spaces, those little spaces are called synapses and neurons literally vomit, well, they don't literally vomit, but they release little packets of so-called transmitter chemical into that space we call a synapse. It travels across the synapse. It attaches to the cell on the other side, the other neuron. And then depending on what that chemical is, it either makes that next neuron more electrically active or less electrically active, so called excitation, it either excites the next neuron to be electrically active also, or it inhibits, it prevents the next neuron from being electrically active. So again, very simply, we have nerve cells that communicate with one another through electricity and chemicals that inspire that electricity and the little gaps between neurons are called synapses. If you can understand that, I'm certain you can make it through the rest of the episode and that you'll get all the depth and important detail that you need to know. But I want to go just a little bit further and explain that neurons don't just talk one-to-one. There are trillions of neurons in your nervous system that allow you to be happy, to be in love, to be sad, to be in grief, to remember things and so on. And what you do at any moment, what you feel and what you think relates to which so-called neural circuits are active. So a lot of times we think about brain areas and we've all seen these pictures of the brain where, you know, someone was in a fMRI scanner, or they were in a brain scanner of some sort, and they saw a picture of something and a certain area of the brain lights up as it's called. That lighting up of the brain really reflects the activity of hundreds, if not thousands, maybe even millions of neurons in that region. Those images of brain areas lighting up and indeed talking about brain areas lighting up, can be a little bit or a lot misleading because in fact, no single brain area controls any one single perception or behavior or feeling state. Rather, we have so-called neuro circuits, chains of neurons, chains of specific neurons that is, that create different states of mind that lead to specific behaviors that lead to specific emotional states. And those neural circuits are made up of lots of different brain areas that light up in particular sequences. And when I say light up, excuse me, what I mean is that particular brain areas either excite or prevent the excitation, that is they inhibit other brain areas in a particular sequence. Much like keys on a piano played in a particular sequence, makes up a particular song, particular brain areas activated or made silent in a particular sequence leads to a particular behavior like getting up out of a chair or a particular feeling state like being particularly happy one day when you wake up or particularly depressed, whether or not that depression is caused by a life event or whether not it arises spontaneously. So we have neurons, we have synapses and we have neural

circuits. And vitally important is the fact that which neural circuits are active and which neural circuits are likely to be less active at any given moment, depends on two major categories of chemicals. It depends on hormones and it depends on so-called neuromodulators. Now we're mainly going to focus on neuromodulators today because those are the things that if you can learn to control them, and indeed there are tools to control them, then you can control which neural circuits are more likely or less likely to be active in you at any given moment. And in doing so, you can control whether or not you are going to be alert and focused or deeply asleep. You can control whether or not you are going to be in a creative state or whether or not you're going to be in a state of mind more fit, more capable that is of doing focused work or math or more so-called linear types of work where there's a correct answer. There's a specific thing to follow and you're simply going to plug and chug as it were through a particular set of steps in order to accomplish something. Or for instance, whether or not you're going to be in a more relaxed and creative state where you're thinking about new ideas or new ideas just seem to be spontaneously coming to mind. All of that can be controlled to a considerable extent by leveraging these so-called neuromodulators. What are neuromodulators? Neuromodulators are particular chemicals that make it likely that certain neuro circuits will be active and not others. And the four neuromodulators that we're going to talk about today that are of the utmost importance for your goals are dopamine, epinephrine also called adrenaline, serotonin and acetylcholine. That's dopamine, epinephrine, serotonin and acetylcholine. Today, I'm going to teach you how each of those different categories of neuromodulators work and the things that you can do to control those neuromodulators, that is increase them or decrease them through behavioral tools and supplementation, in ways that allow you to access the brain and body states that you want

00:31:32 How Neuromodulators Work

at the times that you want. Just very quickly. I want to talk about how neuromodulators are able to work, regardless of whether or not it's dopamine or serotonin or epinephrine, et cetera. There are many features of how neuromodulators work, but for sake of today's discussion, we only need to focus on two of those features. And those are fast-acting features and longer slower features or what we call baseline features. What am I talking about when I say faster or baseline? Well, consider that at any given moment, whether

or not you're asleep or awake, whether or not it's morning or afternoon or night, you have some amount of dopamine being released in your brain and body, some amount of serotonin, some amount of epinephrine and some amount of acetylcholine. It is rarely, if ever the case, that you have zero dopamine or zero serotonin. You know, so often we hear about someone being dopamine depleted or these days, you hear a lot about that anyways. Or you'll hear that people's serotonin is bottomed out. In reality, none of these neuromodulators ever disappear completely, but they tend to be present at different levels or different relative levels. Another important thing to point out is that they don't work alone. In fact, as you'll soon learn, dopamine and epinephrine are close cousins that collaborate in terms of creating states of focus and motivation, for instance, or in creating states of energy and the pursuit of particular goals. When I say they're close cousins, what I mean is that they tend to impact some of the same neural circuits. And believe it or not, dopamine and epinephrine are chemically related, too. I'll just tell you right now that epinephrine is actually derived from dopamine, chemically epinephrine, that is adrenaline, is made from the molecule dopamine. Now dopamine and serotonin can also work together to impact certain circuits in the brain. But in large part, they operate on separate circuits. And acetylcholine, which you'll soon learn is involved in states of focus and can actually open up, it can literally create states in the mind in which your brain is more plastic and able to change and learn more quickly. Well, acetylcholine can do that on its own, but rarely does it do it on its own. More typically, it gets assistance from some of the other neuromodulators. Now that might seem like it complicates the picture, but it actually makes the picture far simpler because what we can say for sure is that the fast actions of dopamine or the fast actions of epinephrine, serotonin or acetylcholine are actions that occur on the order of seconds or minutes or up to about an hour or so. Whereas the slower actions of those neuromodulators tend to occur on the order of hours, days, or even weeks.

00:34:24 Baseline Neuromodulator Levels, 3 Daily Phases

Now perhaps surprisingly, I'd like to focus on the slow actions of the neuromodulators first, because those slow actions of the neuromodulators are happening in you and in me and in everyone right now, and they set the backdrop, the context in which the various tools to manipulate dopamine, epinephrine, serotonin, or acetylcholine will work. What do I mean by the context or the backdrop or the baseline? Well, it's fair to say that most

people are awake during the daytime and asleep at night. I do realize that there are people who are going to be doing shift work or they're raising young children, or that might have a sick person at home that they're tending to, et cetera, or even have insomnia, they're tending to them. So schedules of sleep and wakefulness will vary, but in general, everybody, regardless of whether or not you're nocturnal or you're, so-called, diurnal, your awake during the day, pretty much everybody follows a schedule in which from zero to nine hours after waking, that is from the time you wake up until about nine hours later, the neuromodulators, dopamine and epinephrine, tend to be at their highest levels that they will be at any point in the 24-hour period, in any period of the day. So we can call this zero to nine hour period phase one of the day, just for simplicity. And I've referred to this before in a previous episode, but not in this exact context. From nine to about 16 hours is what we would call phase two. And that's when dopamine and epinephrine levels tend to subside a bit compared to the earlier phase one part of the day and serotonin levels start to increase. And then phase three of the 24-hour cycle, which is from about, and again about the zero approximates, from about 17 hours after waking until about 24 hours after waking is phase three of the day. And during that time, there is chaos in terms of which neuromodulators are most present in the brain. And by chaos, what I mean is that during sleep, you have incredible peaks in acetylcholine and drops in acetylcholine. You have incredible peaks in dopamine and drops in dopamine. You have incredible peaks in serotonin and drops in serotonin. Most often, you are not going to see much if any release of epinephrine, adrenaline, and that's because epinephrine, also called adrenaline, tends to wake us up and put us into action mode behaviors and that's simply not happening during sleep. But for the other three neuromodulators, across the night, it's sort of chaos. You've got peaks and drops and peaks and drops in different combinations than you would ever see in wakefulness. And this plays important roles in dreaming, important roles in some of the reparative functions of sleep. The point is that during that phase three, the levels of neuromodulators are all over the place, but it's not random, right? I say it's chaos, but it's organized according to the specific reparative goals of sleep, the specific metabolic roles of sleep, et cetera. We're not going to focus too much on phase three today because phase three of the 24-hour cycle, that 17 to 24-hour period, is one in which you ought to be deeply asleep, whether or not you're nocturnal or diurnal, right? 17 hours after waking, you ought to be asleep. And there are a lot of episodes of this podcast. And indeed, today, I started talking about two particular studies related to sleep, and there

are a lot of tools to enhance sleep, et cetera. And of course there are things that you can do in the late portion of phase two of the day in order to enhance your transition time into and depth of sleep. But you can't really do much during sleep, right? You're not taking supplements. You're not doing breathing practices. There are things to fall back asleep, but you're not really doing much during sleep. So we're mainly going to focus on what we're calling phase one and phase two. Phase one, being this dopamine epinephrine dominated phase of our day. And phase two being this more serotonergic or serotonin dominated portion of the day. And then you might say, well, what about acetylcholine? You forgot about acetylcholine? Well, we didn't forget about acetylcholine. Acetylcholine is under control more in terms of what we happen to be doing at any given moment, whether or not we're focusing or not focusing, whether or not we're learning or not learning. And here I'm referring to acetylcholine specifically in the context of the brain and thinking, because as some of you are probably shouting out there, right, if you're an exercise physiologist or you know anything about how the brain controls movement, acetylcholine is used at the nerve to muscle synapse, right? So neurons don't just control other neurons electrically. The way you are able to move in fact is because neurons are controlling the electric activity of muscles, literally the contraction of muscle fibers, and that control is exerted through the release of acetylcholine. So acetylcholine is working at muscles, as well, but we're not focused on that today. We're focused on what we can do during phase one of the day and what we can do during phase two of the day to control the specific neuromodulators, dopamine, epinephrine, serotonin, and acetylcholine, toward particular end goals. And as I've been harping on for the last five or 10 minutes or so, it is important to understand that in the early phase one part of the day, again, zero to nine hours, dopamine and epinephrine already dominate the neuromodulator landscape. That is they are already elevated and then they will taper off in phase two. Whereas in phase two of the day, serotonin tends to dominate more than dopamine and epinephrine. And so if you think about that, what it means is that if your goal is to increase serotonin in order to get some particular effect on your mental performance or physical performance or health, or if your goal is to increase your dopamine or epinephrine, to get some particular effect on your mental health, physical performance, et cetera, well, then you need to consider what the background level of dopamine or epinephrine or serotonin happens to be because in doing so, you will know which tool to select and how hard you need to push on that tool, right? If your levels of dopamine are already riding pretty high, because it's the early part of the day, well then it

