Using Caffeine to Optimize Mental and Physical Performance

I'm a professor of Neurobiology and Ophthalmology at Stanford School of Medicine. Today we are discussing caffeine. Caffeine is one of the most widely used substances on the planet. Estimates are that more than 90% of adults and as many as 50% of kids that is adolescents and teenagers use caffeine on a daily basis. Caffeine is an amazing molecule. Most people are familiar with caffeine's ability to increase alertness and to reduce our feelings of sleepiness and fatigue. And indeed, it does that. But what most people are not aware of is that caffeine acts as a strong reinforcer. What I mean by reinforcer is that, when caffeine is present in a drink or food-- and yes, indeed, caffeine is present in many foods even unbeknownst to us. When it's present in drinks and foods, we actively come to like those foods and drinks more than if caffeine were not contained in those foods and drinks. So it reinforces our liking of particular foods and drinks. And indeed, it even reinforces our liking of the containers they are consumed from and the company we keep when we consume foods and drinks that contain caffeine. That is, caffeine is not just a stimulant. Caffeine is a reinforcer. And it's a reinforcer that plays an active role in almost everybody's daily life. We can say that with confidence because, as I mentioned a moment ago, more than 90% of people are consuming caffeine. And most people think that they consume caffeine because it makes them feel more alert. But there are many reasons why you're consuming caffeine. And I'm not going to tell you that consuming caffeine is necessarily bad. In fact, today, I'm going to tell you about many of the positive health benefits of caffeine, including neuroprotective effects, antidepressive effects, and certainly performance-enhancing effects, both for mental performance and for physical performance. Now that said, there are certain situations in which you want to avoid caffeine, and there are certain people who might opt to avoid caffeine. That's especially the case when one thinks about caffeine not just as a stimulant but as a reinforcer. In fact, caffeine is such a strong reinforcer that, if even tiny amounts of caffeine are present in certain foods and drinks, you will very quickly come to prefer those foods and drinks over other choices, which can be a good thing or a bad thing, depending on what sorts of food and drink choices you're trying to make. So today, I'm going to inform you about how caffeine works at a mechanistic level. I promise to do that with a minimum of nomenclature and such that, even if you don't have a background in biology, you will be able to digest that information easily. And then I'll tell you how to use caffeine to your advantage or conversely how to avoid caffeine at certain times to your advantage. So today's episode will focus both on mechanisms and tools that is the use and leverage of caffeine to improve mental health, physical health, and performance. Before we go any further into today's discussion, Tool: GLP-1, Yerba Mate, Satiety & Weight Loss I want to tell you about some recent results about a molecule that's found in certain caffeinated beverages and that has been proven to be very useful for both weight loss, mental performance, and controlling blood sugar levels. And that's GLP-1 or glucagon-like peptide 1. Glucagon-like peptide 1 is found in the brain and body. It acts both on the brain and body. It does many different things. But one of its primary effects that's been discovered is to reduce hunger. And it does that in two ways. It does that by activating certain neurons in your hypothalamus. So that's a brain region that controls hunger and satiety. It makes us feel full at the level of the brain, so it makes us feel sated, that is. And it actually makes us feel full. It turns out that GLP-1 acts on certain receptors in the gut to make us feel as if we've ingested enough food. It doesn't necessarily make us feel as if our gut is distended, but it makes us feel full. That's really interesting because, if you think about it, when we eat, our stomach fills up, obviously. And that information has to be communicated to the brain such that the brain can then send satiety signals that actually shut off our hunger. And believe it or not, the brain actually activates signals to reduce the desire to chew when our stomach is full. And GLP-1, as I mentioned, works on the brain to create these feelings of satiety as if we've had enough and to reduce our desire to eat more. And GLP-1 acts directly on the gut to give us a slight sense of fullness in the gut, which

then is communicated to the brain. So really, there are two parallel signals being sent when we have GLP-1 present in our system. Now a little bit of relevant history on GLP-1. It was actually discovered in Gila monsters. These are these reptiles that can go long periods of time without eating. And a very clever scientist decided to study why it is that certain animals like Gila monsters can go a long period of time without ingesting anything. And it's because they produce very large amounts of GLP-1. They isolate the peptide from GLP-1, then they looked for the analogous peptide in humans. And it turns out that does exist. And as I mentioned, it's released in both brain and body to make you feel full and sated. Why am I telling you all this? Well, today we're going to talk about caffeine. And there's one particular caffeine source, which is yerba maté, and there are some other forms of teas similar to yerba mate that stimulate the release of GLP-1 significantly. There are also nowadays drugs which are called analogues of GLP-1. So these are drugs that mimic or are identical to the kind of GLP-1 that you would make. And those drugs are proven to be very effective for the treatment of certain forms of diabetes and for the treatment of obesity, but they trigger enormous amounts of GLP-1 pathway activation. So those are extreme cases for people that are really struggling for weight loss. But the clinical trials and the data that are out there in the general population now are very, very promising for GLP-1 analogues. Yerba maté tea, provided it's not the smoked variety-- and I mention that because a number of people have cued me to the fact that yerba maté teas come in smoked varieties and nonsmoked varieties. And the smoked varieties are thought to perhaps be carcinogenic. That is, procancer-causing. So I advise people to avoid smoked varieties of yerba maté tea. But yerba maté teas are known to stimulate significant amounts of GLP-1 release. And so they can be effective as a weight loss tool, mainly by blunting appetite. And again, they do that both at the level of the brain and at the level of the gut. Now all of what I just told you has been known for some period of time, but there are new set of findings that were just published in Cell Reports Medicine, Cell Press journal, excellent journal-- which indicate exactly how it is that GLP-1 stimulates both satiety and can trigger additional weight loss through other mechanisms. And I find the mechanism to be really interesting and actually really important, given some other topics we've covered on this podcast before. So the basic finding is that GLP-1, whether or not it's stimulated through the release of analogue drug that one is prescribed or by drinking yerba maté tea, for instance, and stimulate release of your own so-called endogenous GLP-1, yes, it makes you feel more full at the level of brain and body. But it turns out it also stimulates thermogenesis. Now thermogenesis is the active utilization of more metabolic energy. And fat cells, in particular-- so-called beige and brown fat cells-- are a potent source of thermogenic activity in your body. The basic background is that you have white adipose cells, so white fat cells. You have beige fat cells, and you have brown fat cells. And the beige and brown ones are fat cells that you actually want more of. They are not abundant under your skin. They're abundant really around your clavicles and your upper neck. They are the ones that generate heat. And the beige and brownness of them is actually the consequence of having a lot of mitochondria in those cells. When GLP-1 is elevated in your system, it turns out that it communicates to those white fat cells and helps convert them into beige and brown fat cells. That is, it takes fat cells that are not doing anything useful for you except being stored energy. And I think most people out there would like to have fewer of those white adipose cells. There are few of you out there that actually need more of them that are too thin, too lean, but most people are suffering from having too many of these white adipose cells. Well, when you ingest yerba maté tea or you were to take a GLP-1 analogue or stimulate GLP-1 in any number of different ways, yes, you stimulate increased satiety, but you're also stimulating the conversion of these white fat cells into beige and brown fat cells, which makes you more thermogenic and over time raises your basal metabolic rate. So you're burning more calories even at rest. It also makes you feel as if you're more comfortable in colder environments at rest. This is very much the same as the mechanism that's induced when you were to, say, take a cold shower or do regular ice baths or get into cold water regularly. That, too,

stimulates the conversion of white fat cells to beige and brown fat cells. So I like these findings very much because they provide a mechanistic coherence. They provide that is a really nice story as to how something like GLP-1 could be so effective for weight loss. Yes, on the one hand, GLP-1 is reducing appetite, and that, of course, will help people maintain or lose weight. But it's also increasing basal metabolic rate. And we now know how that's accomplished. It's likely accomplished at least through this one mechanism by the stimulation of conversion of these white fat cells, which don't do much for us except as energy storage units to these metabolically mitochondrial-rich beige and brown fat cells, which you can think of as sort of the oil in the candle that allows your furnace, your metabolism to burn at a higher temperature and a higher rate. So that's the mechanism. And the basic tool takeaway is that, if you are somebody who's interested in losing weight and you want to leverage the GLP-1 pathway, drinking a cup or two of yerba maté tea early in the day would be a great way to stimulate GLP-1 release. There are other ways to stimulate GLP-1 release. You can get it through certain forms of exercise. In particular, fasted exercise. This is actually a vote in favor of fasted exercise. There's a debate as to whether or not fasted cardio burns more fat than nonfasted cardio. And the data basically say no, it doesn't really matter. But that doesn't really take into account the longer arc of things like GLP-1 release, so that needs to be taken into consideration. So you could do fasted cardio. You could drink yerba maté tea, keeping in mind that yerba maté tea does contain caffeine. We'll talk more about the specific forms of stimulants including caffeine that maté has. But maté would be a great way to stimulate GLP-1 release. And then, of course, for those of you that are interested in more robust activation of GLP-1, then perhaps you might want to consider some of the new prescription GLP-1 analogues that are out there. But that's a more severe stimulus for GLP-1, of course. And for everybody, regardless of whether or not you're trying to lose weight, gain weight, or maintain weight, I think we're going to be hearing a lot more about GLP-1 analogues and drinks and supplements and things of that sort that stimulate GLP-1 in the very near future because it does appear to be a very important biological mechanism. Before we begin, I'd like to emphasize Let's talk about caffeine. So as I mentioned earlier, caffeine is consumed by basically most all adults every single day Caffeine Benefits for Mental & Physical Performance and consumed at very regular times each day. In fact, if you were to take a look at your caffeine intake or the caffeine intake of somebody close to you, what you would realize is that they don't do so well if their caffeine intake arrives even 10, 20, or 30 minutes past their expected or usual intake of caffeine. That's pretty remarkable, and it brings to mind ideas that we are all, quote unquote, "addicted to caffeine" or that caffeine is somehow bad. I'm certainly not going to make the argument that caffeine is bad. First of all, I'm a regular caffeine user. I wouldn't call myself a caffeine abuser, but I am a regular caffeine user. And caffeine is known to have certain health benefits. I listed off a few of them earlier, but I'll mention those again now before going forward. Caffeine is known to have certain neuroprotective effects. And that is because of its ability to increase neuromodulators, such as dopamine, but also other so-called catecholamines like norepinephrine. If you don't know what those names mean, these are molecules that increase levels of alertness, motivation, and drive. And so then therefore not surprisingly the large scale analyses of the relationship between depression and caffeine shows that, provided people are not drinking so much caffeine, that it makes them overly anxious, that regular intake of caffeine is inversely related to levels of depression. So it may have some antidepressant effects. And those could be direct or indirect. What do I mean by that? Well, you can imagine that if people are ingesting caffeine and they are more motivated to do work and pursue quality social interactions, then the probability that they will have depression could be lower. It could also be that there are direct effects on the chemical systems of the brain that relate to mood and well-being that could offset depression. It is not clear whether or not the effects of caffeine in countering depression are direct or indirect. Nonetheless, there's a relationship there, and it's an interesting and positive one. Or I should say negative correlation, positive effect overall on mood and well-being, to be exact.

