Dr. David Berson: Your Brain's Logic & Function | Huberman Lab Podcast #50

In this episode, my guest is Dr. David Berson, Professor & Chairman of Neuroscience at Brown University. Dr. Berson discovered the neurons in your eye that set your biological rhythms for sleep, wakefulness, mood and appetite. He is also a world-renowned teacher of basic and advanced neuroscience, having taught thousands of university lectures on this topic. Many of his students have become world-leading neuroscientists and teachers themselves.

Here Dr. Berson takes us on a structured journey into and around the nervous system, explaining: how we perceive the world and our internal landscape, how we balance, see, and remember. Also, how we learn and perform reflexive and deliberate actions, how we visualize and imagine in our mind, and how the various circuits of the brain coordinate all these incredible feats.

We discuss practical and real-life examples of neural circuit function across the lifespan. Dr. Berson gives us a masterclass in the nervous system—one that, in just less than two hours, will teach you an entire course's worth about the brain and how yours works.

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- Welcome to the Huberman Lab Podcast, where we discuss science and science-based tools for everyday life. I'm Andrew Huberman and I'm a Professor of Neurobiology and Ophthalmology at Stanford School of Medicine. Today my guest is Dr. David Berson, Professor of Medical Science, Neurobiology and Ophthalmology at Brown University. Dr. Berson's laboratory is credited with discovering the cells in the eye that set your circadian rhythms. These are the so-called intrinsically photosensitive melanopsin cells. And while that's a mouthful, all you need to know for sake of this introduction is that, those are the cells that inform your brain and body about the time of day. Dr. Berson's laboratory has also made a number of other important discoveries about how we convert our perceptions of the outside world into motor action. More personally, Dr. Berson has been my go-to resource for all things neuroscience for nearly two decades. I knew of his reputation as a spectacular researcher for a long period of time. And then many years ago, I cold called him out of the blue, I basically corralled him into a long conversation over the phone after which he invited me out to Brown and we've been discussing neuroscience and how the brain works and the emerging new technologies and the emerging new concepts in neuroscience for a very long time now. You're going to realize today why Dr. Berson is my go-to source. He has an exceptionally clear and organized view of how the nervous system works. There are many many parts of the nervous system, different nuclei and connections and circuits and chemicals and so forth, but it takes a special kind of person to be able to organize that information into a structured and logical framework that can allow us to make sense of how we function in terms of what we feel, what we experience, how we move through the world. Dr. Berson is truly one of a kind in his ability to synthesize and organize and communicate that information. And I give him credit as one of my mentors, and one of the people that I respect most in the field of science and medical science generally. Today Dr. Berson takes us on a journey from the periphery of the nervous system, meaning from the outside, deep into the nervous system layer by layer, structure by structure, circuit by circuit making clear to us how each of these individual circuits work and how they work together as a whole. It's a really magnificent description that you simply cannot get from any textbook, from any popular book and frankly, as far as I know, from any podcast that currently exists out there. So it's a real gift to have this opportunity to learn from Dr. Berson. Again, I consider him my mentor in the field of learning and teaching neuroscience, and I'm excited for you to learn from him. One thing is for certain, by the end of this podcast, you will know far more about how your nervous system works