doesn't take a whole lot more to get dopamine to a level in which it can, for instance, change your level of motivation. Whereas if you are in the late part of the day, let's say eight or 9:00 PM, and you have a lot of serotonin swimming around in your system and you really need to be focused and alert, well, you can do that by leveraging the dopamine and epinephrine system and indeed the acetylcholine system too, but you're going to have to resort to tools that can do that far more potently and that can do that in a much more sustained way if you're going to access the state that you want. So again, it's really important to understand what the backdrop of these neuromodulators is, the so-called baseline and that they vary across the day if you are going to be able to leverage tools to optimize your brain chemistry. Anyone that tells you do this protocol in order to increase your dopamine, do this protocol, or take this supplement to increase your serotonin, they can be telling you the absolute truth, but if you don't consider the backdrop over which that supplement or behavior is going to have its effect, well, then you can't really predict the effect it will have. But if you can understand these backdrop baseline elements to how neuromodulators work, well, then you're in a terrific position to leverage the best tools in the immediate and short-term

00:42:15 Hormones Modulate Neuromodulators

and that is on the order of seconds, minutes and hours. Before we dive into the more pointed, directed effects of specific tools on neuromodulators, I'd like to just briefly mention hormones because they are also important for understanding the background and the context and these baseline levels of neuromodulators. Now here, I'm going to paint with a bit of a broad brush, but what I will say is accurate, even though it might not be exhaustive. What I mean by that is everything I'm about to say is true, but it doesn't cover every example in detail and nuanced possibility out there. Hormones have many different effects on the brain and body and not unlike neuromodulators, some of those effects are very fast. Some of them are very slow. In fact, certain hormones, for instance, the steroid hormones, like estrogen and like testosterone and corticosteroids and here, of course, I'm referring to the steroid hormones for what they are. They are indeed steroid hormones, but I'm not talking about steroids that people inject for sports performance or for physical augmentation. I'm talking about the steroid hormones that you make naturally because indeed you make these naturally. Well, the steroid hormones can actually control gene expression. They can change the identity of cells

and the genes and proteins that cells express. This is why during puberty, for instance, testosterone and estrogen are released into the body, growth hormone is released into the body and bodies and voices and personalities and brains change tremendously because literally there is a transformation of the breast tissue, of the testicular tissue, of the ovarian tissue, of the bones, of the muscles, of the tissues and cells that control hair growth. Gene expression changes in all those cell types. And the child becomes an adolescent, becomes a young adult, right? That's what puberty really is. In fact, puberty is perhaps the most dramatic transformation that we go through in our entire lifespan in terms of our aging, 'cause indeed it reflects a very rapid, I should mention, period of aging and transformation of the identity of cells. So steroid hormones and other hormones can have very slow long-lasting actions in that way. They can also have very fast actions. So for instance, adrenaline, epinephrine, released from the adrenal glands can immediately make your heart beat faster, can immediately change the circumference of your blood vessels and arteries and capillaries and change the way blood flows. It can change the way you see the world, literally. It does change the way you see the world through your visual system. And that all happens on the order of hundreds of milliseconds or seconds, these are extremely fast actions. Corticosteroid also can have fast actions and slow actions. But since this isn't a discussion about hormones per se, and we've done entire episodes like the Optimize Testosterone and Estrogen episode. You can find that at HubermanLab.com. Or the interview with the incredibly knowledgeable and clear and really wonderful tutor of actionable information, Dr. Kyle Gillette, who is also on this podcast, you can learn a lot about hormones there. Today, we want to think about hormones as they relate to these neuromodulators, the dopamine, serotonin, epinephrine and acetylcholine, and in general, testosterone tends to collaborate with and increase the action of dopamine. That's not always the case, but in general, when testosterone goes up, dopamine goes up and sometimes even vice versa. When dopamine goes up, testosterone go up. And this is true for both males and for females. In general, when corticosteroids like cortisol and some related steroid hormones increase, epinephrine levels go up. And in general, when hormones like oxytocin or prolactin are increased, levels of serotonin go up. We can't draw a direct link between any one hormone system and acetylcholine. Acetylcholine kind of sits off in a category of its own in that way. But again, in general, testosterone and dopamine tend to collaborate in the same direction. Cortisol and epinephrine tend to collaborate in the same direction. Oxytocin and prolactin, which are hormones, and serotonin tend to

collaborate in the same direction. And then we have poor old, lonely acetylcholine off on its own, but it's not poor and lonely. It actually has incredibly potent effects on its own. So it's really that it just doesn't mean much help from the hormone systems or at least not the steroid hormone systems in order to have its tremendous effects. Now a lot of what people think about and will do when trying to improve mental health and physical health is they will try and increase or decrease certain categories of hormones of the sort that I mentioned, testosterone, estrogen, oxytocin, and prolactin, so on. But oftentimes, the effects of those manipulations in hormones that are going to be most salient are not going to be due to the direct effects of those hormones. Sometimes it could be. But oftentimes it's going to be due to their effects on the brain and nervous system by way of how those hormones impact neuromodulators. So for instance, there are various things that people can do, both men and women, to increase their testosterone and estrogen in the appropriate ratios. I talked about one such approach in a previous episode, and that is to get sunlight onto a large portion of one's skin each day. Believe it or not, this actually works. And it works because your skin is actually an endocrine organ, a hormone secreting organ. It's a beautiful study. I've covered it on this podcast before. We will provide a link to this study again, but it had people spend at least 20 minutes or so, closer to 30 minutes, each day, trying to maximize sunlight exposure to as much of their skin as they could in terms of still maintaining decent exposure, meaning not over exposing themselves in a cultural way, meaning wearing enough clothes that they were decent, but still getting a lot of sun exposure, a couple of times per week or more. What they found was that people's testosterone and estrogen levels went up. Feelings of well-being went up. Feelings of well, or I should say increases in libido were observed, as well. They subjectively reported more passion, et cetera, testosterone and estrogen did indeed both go up. And again, I want to highlight that increases in estrogen, not just testosterone, are related to increases in libido in both men and women. This is why you never want to crush your estrogen down to zero, whether or not you're male or female, if you want to maintain some sort of healthy libido and general feelings of well-being, unrelated to libido. Well, many of those effects we know are not due to direct effects of testosterone and estrogen, but rather are due to the effects of testosterone and estrogen on the neuromodulators, dopamine and serotonin, because much of libido and feelings of well-being and feelings of relaxation, but also desire, motivation, et cetera, originate because of the activation of neural circuits that dopamine controls and promotes and that serotonin promote and control. So this is very important to understand as we move

toward more specific discussion of the chemicals that we call neuromodulators, because hormones are controlling those neuromodulators in a very slow modulatory way. So yes, I said it, hormones modulate neuromodulators. I sort of said it twice on purpose. And this is a dramatic and potent effect. So I'll just give you one more example. The hormone prolactin tends to be antagonistic. It tends to reduce amounts of dopamine or at least when prolactin levels are high, dopamine levels tend to be lower. You observe this after the birth of a new child, you observe this post coitally after mating, in all species, humans and animals. When prolactin is elevated, serotonin tends to be elevated. And when prolactin is elevated, levels of dopamine and the effects of dopamine tend to subside. Now as I move toward explaining what each of the four categories of neuromodulators do, this will start to make more and more sense as to why this would be. I always say I wasn't consulted in the design phase, meaning I didn't design these circuits. And if anyone tells you that they did, you should back away quickly because none of us design these circuits. This is the way that evolution and nature created these systems. And they tend to work in a bit of a seesaw fashion, prolactin up, dopamine down, right? Dopamine up, prolactin down. In general, that is the way they work. So if we are to take a look at how each of these neuromodulator systems functions on its own, while understanding that they never truly function on their own, we can start to really make sense of the landscape of tools that are available to us and which tools are going to be most powerful to select if our goal is for instance, to be focused or if our goal is to be less stressed or if our goal is to be highly motivated and highly focused for sake of learning. All of that is indeed possible if you understand these four neuromodulators and you understand that while there are many tools ranging from pharmacologic to behavioral that can tap into these neuromodulator systems, that can kind of press on the gas of dopamine, pull back on serotonin and so on, but that there are particular tools, both behavioral and supplementation-based, and to some extent, prescription drug based, too, and we'll touch on a few of those. If you understand that and why they work, well, then you can create a sort of kit, a grab bag of things that you can use in any context or I should say that you can look to depending on the context you're in