Now it's also the case that caffeine can improve mental performance and physical performance. This has been demonstrated in tens of thousands of studies. I will review a few studies on this, in particular, today. But to just give you a sense of how caffeine works at the level of its timing and impact on mental performance and physical performance, when we ingest caffeine, provided that we don't have a lot of food in our stomach and that our blood sugar isn't particularly high, generally, we experience an increase in alertness within about five minutes. And that increase in focus and alertness peaks around 30 minutes after ingestion of caffeine and persists for as long as 60 minutes. Now this is assuming that one takes caffeine in pill form or drinks the entire caffeine drink within a short period of time. But a little bit later, I'll talk about how you can consume caffeine at regular intervals while doing mental work or physical work in a way that can further increase mental performance and physical performance. But let's just touch on what caffeine intake really does for mental performance and physical performance. erhaps the most robust finding across all of the studies that I've examined is that caffeine reduces our reaction time. That is, it improves our reaction time. It doesn't make it longer. It makes it shorter. So, for instance, in a laboratory study where people were asked to hit a lever every time they hear a tone, you can greatly reduce the time between the tone and the pressing of the lever if people ingest caffeine about 30 minutes before they do that task. Now that seems like a trivial task, but this is also seen in the domain of sports performance and even in cognitive performance, where people have to arrive at a particular answer to a question. And the answer to that question has to be pulled from their memory banks within their brain, their hippocampus, for instance, a brain structure involved in memory. And if you are asking people, for instance, to remember the capitals of different states or cities or to remember certain historical facts, they will do that at a particular rate. But if they've ingested caffeine within the hour prior, their ability to recall that information is much, much better. They are faster, and it does not appear that accuracy is reduced. In fact, in many cases, accuracy is enhanced. And that's because caffeine both works on the reaction time systems of the brain and body. I'll talk about the mechanims for that in a little bit. But it also stimulates certain neurotransmitters and so-called neuromodulators within the brain and body that give the neural circuits in the brain that are associated with learning and memory a lower threshold to activation. What does that mean? That means that we are better able to access the brain circuitry involved in learning and memory when we have a certain amount of caffeine circulating in our system. So this makes caffeine an incredible performance-enhancing compound. And I could give you tens of thousands of examples of this in humans. But before I do that, I want to just touch Caffeine in Nature & Positive Reinforcement on what we know about the existence of caffeine in nature and what the existence of caffeine in nature and its effects on other animals tells us about what caffeine does in humans. Because as I alluded to earlier, what caffeine is doing for us is not just making us more alert, improving our memory, improving our reaction time, and so on. It's actually acting as a powerful reinforcer of experience. And it's acting as not just a powerful reinforcer of the caffeine-containing drink that we drink but also the mug that it's contained in, plus the person that we might be sitting across from when we consume that caffeine, and so on and so forth. If it's a little bit hard for you to conceptualize what a reinforcer is and why I'm calling it a reinforcer, let me spell it out in three specific ways. We often hear about the word reward, and we think, OK, if we do certain things and we like the outcome, then those certain things are rewarded. Right? If we're doing something, we receive praise. The praise is the reward. And therefore, we are more likely to do that thing in the future. In fact, a lot of parenting is like that. And a lot of life is like that. However, when we hear the word reward, we often think about something that feels good to us. And certainly, if we've worked hard and we get some praise, that's natural for the praise to feel good to us. Or for instance, if we work very hard and we get a certain outcome-- a trophy, a financial outcome, a degree outcome, recognition, et cetera-- all of those can act as rewards, but those are all conscious rewards. We are aware that they are happening.

Reinforcers are a little bit different because the word reinforcement can apply to conscious rewards of the sort that I just described, but there are also many ways in which caffeine stimulates the release of chemicals in our body that act as reinforcers. But those reinforcers are subconscious. That is, we are not aware that they cause this preference for the activities that cause their release. So the study I'm about to describe beautifully, I believe, encapsulates how is it that humans came to consume caffeine and why caffeine exists in nature and the powerful effects of caffeine as a reinforcing agent both in animals, insects, and in you and me. And the title of the paper is "Caffeine and floral nectar enhances a pollinator's memory of reward." Keep in mind that caffeine is made from plants. Some of you will say, duh, but I think some of us don't realize that the reason why there is caffeine in coffee is because coffee comes from a plant. It's a coffee bean, certain teas, which, of course, are plants that people brew. Caffeine is contained in those teas, such as yerba maté. Well, why would this bitter substance-- because, in fact, caffeine is quite bitter in high concentrations. Why would this bitter substance be something that insects or animals would want to consume at all? It turns out that, in most plants, caffeine is present in small enough quantities that insects and other animals-- and in fact, we can't actually taste the caffeine. If I were to give you a little bit of pure caffeine, yes, it would be a stimulant for you, but you would say that it tasted awful. It's in a category of compounds that would strongly stimulate the bitter receptors on your tongue and would make you cringe and pucker and essentially walk away from whatever it is that contain that caffeine and from the experience that contain that caffeine. Well, in nature, caffeine is present in very low concentrations or is masked by other flavors within flowers, beans, and plants. And what this paper really points to is that caffeine in nature is acting as a reinforcer for bees that are consuming different nectar. So the way that it works is that bees, of course, go from flower to flower, and they are consuming the nectar. They are bringing nectar and pollen back to the hive, and that provides critical nourishment for the bee colony. The bees are foraging in a way that includes information about color, in particular, ultraviolet color, things that we can't see but they can see, because they have different photoreceptors than we do. And what the study shows is that plants and nectars that contain very small amounts of caffeine are the preferred sources of food for bees. And the study is beautiful because they were able to confirm that they could mask the caffeine taste. So they know that the bees are not preferring the taste of caffeine. But what they do is they pair caffeine with different food sources for the bees, then they remove the caffeine. And what they find is that the bees very strongly prefer flavors that contain caffeine, not because they could taste the caffeine but rather for the way that those caffeine-containing flavors made the bees feel. So how do those caffeine-containing flavors make the bees feel? The same way that they make you and I feel, a little bit more alert and thereby able to do more work. For the bee, the more work is the consumption of more food, which then has a further reinforcing effect. So what we're really talking about here is the fact that A, caffeine exists in nature, in plants. It exists in concentrations that are very low, so low, in fact, that they are not detectable to the taste receptors of insects, and, in many cases, to the taste receptors of humans. And, of course, there can be high levels of caffeine in a plant. But if the plant also contains compounds that mask the flavor of caffeine, well then, those plants are going to essentially be even stronger reinforcers for the flavor of the plant, OK? So now we're talking about strong flavors plus strong neurostimulant effects of caffeine. And the most important point here is that all of these effects of caffeine are subconscious. It is not because the bee or you likes the taste of caffeine. In fact, most people, when they take their first sip of coffee, they find it taste bitter and kind of noxious. They don't like it. You may not even remember that because it happened so long ago and because caffeine is such a strong reinforcer that very quickly you come to like the taste of coffee. You might even come to like the feeling of your mug in your hand. You might even come to like the smell of coffee and so on and so forth. And that's because caffeine stimulates Caffeine Effects on Brain; Reward Pathways the release of certain neurochemicals in the brain, in particular, dopamine and

acetylcholine, two neuromodulators that increase our focus and alertness and our feelings of well-being. A little bit later, I'll tell you that caffeine stimulates the release of dopamine in a way that's very much distinct from the classical dopamine pathway associated with addiction and reward. In fact, we can think of caffeine as having a somewhat privileged access to the reward systems. I'll give you a bit of a hint of where this is going. Caffeine stimulates the release of dopamine and acetylcholine not within the classic so-called mesolimbic reward pathway. That's just fancy nerd speak for the reward pathways of the brain. They're associated with things like sex and food and drugs of abuse, like cocaine and methamphetamine. But rather, caffeine seems to stimulate the release of dopamine in the parts of the brain that are associated with alertness and cognition, meaning the forebrain. This is very important. We have multiple dopamine systems in the brain and body, and caffeine seems to stimulate dopamine directly within the components of the brain that are associated with clarity of thought and well-being, but more so clarity of thought. Now, I'm also talking about caffeine as a strong reinforcer in that it makes you feel good overall. And it does. And that suggests that it also taps into the more classic reward pathway. But it does that in a very interesting and frankly almost diabolical way. When we regularly ingest caffeine, it stimulates the increase in dopamine receptors at multiple sites throughout the brain but, in particular, within the reward pathways of the brain. So not the areas of the brain that are associated with focus and clarity of thought and cognition. It does that, but it is also increasing the level of dopamine receptors in the reward pathway. And what that means is that, for any dopamine that's released in response to a positive experience, social experience, or any number of the other things that can stimulate dopamine release, there are more receptors, more parking spots, if you will, for that dopamine to arrive at and to exert its increases in mood, increases in motivation, and overall feelings of drive and excitement. So there are four ways that caffeine works that we need to understand. First of all, caffeine acts as a reinforcing agent. It increases the probability that you will return to and engage in a certain activity or consume a certain beverage or food. Second of all, caffeine increases dopamine and acetylcholine, which are both neuromodulators in the forebrain, which helps us improve our ability to think, to modify our rule sets. That is, to adjust our strategies for different social situations and mental demands and physical demands. And third, it increases the number and efficacy of dopamine receptors in the reward pathways of the brain. That is, it makes things that would feel pretty good feel even better. And fourth, caffeine acts as an antagonist to adenosine, which offsets the sleepiness that we would otherwise feel from the accumulation of adenosine that occurs as we are awake for more and more hours throughout the day. So let's talk first about caffeine as a reinforcing agent. Again, this was first most beautifully demonstrated Caffeine as a Reinforcing Agent in this study on honeybees where the bees prefer nectars that contain caffeine. And that all makes perfect sense in terms of the ecology of bees and flowers that contain nectar. There's an advantage, at least in terms of adaptation, that the flower benefits because of distribution of things from the flower, which is good for the flowers and the bees benefit, because they're getting food. And so there's a kind of a symbiosis there. But with humans, we're consuming caffeine-containing beverages for our sake. I don't think we have it in mind, nor do the bees have it in mind, frankly, that we're trying to preserve the plants that provide the caffeine. I think we would all suffer, or I should say 90% of adults would suffer greatly if all the caffeine-containing coffee and tea plants were gone, certainly. But most of us are not consuming coffees and teas and caffeine-containing foods because we're thinking about the plants they come from and we want to help those plants. We're thinking about how we want to help ourselves. And yet the point of the reinforcing effects of caffeine are that they are largely subconscious. We are not aware of them. Now you might say, no, that's not true. When I drink caffeine, it makes me feel really good. So I'm aware that it makes me feel good. In order to illustrate how reinforcement really works, let me give you the counter example, which would be an aversive agent. So we have reinforcing agents and we have aversive agents. Let's say that there were

compounds in nature that exist in plants that are aversive. And indeed, they are. And let's say that these compounds were present at such low concentrations that you couldn't taste them. Let's say you wake up in the morning and you go to your refrigerator and you open it up and you are thirsty, and so you reach for a nice rich red-containing beverage in a glass jar. Maybe it looks like cranberry juice or something of that sort. Or even a nice clear glass of water. It looks like a jug of water or a glass of water, and you drink that. Taste fine to you. Maybe even tastes great to you. And then let's say about 30 minutes later, you feel a little queasy, you feel a little off, you feel like going back to sleep, you just don't feel very good. You don't know why, but your nervous system is a predictive machine, and it has a process in which it back integrates. Or I should say integrates backwards into your immediate experience that preceded that not so good feeling. We can reliably say that there is a much lower probability that the next day when you wake up that you would reach for that same beverage or for that same container even. And maybe if you're in a novel environment, maybe you're staying in an Airbnb or a hotel or something of that sort, you might even find that you don't really like the kitchen in which you consume that beverage in the first place. And you don't know why. And unless you got very, very sick the day before, it's unlikely that you would have such a strong response that you would entirely avoid, for instance, water or glass jars containing liquids, et cetera. Let's say you went back to the refrigerator and you consume a beverage again and you just didn't feel so well, you felt less good than you normally would. Well, even without any ability to taste I'd like to just briefly talk about adenosine and some Caffeine, Adenosine & Reduced Sleepiness of its molecular features. And again, if you don't have a background in biology, don't worry. I promise to make this very clear to everyone. First of all, caffeine is what's called a methylxantine. It's a plant alkaloid. That's why caffeine itself is very bitter. Again, if I were to give you just the tiniest little bit of pure caffeine, you would find it to be extremely aversive. So these plants that have snuck small enough amounts of caffeine into them or that have masked the flavor of caffeine with other flavors such that bees and humans want to consume them, while we don't know what plants think, it does seem very diabolical and very clever in that we are seeking out these caffeine-containing plants, beverages, and foods even though caffeine itself is this alkaloid that is very, very bitter. Methylxantine-- that is caffeine-- binds to adenosine receptors. And there are really two types of adenosine receptors. There are these so-called A1 receptors and the A2 receptors. And they are present in different parts of the brain and body at different levels. We don't have to get too far into receptor subtypes. More importantly to understand is that adenosine makes us feel tired because of the way that it taps into the ATP pathway. The ATP pathway is central to energy production and feelings of overall energy in our brain and body in all cells and organ systems. When caffeine binds to adenosine receptors, it prevents adenosine from breaking down certain components of the energy production pathway. And the net consequence of that is increased cyclic AMP. So basically, when we ingest caffeine, we are biasing our system towards the pro-energetic aspects of these cellular pathways. Now it's really important to understand that, in biology, even if you block a receptor or you prevent the activity of an enzyme and-- at least, in this case, you end up with more cyclic AMP, more energy. You're not really getting more energy. You're actually borrowing energy against an overall system that is frankly nonnegotiable. What do I mean by that? Well, let's say that you were to wake up after six or eight hours of sleep and to drink a lot of caffeine and keep drinking caffeine throughout the day blocking those adenosine receptors. Yes, you'll offset fatigue. You'll offset sleepiness because that adenosine simply can't function. But at the point where the caffeine becomes dislodged from the adenosine receptors, you will have a massive glut, a backlog of adenosine, and you will feel extra, extra sleepy. So really, there's no way to create more energy in your system. Really, what you're doing is you're changing the timing in which the sleepy signals and the more energetic signals are arriving. And this is really important to understand as the backdrop to the various tools that we're going to get into next, in which you can use caffeine for enhancing mental performance and physical performance and