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than the vast majority of people out there including many expert biologists and neuroscientists. Before we begin, I'd like to emphasize that this podcast is separate from my teaching and research roles at Stanford. It is however part of my desire and effort to bring zero-cost to consumer information about science, and science-related tools to the general public. In keeping with that theme, I'd like to thank the sponsors of today's podcast. Our first sponsor is Athletic Greens. Athletic Greens is an all-in-one vitamin mineral probiotic drink. I've been taking Athletic Greens every day since 2012. So I'm delighted that they're sponsoring the podcast. The reason I started taking Athletic Greens and the reason I still take Athletic Greens is that, it covers all of my vitamin mineral and probiotic needs. Nowadays there's a lot of data out there pointing to the fact that a healthy gut microbiome literally, little microbes that live in our gut, that are good for us is important to support our immune system, our nervous system, our endocrine system, and various aspects of our immediate and long-term health. With Athletic Greens I get all the vitamins and minerals that I need plus the probiotics ensure a healthy gut microbiome. It also tastes really good, I mix mine up with some water, a little bit of lemon juice, I'll have that early in the day and sometimes a second time later in the day as well. It's compatible with intermittent fasting, it's compatible with vegan diets, with keto diets, and essentially every diet that you could possibly imagine out there. It's also filled with adaptogens for recovery, it has digestive enzymes for gut health, and has a number of other things that support the immune system. If you'd like to try Athletic Greens, you can go to athleticgreens.com/huberman to claim their special offer. They'll give you five free travel packs that make it really easy to mix up Athletic Greens while you're on the road, and they'll give you a year's supply of vitamin D3K2. There's now a lot of evidence that vitamin D3 supports a huge number of metabolic factors, immune system factors, endocrine factors, basically, we need vitamin D3, we can get it from the sun, but many people are deficient in vitamin D3 even if they are getting what they think is sufficient sunlight. And K2 is important for cardiovascular health. So again, if you go to athleticgreens.com/huberman, you can claim their special offer, the five free travel packs, plus the year supply of vitamin D3K2. Today's podcast is also brought to us by InsideTracker. InsideTracker is a personalized nutrition platform that analyzes data from your blood and DNA to help you better understand your body and help you reach your health goals. I've long been a believer in getting regular blood work done for the simple reason that many of the factors that impact your immediate and long-term health can only be analyzed from a quality blood test. And now with the advent of modern DNA tests, you can also get information about how your specific genes are impacting your immediate and long-term health. Now a problem with a lot of blood tests and DNA tests out there, is you get the numbers back but you don't know what to do with those numbers, with InsideTracker they make it very simple to figure out what to do to bring those numbers into the ranges that are right for you. They have a dashboard that's very easy to use, you can see the numbers from your blood and/or DNA tests, and it will point to specific lifestyle factors, nutritional factors as well as supplementation maybe even prescription factors that would be right for you to bring the numbers into range that are ideal for your immediate and long-term health goals. Another feature the InsideTracker has is their inner age test. This test shows you what your biological age is and compares that to your chronological age and what you can do to improve your biological age, which of course is the important number. If you'd like to try InsideTracker you can visit insidetracker.com/huberman to get 25% off any of InsideTracker's plans. Also an interview I did with Longevity Research Doctor and InsideTracker's Founder Dr. Gil Blander, is out now on their podcast, the longevity by design podcast and a link to that interview can be found in today's show notes. Today's episode is also brought to us by

Magic Spoon. Magic Spoon is a zero sugar, grain-free, keto-friendly cereal. I don't follow a ketogenic diet. The way that I eat is basically geared toward feeling alert when I want to be alert and feeling sleepy when I want to go to sleep. Which for me means fasting until about 11:00 am or noon most days, then I eat low carb during the day. So I'll have some meat or fish or chicken and some salad that's what works for me, and in the afternoon, I remain on a more or less low carb-ish diet, and then in the evening, I eat pastas and things primarily and I throttle back on the protein and that's what allows me to fall asleep at night. That's just what works for me. So if I want a snack in the afternoon, I want that to be a ketogenic or low carb snack and that snack these days is Magic Spoon. Magic Spoon is really terrific, it has zero grams of sugar, 13 to 14 grams of protein, and only four net grams of carbohydrates in each serving. It's really delicious, they have a number of different flavors like cocoa, fruity, peanut butter and frosted, I particularly like frosted. It tastes like donuts and I really like donuts although I try not to eat donuts too often if ever. What I do lately, is I take Magic Spoon, I put it in some Bulgarian yogurt which is really good and I mix that up, I put those in there and sometimes I put some cinnamon on them. And as I'm describing this, I'm getting hungry for Magic Spoon. So if you want to try Magic Spoon, you can go to magicspoon.com/huberman to get their variety pack. Just use the promo code Huberman at checkout to get $5 off your order.