00:52:12 The 4 Major Types of Neuromodulators

and create the states of body and mind that you want. Now once again, painting with a somewhat broad brush, but nonetheless, an accurate brush, we can say that dopamine,

when elevated above baseline, tends to increase states of motivation, both mental and physical motivation, drive and to some extent focus. I've said it many times before, and I'll say it again, there's a lot of misconception about dopamine. Many people out there think that dopamine is all about pleasure. You hear about dopamine hits or people chasing dopamine or the need to have a dopamine fast, et cetera. Dopamine is not about pleasure. Dopamine is about motivation, craving and pursuit for goals or for things that are outside our immediate possession and experience. The motivation and pursuit of a mate. The motivation and pursuit to mate. The motivation and pursuit of food. The motivation and pursuit of a career goal, et cetera, et cetera, things we do not yet have, but that we want and we get into sort of a forward center of mass and a pursuit of, and that pursuit can be physical. That pursuit can be cognitive. It can be both cognitive and physical. And it can involve talking about something, right? Because in some professions, pursuit of things involves talking. I think about lawyers, they talk a lot in pursuit of winning cases and money, et cetera, putting people in jail or keeping people out of jail, et cetera, that's done with their mouths, not with their bodies. Athletes in a state of motivated training or in motivated competition use their bodies. All this is obvious of course, but perhaps what is not so obvious is that one molecule not working alone, but predominantly one molecule, dopamine, is responsible for all of those motivated states, which again, underscores the power of these neuromodulators. So dopamine, we can think of at least in the context of today's discussion as controlling and indeed promoting motivation, drive and pursuit and to some extent, focus. Epinephrine and a closely related molecule called norepinephrine and again, I want to emphasize that epinephrine is adrenaline and adrenaline is epinephrine. Norepinephrine is noradrenaline and noradrenaline is norepinephrine, but today we're going to just simply talk about epinephrine and norepinephrine. That category of neuromodulator is mainly responsible for generating our energy, our level of fuel and baseline level of forward center of mass, as I like to call it. You can also think of it as how high your RPM are. Now we're not a car and the car analogy sort of falls apart as we go further into the biology, but it's a decent one for now. When epinephrine levels are high, we tend to feel agitated, we tend to feel like we want to move, we tend to feel like we can't shut down our thinking and our anticipation of what's going to happen next. And when epinephrine levels are very, very low, we actually have less physical energy. We tend to have less mental energy in terms of generating thoughts very quickly and so on and so forth. And as I mentioned before, dopamine and epinephrine are closely related so much so that

we know for a fact that epinephrine is actually manufactured from the molecule dopamine. So that's why I'm talking about these two neuromodulators in very close juxtaposition because they do indeed collaborate with one another. But for sake of today's discussion, we can just think of epinephrine as increasing energy, adrenaline increases energy in our state of readiness. It also, I should mention, activates our immune system. Contrary to popular belief that stress inhibits our immune system, epinephrine is deployed, it's released at great levels in our brain and body when we are stressed. And that actually protects us against infections of multiple kinds, at least in the short-term. That and all the details of that and tools related to that were covered in our episode on the immune system, if you want to check that out. Now the neuromodulator serotonin creates a number of different states in the brain and body, but for sake of today's discussion, we're going to think about the predominant states that it creates and those are states of contentness, being happy, feeling fairly relaxed, feeling soothed and to some extent, even some relief from pain or lack of pain. Serotonin is associated with a feeling of satiety of having enough of what we already have. Now when serotonin is very, very high, people can even be sedate. They can be completely amotivated, no motivation to seek out things like food or sex or work or et cetera. Whereas when serotonin levels are very low, people can actually exhibit agitation and high levels of stress. So the levels matter here, but again, for sake of today's conversation, when we leverage serotonin, we are really leveraging a neuromodulator that tends to increase the activity of neural circuits in the brain and body that make us feel relaxed and happy. And it tends to decrease the activity of neural circuits that make us rabidly in pursuit of things that we don't have, right. The opposite of content and sated is motivation, desire and hunger and thirst for things that we don't have. So serotonin is the molecule of peace. It is the molecule of contentness. It is the molecule of having enough, at least for the time being or the feeling that we have enough for the time being. Now acetylcholine is a fourth category of neuromodulator that as I mentioned earlier, is somewhat not totally, but somewhat distinct from any direct control by the major hormone systems of the body, or at least the major steroid hormone systems. And acetylcholine we can say is mainly associated with states of focus. And we can go a step further and say that it's mainly associated with steps of focus as they relate to learning and encoding new information, so called neuroplasticity. Now neuroplasticity, or the brain and nervous system's ability to change in response to experience can be impacted by an enormous number of different chemicals, not just acetylcholine, but acetylcholine has a particularly potent

ability to open up the thing that we call neuroplasticity to allow plasticity to happen in one moment whereas in a previous moment, it could not occur because acetylcholine had not been released in the brain or in the spinal cord. So acetylcholine is involved in focus and in learning, but it is not necessarily always associated with learning in the context of highly motivated, really ramped up states. It can be, but acetylcholine can also be released and can encourage the learning and neuroplasticity associated with calm states. For instance, if somebody has a newborn child, we know that they are flooded with oxytocin, which has actually even been called the love hormone or it does many things in addition to control feelings of romantic attachment and attachment to children, et cetera. It does all of that, but it does a lot more, as well. But when people have a new child, they also tend to be hyper-focused on that child, not just its well-being, but they narrow all their thinking, all their vision, all their hearing to that child and there are obvious adaptive reasons for wanting to do that. I recall a family dinner we had. Gosh, this was over 10 years ago. We had a couple over. My mom was in the habit of inviting people over who didn't have places to go on the holidays, 'cause that's just who she is and I think it's quite nice. So she brought over this couple, they had a newborn, I think this baby had been born maybe two or three weeks before and it was seated or not seated [laughs]. It was lying down. I couldn't see it. It was like a potato bug. It could barely hold its head up. But it was lying in a little bassinet on the floor as we ate dinner. And it was almost hilarious, it actually was hilarious. We laughed a lot about this, that the entire meal, they were basically staring at this baby. They were so clearly in love with the baby and so flooded with oxytocin and also prolactin that they couldn't take their focus off this baby. It was actually really wonderful and endearing to see. But in addition to that, I'd be willing to bet had I been able to do a little bit of microdialysis, which is a ability to measure the amounts of neuromodulator given location in the brain, had I been able to do that experiment on them in that moment, I would've found that levels of acetylcholine were exceedingly high because they were so hyper-focused on this child, not just in love with, but focused on that child. And without a doubt, the neural circuits related to focus and plasticity were heavily engaged again for obvious adaptive reasons related to child rearing and learning the coos and cries and pain signals and pleasure signals of one's offspring. So we have dopamine associated with motivation, drive and pursuit and to some extent, focus. We have epinephrine and norepinephrine associated with energy of having a forward center of mass, mentally and or physically. We have serotonin, which is associated with a peaceful, content, sated state of being. And we

have acetylcholine, which is associated with focus and in particular focus as it relates to learning

01:01:45 Tool Kit 1: Increase Baseline Dopamine & Focus

and encoding new information. So let's say you want to be more motivated. You want to be more in pursuit of goals. And you want to have more energy and to be more focused. There are many ways to go about that. In fact, there's a near infinite cloud of opportunities, everything from prescription drugs to illicit drugs, which I certainly do not recommend, supplements, nutrition. You can listen to particular music. You can do all sorts of cognitive behavioral, nutritional supplementation tricks. Or you can just understand that what you're really after are increases in dopamine above baseline that you control and there are ways to control them that are quite potent and science tells us which tools are going to be the most potent and the most versatile for you. So I'm going to share those tools with you now with the caveat that each one of those tools could be its own entire podcast episode, and that we've done near entire episodes on each of these tools or small collections of these tools. So I'm going to cover these in somewhat superficial manner. We can provide links to previous episodes that relate to each of these tools in detail, but I'll give you enough detail about them that would allow you to incorporate them into your routine should you choose. Let's say you want to increase dopamine for sake of increasing motivation. The first thing to do is to understand what the natural behavioral tools are for increasing dopamine and to do those as consistently as possible. Again, these are tools that you'll want to do nearly every day, if not every day. And I know I'm sounding like a broken record on this one, but here again, we come to sunlight and I should say, not just the desire to, but really the need for viewing the maximum amount of sunlight that one can reasonably get given schedules and locations in the world, time of year, et cetera, in the early part of the day, within the first hour of waking, ideally, but certainly in the first three hours of your day, you are going to want to maximize sunlight exposure to your eyes. Never look at the sun or any other light so bright that it's painful to look at. And yes, of course blinking is fine, but no, take sunglasses off, go outside once the sun is out and get some natural light in your eyes. And if it's appropriate or I should say in a way that's appropriate, maximize the amount of sunlight exposure to your skin, but please don't get burned. Please do wear sunscreen if you're prone to getting burned. Typically early day sunlight is not going to burn you, at

least not most people, unless you're extremely fair-skinned. So don't get burned. Do what you need to in order to protect yourself from burn. There's some emerging controversy about sunscreen and which ones are safe and which ones aren't safe. We have not done an episode on that yet, but I find it to be an important and interesting topic. Darya Rose, Dr. Darya Rose, I should say, has a podcast called The Darya Rose Podcast and did an episode all about sunscreens, which are safe, which are not safe, by interviewing an expert on that so I refer you to that podcast as it relates to sunscreen. But get some natural light exposure in your eyes. And if you wake up before the sun comes out, turn on as many bright lights inside as you can turn on reasonably given your electric bill, et cetera. Get a lot of bright sunlight exposure early in the day and get a lot of sunlight exposure to your skin in the early part of the day, in a way that doesn't burn you, meaning burn your skin or blind you, please. Please don't do anything that harms your vision like stare into a bright light, that's painful. What does that do? Well, it sets in motion a number of different biological cascades. Some are very fast. There are fast actions of sunlight that will trigger for instance, dopamine release from different parts of your brain and your endocrine system. And we now know that it increases levels of genes related to thyroid hormone and actually increases certain dopamine receptors. So there's a wonderful paper. We will provide a link to this paper that shows that sunlight exposure can actually increase the amount of so-called DRD4. This is a particular type of dopamine receptor, the dopamine receptor four. The genes for dopamine receptor four are actually under photic control. So if you get sunlight exposure to your eyes and it does have to be to your eyes in the early part of the day, you increase the amount of dopamine receptor that you have, which allows whatever circulating dopamine happens to be there to have a greater effect on motivation and I should say also on mood and feelings of being in pursuit and generally, in craving and pursuit of things in life. Now there's another way to increase the effect of whatever dopamine happens to be circulating in your brain and body. And this again, relates to increasing the number or the efficacy of the receptors for dopamine. Now here we're not talking about the dopamine receptor four, but a different category of dopamine receptors, the D2 and D3 receptors, which are expressed multiple places in your brain and body and bind dopamine, meaning dopamine parks in them like a parking spot and allows dopamine to generally increase the activity of the neurons and cells that express those dopamine receptors. How do you do that? Well, turns out that regular ingestion of caffeine at safe and appropriate levels, about a hundred to 250 milligrams is going to increase the number of