other aspects of health. But it's very important to understand this concept that, when you wake up in the morning provided that you slept well and enough the night before, your levels of adenosine will be about as low as they will ever be. Actually, in order to get your adenosine levels really bottomed out, you want to avoid caffeine in the first 90 to 120 minutes after waking. We'll talk about why that is because it turns out there's a way to completely clear adenosine out of your system in the hour or so after waking. But for most people, adenosine levels are going to be close to their lowest after a good night's sleep. But there's really no negotiating the accumulation of adenosine that's going to occur and going to bias you towards feeling more sleepy than you would. Otherwise, that's going to occur throughout the day. There's really no way to eliminate adenosine. All you can really do is block its function. So it's sort of like borrowing energy against the fatigue that you will inevitably feel. Now this actually has a very important socioeconomical relevance. Before caffeine was regularly consumed by human beings, we were really slaves to the light/dark cycle. And this was especially true before the presence of artificial lighting. But even before the advent of artificial lighting, humans were largely constrained to the outside light/dark cycle. We need to be active during the day and working during the day, and we need to be asleep at night. Caffeine allows us to divorce ourselves from that circadian cycle. Circadian just means about 24 hour. Caffeine allows us to do that at least somewhat by way of increasing our alertness. That is, spiking our alertness at various times throughout the day and even at night. This is how we can have shift workers, for instance, that can sleep during the day and then drink a strong cup of coffee at 8:00 PM and then work into the night. That ability completely transformed our society. Now, of course, the healthiest schedule-- and we know this with certainty. The healthiest schedule for brain and body is going to be alert during the daytime and asleep at night. There's no question about that. Shift workers run into all sorts of health problems. And thank you shift workers for doing the important work that you do. We need you. Air traffic controllers, paramedics, firefighters, police officers, et cetera. But we know that there are serious health consequences, negative health consequences, that is, for shift workers. But for most people out there, about 95% of people follow a typical schedule. They're awake during the day and asleep at night. And yet it used to be before the advent of caffeine-containing beverages that, if you were sleepy in the afternoon, you either had to take a nap or battle that sleepiness, that your activity rhythms and your sleep rhythms were governed by these circadian changes in availability of sunlight and when you slept. And you just didn't have the ability to ingest a beverage that would increase your levels of alertness because you block adenosine. So this is important to understand that, nowadays, we certainly live in a time in which we use-- in fact, 90% or more of adults and half or more of adolescents and teenagers use caffeine as a way to negotiate with, to borrow against this natural pattern of adenosine making us sleepy. But again, you're just offsetting the effects of sleepiness that adenosine causes. You can't eliminate the adenosine entirely. The important point is that adenosine as a pro-sleep molecule is a nonnegotiable aspect of your biology. In fact, it's so nonnegotiable that, every 24 hours, you are going to release adenosine, and you're going to release adenosine in direct proportion to how long you've been awake. So the longer you've been awake, the more adenosine circulating in your system. There are really only a handful of ways to completely clear out adenosine. The major one being to get sleep. The other is to take a short nap, which, of course, is sleep, but it's shallow sleep. Or non-sleep deep rest, so-called NSDR, has been shown to reduce levels of adenosine. And there are certain things such as viewing morning sunlight, which because of its effects on cortisol, can quote unquote, "clear out adenosine." We'll talk about this in more detail in a few minutes. And there's also evidence that certain forms of exercise, provided that it's brief and intense, can also reduce adenosine, not just block its effects. Tool: Caffeine Dosage, Caffeine Adapted Now that we've talked about some of the incredible mechanisms by which caffeine changes our experience of life, increases alertness and mood, et cetera, I want to talk about the use of caffeine as a tool. Now caffeine is a very potent and useful tool for enhancing mental health,

physical health, and performance. But there are certain considerations one has to keep in mind, in particular, dose. Now, first off, not everybody will respond to the same dose of caffeine the same way, but we can reliably say that your body weight is a good measure by which you can estimate what a healthy, useful dose of caffeine would be. So for most people, ingesting 1 to 3 milligrams of caffeine per kilogram of body weight is going to be the range in which caffeine can have positive effects without making us feel overly anxious and give us that feeling that we're jumping out of our skin and turn the otherwise positive experience of caffeine into an aversive one. For those of you that aren't familiar with thinking in terms of kilograms and normally think in pounds, I'll just quickly give you some general estimations that, for instance, 100 kilograms equals 220 pounds. So for me, I weigh 100 kilograms. That means that 1 to 3 milligrams-- again, milligrams, thousandth of a gram. 1 to 3 milligrams of caffeine per kilogram of body weight would mean for me. I could safely ingest 100 to 300 milligrams of caffeine in a single dose, in a single drink, if that's the way I'm consuming it, or pill form if that's the way that I'm consuming it. And it's very likely that that will be a tolerable dose. However, if you are not somebody that's accustomed to drinking caffeine on a regular basis, I suggest you start on the lower end of that 1 to 3 milligrams per kilogram of body weight range. So for instance, if you're somebody who weighs 50 kilograms, that's approximately 110 pounds. And you would be pretty comfortable ingesting somewhere between 50 and 150 milligrams of caffeine. So what I recommend is that people who are considering using caffeine as a tool or who are already ingesting caffeine, start to think about the dosage of caffeine that you are ingesting or plan to ingest and the timing in which you ingest that caffeine relative to certain tasks throughout your day, your waking, and your sleep. And we'll talk about that in just a moment. But the first step for you is to figure out how much you weigh in kilograms and then to go to that number of 1 to 3 milligrams of caffeine per kilogram of body weight. And that's a good range in which you might want to explore the use of caffeine in a single application, meaning a single dose. Now, I do realize that some people out there are drinking coffee all day long or having coffee in the morning and again in the afternoon. What I'm referring to here is the ingestion of caffeine in a single bout, right? 1 cup of coffee or 2 cups of coffee, for instance, to achieve that 100 to 300 milligram range if that's what's appropriate for your body weight. But to avoid any confusion, when I talk about dosage of caffeine, what I'm really talking about is not the total amount of caffeine ingested per day. I'm talking about the total amount of caffeine ingested in one sitting or setting, that is. And if you're somebody who's drinking caffeine multiple times throughout the day, you can imagine-- for instance, let's say the appropriate dose for you in order to get an enhancement in mental performance or physical performance is 200 milligrams. And you are somebody who's doing some work in the morning, and you want to have that lift in the morning to be able to focus better. And you're doing some physical exercise in the afternoon or vice versa that you would ingest 200 milligrams of caffeine at two separate times per day separated by about four hours. Now you don't have to separate them. You could put them two hours apart, for instance. But we'll talk about half-life of caffeine and so forth. Just keep in mind that, if you're ingesting 200 milligrams of caffeine and that's the appropriate dose for you based on your body weight and then you are ingesting another 200 milligrams of caffeine an hour later, you are effectively ingesting approximately 400 milligrams of caffeine, which is going to start exceeding the dose in which you can normally tolerate without feeling anxious and jittery. With all of that said, there is a range of tolerance for caffeine that's based on two things. One is a preexisting disposition that is whether or not your genetics and nervous system and the backdrop of your life, how much stress you're experiencing tends to make you feel more anxious and alert and jittery before you ingest any caffeine. And the other is how so-called caffeine-adapted you are. We often hear about tolerance. Tolerance means something very specific. It's the ability to ingest more and more of something with a plateau that is a no increase or an actual reduction in the effectiveness of that thing. But here we're not really talking about tolerance to caffeine. What we're talking about is being

caffeine-adapted. A simple way to understand whether or not your caffeine-adapted or not is that, if you drink caffeine and it tends to increase your heart rate and make you feel more alert and a bit more anxious, then chances are you are not caffeine-adapted, provided the amount of caffeine is within the healthy range for you, that is, the ranges we talked about a moment ago. However, here's somebody who drinks caffeine and you actually feel alert and relaxed, chances are you are caffeine-adapted. And so at various times during today's episode, I'll talk about people who are caffeine-adapted and people who are not caffeine-adapted. We'll talk about the use of caffeine every other day. I know a few habitual caffeine drinkers including myself, just the simple mention of that probably sounds aversive. But there is actually great utility to using caffeine every other day as opposed to every day. But just keep in mind that some people will drink caffeine and not get much of a lift from it at all. Other people will drink caffeine, and they will feel extremely anxious even at dosages far lower than that 1 to 3 milligrams per kilogram of body weight range that I described a moment ago. So you have to take into account individual differences. That said, 1 to 3 milligrams of caffeine per kilogram of body weight for a given sitting. For your morning coffee or your morning yerba maté tea is a good range from which to start. And I do encourage you to go online and look up the various beverages and foods that you might be eating that contain caffeine. For instance, some people are surprised to discover that the coffee that they get from some of the more standard popular vendors out there, the small coffee or the medium coffee, for instance, can contain as much as 400 to 600 milligrams of caffeine. And the large coffee that is often sold at those commercial vendors can contain as much as 1 gram, 1,000 milligrams, of caffeine. Now you may be adapted to that such that it doesn't make you feel anxious, but if you wonder why you feel irritable and you get a headache when you don't get that caffeine or that amount of caffeine at precisely the time that you're used to getting it each day, that's because you are consuming quite large quantities of caffeine on a regular basis. So I do recommend whether or not you drink soda or coffee or tea that you figure out the source of that. OK, so figure out what vendor you purchase it from, what kind of coffee, and go online and spend a little bit of time because the information is out there to discover what levels of caffeine you're actually ingesting. Now if you happen to be ingesting more than 1 to 3 milligrams per kilogram of body weight of caffeine, that's not necessarily bad. However, you do want to be careful about ingesting very high levels of caffeine over long periods of time in your life because there can be issues that start to arise. In particular, a bias towards higher levels of anxiety and depletion of certain electrolytes. Because caffeine is a diuretic can cause you to lose sodium and other things of that sort. And also just from simply a dependent standpoint, it does appear that if you ingest high levels of caffeine that is exceeding the dosages that normally you could get away with and get just as much mental-enhancing and physical-enhancing benefits that you can cause some disruption to the microvasculature. You can bias yourself towards headaches, anxiety attacks, and you can become actually quite irritable when you're not getting those higher levels of caffeine. So I do encourage you to figure out not just what an appropriate caffeine dosage would be for you but also how much caffeine you might already be ingesting. The first tool I'd like to talk about is one that I've mentioned before on this podcast several times. Tool: Delayed Caffeine Intake, Afternoon Crash & Sleep And it's something that if you haven't heard of will be very useful to you. And if you have heard this tool before, I'm going to add some additional features to the description of this tool that should make this worthwhile for you as well. And that is to delay your caffeine intake to 90 to 120 minutes after waking up on most days. And I'll be very clear as to days in which you might want to ingest caffeine more closely to when you wake up. Why would you want to delay your caffeine intake to 90 to 120 minutes after waking? The answer to that is very simple. Many people wake up in the morning. They drink caffeine within 10, 20, 30, sometimes within 2 minutes of waking. And they feel more alert naturally. That makes sense because of the effects of caffeine in blocking the effects of adenosine that I talked about earlier and its effects on other neurotransmitter systems. But then what they find

is that, in the early afternoon, in particular, after lunch, they experience a dramatic dip in their overall levels of energy, the so-called afternoon crash. And in most cases, the way they respond to that is to ingest more caffeine, which indeed can increase their levels of mood and alertness. However, as we'll soon talk about, there is a problem with ingesting caffeine in the afternoon if it falls within 8 or 10 or dare I even say 12 hours of going to sleep. And that is, the caffeine ingested in the afternoon-- for most everybody, let's say for 95-plus percent of people-- disrupts the architecture and quality of their nighttime sleep. And I should say that it doesn't necessarily impact their ability to fall asleep and maybe even sleep through the night but that the depth and quality of that sleep is disrupted by consuming caffeine in the afternoon. A little bit later, I'll talk about how you can offset some of those negative effects if you absolutely require caffeine in the afternoon. But there's a huge advantage to restricting your caffeine intake to the early part of your day but not consuming caffeine within the first 90 to 120 minutes after waking. In fact, many people find that if they delay their caffeine intake to 90 to 120 minutes after waking up that they feel more alert in the morning, and they completely avoid that afternoon crash. Now that said, many people, including myself, do need a short nap or non-sleep deep rest or other form of relaxation for 10 to 30 minutes in the afternoon. That is natural and healthy. I'm not referring to the need for that when I refer to the so-called afternoon crash. What I'm talking about in the afternoon crash is a inability to recover energy and focus and a need to consume more caffeine just to make it through the afternoon. By delaying caffeine intake to 90 to 120 minutes after waking, there are a couple of things that are accomplished. First of all, you offset that afternoon crash. And this is an effect that many people experience the very first time they start delaying their caffeine intake to 90 to 120 minutes after waking. And the reason this works so well is the following. As I mentioned earlier, adenosine is a molecule that builds up the longer that we are awake. It is a molecule that is reduced or cleared from our system by sleep. So when we emerge from sleep regardless of how long we've slept, our adenosine levels are lower than they were when we went to sleep the previous night. If you slept well enough and long enough, those adenosine levels can be very, very low, but they are never completely zero. When you wake up in the morning, even if you're one of these people that springs out of bed and is ready to attack the day-- and here I'm certainly not describing myself. I'm not one of those people. I tend to wake fairly slowly. But if you're one of those spring up and attack the day or you're one of the people who moves more slowly into your day, regardless, there's still some residual adenosine in your system. And this is particularly the case if you did not get enough sleep or enough depth of sleep the night before. The correct ratio is a slow-wave sleep and rapid eye movement sleep. And for those of you interested in optimizing sleep, I'll just refer you to our master your sleep episode of the Huberman Lab podcast, the perfect your sleep episode of the Huberman Lab podcast. And we have a tool kit for sleep all of which are available, zero cost, time-stamped, et cetera at hubermanlab.com. You wake up in the morning. And your adenosine levels are low, but they're not zero. And if you didn't sleep that well or deeply enough the night before, you're going to have more adenosine in your system. You might think the logical thing to do is therefore to drink caffeine and to block the adenosine that's there. But what happens if you do that is there's an accumulation, a sort of glut of adenosine that hangs around. And then in the afternoon, when the effects of that caffeine start to wear off, you will experience the so-called afternoon crash. As I mentioned earlier, there is a way to clear out the adenosine that's present when you wake up in the morning and to clear it out essentially completely without just blocking its receptors and letting it accumulate or hang around. And the way to do that is to deliberately spike your cortisol. Now, many of you have heard of cortisol, the so-called stress hormone, as a bad thing. And indeed, chronically elevated cortisol is a bad thing. It depletes your immune system. It's bad for psychosocial effects. It tends to make us feel anxious and on and on. But cortisol itself is not bad. Cortisol is wonderful. Cortisol enhances the efficiency of the immune system. It makes us alert and focused. It stimulates our metabolism. It does a huge number of

positive things, provided that it is released in a circadian fashion. That is, at the appropriate times every 24 hours and that it tends to peak very close to waking. In fact, one of the reasons you wake up in the morning, assuming that you weren't woken up by some noise or sleeping in an environment that's too warm, et cetera, is that your cortisol levels start to rise. And shortly after waking, your cortisol levels will start to reach their peak. And when I refer to a cortisol pulse, that's just biology nerd speak for a rise and peak in cortisol. You want that cortisol pulse to occur early in the day close to waking, and you want that for a couple of reasons. First of all, if you don't restrict that cortisol pulse to early in the day, it will tend to bleed into the later parts of the day. And actually, a late shifted cortisol peak is one of the hallmark signatures of depression, low-level depression, and serious depression. And it can start to disrupt sleep and certainly can disrupt mood metabolism and your immune system. So you want that cortisol peak early in the day. How do you ensure that that happens? Well, you wake up in the morning. And whether or not you're a bounce-out-of-bed type or you're more groggy, you kind of wade slowly into the day type like I am, you wake up, and you don't ingest caffeine. Fine and, in fact, beneficial to hydrate with water and electrolytes. Terrific. In fact, I would say necessary to get bright light in your eyes ideally from sunlight. I've talked about this many, many times before on the podcast. If you wake up before the sun comes out, then turn on bright artificial lights. But then certainly once the sun is out and even on cloudy days, in fact, especially on cloudy days, get outside for anywhere from 5 to 20, maybe even 30 minutes. Do some work outside, take your breakfast outside if you're a breakfast eater. Get something done outside even if it's just to get outside and get bright light in your eyes. Why? Well, because it's been shown in studies on humans that getting bright light in your eyes in the first hour after waking or as soon as possible after waking increases the peak of that cortisol pulse by 50%, 5-0. And that cortisol pulse, yes, increases mood, yes, increases alertness, but it does one other very important thing, which is that, through an indirect pathway, it can clear out any residual adenosine that might be present in your system when you wake up in the morning. Again, this is going to be especially important for those of you that are not getting as much sleep or as much quality sleep as you would like. It's going to be very important for you to get that morning bright light ideally from sunlight, get that cortisol peak going. Other ways to increase that cortisol peak would be to do some physical activity. If you don't have time to do a full workout, well then, getting some movement-- 10 minutes of skipping rope or even 5 minutes of skipping rope or jumping jacks or walking if that's all you have time for ideally while getting the sunlight in your eyes. But that's going to zero out the adenosine present in your system. If, however, you were to wake up and immediately drink caffeine-- caffeine itself can stimulate the release of cortisol a little bit more than it would otherwise be present in your system. But by blocking those adenosine receptors and because of the indirect effects of caffeine on the cortisol system, you actually are reducing the clearance of adenosine that would otherwise occur. So I realize that's a mouthful. Just to be very clear, if you wake up and you ingest caffeine right away, you're blocking the adenosine receptor, but you're not clearing it out. You're also preventing cortisol from having its normal increase and rise such that it can directly clear out adenosine because cortisol can clear out adenosine. And that's what you want. You want to be at maximum alertness and focus in your morning and throughout your day. And by delaying your caffeine to 90 to 120 minutes after waking, you set up your system so that you get that morning cortisol peak. Ideally, a peak that's even greater because you're getting your bright light viewing. And then when you ingest your caffeine 90 to 120 minutes after waking, not only will you be craving it just a little bit, but you will be drinking that caffeine on an already existing backdrop of increased alertness for two reasons. One is adenosine is zeroed out, and your cortisol peak is higher. And so now when you ingest caffeine, you can actually ingest levels of caffeine that are a little more reasonable that almost with certainty are going to fall in this 1 to 3 milligrams per kilogram dosage and will allow you to feel really alert and will carry that alertness well into the afternoon hours without the need to drink more caffeine and thereby will

prevent you from drinking caffeine and disrupting your nighttime sleep. And, of course, by getting better nighttime sleep, you're going to zero out your adenosine even more. So what I'm describing here are essentially two tools. I'm telling you to get morning sunlight and maybe some exercise in conjunction with that even if it's brief exercise. But the main tool of delaying caffeine 90 to 120 minutes after waking has immediate effects, but it also sets in motion a cascade or domino falls that lead to better sleep and more wakefulness the next night and the next day and so on and so forth. Now I realize there are some people who just simply cannot Morning Exercise & Residual Caffeine Effects or will not delay their caffeine 90 to 120 minutes after waking for whatever reason. First off, let me say that, if you are somebody who likes to wake up and do very intense exercise within the first 90 minutes after waking, well, in that case, it would be appropriate to ingest your caffeine just prior to doing that exercise. Not a problem. Not a problem. But you should expect that the combination of drinking caffeine very shortly after waking plus exercising very intensely shortly after waking will increase the intensity of that early afternoon and afternoon fatigue that you feel. Now for some people, that's a great thing. They can afford to take a nap or do non-sleep deep rest, step away from work, and so forth. In that case, I strongly encourage you to do whatever it is that allows you to get regular exercise because regular exercise is going to be very beneficial. In fact, we did an entire episode called tool kit for fitness that describes a couple of different but really one main structure that allows you to get the appropriate amount of resistance training and cardiovascular training and flexibility training throughout the week. I happen to follow that program, and it works very well. And it does involve some of those workouts to come very early in the morning shortly after waking. And in those cases, I do ingest caffeine just prior to those, so within 10, 20 minutes of waking. However, on other days, I personally delay my caffeine intake 90 to 120 minutes, and I've done that to great benefit. And most people, if not, all people that try that, have reported the same. I should mention that some people will find getting out to that 90 minutes to be excruciatingly difficult because they're so accustomed to ingesting caffeine close to waking up. In that case, maybe just push out your caffeine intake by about 15 minutes each day until you hit that 90 to 120-minute mark. And that will make it much easier. It might take you a week or so to get there. But once you get there, you'll find it to be quite easy to maintain. The other thing is that, if you are somebody who insists on drinking caffeine very shortly after waking, I would encourage you to drink half of your caffeine then and then the other half of your caffeine about an hour later. That also will help offset some of the afternoon crash for reasons related to the so-called kinetics of caffeine. Caffeine has a quarter life of about 12 hours. That means that if you were to ingest a cup of coffee at let's say 8:00 AM-- and let's say 100 milligram coffee just for sake of simplicity, that about 25% of that caffeine action-- we wouldn't really say 25 milligrams, but about 25% of that caffeine action will still be present at 8:00 PM that night, which is pretty remarkable. So there's a long arc of caffeine effects, and this is why it can impede sleep if we take caffeine in the afternoon. But again, if you're somebody who wakes up and you really need caffeine right away and you refuse to do this 90 to 120-minute delay thing that I'm talking about, well then, in that case, I would drink half of your caffeine upon waking and then a little bit more or the other half about an hour later. And that will extend the arc of that caffeine effects such that you don't need it again in the afternoon because you won't experience the afternoon crash. Because of the way caffeine works, I should mention that, if you ingest caffeine Tool: Theanine & Jitteriness; Fasting, Intermittent Caffeine Use on an empty stomach, it will have a more potent stimulant effect. That will also tend to increase the level of jitteriness that caffeine can produce. Later, I'll talk about ways to offset that jitteriness, but I'll just tell you one tool now. Many people opt to take 100 milligrams of theanine, T-H-E-A-N-I-N-E, theanine, as a way to offset some of that jitteriness. Theanine will reduce the jitteriness of caffeine, which is why many energy drink manufacturers and even some coffee manufacturers are now putting theanine in energy drinks and in ground coffee because, no surprise, it allows people to consume more of that beverage and

thereby purchase more of that beverage, which is what these vendors want without feeling overly anxious and jittery. So you can take pill form theanine if you want with your caffeine. I don't tend to do that. Rather, I control the total dosage of my caffeine. I do tend to consume caffeine on an empty stomach because I do restrict my caffeine intake to the early part of the day. And I generally eat my first meal somewhere around 11:00 AM, and then I generally my last meal some time around 8:00 PM or so. Those are averages. I would say plus or minus an hour. And that's not because I'm religiously following any kind of time-restricted feeding. It's just that tends to work best with my schedule and my appetite. But again, that's a general theme. There are days in which I wake up and I'm very hungry, and I might ingest something, small snack or something. Or if I'm meeting somebody for breakfast, sometimes I'll have breakfast. Sometimes I won't. And so on and so forth. The point is that you can get away with drinking less caffeine to get the stimulant effect if you do it on an empty stomach. And if you're somebody who likes to exercise on an empty stomach-- and I'm one of those people-- well then, ingesting caffeine just prior to exercise can be a fantastic tool. A little bit later, we'll talk about some of the physical performance-enhancing effects of caffeine. But I'll just briefly jump to a point about that as we relate to morning exercise. If you are somebody who regularly ingests caffeine-- and we can define regularly by, if you've ingested caffeine every day for the last two weeks, you're a regular consumer of caffeine. Whereas if you're somebody who only ingests caffeine somewhere between two and four times per week, well then, you are not a regular consumer of caffeine. You're an intermittent user of caffeine. Well, if you're somebody who's a regular user of caffeine, the performance-enhancing effects of caffeine are going to be most dramatic if you take two or three days off from drinking caffeine, which to my mind as a-- I don't want to call myself a caffeine addict but a regular caffeine user. That's a horrible notion to me, it is an aversive notion, because I do like the effects of caffeine so much. But if you really want to see the maximum performance-enhancing effects of caffeine, you will do either one of two things. You will either abstain from caffeine for a few days or three days prior to ingesting caffeine, or you will use caffeine on an empty stomach. It's very clear that caffeine on an empty stomach enhances both the mental and physical enhancing effects of caffeine. And, of course, all of that has to be stated on the backdrop of consideration that you're very, very hungry, it can be make it hard to concentrate and so on and so forth. So I'm not encouraging people to starve themselves by any means. Certainly, don't do that. But if you want to maximize the performance-enhancing effects of caffeine, you will consume it on an empty stomach. And then as a final point to that, caffeine is a diuretic. It causes us to lose fluid and, along with that fluid, to excrete sodium because of the effects of caffeine on various processes within the kidney. So one thing that works very well to maintain mood and alertness longer given a certain amount of caffeine intake and to avoid the jitteriness and what can sometimes feel like a crash or low blood sugar feeling or even blurry vision is to make sure that you consume at least an equal volume of water with your caffeine. And ideally, that water would contain maybe a small pinch of salt or some sort of electrolyte drink-- or powder, rather. For me, I use element. Full disclosure, they are a podcast affiliate and sponsor. But you don't need to do that. You could simply just have a glass of water alongside your coffee or espresso or your yerba maté and just put a small pinch of sea salt in that or evem just playing table salt. And that will help offset some of the jitteriness of caffeine. A lot of people think that, when they ingest caffeine, they get the jitteriness and crash because their blood sugar is low. And while that can be the case, oftentimes, it's simply because of the excretion of sodium that's occurred when they've ingested caffeine. So I encourage you to hydrate well and to hydrate with something that contains a little bit of sodium. Obviously, not so much that increases hypertension or something of that sort but a small amount of sodium or an electrolyte drink like Element. And there are other electrolyte drinks out there that can accomplish the same, of course. Just a couple of quick notes about theanine because there are a growing number of products out there that contain theanine. And there's certainly a growing number of people out there who are