D2 and D3 dopamine receptors. I talked a little bit about this on a previous episode. Again, we'll provide links to these studies, but this is an important finding, I believe, because this is not about the acute, the immediate effects of caffeine on alertness, although those occur, too. When you drink caffeine, it's going to increase your levels of adrenaline and so-called epinephrine, which will increase your energy levels. It's going to decrease levels of something called adenosine, which builds up while you're sleepy. It's going to make you feel less sleepy, more alert, more energetic. That's sort of obvious. But what's less obvious is that it's increasing the number and efficacy of dopamine receptors so that whatever dopamine happens to be around in your system is going to have more of a potent effect. So how much caffeine should you drink? That's going to vary from person to person. Some people are very sensitive to caffeine, others are not. I tend to be fairly insensitive to caffeine, 'cause I've been drinking it for a long period of time. But you know, after one or two cups of espresso or coffee, I feel like I've had enough. I tend to drink my caffeine early in the day, which is what I'm going to recommend that you do, not drinking caffeine past two and certainly not 4:00 PM, if you're on a typical schedule and you want to be able to sleep that night, even if you can fall asleep. Having too much caffeine in your system is not good because it disrupts the architecture of sleep. And now knowing about all the metabolic variability across the night, according to different stages of sleep, it should be even more obvious as to why disrupting the architecture of sleep would be bad for you. So limit that caffeine intake to early in the day and don't go ballistic. Certainly don't go ballistic in any case, but for most people anywhere from 100 to 400 milligrams of caffeine is going to have this effect. And this effect again is a slow accumulating effect by drinking caffeine consistently day-to-day. I get my caffeine mainly from Yerba Mate tea. I want to emphasize that it's probably a good idea to stay away from the smoked mates. There's some evidence those can be carcinogenic, but I brew my own Yerba Mate tea, or sometimes I'll drink coffee or espresso, or sometimes both frankly, as long as I'm hydrating enough and I'm getting enough salt, then I tend to feel fine with that much caffeine.

01:08:52 Tyrosine-rich Foods & Dopamine

The other way to increase dopamine and to make sure that your baseline levels of dopamine are high enough is to make sure that you're eating sufficient numbers of tyrosine-rich foods. You can look up which foods include tyrosine. Tyrosine is a

precursor to dopamine. It's an amino acid that is in direct pathway to dopamine synthesis and tyrosine foods include things like certain meats, Parmesan cheese, very high in tyrosine, for instance. In fact, there's something called the cheese effect, believe it or not. I don't want to go too far off topic, but the cheese effect is kind of interesting because certain people will take antidepressants that are so called MAO inhibitors, monoamine oxidase inhibitors. Anytime you hear ASE, that's an enzyme. They will take these inhibitors that prevent the breakdown of dopamine and other so-called catecholamines, which allow more dopamine to be in circulation. But if these people eat certain cheeses, including Parmesan cheese, and there are other foods, of course that include not just tyrosine, but one of the derivatives of tyrosine, called tyramine, that generates what's called the cheese effect, which is people get potent migraines, headaches, blood pressure goes up. Why, well, because they've got a lot of tyrosine in their system and dopamine in their system. And they've got less of the enzyme that removes that dopamine or limits its action and so they have an excess of dopamine and dopamine has effects on blood pressure, et cetera. So the cheese effect is something to avoid if you are somebody who's taking drugs that tap into or manipulate the dopamine pathway, either for Parkinson's or depressions, obviously you're going to want to be careful about adjusting up or down levels of dopamine too potently. So mind the cheese effect if you're taking an MAO inhibitor. There's a lot of information about this online. For most people, eating foods like Parmesan cheese, eating foods like certain meats and certain vegetables also can increase tyrosine levels, which will increase dopamine synthesis. So these are ways of modulating, more or less, the baseline of dopamine that you are able to produce and the ways that dopamine can have its action

01:10:59 Dopamine Supplementation: Mucuna Pruriens, L-tyrosine & Phenylethylamine

by way of binding to receptors more potently. Now there are other ways to increase dopamine in a more acute or directed way, ways to spike your dopamine, to enhance your state of motivation, mood, focus and so on. And in thinking about the vast landscape of tools that can do that, we have one category of tools, which are the really, really bad things that I don't recommend anybody do. In fact, I recommend nobody do ever, which are things like cocaine, methamphetamine, et cetera. They are incredibly destructive for lives because of the way that they so potently increase dopamine and then the crash in dopamine that occurs later. I mean, they can indeed and often do ruin

lives. So we're leaving those off the table. There are of course, prescription drugs that many people, especially people who have clinically diagnosed ADHD, attention deficit hyperactivity disorder, rely on and in fact benefit from in many cases, things like Ritalin, Adderall, Vyvanse. Nowadays, there's also a lot of interest in use of things like Modafinil, Armodafinil. I covered all of those in the episode on ADHD. And you can find that on HubermanLab.com and the other places this podcast is found. Prescription drugs aside because they require a prescription and a discussion that's in-depth and appropriate with your physician, healthcare provider. There are supplements that can very potently increase dopamine as well, perhaps not to the extent that some of those other prescription drugs can, but certainly to a degree that will impact and increase dopamine and motivation and the other states dopamine is associated with. And the two main categories of supplements that are very effective in raising dopamine and here I should provide the caveat that anytime you're going to add or remove anything from your supplementation protocols, please talk to a physician who is knowledgeable on these topics. If you're somebody who has, or is taking drugs for depression or mania, please be very cautious about manipulating your dopamine in any case. I don't just say that to protect us, I say that to protect you. But if we were to look at the supplement landscape and ask which supplement increased dopamine, there are a vast number of them, but the three main ones, the most effective ones that are readily available out there without a prescription are mucuna pruriens. This is actually the outside of a velvety bean that has been extracted and put into a supplement. Mucuna pruriens is actual L-dopa. It's 99% L-dopa, which is a prescription drug that is given for Parkinson's and for other purposes where increasing dopamine is important. I don't recommend mucuna pruriens. I'm not saying that no one should take it, but I don't take it. And I don't recommend it because it tends to so potently and acutely increase dopamine, that there's a pretty substantial crash afterwards. So I avoid it and I don't generally suggest that anyone take it unless there's really a clinical need, or they're working very closely with somebody that can really monitor that. The other two supplements that can increase dopamine in a short-term way, but in a significant way, are L-tyrosine so you can buy that as a supplement amino acid. I sometimes take this. I would say, I probably take it about once a week maximum for work bouts or workouts. I'll take it in dosages of anywhere from 500 milligrams to a thousand milligrams. People vary tremendously in their sensitivity to supplementing L-tyrosine. I know people that can take two grams. I know people that can barely take a hundred milligrams. I know people that the best dose for them is zero

milligrams. So there's a lot of variation there depending on sensitivity and they're natural baseline levels of dopamine and whether or not they're doing a lot of other things to support dopamine, but nonetheless, taking L-tyrosine will lead to fairly substantial increases in dopamine within about 15 to 45 minutes and it lasts for about 30 minutes to two hours and then there's kind of a tapering off. Some people experience a little bit of an emotional and or I should say energetic crash, some people don't. And then the other supplement that I certainly use, and that I know a number of other people use is more fast-acting, but more potent, which is phenylethylamine. This relates to the so-called PEA molecule, PEA, P-E-A, and phenylethylamine increases dopamine and some metabolites related to dopamine in ways that really increase energy and feelings of well-being and motivation. And again, it's fast-acting. So my particular protocol, the one I use is I'll take phenylethylamine at dosages of about 300 to 600 milligrams along with some L-tyrosine, or I'll take it on its own with a molecule, or I should say a compound that we'll talk about a little bit later as it relates to acetylcholine, Alpha-GPC, but tyrosine and phenylethylamine taken alone or together will make you feel more motivated and more alert, more willing and able to lean into particular motivated behaviors, whether or not they're physical or cognitive. If you'd like to learn more about these compounds and their supplementation and their effects, I encourage you to check out the ever valuable website, examine.com. It's zero cost to access, and they provide references and some more details

01:16:00 Deliberate Cold Exposure & Dopamine

about these sorts of compounds and other related compounds. Now if we are going to look at behavioral tools for potentially increasing dopamine, that too is a vast landscape. And we know based on hundreds, if not thousands of studies that things like winning at some sort of competition or succeeding in reaching a goal can certainly increase dopamine. We talk a lot about this in the episode on dopamine, motivation and drive, but leaving that aside, there are certain behavioral protocols that are unrelated to your overall goals and motivations that can increase dopamine in a very sustained way. And without question, the most potent behavioral tool for doing that is going to be deliberate, cold exposure. Deliberate cold exposure has been talked about a lot here and elsewhere in terms of its ability to do things like reduce inflammation as a way to test and improve resilience because uncomfortable cold, provided its applied safely is a great way to learn

to be more resilient because you're essentially staying or forcing yourself to stay in a circumstance where your system is flooded with adrenaline. But one lesser known aspect of deliberate cold exposure is one that's been demonstrated quite convincingly in humans, comes from a study published in the year 2000. I'll link to this study. I love this study by the way. Covered it many times on this podcast because I love it so much and I think it's truly important. And that's the study from Srámek et al, entitled, "Human physiological responses "to immersion into water of different temperatures". I'm not going to go into this into a ton of detail for sake of time, but basically what they show is that putting people into cold water, and I should mention the water that they used in this study wasn't that cold. They had a bunch of different conditions, but they had people that got into, for instance, 60 degree Fahrenheit water for up to two hours, had them sitting there, had them in a lawn chair up to their neck, had very long sustained increases in dopamine transmission and dopamine circulation in their brain and body. And also some of the other catecholamines, as I mentioned before, dopamine tends to collaborate with epinephrine and vice versa. Now you don't need to put yourself into 60 degree Fahrenheit water to get these kind of sustained increases. And you certainly don't need to do it for two hours. We have a strong reason to believe based on subsequent studies, in fact, published just this last year, that getting into much colder water of say 50 degrees or 55 degrees or even 45 degrees Fahrenheit can potentially increase dopamine and epinephrine, as well. And that you don't need to expose yourself to that cold water for nearly as long. So perhaps even as short as one minute or even 30 seconds exposure to really cold water, can lead to these potent long-lasting increases in dopamine. Many people will ask which protocols to follow. For instance, will a cold shower suffice? Very likely, yes, if your shower gets cold enough. Do you need ice floating in the bath? No, it's all about the temperature not whether or not there's ice present or not. How long to stay in there? There are a lot of details that we don't have time to go into this episode. Please see the episode on the Use of Deliberate Cold for Health and Performance. You'll find that at HubermanLab.com. We have a newsletter related to this. It gets into a lot of detailed protocols, but in general, we can say that the way to evoke dopamine and epinephrine release using cold water is to ideally you would do cold water immersion. If you can't, you'd use cold shower, but you want to use a temperature that is safe, meaning you're not going to have a heart attack, but that is uncomfortable such that you really want to get out and then staying in for anywhere from one minute to 10 minutes, depending on how cold adapted you are, and then getting out

and drying off and going about your day, unless you have some other protocol that you're trying to extract from the cold. So this is a cold exposure protocol specifically aimed at increasing dopamine. For some people out there, you might think this is kind of silly using cold water to increase dopamine. But when you look at the data in humans on the effect of cold water exposure to stimulate long-lasting, very significant increases in dopamine and epinephrine, I think you'll agree that this is a really potent tool that provided its given safely and gone about safely, is giving you the kinds of increases in dopamine that you would seek using prescription pharmacology. Now it shouldn't be used as a replacement for prescription pharmacology, although people have done that to success. One of the previous guest on the Huberman Lab Podcast was Dr. Anna Lembke, our director of the Dual Diagnosis Addiction Clinic at Stanford. She has an amazing book called "Dopamine Nation", all about dopamine and both its uses, healthy, and its perils in things like addiction. And she describes a patient of hers that used deliberate cold exposure to try and maintain dopamine levels while coming off of drugs that were increasing dopamine so potently that they were putting him down the path of addiction. So the use of cold water for increasing dopamine is a real tool. It's, I would say, a power tool. In fact, it's the kind of thing that if you want to increase dopamine for sake of motivation, it might be your first go-to provided you're also doing the things to maintain dopamine baseline like sunlight exposure in particular, making sure you're getting sufficient amounts

01:21:12 Tool Kit 2: Additional Tips to Increase Dopamine

of tyrosine-containing foods and so on. And now just very briefly, I want to point to a few quick tools that good peer review data tell us can be leveraged in order to make sure that you have sufficient dopamine when you want it or that it's available for it to be released by any number of the tools I provided thus far. And those are sufficient number of B vitamins. So it turns out that B vitamins, in particular B6 or vitamin B6, can potently reduce prolactin levels. And again, prolactin and dopamine tend to work in kind of push pull fashion. That said you should be cautious about taking excessive levels of B6. It is a vitamin that if you take too much, you'll likely excrete it through your urine, but there is evidence that having excessively high levels of B6 or supplementing with excessively high levels of B6 can cause some peripheral neuropathy, some death of nerves in the periphery. If you want to know what dosage levels are relevant there just simply look it

up online. There's a lot of information about this. But you do want to make sure that you're getting enough B6, B12, et cetera, such that you can keep prolactin levels in check. And if you suspect that you have a dopamine deficiency, please talk to your doctor and talk to them about ways you might adjust that prolactin down and thereby dopamine up. The other way to ensure that dopamine levels stay high or put differently, that you don't quash whatever dopamine you have in your system is to really avoid bright light exposure to your eyes between the hours of 10:00 PM and 4:00 AM or another way of putting this because I realize people sleep at different times, et cetera, is to avoid bright light exposure to your eyes, not just blue light, but all colors of light in phase three, that is 17 to 24 hours after waking up because that's really when you should be asleep or trying to get asleep, if you're having trouble sleeping. Work from Samer Hattar's lab, the director of the chronobiology unit at the National Institutes of Mental Health, again, a previous Huberman Lab Podcast guest, tell us that bright light exposure in phase three of your circadian cycle, 17 to 24 hours after waking, can have dramatic effects in reducing dopamine levels by way of activating a neural circuit involving something called the habenula. I don't want to get into too many details right now, but really try and keep the lights dim in the middle of the night or off, if you can do that safely. It's really going to help if you're turning on your phone brightly, if you are turning on bright lights, it's not just going to negatively impact melatonin, the hormone that helps you fall and stay asleep. It's also going to negatively impact dopamine levels, not just that night, but the subsequent day. So that more or less summarizes our coverage of ways to use behavior and supplementation and nutrition to increase dopamine and dopamine receptor efficacy and number, and to keep sufficient amounts of dopamine in your system day-to-day for motivation, mood and focus. And of course, keep in mind those things that can suppress dopamine, the bright light exposure, elevated prolactin, and so on. My hope is that by understanding those tools and how they work and understanding that dopamine does certain things and not others that you can assemble a versatile kit of behaviors and other things that you can do in order to adjust your dopamine levels according to your particular goals. I want to just briefly return to the fact, however, that all of that is riding on that phase one, phase two background, meaning, it's probably going to take less cold water exposure, or I should say less time doing cold water exposure early in the day to get a big increase in dopamine than it would later in the day. Because later in the day, your baseline levels of dopamine are lower and you've got more serotonin circulating. That should make sense to you now as to why that's the case. And does that mean that

you should really modify your protocols dramatically? Probably not, but you might keep that in mind that if, for instance, you need to be in a highly motivated, focused state in the late part of the day, for whatever reason, it might take a few or more of these tools in combination in order to accomplish that. Whereas if you're somebody who feels pretty good during the day, but you're kind of lacking motivation and you want to increase dopamine levels and you don't yet need to, or want to resort to prescription drugs or supplementation, well, then you might layer in a couple behavioral protocols paying attention to of course, the things that you might be doing that would also potentially suppress dopamine. So again, that kit of tools is designed for you to play with, if you choose, if it's safe for you to apply them, then do that. Consider doing them individually, not trying to hit all the tools all at once, right? I mean, why throw all those tools at your dopamine system at once? Better would be to have those tools in your kit and be able to deploy them depending on whether or not you're on travel, whether or not you're eating well or less well, whether or not you're sleeping well or less well. That's highly individual and I'd like to think that in having those tools in hand, you'll be able to adjust them and apply them in the ways that allow you to access the dopamine increases that you're after.

01:26:10 Tool Kit 3: Increase Epinephrine (Adrenaline) & Alertness

So next I'd like to talk about epinephrine, also called adrenaline. I want to point out that epinephrine is released both in the brain and the body. In fact, there's a barrier between brain and body that prevents the epinephrine that's released from your adrenal glands, from crossing the blood brain barrier. So your brain has a separate site called the locus coeruleus. This is a collection of neurons in the back of the brain that kind of sprinkler the rest of the brain with epinephrine and essentially wakes up whatever neural circuits happen to see, or I should say, wake up any circuits where that epinephrine happens to arrive, right, and generally increase the excitability of those networks. That's why we say epinephrine increases energy. I'm not talking about caloric energy, although that's distantly related to this, but really energy and the desire to move, the feeling that we can think, the feeling that we can be alert. In fact, if you look at somebody and their eyelids are wide open, in large part, that's because of a lot of adrenaline in their system. If their pupils are really big and their eyes are really wide open, in general, that means they have a lot of epinephrine circulating there, whereas when we're tired and we're kind of

hood-eyed and we're sort of sleepy, or our pupils are really small, in general, that's because levels of epinephrine and also dopamine, remember they work together, levels of epinephrine and dopamine tend to be lower. This is also why when people take any drug, like again, not recommending this, amphetamine or cocaine or any stimulant, their pupils tend to be huge. Their eyes tend to be wide open. They don't blink very often. And the opposite is true when people take sedatives. So it all starts to make sense when you think about the basic actions of these things. For many people, increasing adrenaline or epinephrine might seem like a crazy idea. Most people probably associate this molecule with stress and then would like to be less stressed. And we've done entire episodes about stress, how to master stress, how to leverage stress, how to conquer stress. There are a lot of great tools to do that that are behavioral, supplementation-based. Please see the episode on Mastering Stress for those tools, but there are people, including me, that want to increase our levels of epinephrine at least early in the day. I'm somebody who wakes up rather slowly. In fact, right after waking up, I rarely want to bounce out of bed. I try and push myself to do that. I'm always impressed by these chakra-willy types that are up at 4:30 or up at five and already into action. I tend to be kind of thinking about thinking about maybe being in action early in the day, but I try and push myself to get into action, which itself can increase epinephrine. I should mention that any physical activity, any physical activity, walking, running, weight lifting, swimming, even talking for that matter is going to increase levels of epinephrine. Locus coeruleus is a brain structure that is tightly coupled with behaviors in a bidirectional way. That is, when you are in action, you increase the amount of epinephrine released from locus coeruleus. You wake up the brain. And conversely, when locus coeruleus is active, the brain wakes up, so it's reciprocal. It goes both directions. So I saw a funny tweet actually earlier today, it was something like going to the gym gives you energy, but you need energy to go to the gym. Sounds like a pyramid scheme to me, which made me chuckle. But of course overlooks the fact that, indeed, if you have energy, you are more likely to be willing to get into physical movement or cognitive movement and thinking hard or thinking a lot about something. But also it is absolutely scientifically proven that being in action increases levels of epinephrine. This is why exercising early in the day gives you more energy for rest of day. You still might experience a little bit of a crash in the afternoon, especially if you're getting up extra early, or if you're drinking caffeine too close to waking. I've talked about this before. If you drink too much caffeine close to waking, you're going to have an afternoon crash. Better to push that caffeine intake out