using theanine for the effect that I described before, which is to offset some of the jitteriness associated with caffeine-containing beverages or foods. And, of course, I should mention that I've Theanine: Effects & Dosage talked about the effects of theanine on sleep at that sleep tool kit that you can find as a free download. You don't even have to sign up for. Anything you just download it from hubermanlab.com. Go to the menu, go to a newsletter. You'll see the tool kit for sleep. You'll see that the so-called sleep stack that I use and recommend includes magnesium 3 and 8, something called apigenin and theanine, although that sleep stack is designed to be taken 30 to 60 minutes prior to sleep. And I make the point there, and I'll make it again here that ingesting theanine prior to sleep is not a good idea if you are somebody who tends to have very vivid dreams, night terrors, or night walk-- sleepwalking, excuse me, et cetera. In that case, eliminate theanine from the sleep stack.. . However, a number of people are using theanine, and products are using theanine to offset jitteriness from caffeine-containing products during the daytime, daytime consumption, that is. A couple of notes about theanine-- theanine is something that is present in green tea, right? It's now been created as a supplement. It's what's called a nonprotein amino acid. So while there are amino acids and proteins, there are, of course, amino acids and nonproteins. And theanine is one such nonprotein amino acid. Theanine tends to stimulate the so-called glutamate and glutamine pathway. It's actually very similar to glutamate and glutamine, and it has a lot of effects on a lot of different aspects of the nervous system. But the general effect of theanine is to compete for the receptors for certain neurotransmitters. And the neurotransmitters I'm referring to are all excitatory neurotransmitters, things like glutamate. And they govern a tremendous amount of our daily thinking and action and feeling, et cetera, because they're present at so many connections between neurons in the brain. Theanine competes for the receptors for glutamate and tends to reduce our overall levels of alertness. So really, when people take theanine along with caffeine, what they're doing is they're really taking a slight-- I don't want to call it depressant to the point Let's talk for a moment about when to avoid caffeine. Other Effects: Osteoporosis, Hormone Levels, Depression And in the same stroke, let's also talk about some of the myths around caffeine. For instance, one of the major myths around caffeine is that it can increase osteoporosis. It turns out that, while there is a relationship, of course, between calcium and osteoporosis-- that is reductions in bone density. And it is the case that caffeine can extract calcium from certain tissues. The large scale studies that are out there essentially prove that, if people are ingesting enough calcium through their diet, which most everybody is-- although certainly, there are some people that need to supplement calcium or make it a point to consume more calcium-containing foods. But assuming that you are getting adequate levels of calcium, there is no direct relationship between caffeine intake and osteoporosis, at least not that I'm aware of. I know this was debated for a number of years in the literature, but the literature seems to have arrived at a general consensus now that caffeine itself is not going to create or exacerbate osteoporosis, provided people are getting enough calcium through their diet. That is, through foods, through supplementation, or both. Some of the other myths around caffeine are that, for instance, caffeine will reduce testosterone levels or will reduce estrogen levels. Other myths out there are in exact opposite to that, that caffeine will increase testosterone levels, in particular, free testosterone levels. There have been some large scale studies addressing the hormone effects of caffeine. They are a little bit difficult to do. I should just mention that caveat. And the reason they are difficult to do is because 90% of adults are consuming caffeine. And therefore, you can imagine it's very hard to find a control group to compare the caffeine consumers to. In particular, a control group that's well controlled for other things like lifestyle, diet, exercise, et cetera. However, when one controls as well as one can for all the various factors that could impact hormones, what one discovers is that caffeine intake, at least at the dosages we talked about earlier, 1 two 3 milligrams per kilogram of body weight or even up to double that, that there are no consistent increases or reductions in testosterone or estrogen in men or women that can be directly attributed to the

caffeine intake. And I say directly attributed because in these association studies, one always has to wonder, for instance, if because people are ingesting more caffeine, they have more energy and therefore exercising more. And exercise is known to have effects on testosterone, estrogen, and other hormones, whether or not the effects of caffeine on those hormones is indirect and so on and so forth. And this all just underscores the challenges of doing studies on humans in the wild in their natural habitat of living as opposed to an acute study as it's called to bring someone into the laboratory and studying them just for those hours or moments. With all that said, there does appear to be a relationship between caffeine intake and so-called sex hormone binding globulin, which is a protein present in the body of both men and women that binds to the sex steroid hormones-- testosterone and estrogen-- and prevents them from being in their free or active form. It has been shown that ingestion of caffeine-- even in the sorts of dosage ranges that are considered safe and that we've been discussing-- can increase sex hormone binding globulin such that it can slightly reduce overall levels of free testosterone and free estradiol in women. Now those effects are relatively minor, but they do exist. If any of you are interested in reading further into the effects of caffeine on hormones, I'll just refer you to a couple of studies. We will link to this in the show note caption. The title of the study is "Consumption of caffeinated beverages and serum concentrations of sex steroid hormones in US men." And within this study, there is a reference to a equally sized empowered study done on women, both of which converged on the same conclusion, by examining more than a thousand. So in this case, 1,410 men or more than a thousand women, that there are increases in sex hormone binding globulin associated with increased intake of coffee, in particular. But they were able to narrow that down specifically to ingestion of caffeine. So it's not coffee per se that's causing the increase in sex hormone binding globulin. It's actually caffeine itself. So again, the increases in sex hormone binding globulin were not so significant that, at least to my mind, they seem like a concern, although I think that it is worth noting that if you're going to consume caffeine that you probably want to consume caffeine in a way that is in dosages and with the sort of timing that will allow you to get away with ingesting caffeine but not to excess, so to derive the benefits of caffeine without for instance driving up sex hormone binding globulin too far. Now why would that be a good idea? Why would you want to make sure that you have enough free testosterone and free estrogen? Well, some of that is related to the acute effects of those hormones in terms of well-being and libido and strength and mood, et cetera, but some of those also relates to the longer term effects of sex steroid hormones. Many people don't realize this, but the sex steroid hormones operate on the receptors at the surface of cells to have immediate effects. But they also can enter cells and actually go into the nucleus of cells where the DNA of those cells are contained and control gene expression in those cells. So the sex steroid hormones, testosterone and estrogen, are controlling a lot of different cellular functions over long periods of time. So blunting their action over long periods of time is probably not a great idea. But again, at the dosages of caffeine that we're talking about today, 1 to 3 milligrams per kilogram of body weight, unlikely that the increases in sex hormone binding globulin that one experiences from that are going to be detrimental. And certainly, the positive effects of caffeine that one experiences in terms of mental performance and physical performance and the fact that it increases energy to do the sorts of things like exercise that we know can profoundly improve hormone profiles, twofold or threefold improvement in hormone profiles. In that case, it seems that ingesting caffeine is overall a good thing, provided it's not in excess. That also makes this the appropriate time to mention one of the more impressive effects of caffeine, which is on overall levels of mood and mental health. There are several studies on this, but the one that I'm particularly fond of was published in 2019 in Psychiatry Research. And the title of the paper is "Inverse association between caffeine intake and depressive symptoms in US adults." And these are data from the National Health and Nutrition Examination Survey. And the basic takeaway is that, while, of course, there are a ton of different factors that are going to relate to whether or not people

are depressed or not, life circumstances, genetics, and so on, that-- and here I'm quoting from the study. "Caffeine's psychostimulant properties-- that just means the ability to make us feel more alert and positive-- appeared to protect against depressive symptoms." And, of course, they acknowledge that additional studies are needed, but this is just one of several studies pointing to the fact that people who regularly ingest caffeine in the appropriate dosages do seem to enjoy an antidepressive effect overall. I wouldn't want anyone to consider caffeine a treatment for severe depression or at least not alone a treatment for severe depression. But provided the anxiety-inducing effects of caffeine can be kept in check through use of theanine or making sure that the dosage and the timing of caffeine ingestion is correct, then caffeine overall seems to be good for our mood and prevent depression or at least keep depression at bay when depression might otherwise surface or be more severe. Afternoon Caffeine & Sleep And, of course, there are the don'ts surrounding caffeine intake as it relates to sleep. And to put it very simply, sleep-- that is getting enough quality sleep each night-- is the foundation. It is the bedrock of mental health, physical health, and performance. Sleep and the power of sleep far exceeds any nootropic you could ever take, any prescription drug you could ever take, any health-promoting tool for your immune system, your metabolism, your mental function, your physical function you could ever take. Sleep is the bedrock. I know a lot of people experience challenge with sleep. Nobody is perfect about sleep. That's important to keep in mind. I think a good goal is to get enough quality sleep of sufficient duration 80% of the nights of your life and then as much as possible to make sure that the remaining 20% of nights you are not getting enough sleep for good reasons as opposed to hard reasons. Good reasons would include raising children. That's important. After all, every species desires to make more of itself and to preserve and extend the well-being of its young, so child-rearing is a perfectly legitimate reason to get a lack of sleep. But you really want to strive to get quality sleep most nights of your life, which means that, even if you're somebody who can, quote unquote, "drink an espresso" and then fall right asleep, that you avoid caffeine intake in the 12 hours prior to sleep. I realize not everyone will be able to do that. And in fact, I sometimes violate that, so I tend to go to sleep around 10:00 PM every night, sometimes 11:00, occasionally 12:00 midnight, but usually around 10:00 PM every night. I confess that my last ingestion of caffeine is not always 10:00 AM or prior to that, so sometimes I will have caffeine up until 11:00 AM or maybe noon. And very, very rarely, I'll have an afternoon coffee or espresso or noncalorie-containing soda or tea or something that's of that sort. But I really tried to restrict my caffeine intake to the early part of my day that is before noon, given that I go to sleep around 10:00 PM each night. And I strongly encourage everyone out there to try and limit their afternoon caffeine intake. This is something that Dr. Matt Walker, who's an expert sleep researcher out of University of California Berkeley Psychology and neuroscience department there, author of the incredible book Why We sleep. He's been on this podcast, many other podcasts, talking about the importance of sleep. He will remind us, and I'll remind you now that the quarter life of caffeine is 12 hours. I mentioned this earlier, but I'm going to repeat it again. And that means that, if you ingest caffeine at noon, 25% of its effects more or less, OK? I'm using a broad stroke here to talk about quarter life. 25% of that is still going to be bioactive at midnight that night, which will disrupt the early phase of your night, the amount of slow-wave sleep, which then in turn will disrupt the amount of rapid eye movement sleep, which will disrupt your emotional processing during the following day and so on and so forth. None of this is to say that if you have the occasional cup of coffee in the afternoon, that it's going to completely demolish your sleep/wake cycle forever. But I really encourage people to avoid drinking caffeine in the 12 hours prior to sleep. And if you can't do that, within the 10 hours prior to sleep. And if you can't do that, within the 8 hours prior to sleep. So really try and limit your caffeine intake in the 8 to 12 hours prior to going to sleep at night. And, of course, slow-wave sleep, aka deep sleep, is the sleep that's associated with somewhat mundane dreams, which makes it sound like it might not be that important. But it's also the sleep that's associated with