about 90 to 120 minutes after waking. I know this is really painful for certain people, but caffeine does increase epinephrine. Caffeine does other things to limit sleepiness. And by pushing it out 90 to 120 minutes after waking, you will avoid the afternoon crash to a large degree. And if you get up and you exercise or even do any movement of any kind, a hundred jumping jacks or a walk, if you can't do that, anything like that will increase the total amount of epinephrine that you secrete into your bloodstream and in your brain and will get you more energy, not just in that moment, but throughout the day. So keep that in mind. Exercise does indeed give you energy. It burns caloric energy, but it gives you neural energy by way of increasing epinephrine transmission from locus coeruleus. And presumably if the exercise is intense enough, adrenaline, epinephrine release, from the adrenals within your body, as well. So we have exercise and we have caffeine as potent tools for increasing epinephrine and thereby, energy. Another potent tool that's purely behavioral, but is known to work, based on excellent studies in humans. And actually my laboratory has been doing similar types of studies that are soon to be published, we hope, is so-called cyclic hyperventilation. Some of you may be familiar with Wim Hof breathing. There's also Tummo breathing, which is very similar, Kundalini breathing. All of those styles of breathing involve cyclic hyperventilation, deep inhales, and either passive exhales or active exhales, but repeating, inhale, exhale, inhale, exhale, in a very deep and repetitive way. If you were to do that right now, doesn't matter if you do it through your nose or mouth, although ideally you would do the inhale through your nose and the exhale through your mouth, if you did that for 25 repetitions, 25 inhales and exhales, you would feel more alert. You'd also feel more warm, why? Because you increased epinephrine, adrenaline release in the brain and body. It works the first time and it works every time to increase epinephrine and thereby energy. And in fact, there are protocols and great scientific studies of using cyclic hyperventilation for periods of minutes, if not longer, where for instance, you would do 25 big inhales and exhales followed by a brief breath hold with your lungs empty, then repeat 25, then brief breath hold, excuse me, exhale, hold your lungs empty. And then repeat again for a third round, if you like. If you do that over and over, you're going to be very alert. You're going to have more energy. You're going to feel like you want to move around a lot more. In fact, you might even feel agitated. So people with a lot of anxiety or prone to panic attack might want to be cautious in how they train and embark on that type of breathing, might want to approach it a little more carefully or avoid it altogether. But for most people, cyclic hyperventilation is simply going to get you more energized and feeling like you

want to move, feeling like you can think more clearly, and you'll be more wide-eyed and alert because you are releasing adrenaline. And the cold water exposure protocol that I talked about earlier and that's covered in our episode on cold and in the newsletter on cold. Well that, as I mentioned earlier, potentially increases dopamine, but also epinephrine. So that's another terrific tool, whether or not it's applied by cold shower or cold immersion or some other thing like cryo, that is going to make you more alert because it releases adrenaline. Now we can't really say that there are foods to increase epinephrine. Rather, there are foods that include a lot of tyrosine that will increase dopamine. And remember, dopamine is the molecule from which epinephrine is synthesized. So we can't really point to a particular food or categories of food for increasing epinephrine. I think caffeine and things like it will increase epinephrine. There are of course prescription drugs that will increase epinephrine. And of course, there are all sorts of so-called beta blockers that will block the receptors for epinephrine to make you feel calm for public speaking or for various heart conditions, et cetera. That's really the domain of physicians and should really be worked out with your cardiologist, with a physician et cetera. I think the tools of exercise and should you want very potent increases in adrenaline, high intensity exercise, as well as the tools of caffeine, cyclic hyperventilation and deliberate cold exposure, really combine to give you a nice little kit, I would say a versatile kit, of ways to increase epinephrine

01:34:34 Tool Kit 4: Increase Acetylcholine & Attention/Learning; Choline-rich Foods

for sake of having more physical and mental energy. So next is the neuromodulator acetylcholine. And as I mentioned earlier, acetylcholine is associated with states of focus and those states of focus can be high energy states of focus. So the ones that are accompanied by high levels of dopamine and epinephrine and where we're really excited about and really lasered in on something, or they can be the calmer, more relaxed states of focus like reading a book or practicing music or listening very carefully to somebody in a way that's relaxed and calm. And yet nonetheless, where we have a narrow cognitive and typically a narrow visual aperture, and typically also a narrow auditory aperture. That is our auditory system and our visual system and our thinking can be very broad. It can be all over the place. Or it can be very narrow. And it can be very focused. Acetylcholine is released from two major sites in the brain, nucleus basalis, which is in the forebrain and extends connections out to many different brain areas to offer the opportunity to

release acetylcholine locally and more or less in a chemical way, highlight those particular neurons and synapses for strengthening, for plasticity later. And it is released from sites in the back of the brain in a way that can increase the so-called fidelity of information coming in through our eyes, our ears, our nose, et cetera. What do I mean by fidelity? Well, we are constantly being bombarded with sensory information through all of our various senses and acetylcholine released from this area in the back of the brain, has the ability to increase the extent to which say, visual information or just visual and auditory information would make it through to our consciousness whereas all the other types of sensory information that are coming in are filtered out. So your brain, because it's taking in all this information needs to decide what to pay attention to. And in this way, we can say that acetylcholine has a lot to do, not just with "focus", in air quotes, but literally attention, which neural signals become relevant to our consciousness. There's a whole discussion to be had there and we don't have time for that. Rather, I'd like to focus on what are the tools that one can use to maintain healthy baselines of acetylcholine and increase acetylcholine for sake of learning any type of information, physical, cognitive, or otherwise. Now it turns out there have been a lot of studies, including many quality peer reviewed studies carried out in humans, looking at what happens when you increase acetylcholine levels in the brain and you accompany that with the attempt to learn. And what you find almost always is that people experience increased focus, that when measured the neuronal responses become more specific, so less broad scale activity in the brain and more specific neural circuit activity

01:37:29 Acetylcholine Supplements: Nicotine, Alpha GPC, Huperzine

and that this triggers immediate and long-lasting changes in the way those circuits work, even when acetylcholine is not being deployed, so-called neuroplasticity, the circuits literally change. So this is great. The work of Michael Silver at Berkeley, the work of Mike Merzenich at UCSF, the work of Michael Kilgard down in Texas, all of those laboratories see this again and again, and again. Increase acetylcholine before and during learning. And there's a much higher probability that the learning will quote, unquote, "sink in", that the information will be retained because those neural circuits change. Now ways to increase acetylcholine in a potent way include again, nutrition and supplementation. It is important to have baseline levels of acetylcholine be sufficiently high, as well. And for that really the ideal situation is to regularly ingest foods that provide enough of the

precursors for acetylcholine to be made. If you go online and you were to do a search of which foods contain a lot of choline, which is related to the synthesis of acetylcholine, you would get some interesting information back. For instance, beef liver is the most potent source of choline. I know nowadays there's kind of a growing micro trend if you will, of ingesting beef liver, even raw liver, which to be honest, the thought of ingesting raw liver of any kind activates my area postrema, which is the area of the brain that triggers nausea. In fact, I'm starting to salivate a bit, not because I'm hungry, but I think the whole concept makes me ill. Nonetheless, cooked liver or raw liver for that matter, or liver of any kind seems to contain a lot of choline. I realize most people, most people are not going to be running out and ingesting large amounts of beef liver. Eggs contain a lot of choline. Beef contains choline. Soybeans contain choline. So there are vegan or non-meat sources, chicken, fish, mushrooms, kidney beans, these sorts of things contain a lot of choline and there are other vegetables that contain choline. So depending on your dietary preferences and needs, you can select certain foods to ingest, to get enough choline to synthesize enough baseline acetyl choline. In the realm of supplementation, there are some excellent tools for increasing acetylcholine in the acute short-term, meaning over the course of about 30 minutes out to about two hours or maybe even four hours. And the number of different molecules that can do that, that are available without a prescription, at least in the US, is pretty vast. The most common of those molecules is actually nicotine. Nicotinic acetylcholine receptors are abundant throughout the body and brain. They're in various brain circuits. They are on muscle and yes, smoking nicotine either by vaping or cigarette will activate those nicotinic receptors. But of course, smoking is a terrible thing. It will also activate things like lung cancer. So I definitely don't recommend that. It also activates addiction because of the ways that it triggers activation of the dopamine circuit. So I think that triggering activation of acetylcholine-related pathways by ingesting nicotine by way of inhalants is generally a bad idea. However, some people will chew Nicorette or other nicotine type gums. I've never done that, but I have friends who actually rely on that. These are typically former smokers that are trying not to smoke, but still want to get some of the focus enhancement that they experience from nicotine. Some people are very sensitive to nicotine, and this is important. Some people are very sensitive to ingested nicotine. So nowadays there are nicotine-dipped toothpicks, there of course, is nicotine gum and other sources of nicotine. Some people can take that and feel fine. Some people take it and feel absolutely terrible. I confess, I've never actually tried nicotine in any of those forms so I don't know how they work for

me, but some people do use them as cognitive enhancers. In fact, I know one Nobel prize winning neuroscientist, who's quite well known in our field for chewing Nicorette all day long. He insists that it really helps him with his focus and he is exceedingly smart and productive, although I'm sure there are other reasons for that. Supplements that I have used and do use for increasing acetylcholine are things like Alpha GPC or Huperzinene. Alpha GPC is in the choline pathway, such that more acetylcholine is synthesized after you ingest it. That's the general logic or framework of how it works. Whereas Huperzinene is mainly in the enzymatic pathway. It tends to adjust how much acetylcholine is broken down and lead to net increases in acetylcholine. I will often take 300 milligrams of Alpha GPC prior to workouts or prior to cognitive work bouts. But when I say often, I tend to do this anywhere from three to four times a week, typically not every day. Although there are people including people who are trying to offset age-related cognitive decline, that will take 300 milligrams of Alpha GPC three times a day, every day, which closely mimic some of the studies that have been done on humans, looking at offsetting age-related cognitive decline, using things like Alpha GPC. I should point out that there have been a few studies, a few, not many, but these studies emphasize that people who take a lot of Alpha GPC chronically over time may be at increased risk for stroke. I think the data are still out on that and we need more data. But for me, in terms of thinking about the risk benefit profiles, taking 300 milligrams of Alpha GPC, most certainly does increase my ability to focus. I've noticed that. I tend to take it alongside caffeine and phenylethylamine. So I take that in combination either before workouts or workbouts, really sharpens my focus. And again, I'm doing that three, maybe four times per week. And I'm careful to do that in the early part of the day so that it does not disrupt my sleep. Although I have taken Alpha GPC in the second half of the day, and I had no trouble sleeping at all. I don't know what the exact half life is of the given form that's typically in supplementation. It's actually hard to get that information. But typically the focus effects wear off after about two, maybe four hours maximum. Now one thing that I don't think has ever been discussed before, certainly not on this podcast is that if you take Alpha GPC, even semi-regularly, you may notice that a particular feature of your blood work will increase and that's TMAO, which is sometimes associated with increased cardiovascular risk. This may, again, may relate to some of the potential risk of very high levels of Alpha GPC ingestion over many years, increasing stroke risk. Again, those studies looked at people who've been taking it for up to a decade, but in any case, one way to prevent the increase in TMAO, if you're taking

Alpha GPC at all is to take 600 milligrams of garlic because it contains something called allicin. This was a trick that was handed off to me by Dr. Kyle Gillette, who again, was a guest on this podcast some time ago, talking about hormones and hormone health. Turns out that ingestion of 600 milligrams of allicin alongside or even just same day as Alpha GPC can really clamp those TMAO levels that would otherwise increase if you're taking Alpha GPC. And indeed I've done the blood work and that turns out to be the case. I saw a spike in TMAO. I started taking 600 milligrams of garlic

01:44:47 Tool Kit 5: Behavior to Increase Focus & Acetylcholine

and those TMAO levels came down. And last as it relates to acetylcholine, but certainly not least, just as acetylcholine can increase focus, focus can increase acetylcholine. I talked a lot about this in the episode on focus, but there are behavioral tools that you can use to enhance focus. Things like staring at a particular visual target at the same distance at which you're going to perform some work and doing that for 30 to 60 seconds, narrowing in a very deliberate way, your visual field, and then moving into a focused work about. That behavioral practice of narrowing your visual aperture will increase the amount of acetylcholine transmission in particular neural circuits that will then make it easier to focus. How do we know that? Well, I covered in that episode, some of the peer reviewed studies that relate to protocols that are now actively being deployed in schools in China and elsewhere, where kids are doing deliberate visual focus exercises in order to increase their mental focus. And while they're not doing microdialysis or brain imaging on those kids in real time, the cognitive effects and indeed the performance effects in terms of academic ability and output are pretty impressive. So acetylcholine increases focus. We talked about some dietary and some supplementation-based ways to improve acetylcholine, or I should say increase acetylcholine. And that does in fact lead to increases in one's ability to focus. This is why a lot of the prescription drugs for the treatment of Alzheimer's age-related cognitive decline and indeed, even some of the drugs that tap into treatments for ADHD also involve the acetylcholine system. So there's nothing surprising or heretical here, but it is important to point out that your behavioral ability to focus is also related to your ability to access and deploy acetylcholine. So never do we want purely pharmacologic treatments to be the only way that people are increasing a given neuromodulator. I always say behaviors first, then nutrition, then supplementation. And then if there's a need, certainly

a clinical need, then prescription drugs,

01:46:56 Tool Kit 6: Behavior to Increase Serotonin & Feelings of Well-being

et cetera, of course administered through a physician. So let's discuss serotonin. Serotonin, as I mentioned earlier, is associated with brain and body states of well-being, of comfort, of satiety, and therefore should come as no surprise that a lot of the prescription drug treatments for things like depression involve increasing levels of serotonin in the brain and body. That said, anytime you talk about prescription drugs for serotonin, we also want to acknowledge that there are often side effects associated with increasing serotonin, in particular, if serotonin levels go too high, that is if the dosages of those treatments go too high, people will, for instance, feel reduced appetite, reduced libido, increased lethargy, et cetera. And there's a so-called serotonergic syndrome. All of that can and should be considered with a well-trained physician, so because they're prescription drugs, controlling the dosage, deciding what dosage to take, deciding which SSRI to take and whether or not to come off those drugs, how to come off those drugs. Again, all of that should be handled with a licensed physician. That said, there are behavioral tools, nutritional tools, and supplementation tools that can tap into the serotonin system, not to the same degree in potency, but nonetheless, in ways that can still impact our feelings of well-being in positive ways. So let's focus first on the behavioral tools and some of these might make people chuckle a little bit, but I want to point out that a lot of these tools are quite potent. In fact, they are power tools for modulating serotonin. And we know that based on human neuro imaging studies, human and animal microdialysis studies and other studies that really have evaluated circulating levels of serotonin and the particular brain circuits that release serotonin when people do certain things. What sorts of things? Well, for instance, physical contact, in particular with loved ones, this can be romantic love. This can be children, so your own children or your spouse, even if it's not sexual contact, friend to friend contact, even friend to animal contact, you know, as a former dog owner, I hope to have another dog soon 'cause unfortunately Costello passed away, but there is something really comforting and wonderful about petting your dog. And certainly, given that many of the studies on serotonin and these other neuromodulators were done on animal models, we also know that serotonin is being evoked in the dog and of course in the child and in the significant other, et cetera. So things like holding hands, believe it or not, hugs, cuddling, et cetera,

can increase serotonin transmission and they make people feel good. This shouldn't really come as a surprise. There's also gratitude. And we did an entire episode about gratitude. There's a lot of misunderstanding about gratitude. Oftentimes when people hear gratitude, they think, oh, gratitude, this is just being thankful for what you have and it's kind of a weak sauce effect, meaning, you know, it's kind of like, maybe a little serotonin goes up or maybe there's a little bit of increased feelings of well-being. Nothing could be further from the truth. It turns out, first of all, that receiving not giving gratitude is what has the most potent effects on increasing serotonin and activity of the brain circuits that involve serotonin and that lead to increases in feelings of well-being. So this is interesting. Receiving much more than giving gratitude is what activates those serotonergic pathways. So the takeaway from that is both give and receive gratitude and of course, do it in an authentic way. The other thing about gratitude that's somewhat counterintuitive is that observing others giving and receiving gratitude is immensely powerful for evoking serotonin and the activity of serotonergic circuits in you, the observer. So receiving and observing gratitude turns out to be the most potent way to increase serotonin in the brain and body. And these again are dramatic effects that are quite long-lasting and not the sorts of effects

01:50:51 Tools: Tryptophan-Rich Foods & Serotonin

that are going to lead to side effects, at least there's no reason to think they would. Now what about nutritional approaches to increasing serotonin? Well, just as we have tyrosine as an amino acid precursor upstream of dopamine synthesis, we have the amino acid tryptophan, which is upstream of serotonin synthesis. And one simply has to go online and put in tryptophan containing foods and you will discover that there are a lot of foods that are enriched in tryptophan that can lead to net increases in the amount of serotonin available in the brain and body. The most kind of famous or infamous of these is white meat turkey, the so-called tryptophan effect where people get very sleepy after eating white meat turkey. And it is indeed highly enriched in tryptophan although typically the getting sleepy after eating turkey is most often associated with the Thanksgiving meal and the Thanksgiving meal, at least in the US, is often associated with people vastly overeating. And so I do want to point out that if you fill your gut with food, no matter what that food is, there's going to be a diversion of blood to your gut that's going to make you feel sleepy because there's a diversion of blood away from other tissues.

So if you eat a lot, you're going to get sleepy, period, whether or not you eat turkey or some other substance. Nonetheless, there are a number of foods that contain a lot of tryptophan and that some people will leverage in order to try and increase the total amount of circulating serotonin available to them in order to have a modest increase in overall mood and well-being. So what are some of these foods? These are things like milk, in particular, whole milk, so full fat milk. I know a number of people choose not to drink milk 'cause they're lactose intolerant. I'm raising my hand 'cause I'm one such person, although when I was a kid, I did enjoy milk. Canned tuna. Turkey, as we mentioned before, high in tryptophan. Oats, I am a consumer of oatmeal so that resonates with me. Cheese and here I read, although not as high in tryptophan as meat and other dairy sources, certain cheeses like cheddar cheeses can be rich in tryptophan. Certain nuts and seeds, certain breads. Chocolate, I know a number of people will be relieved to hear that. I know chocolate lovers are always looking for an excuse to eat chocolate. I confess I've never really liked chocolate, except dare I say, I like the smooth 100% percent chocolates. I know many people gag when they hear a hundred percent, but I actually really like them. And some fruits can be highly enriched in tryptophan, things like bananas and apples and things of that sort, although not nearly to the degree of things like turkey, canned tuna and milk. I'm sure there are other excellent sources of tryptophan from the diet, including vegan sources so please peruse the internet to try and find the sources that are compatible with your nutritional program,

01:53:31 Tools: Serotonin Supplements: Cissus Quadrangularis, 5-HTP, Myo-inositol

if indeed your goal is to increase tryptophan. Now there are supplements that can increase tryptophan and can do so quite potently. One of the ones that has received increasing attention as of lately is cissus quadrangularis, complicated name, when taken in dosages of about 300 to 600 milligrams can pretty dramatically increase serotonin levels. In fact, anywhere from 30% to 39% increases in circulating serotonin. That's a big increase and I can provide a link to that study. The study was focused, not so much on serotonin, but was focused mainly on treatment of obesity and appetite and weight loss. And it should come as no surprise that serotonin, if increased, might lead to decreases in appetite. A cautionary note, cissus quadrangularis may need to be cycled. How quickly to cycle it, meaning do you do two weeks on, two weeks off? Whether or not you need to do more rapid cycling like two days on, two days off, is a matter of debate. There