growth hormone release, which is important for protein synthesis, repair of all bodily tissues and metabolism. And slow-wave sleep is also critically attached to your immune system's ability to clear out bacteria and viruses that might otherwise infect your tissues. Now I'd like to talk about caffeine and performance. And that includes both mental performance Tool: Caffeine & Mental/Physical Performance; Cortisol & Caffeine Abstinence and physical performance. Now I'd like to talk about caffeine and its positive effects on performance when used correctly. And here we are referring to both mental performance and physical performance. The exploration of caffeine as a pro-performance tool has been explored since the 1930s, at least that's some of the earliest documented literature on this. Although I have to imagine, given that people have been using caffeine for much longer than that, that long ago somebody realized that, by ingesting a certain plant, that they felt much more alertness and were able to hunt and gather or do any number of different things better and, as a consequence, decide to consume more of that plant. Now these days, we consume a lot of caffeine in the form of coffee and tea mainly, and some people consume it in the form of caffeine tablets or energy drinks, et cetera. Across the board, one finds that caffeine intake at a level of 1 to 3 milligrams per kilogram of body weight improves reaction time. That is, it reduces the amount of time to take a physical action or to answer a question correctly with a verbal response. It can also improve coordination. It can also improve memory, although I do want to mention that, whereas most studies of the effects of caffeine on improving mental and physical performance involve taking caffeine at 1 to 3 milligrams per kilogram of body weight before the mental task or physical task, there is also a pro-performance effect of caffeine on memory if one takes caffeine after learning certain material or I should say being exposed to certain material. We'll come back to that in a few minutes. If one examines reaction time, mood, alertness, focus, and memory or the ability to call up information from memory, or physical dexterity, power output, endurance, and overall feelings of well-being during exercise and exertion, caffeine has been shown in numerous studies in both men and women to improve all of those metrics significantly. So this is all just to say that caffeine is an incredible performance-enhancing tool. Now, what's not obvious from the statement that caffeine is a performance-enhancing tool across the board and in men and women and in different contexts is that the way in which caffeine is taken is very important. Because 90% or more of adults consume caffeine, finding controls for studies of caffeine is really challenging. That is, finding people who don't ingest caffeine regularly is a very challenging task for the researcher. And as a consequence, many of the studies of caffeine on human beings involve depriving regular caffeine users of caffeine and then examining the effects of caffeine given after a period of, say, 5 to 15 days of abstinence in a person that is essentially experiencing mild withdrawal symptoms because they haven't had the caffeine that they were used to getting. So this is an important point. And it's a point that likely exacerbates the observed pro-performance effects of caffeine. Now all of that isn't necessarily a problem, provided you keep it in mind. And it actually points to a way in which even if you're a regular caffeine user, you can extract more of the benefits of caffeine. The simplest way to do this, for instance, is to look back to what we talked about earlier in terms of the need to have most of your cortisol increase restricted to the hour or hours just after waking in terms of mood and alertness and performance. One of the ways to increase the peak of that cortisol early in the day is to consume caffeine shortly after that peak occurs. And this was really nicely demonstrated in a study entitled caffeine stimulation of cortisol secretion across the waking hours in relation to caffeine intake levels. We will provide a link to this study. It's a somewhat complicated study because they looked at a bunch of different times of day for caffeine intake. And I should mention, in this study, they use this 300 milligrams per day or 600 milligrams per day. So that's quite high, although for people of sufficient body weight and who are accustomed to taking caffeine, it's certainly not going to be in excess of what a lot of people out there are taking. But basically, what they observed was the following. Cortisol responses to caffeine are reduced but not eliminated in people who consume caffeine on a

daily basis. What this means is that, if you wake up-- as I recommended earlier, you avoid drinking caffeine for the first 90 to 120 minutes after waking, but you do get some sunlight or other bright light in your eyes in that time, maybe even get some exercise in that time, which would be even better-- and then you ingest caffeine, you will get a further increase in cortisol, which, provided it's restricted to the early part of the day, is a good thing overall for mood and alertness. So this is a simple performance-enhancing tool, which is to stack caffeine on the tail of that early cortisol peak. I should also mention, however, that, in this study, they had people do a five-day caffeine abstinence prior to being tested with 300 milligrams or 600 milligrams of caffeine. So the simple tool to extract from this and other studies like it is that, if you want to experience the maximum alertness-promoting effects of caffeine when you ingest it early in the day, you would abstain from caffeine for five days and then ingest caffeine 90 to 120 minutes after waking. I would still hope that you were doing all the other things that I described-- morning sunlight, exercise, et cetera-- correctly. But regardless, it's very clear that a five-day abstinence from caffeine however painful that might be will increase the performance-enhancing effects of caffeine when you take caffeine on that sixth day. Now, I'm sure many of you out there are saying, why would I ever want to abstain from caffeine for five days in order to just get this six-day performance-enhancing effect? Well, there are a couple of reasons for doing that. Perhaps you're planning to travel to a new time zone, and you want to use caffeine as a stimulant to stay up during the day in the new time zone. That's a somewhat unusual case. Others of you might be interested in the pro-physical performance effects of caffeine. We'll talk more about these in a little bit. But you want to get the maximum strength increase or the maximum endurance increase from ingesting, in this case, 300 to 600 milligrams of caffeine. Well, in that case, abstaining from caffeine for five days will greatly exacerbate the pro-performance effects of caffeine when you take it on that sixth day, although admittedly, those five days are likely to be pretty painful if you're a regular caffeine user. Another variation on this, however, might be to have the amount of caffeine that you ingest on a daily basis and then go back to your regular level of caffeine intake on that day in which you need the caffeine to really boost your mood, energy, and performance. Another reason why you might want to abstain from caffeine or reduce your caffeine intake for a period of time and then go back to your regular caffeine intake is simply to identify how much of an effect caffeine is really having on your overall level of daily functioning and mood. This was something that was actually covered in beautiful detail in a book by Michael Pollan all about caffeine. It's available on Audible. I really enjoyed that book. It describes his experience with the decision to completely abstain from caffeine for a period of months, although I confess that after hearing that book, what it basically made me want to do is never quit drinking caffeine because it sounded as if, at least my interpretation was, that even after several weeks or months of abstaining from caffeine, that he still fantasized about the effects of caffeine. But he did mention that, when returning to ingesting caffeine after a period of long abstinence, that it had almost a-- let's not call it a psychedelic property, but it had such obvious effects on mood and alertness and feelings of well-being that it really highlighted for him the extent to which caffeine normally was allowing him to just function what he thought was normally. So in other words, many of us don't even really know what our normal basal level of cognitive and physical functioning is because we're ingesting caffeine on such a regular basis. I confess that, as much as I enjoyed that book and as intriguing as his description of caffeine abstinence and then the return to caffeine was, I don't intend to ever find out personally. Now a very good reason why you might want to abstain from caffeine for a deliberate period of time and then return to caffeine intake is for its physical performance-enhancing effects. And here we can look to a really interesting study. The title of which is "Time course of tolerance to the performance effects of caffeine." And what I like about this study is that, while yes, it does say that abstaining from caffeine and then returning to caffeine intake can enhance physical performance in a very specific way, it also says that, if you take caffeine regularly, you can still see the physical performance-enhancing effects

of caffeine. Although they are not quite as robust as they would be had you abstained from caffeine. The design of the study is pretty straightforward. They had people either ingest 3 milligrams per kilogram of caffeine for 20 consecutive days. Many people are already doing that, I realize, but they had people do that or ensure that they were doing that. Or others ingested a placebo for 20 days, so they abstained from caffeine without realizing it. Then after that 20 days of either ingesting caffeine or a placebo, their peak performance was measured in terms of aerobic output. But prior to that measurement, they had caffeine, OK? So it's 20 days of caffeine and then a 21st day of caffeine and then the physical task on that 21st day. Or it's 20 days of abstinence from caffeine. And then on day 21, you get caffeine, and you get the same physical test. And what they discovered was that the ingestion of caffeine increased peak performance in this aerobic output dramatically if people had abstained from caffeine. But for people that had consumed caffeine all the way through up until that day, it still was effective to ingest caffeine on day 21 but not as effective as it would have been had they abstained. And in fact, the magnitude of what they call ergogenic effect, which is the pro-performance-enhancing effect of caffeine, was higher on the first day than in subsequent days when they allowed people to continue caffeine intake. So the takeaway from this study is really straightforward. If you want to get the maximum physical performance-enhancing effects of caffeine, you abstain from caffeine for 20 days. Then on day 21, when you're going to do the physical thing, the task, you ingest caffeine about 30 minutes to an hour before you do that physical challenge. Now 20 days of abstinence is going to be rough for a lot of people. I certainly don't want to sign up for this study. In which case, you might want to do five days of abstinence as we talked about before. And then on day six is the day that you ingest caffeine and do the physical task. There are even some studies showing that you can abstain from caffeine for just two days, for just 48 hours. And, in particular, if you are a regular user of caffeine, this allows you to, on day three, ingest caffeine at the dose that's appropriate for you and do the physical, or I should mention mental performance task and perform significantly better than those that have been taking caffeine throughout the entire period leading up to the challenge. So you don't necessarily need to abstain for 20 days in order to get the pro-performance effects of caffeine on day 21. You could do five days of abstinence prior or even two days of abstinence prior. Or if that's intolerable to you as it is in my mind, to me, to just reduce your caffeine intake slightly or even perhaps have it if you can tolerate that in the week or two weeks or maybe even three weeks preceding some physical or mental challenge. Now again, this sort of implies that you're going up against a marathon, or you're going up against a series of long tests, maybe standardized tests in one day. There, I just really want to point out that there is an abundant literature showing that people perform best on mental tests if they are in the state that they were when they studied for that material. Now in college, I knew a number of people who took this to the extreme, thinking that if they were to study under the effects of alcohol, that they would be best off consuming alcohol prior to taking exams. And it turns out to not be the case. Here we're talking, in particular, about psychostimulant effects of caffeine and other compounds. So don't think that you can drink or be under the influence of THC and then take-- when you study and then take an exam under the same influence and do just as well as you would had you not ingested anything. Please don't let that be the takeaway. However, do let it be the takeaway that caffeine's effects are made more potent by a brief to not so brief period of abstinence prior to taking a dosage of caffeine. And then the final point to make is that, if you are somebody who is not accustomed to drinking caffeine, meaning you're hypersensitive to caffeine or you don't regularly ingest caffeine, please do not ingest caffeine on the day of any important mental or physical challenge or performance, because what you will find is that because you are not caffeine-adapted, you will experience changes in your thermal regulation, in your levels of anxiety and jitteriness, and your levels of focus that could be very detrimental to mental or physical performance. So you don't want to throw yourself in the deep end by ingesting caffeine if you're not used to it. And I should mention that for people that are

not accustomed to ingesting caffeine or are very sensitive to caffeine. Even 25 to 50 milligrams of caffeine in the amount that's found in, for instance, a piece of certain types of chocolate can actually cause anxiety. So be careful there. Here, I'm referring only to people that are accustomed with caffeine intake. So what I recommend is to explore the ergogenic effects of caffeine during your training and then to make a decision about what you can reasonably and reliably do in terms of abstinence and then pulse with caffeine on the day of the challenge. I get a lot of questions as to whether or not Caffeine, Performance & Menstrual Cycle caffeine has different effects on the nervous system and on performance in particular, depending on phases of the menstrual cycle. So I explored that in my research for this episode, and I found two studies both of which we will reference in the show note captions. The first one is entitled "Caffeine consumption and menstrual function." So it's actually the relationship between caffeine and menstrual function. We will do an entire episode about the menstrual cycle and menstrual function. But the other one as it relates to performance was published in 2020 in the European Journal of Nutrition, which is "Ergogenic effects of caffeine on peak aerobic cycling power during the menstrual cycle." And the basic takeaway of this study is-- frankly, a very nice study, showed that quote, "Caffeine increased peak aerobic cycling power in the early follicular, preovulatory, and midluteal phases of the menstrual cycle." Thus, the ingestion-- and again, here they use 3 milligrams of caffeine per kilogram of body mass might be considered an ergogenic aid for women who are in the menstrual cycle during all three phases of their cycle. So keep that in mind, women-- for those of you that are regular users of caffeine or you're using caffeine to enhance physical performance, there does not seem to be any menstrual cycle phase-dependent effects of caffeine on performance. That is, caffeine seems to always increase physical performance regardless of the phase of the menstrual cycle you might happen to be in. Tool: Memory & Caffeine Timing; Adrenaline & Cold Exposure I'd like to touch on a little bit more of the use of caffeine for enhancing mental performance. Yes, it is the case that ingesting 1 to 3 milligrams of caffeine per kilogram of body weight in the 30 minutes or so prior to doing a memory task or sitting down to doing some studying or learning of any kind, physical or mental performance, of any kind is beneficial for all the reasons we talked about before, relate to dopamine and acetylcholine, et cetera. But it turns out that it is also the case that spiking one's adrenaline and other so-called catecholamines-- so this would be dopamine, norepinephrine, and epinephrine-- after a bout of learning can greatly enhance memory for the information that one was trying to learn. That's right. Spiking your adrenaline after learning can greatly increase memory for the material you're trying to learn. In fact, this is a practice that dates back centuries and was written about in a beautiful Annual Review of Neuroscience on the biology of memory by James McGaugh, where he talks about medieval practices of children being taught information and then being thrown literally into cold water to stimulate the release of adrenaline and that increase in adrenaline. While the mechanism wasn't completely understood, it was understood that that sort of shock to the system from the cold water led to better memory and retention of the information that these children had been exposed to. And it turns out the exact same thing is true for adults in the laboratory or kids in the laboratory. And here I'm not suggesting throwing anyone into cold water. If you want to get into cold water, there's a reason we call it deliberate cold exposure on the podcast is that it should be deliberate and controlled by you, not by somebody else. And if it's controlled by somebody else, that might be military screening or something. But here we're talking about deliberately increasing your levels of adrenaline and other catecholamines, dopamine, norepinephrine, et cetera. You can do that certainly by deliberate cold exposure with a cold shower or getting in up to your neck in cold water of any kind. But the other way to do that is to spike your adrenaline by ingesting 1 to 3 milligrams per kilogram of caffeine after sitting down to try and learn some material I confess that, more often than not, I use caffeine in the same way that most people use it, which is OK. I'm going to sit down. I'm going to research information for a podcast or assemble some information for a paper or grant, and I