are not a lot of data on this just yet. There are a lot of opinions about this on the internet, but again, not a lot of quality peer review data. Nonetheless *cissus quadrangularis* has been shown to increase serotonin in humans and for people that are seeking to increase serotonin maybe in particular, for sake of appetite and weight control, that might be a useful compound. I know many people also take 5-HTP, one of the precursors to serotonin in dosages of anywhere from 300 to 500 milligrams. Typically people are doing this in anticipation of sleep, meaning in the final hour of wakefulness before going to sleep. I myself have tried 5-HTP prior to sleep and all I can tell you is that it led to very deep sleep for about one to three hours. And then I woke up and I could not fall back asleep. I ran that experiment twice before I decided to abandon 5-HTP as a sleep aid. And that's why I've never put it into our sleep kit or at least my sleep kit. And when I refer to the sleep kit, that's something you can find at HubermanLab.com. This is zero cost resource where you can see behavioral tools and also supplementation tools that can improve the transition time into and the depth of sleep. And none of those rely on 5-HTP supplementation. That said, I know a number of people use 5-HTP supplementation outside of sleep, or I should say during the daytime to try and increase serotonin and it will indeed increase circulating serotonin. But again, people vary in their sensitivity to these sorts of things. Some people might find for instance, that 300 milligrams of 5-HTP is just far too much. It blunts their appetite, might even reduce libido. There aren't a lot of very well controlled studies looking at this and so it has to be figured out on an individual basis, if you decide to approach it at all. Now one molecule that I've found to be particularly interesting and useful and this is one that I haven't talked about yet on this podcast is inositol, in particular myo-inositol. Myo-inositol can have the effect of increasing serotonin and other neurochemicals, but primarily at least in terms of the neuromodulators discussed today, serotonin. I've been taking 900 milligrams of myo-inositol every third night or so as a test of its ability to improve sleep. And I have to say, the depth and quality of sleep that I've been obtaining on myo-inositol is pretty remarkable. In fact, I've used it alone and in combination with the magnesium threonate, apigenin, theanine sleep kit that I've talked about and that's included in that, again, zero cost kit that's available as a PDF on our website. So myo-inositol is known to increase circulating levels of serotonin. It has been explored extensively in both animal models and in humans for its daytime use for treating anxiety. It does seem to reduce anxiety. And for all sorts of things. It's been explored for bipolar disorder. We're going to do an episode about bipolar disorder coming up. It's been explored for the treatment of

migraine. It's been explored for ADHD. It's been explored for a huge number of different conditions of brain and body. Again, I've been using the 900 milligrams of myo-inositol in the 30 to 60 minutes before sleep to improve my sleep and it has been doing that very dramatically, especially when I take it alongside the rest of those sleep kit supplements. A quick note about myo-inositol for sake of increasing serotonin. If you look at the human studies on myo-inositol that are out there and in particular focus on the human studies, what you'll find is that the dosages that are often used are tremendously high, things like five grams, eight grams, 18 grams of myo-inositol taken throughout the day. I don't know how people stomach that. And in fact, many people drop out of those studies because of gastric discomfort. And yet I also wonder how people tolerate it because it has somewhat of a sedative effect and this kind of anti-anxiety effect. And I can't even imagine given my experience with 900 milligrams, what one would experience taking multiple or many more grams per day. So I certainly am not encouraging that. And the only reason I mention myo-inositol is that it has a known effect of increasing serotonin. At least in my experience, it does not lead to this falling deeply asleep and waking back up. Actually to the contrary, if I wake up in the middle of the night to use the bathroom, or I wake up at the middle of the night, for whatever other reason, I find it far easier to fall back asleep if I've taken 900 milligrams myo-inositol prior to sleep. So for me, it's proving to be a quite useful compound. I'm not aware of having any serotonergic deficiency overall. I don't consider myself depressed. And of course I should mention that no supplement either added or withdrawn from your protocol should ever be used as a direct replacement for prescription drug treatments that your physician has given you. You should always talk to your physician anytime you remove or add something to your drug protocol or prescription protocol, of course. So we've got behavioral protocols that as silly as it feels to say, have been shown to potently increase serotonin, things like physical contact, cuddling, holding hands with people that you love, of course, right? I think if they were people that you despise, it would have the opposite effect for obvious reasons. But also receiving gratitude and observing gratitude, very potent increases in serotonin and things like cissus quadrangularis, things like 5-HGP may have their uses, right? They're very potent at increasing serotonin, but they do seem to have the need to cycle them and they are nuanced. Some people respond well to them, others like myself don't and of course, always be on the lookout for dramatic or even subtle decreases in appetite or libido or things that you might not want if you are going to be tinkering with your serotonergic levels and pathways. And then myo-inositol actually is proving to be

quite useful to me and whether or not that's because of its effects on serotonin or through some of its other effects on maybe reducing anxiety, which certainly I experience if I wake up in the middle of the night, I don't like waking up in the middle of the night, but on myo-inositol, I sort of seem to not really care that I woke up and I fall right back asleep. So the direct source of the positive effects that I'm getting aren't clear, but nonetheless, I thought I'd pass it along as a useful tool because it is out there and it is available over the counter and provided you're taking the appropriate safety steps in considering whether or not to use it or not, I think it might be a useful tool. And of course, as with all the other neuromodulators we discussed, you have both a baseline of serotonin and the ability to give or provide yourself peaks of serotonin through these various protocols. The dietary interventions of the sort that I mentioned, meaning eating foods that are enriched in tryptophan, those are mainly going to adjust your baseline levels of tryptophan. For instance, if you really want to be sleepy, sure you could eat some white meat turkey in hopes that that tryptophan will convert to serotonin and make you sleepy, et cetera. But in general, those are going to be pretty long-lasting effects, especially given the fact that not all of the tryptophan you will ingest is going to be converted into serotonin in your brain. It's going to have other effects on other tissues and organs of your body. Nonetheless, if you want to increase serotonin, providing the appropriate baseline context is going to be useful. And again, this is a general theme of all four of these neuromodulators, dopamine, epinephrine, acetylcholine and serotonin. You want to make sure that you have sufficient baseline levels of those things through things like diet, regular behaviors, and then you have the opportunity to use supplementation and if it's appropriate for you, prescription drugs, and certain behavioral protocols to try and get these potent increases, these acute increases in whichever the neuromodulators

02:02:14 Use the Neurochemical Toolkit to Meet Individual Goals

you happen to want to leverage for your particular goals. So that brings us to the end of at least this exploration of the neuromodulators, dopamine, epinephrine, acetylcholine and serotonin. Some of you who are regular listeners of this podcast might be saying, well, we've heard all this before, right? You had an episode on dopamine. You had an episode on anxiety. You had an episode on sleep. And indeed that's true. But what I've tried to provide today is a framework that cuts through all those episodes and at the

same time builds out a new and what I believe to be a really important theme and principle, which is that whether or not you're using nutritional tools or supplementation or prescription drugs or any other sort of protocol to try and create a desired effect of focus or energy, motivation, relaxation, you are playing with the same neurochemical ingredients, just as in the realm of nutrition, you have macronutrients, you have proteins, carbohydrates, and fats that can be adjusted in different ratios and arranged at different times in order to achieve certain desired effects. Well, when it comes to your neurochemistry and your ability to perform mentally, to perform physically, and your overall well-being, you are dealing with a small handful of especially potent molecules. And I acknowledge that there are many neuromodulators. There are indeed many neurotransmitters, glutamine, glycine, GABA, et cetera. But today we focused on the main four, meaning the most potent and most widespread neuromodulators in the brain and body that give you access to particular brain states and body states of the sort that most people desire. So what I'm hoping is that rather than decide that any one tool is the most useful or that any one neurochemical is most useful for that matter, that the information that I've provided today allows you a kit of versatile tools that allows you to figure out what levels of dopamine and augmentation of dopamine are appropriate and necessary for you. What levels of acetylcholine and tools for manipulating acetylcholine are going to be most useful for you and so on and so forth because at least at this stage in time, that is June, 2022, there is no simple at home test. In fact, there is no simple laboratory test that allows us to know whether or not our dopamine levels are high and our serotonin levels are low. We can look at somebody and their behavior. We can look at ourselves and our own mood and behavior. And we can infer what those levels may or may not be. But unfortunately, we don't have a really good test of dopamine levels or serotonin levels that would allow us to say, okay, this person, or I need to increase dopamine two-fold in order to achieve the kind of motivation that we want. Unfortunately, that doesn't exist. Rather, we are confronted with a situation where we understand generally what these different neuromodulators do, the different mental states and physical states that they tend to put us into. And we reviewed those. And we know that there are really potent tools to adjust those neuromodulators, if not alone, but in certain combinations, that is ingestion of caffeine will tap into and support dopamine and epinephrine. Increasing dopamine and epinephrine alongside increasing acetylcholine will allow us to access certain brain states, that is focused, alert, energized, brain states, great for learning and plasticity of all kinds. Whereas augmenting serotonin is going to

put us into a more relaxed state and so on and so forth. And I'd like you to keep in mind that there is no negotiating the fact that we all have different phases of our 24-hour cycle during which those very same neuromodulators tend to be naturally higher or naturally lower and I reviewed that at the beginning of the episode. So my wish for you is that you will take this information, experiment with it as you see fit for you and in a safe way. And as you go forward, to really try and gain intuition and understanding as to not just how these protocols work, but how any protocol that you might encounter, supplement-based, drug-based, behavioral-based, how those might tap into these different major neuromodulator systems. And from that, to be able to better predict and evaluate whether or not they're going to be useful to you, detrimental to you,

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or whether or not they should be used in combinations that would be more useful to you. If you're learning from and are enjoying this podcast, please subscribe to our YouTube channel. That's a terrific zero cost way to support us. In addition, please subscribe to the podcast on Spotify and Apple and on both Spotify and Apple, you can leave us up to a five star review. If you have feedback for us or you have topics or guests that you'd like us to cover on the Huberman Lab Podcast, please put that in the comment section on YouTube. We do eventually read all those comments and that's the best place to give us that sort of feedback. In addition, please check out the sponsors mentioned at the beginning of today's episode. That's the best way to support this podcast. During today's episode, we talked a lot about supplements. While supplements aren't necessary for everybody, many people derive tremendous benefit from them. As mentioned at the beginning of today's episode, we partnered with Momentous supplements because they're extremely high quality, they ship internationally, they are available in the dosages and single ingredient formulations that are ideal for building a supplementation protocol. You can find all those at liveMomentous.com/huberman. If you're not already following us on social media, we are @hubermanlab on Twitter and @hubermanlab on Instagram. There, I cover science and science-based tools, some of which overlap with the content of the Huberman Lab Podcast, but much of which is distinct from the content of the Huberman Lab Podcast. And if you're not already subscribing to our newsletter, we have a Neural Network Newsletter as it's called. It comes out about once a month. We provide

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