want to focus. So I will drink a cup of coffee at the beginning of that and maybe even throughout that or a couple of yerba maté at the beginning or throughout that. Or I'll sip on one or both throughout trying to learn. And that works quite well in terms of maintaining focus and alertness and retention of information, but it is indeed the case. That is, the research supports the fact. And I've experienced the fact that, if I abstain from caffeine while I'm trying to learn something-- but then I drink caffeine immediately after. Somewhat surprisingly to me but certainly in a way that's consistent with the research literature, memory for the information that I was focused on prior to ingesting that caffeine is much greater. And here I'm talking about as a personal anecdote, but this is actually what the data point to both in animals and in humans. And if you think about it, it makes perfect sense because the way that the memory systems of the brain are organized is that we go through life experiencing things. We encounter surprises both good and bad. We go through the motions of things both typical, mundane, exciting, and novel, and not novel. And then every once in a while, something will happen that will spike our catecholamines. Dopamine, typically if it's a positive surprise. Adrenaline, which can be associated with both positive surprise or positive events and negative events or surprises. And without fail, increases in the catecholamines tend to lock in memories for things that preceded the increase in those catecholamines. Again, the catecholamines being dopamine, epinephrine, and norepinephrine, sometimes all three in combination, sometimes just two of those, sometimes just one of those, depending on the experience. So it makes perfect sense that using caffeine at the end of a learning bout would enhance our memory for the information that we are trying to learn. So if you decide that you want to try and extract this performance-enhancing effect of caffeine, what I recommend would be to try and abstain from caffeine for a day or two prior. But if you can't, you just continue with your normal caffeine intake. But then when you sit down to study or learn something to not ingest any caffeine as you do that but then afterward to ingest caffeine. Now in theory, you could probably further enhance the memory encoding effects of adrenaline and the other catecholamines by drinking caffeine and then taking a cold shower or doing deliberate cold exposure if you really wanted to or had the ability to or doing some sort of intense form of exercise. And we'll talk in a moment about how caffeine, exercise, and the adrenaline system interact. But as a brief but relevant to side, brief bouts of intense exercise ranging from 10 to 50 minutes or so have been shown to improve memory for information that one was trying to learn prior to the intense exercise. This is work from Dr. Wendy Suzuki's lab at NYU as well as other laboratories, some of the work that's being done at Stanford in the Mind, Body Laboratories. And our laboratory points in the direction of these kinds of effects as well. They all come back to the same general neurochemical theme, which is that, when we experience an increase in these catecholamines that include adrenaline, dopamine, and norepinephrine, the memory systems of the brain flip on in a way that try to capture the information and the perceptions and the experiences that we were exposed to just prior to the increase in catecholamines and caffeine but also exercise and also cold water. And, of course, any of those alone or in combination all increase the levels of catecholamines, so it makes perfect logical mechanistic sense as to why this would work. And in fact, it does work. If you want to remember specific information, you might consider using caffeine as you move through and absorb and are exposed to that information. But you might also consider using caffeine after being exposed to that information because studies in animals and humans show that that is a potent way to increase memory for what you are just exposed to. I should mention that what I just described also pushes back on something that I know a number of people Caffeine & Naps perhaps have heard about and maybe even use, which is this notion of the nappuccino. I remember hearing about this a few years back. It was sort of trend, if you will. The trend involved drinking a cup of coffee or a double espresso and then going down for a nap typically in the afternoon and then waking up. And the idea was that the caffeine would hit your system right at the time that you awake from the nap and that you would be better able to focus and exercise. There are a couple of things about that

practice that I don't like. First of all, it implies, in most cases, that you're napping and ingesting caffeine in the afternoon, which I realize for many students and for people that are comfortable staying up until the wee hours of the night and then waking up late the next day might be compatible with their schedule. But again, because of the sleep-diminishing effects of caffeine-- and we talked about earlier. I'm not crazy about the idea of people ingesting caffeine in the late afternoon in order to perform better in the late afternoon. Far better would be to restrict caffeine intake to the early part of the day as we talked about earlier. The other reason is that the data on things like non-sleep deep rest and naps in the afternoon-- and again, the rule here is that you don't have to nap. But if you want to nap, it's been shown that naps of 90 minutes or less or non-sleep deep rest protocols-- and you can find those-- for instance, there's one with me speaking.. There are other NSDR scripts out there now, of course, if you prefer those, that those can all lead to increases in one of the catecholamines at least, which is dopamine. That's been shown in a really nice neurotransmitter labeling study, not from my laboratory, but from another laboratory, but also can improve mood, focus, and alertness on its own without the need to ingest caffeine prior to going into those states. And in fact, ingesting caffeine prior to a nap or ingesting caffeine prior to NSDR is most certainly going to reduce the effectiveness of that nap and NSDR in restoring natural levels of alertness and focus that would lead to the performance-enhancing effect. So I'm not such a fan of the so-called 'nappuccino', although if any of you out there have derived great benefit from it, definitely let me know your protocol and what you've experienced. Put it in the comment section if you would. I'd appreciate that. There's another very important and potent use of caffeine Tool: Exercise, Caffeine, Dopamine & Positive Reinforcement for enhancing performance. And this relates not just to the dopamine and epinephrine and the arousal-inducing effects of caffeine. And it doesn't even just relate to the effect of caffeine on enhancing frontal lobe function. It does include all that, but it also includes those reinforcing effects of caffeine that we talked about at the beginning of the episode. And the best way to illustrate these performance-enhancing effects of caffeine that stem directly from its association with reinforcement is to highlight a study. And the title of the study is "Blood dopamine level enhanced by caffeine in men after treadmill running." And as the title suggests, this was carried out in men, but there's no reason to think that the same results wouldn't also be present in women. There are some sex-dependent effects of caffeine. I'll touch on just briefly at the end. But those are largely present in kids. That is, adolescents and teens as opposed to adults. So this study is really interesting. What they had people do was run on a treadmill and either ingest caffeine-- again, 3 milligrams per kilogram of body weight-- or to not ingest caffeine. And then they looked at levels of dopamine and other neurotransmitters and hormones, such as prolactin and cortisol. And the basic takeaway is, as the title suggests, that exercise, while on its own, can increase cortisol in healthy ways, provided it's not too intense and too long. A little note here, if you have trouble recovering from exercise or you want to continue to derive the benefits from exercise, in general, best not to do high-intensity exercise for longer than 75 minutes. Or 90 minutes probably being the outer threshold. I realized that there are some genetic freaks out there or people that are chemically assisted that can recover from very intense long bouts of exercise. But most people don't do well through long bouts of intense exercise on a regular basis. And limiting their intense exercise to 60 minutes or less-- that doesn't include the warm-up-- is going to be beneficial. See the episode on tool kit for fitness if you'd like details on that. Exercise is known to increase levels of dopamine, cortisol, and other catecholamines and neurotransmitters very potently and things like testosterone and estrogen in ways that we know are beneficial to us and, of course, have all these positive effects on the musculoskeletal system and cardiovascular effects. But unbeknownst to most people, ingesting 3 milligrams per kilogram of caffeine prior to exercise further increases the dopamine release associated with exercise specifically. And this has two important effects. First of all, that increase in dopamine is great because it provides a long-lasting increase in focus alertness and motivation, not

just during the exercise, but also after the exercise. And second, it-- that is, caffeine and dopamine in combination-- act as a reinforcer to make the experience of exercise and the period immediate after exercise more pleasant and, in fact, reinforcing. So in other words, one way to enjoy exercise more and to enjoy the activities that follow exercise more and to experience a genuine increase in dopamine that's beneficial for mood and alertness is to ingest caffeine prior to exercise. Now this is important because a number of people out there are exercising, love exercise, love eating great, love doing all the things that are beneficial for their health, but a number of people out there really don't like to exercise. And that serves as a serious block for their willingness and their consistency to exercise. Ingesting caffeine gives us energy to exercise. It increases the release of neurochemicals and hormones that are good for us during exercise. But as I'm highlighting here, it also increases the reinforcement pathways associated with exercise. That is, it creates a positive feeling about the general theme of engaging in exercise, and it creates a general positive experience of the things that follow exercise. So I think this, if nothing else is a call for or support for the idea, that ingesting caffeine as a performance-enhancing tool makes perfect sense. But for those out there that don't enjoy exercise, in particular, certain forms of exercise, ingesting caffeine can change your relationship to that exercise. In other words, make it more positive, much in the same way that ingesting caffeine alongside a certain taste that would otherwise be neutral or maybe even negative can actually make the taste of that particular drink or food positive. So again, this brings us back to the reinforcing properties of caffeine that are subconscious. It's not just about the enhanced performance in the test or the enhanced performance on the treadmill or with the weights in the gym. It's enhanced feelings of mood and well-being that are genuine because of the effect of caffeine on certain neurotransmitter and hormone systems, but it also is creating an overall milieu of reinforcing all of the things that led in to occur during and occur after exercise. Dopamine Stacking I do want to point out something that's very important as it relates to combining things like caffeine and exercise in order to increase dopamine. This is something that came up in the episode that I did on dopamine, motivation, and drive, which turns out to be one of our most popular episodes. Again, you can find that at hubermanlab.com and links to all formats with time stamps, et cetera. This also came up in the episode on ADHD because of the relationship between ADHD and dopamine. And that's this notion of dopamine stacking. In the episode on dopamine, motivation, and drive, I pointed out that, while there are a near-infinite number of things that can increase dopamine release, most notably positive surprise or positive anticipation or experiencing a win. Certainly, there are compounds, both drugs of abuse, food, sex, and certain supplements that can increase dopamine to varying levels and to varying degrees, both healthy and unhealthy. That's all contained in that episode on dopamine, motivation, and drive. But what I pointed out is that, if you are somebody who tends to experience difficulty with motivation-- that so-called dopamine stacking as I called it might be something that you want to avoid. What's dopamine stacking? Dopamine stacking would be combining a highly caffeinated energy drink that also includes the amino acid tyrosine, which is a precursor to dopamine, plus loud music plus getting yourself really ramped up then an intense workout. All of that can be great if you do it every once in a while. But what you will quickly find is that the extent to which your dopamine peaks also dictates the extent to which your dopamine will drop after that peak. And when I say drop, I mean drop below baseline. So a lot of people find that, if they stack a lot of things to peak their dopamine, then they experience a low, and it does take some time for them to return to baseline. And I highly recommend not engaging in activities or consuming compounds that are in attempt to accelerate that return to baseline because all it will do is drive that baseline lower and lower. So this requires being able to tolerate a drop in dopamine baseline for a period of time, et cetera. Now the reason I'm bringing this up now in the context of this caffeine episode is I just described a study in which using caffeine prior to exercise increases dopamine after exercise. And so you might be saying, especially if you heard that earlier episode, wait, isn't that

dopamine stacking? Aren't you encouraging me to stack my dopamine? Well, in some sense, yes. But keep in mind, I'm not suggesting that you do this every time you exercise. So just as in that earlier episode, I emphasized the fact that, while stacking multiple stimuli-- caffeine or energy drinks and music and et cetera-- for exercise or for mental work or for any experience for that matter is OK to do every once in a while for most people, you don't want to get in the habit of doing it consistently every time you exercise or every time you go out, for instance. And so you really want to be cautious. That is, you want to protect your both baseline levels of dopamine and your peak levels of dopamine. That said, for people that want to experience an increase in mood, alertness, and performance, or who want to condition themselves-- because that's really what it is. It's conditioning yourself by the reinforcing effects of dopamine to increase your liking or maybe even your loving of exercise. Occasionally, using caffeine or frequently using caffeine prior to exercise is fine but be very careful. And by being very careful, what I mean is pay attention to how you feel in the hours and days after that dopamine increase wears off. So for instance, if you ingest caffeine and then exercise very intensely and you're feeling great afterwards but then eight hours later or the next day, you're feeling a little bit low, I suggest you don't go back and do the exact same thing right away. I would give yourself a little bit of time to let that baseline of dopamine return to normal. So again, stacking different things, chemical and behavioral, in order to increase dopamine can be done in a safe way that's beneficial to you, depending on your goals. But be careful about not stacking too many stimuli for dopamine too often. That's the key. Early in the episode, I mentioned one possible caffeine-consuming schedule Scheduling Caffeine to Maximize Its Effects that works very well that doesn't fortunately subject you to long 20-day bouts or 5-day or even 2-day bouts of abstinence. And that's the every other day schedule of caffeine. If you look at the half-life of caffeine and you look at its effects on the dopamine system and its performance-enhancing effects and how a period of abstinence can, in fact, increase the performance-enhancing effects of caffeine-- but also take into consideration that caffeine can be habit-forming, and we can develop a sort of tolerance to caffeine. Well then, what emerges from all of that is that being a person who consumes caffeine every other day can actually help you maximize most of the positive effects of caffeine without subjecting you to the kind of misery that occurs if you're accustomed to consuming caffeine every single day and then suddenly go into a 2 or 5 or 20-day abstinence. So I myself have never tried an every other day caffeine approach, although I'm considering doing it based on the literature that I've read. And I'm considering doing it in a very specific way, which would be to only consume caffeine on the days in which I resistance train. And since I tend to do that about three or four days per week organized in a way that's every other day-- again, if you want to see the exercise schedule that I follow, including cardiovascular exercise and weight training and all the reasons and rationale for what I do and how it maps on to the scientific literature, relate to health span and lifespan, vitality, et cetera, you can find that at hubermanlab.com. And we had a tool kit for fitness that ought to be posted to our website before long. The every-other-day schedule of caffeine intake, to me, seems like the most rational one if one wants to maximize on the performance-enhancing effects of caffeine without suffering the effects of caffeine withdrawal that are associated with being a regular consumer of caffeine and then stopping caffeine intake, such as headache and irritability and so forth. Not I nor anyone in my life wants me to experience those effects, and I'm sure you don't want to experience those effects for you either. So if you're somebody that decides to try the every other day protocol or you are somebody who's already doing that protocol, please let me know what your experiences with that are. At least by my read of the literature on caffeine and it's performance-enhancing effects but also the effects of caffeine on neurotransmitter and hormone systems, the every-other-day caffeine schedule does seem to be the most rational and scientifically grounded one in order to maximize on all those effects. In addition to so-called performance-enhancing effects of caffeine, there are also the well studied and now fairly Pro-Health Effects of Caffeine well mechanistically understood pro-

health effects of caffeine. Now, here when I talk about pro-health effects of caffeine, I want to be very clear that, if your schedule of caffeine intake-- that is, your timing of caffeine intake or anything else for that matter-- offsets getting regular high quality sleep of sufficient duration, well, then you are undermining the pro-health effects of that thing. This is true for exercise. This is true for caffeine. This is true for supplementation. This is true for prescription drugs. Again, you don't want to be neurotically attached to the idea that you have to get perfect sleep every night because that's simply not true but is absolutely the case that anything, whether or not it's good for you or bad for you in the short term, that disrupts your sleep because of the timing in which you're doing that thing is going to undermine your immediate and long-term health before long. So with that said, there are several well described health-promoting effects of caffeine ingestion. And once again, when I say caffeine ingestion, I'm referring to that 1 to 3 milligrams per kilogram of body weight dosage. There are really nice studies showing that being a regular consumer of caffeine can help offset some of the probability, some of the probability of developing Parkinson's and maybe Alzheimer's-related dementia as well. These are not terribly controversial data because of the fact that caffeine is known to increase the release of those catecholamines, dopamine, epinephrine, and norepinephrine, as well as acetylcholine. All those neurotransmitter and neuromodulator systems are the ones that are known to be defective in Parkinson's and Alzheimer's, although there are other transmitter and hormone systems that are defective as well. There are beautiful reviews on the neuroprotective effects of caffeine and neurodegenerative diseases. They're quite extensive. And I'll just refer you to one and the references therein, and we'll provide a link to this in the show note caption. So the title as the topic at hand suggests is the neuroprotective effects of caffeine and neurodegenerative diseases. This was published in 2016. I'm sure there have been other reviews since then, but it includes many, many quality references and studies, both in animals and in humans, pointing to the fact that specific enzymes that are associated with the health of, in particular, dopamine neurons are made more robust by regular ingestion of caffeine. It also points to the fact that the increase in dopamine receptors that is induced by regular ingestion of caffeine that I referred to earlier is another way in which dopamine, however many dopamine neurons remain around in people with Parkinson's or people who are aging that lose dopamine neurons naturally, that dopamine can have its maximal effect because of the increase in receptors for dopamine that caffeine induces. And there are other biological mechanisms that further support why caffeine ought to be neuroprotective, including its effects on the acetylcholine system, which is one of the major systems disrupted in Alzheimer's dementia. So in other words, it makes perfect sense as to why caffeine would be neuroprotective. Caffeine has also been shown to diminish headache, particularly when taken in combination with aspirin. And that's because of the effects of caffeine and aspirin on blood flow. There's also evidence that caffeine can provide brief but substantial relief from asthma. So I wouldn't want people to rely on caffeine as a lifesaving approach to an asthmatic attack. That said, for people that suffer from minor asthma, that caffeine intake-- again, of the dosages that we talked about before has been shown to alleviate some of the major symptoms of asthma for anywhere from one to four hours. And I know this is of relevance to a lot of people out there. Because caffeine increases the catecholamines and in particular because caffeine increases dopamine transmission in the prefrontal cortex-- this area of the brain that's associated with focus and rule setting and context and task switching-- caffeine is known to improve focus and alertness, in particular, in people who have symptoms of ADHD or other attention and focus issues. Now caffeine alone does not appear to be as potent for the treatment of ADHD as are things like Ritalin, Adderall, modafinil, or modafinil and Vyvanse. If you would like a sort of head by head comparison of prescription drugs, supplements, and things like caffeine as well as coverage of behavioral tools and nutritional tools, et cetera that can positively offset some of the symptoms of ADHD, please see the episode that I did on ADHD. Again, that's available at hubermanlab.com in all formats. But that said, caffeine does increase focus,

and it does it through a number of different mechanisms, not the least of which is to increase dopamine transmission in the forebrain just as a drug like Ritalin or Adderall would, although not to the same extent as a drug like Ritalin or Adderall does. Before we close today, I do want to just briefly return Tool: Sugar Cravings & Reinforcing Effects of Caffeine to the reinforcing effects of caffeine that we talked about earlier. This study on the honeybees that showed that bees prefer certain vectors because they contain caffeine. Even though they are not aware that those vectors contain caffeine, they just come to like the feeling that those nectars provide them so much that they associate that in a subconscious way with the flowers themselves, and they come to like those flowers. Or human beings. For instance, children that ingest caffeinated beverages come to adore the taste of those beverages. And beautiful studies have been done that describe how children and adults truly cannot distinguish between the taste of a caffeinated and noncaffeinated beverage. And caffeine can be placed into essentially any beverage in order to give us a preference for that beverage or food. In fact, the studies have been done with yogurt. If you put caffeine into yogurt of different flavors-- even plain yogurt which most kids don't like-- they will come to prefer whatever flavor contain the caffeine even if then you remove the caffeine from that flavor. Now eventually, their preference for that flavor will be extinguished, but all of this is just to say that so many of the things that we like, whether or not it's coffee or tea or a given flavor of food or a given experience or even exercise, occur because we ingest caffeine in conjunction with those activities. Now these are not tricks that your nervous system plays on you. These are real neurochemical-reinforcing effects. And I think that we would all do well to think about and to leverage these reinforcing effects much in the same way we would do well to think about and hopefully not leverage aversive effects of certain compounds, right? The simple way to put this is I or anyone could get you to dislike something, someone, or some place by making you feel slightly less good, lower mood. I don't even have to make you feel nauseous but less good after ingesting something or having a certain kind of interaction or being in a certain environment, very straightforward to do that, because of the way that your nervous system is wired for conditioning. However, there's the positive side of all this, which is that it's very straightforward to reinforce the experience of a given food, including its taste, but all the context around it, the container, the texture, the people you consume it with, where you consume it, et cetera. For instance, I wonder why we are not pairing caffeine with broccoli. And here I'm not suggesting that people actually do that experiment or play that trick on people, but you have to sort of imagine that, if caffeine is this incredible reinforcer of all sorts of things, in particular, things that we ingest and would want to ingest more of if it's paired with caffeine, well then, you actually can use caffeine as a tool to increase reinforcement of different things. And you can avoid caffeine as a way to further reinforce things that you would like to stop. And here I'd like to just give the example of sugar cravings. A lot of people ask me, how do I avoid sugar cravings? I've talked about the use of L-glutamine for that. I've talked about making sure you're getting enough essential fatty acids and essential amino acids as a way to reduce sugar cravings. Please note, however, that if you are somebody who likes to have your sugar, whether or not it's a piece of chocolate or your dessert, et cetera-- I'm not saying that's bad, but if you're trying to reduce your sugar cravings, ask yourself, are you ingesting sugar along with caffeine? Could be the caffeine contained in that sugar-containing food like chocolate. Or it could be that you're having a cup of coffee along with your pastry, and then you're struggling with sugar cravings. Well, think about it. You're not just being reinforced by the sugar and the effects of sugar on dopamine which are real and both conscious and subconscious through the gut to the brain dopamine system and direct on the brain dopamine system. But by co-ingesting caffeine, you are also further enhancing the reinforcing effects of sugar. The flip side to all of this is that you could use caffeine as a way to increase your appetite for certain things. I actually know somebody. I won't reveal who this person is, but they are quite prominent podcaster who ingests 125 to 150 milligrams of in tablet form along with herbal tea and use this as a way to develop

a preference for herbal tea because they found that coffee was giving them other effects that weren't good for them. So it works quite well in animals, and it works quite well in insects. And it works quite well in humans. I suppose animals, insects, and humans are all animals at the end of the day, so no surprise there. But it all underscores the extent to which caffeine is an absolutely fascinating molecule. I mean, its ability to offset the sleepiness system, if you will, this adenosine system, and to control our schedules in that way to essentially take a withdrawal against the bank that is adenosine and then pay that back later in the form of getting sleepy later as opposed to when we want to be alert, its ability to enhance focus, alertness, and mood. And if taken after trying to learn something and remember it, to enhance memory, especially. And its ability to increase VO2 max, increased strength. We didn't even talk today about it, but I'll just briefly mention that caffeine ingested in the sorts of doses we talked about earlier. Because its effects on the neuromuscular system and the calcium system associated with neuromuscular exertion and fatigue can increase peak power output and muscle contractability. It's enhancing performance there as well. And, of course, caffeine does a number of other things just generally related to overall and basal level of mood and alertness, not the least of which are these increases in dopamine. So caffeine is really an incredible molecule. It's affecting all these various neurotransmitter systems but not haphazardly. It's increasing dopamine and acetylcholine in the forebrain to increase attention. It's reducing fatigue. It's improving mental and physical performance for some obvious and some not so obvious reasons. And what I think is among the more miraculous and powerful effects of caffeine, it is a potent, potent, potent reinforcer of things, foods, people, and experiences. And it's one that you can leverage in any direction that you like once you understand the way that caffeine exerts those reinforcing properties. So today, I've really tried to cover as much as I could about the mechanisms of caffeine action in the brain and body, as well as tools and schedules and dosages in which you can leverage caffeine in order to meet your physical performance, mental performance, and frankly mental health, and overall health goals.