00:08:02 How We See

Again, that's magicspoon.com/huberman and use the code Huberman to get $5 off. And now for my discussion with Dr. David Berson, welcome. - Thank you. - Yeah. - So nice to be here. - Great to have you. For more than 20 years you've been my go-to source for all things, nervous system how it works, how it's structured. So today I want to ask you some questions about that. I think people would gain a lot of insight into this machine that makes them think and feel and see, et cetera. If you would, could you tell us how we see? A photon of light enters the eye, what happens? - Right. - How is it that I look outside, I see a truck drive by, or I look on the wall I see a photo of my dog, how does that work? - Right, so this is an old question obviously. And clearly in the end, the reason you have a visual experience is that your brain is got some pattern of activity that associates with the input from the periphery. But you can have a visual experience with no input from the periphery as well. When you're dreaming, you're seeing things that aren't coming through your eyes. - Are those memories? - I would say in a sense they may reflect your visual experience they're not necessarily specific visual memories, but of course they can be. But the point is, that the experience of seeing is actually a brain phenomenon. But of course, under normal circumstances, we see the world because we're looking at it and we're using our eyes to look at it. And fundamentally, when we're looking at the exterior world, it's what the retina is telling the brain that matters. So there are cells called ganglion cells, these are neurons that are the key cells for communicating between eye and brain, the eye is like the camera, it's detecting the initial image, doing some initial processing, and then that signal gets sent back to the brain proper and of course, it's there at the level of the cortex that we have this conscious visual experience. There are many other places in the brain

00:10:02 Color Vision

that get visual input as well doing other things with that kind of information. - So I get a lot of questions about color vision. If you would, could you explain how is it that we can perceive reds and greens and blues and things of that sort. - Right, so the first thing to understand about light, is that it's just a form of electromagnetic radiation, it's vibrating, it's oscillating, but. - When you say it's vibrating, it's oscillating, you mean that photons are actually moving? - Well in a sense, photons they're certainly moving through space, we think about photons as particles and that's one way of thinking about light, but we can also think of it as a wave like a radio wave, either way is acceptable. And the radio waves have frequencies like the frequencies on the your radio dial, and certain frequencies in the electromagnetic spectrum can be detected by neurons in the retina, those are the things we see, but there's still different wavelengths within the light that can be seen by the eye. And those different wavelengths are unpacked in a sense or decoded by the nervous system to lead to our experience of color. Essentially, different wavelengths give us the sensation of different colors through the auspices of different neurons that are tuned to different wavelengths of light. - So when a photon, so when a little bit of light hits my eye goes in, the photoreceptors convert that into electrical signal? - Right. - How is it that a given photon of light gives me the perception eventually, leads the perception of red versus green versus blue? - Right, so if you imagine that in the first layer of the retina where this transformation occurs from electromagnetic radiation into neural signals that you have different kinds of sensitive cells that are expressing, they're making different molecules within themselves for this express purpose of absorbing photons which is the first step in the process of seeing, now it turns out that altogether, there are about five proteins like this that we need to think about in the typical retina, but for seeing color really it's three of them. So they're three different proteins, each absorbs light with a different preferred frequency, and then the nervous system keeps track of those signals compares and contrasts them to extract some understanding of the wavelength composition of light. So you can see just by looking at a landscape, or it must be late in the day because things are looking golden that's all a function of our absorbing the light that's coming from the world and interpreting that with our brain because of the different composition of the light that's reaching our eyes. - Is it fair to assume that my perception of red is the same as your perception of red? - Well, that's a great question. - And that mine is better? I'm just kidding, I'm just kidding. [laughs] - It's a great question, it's a deep philosophical question. It's a question that really probably can't even ultimately be answered by the usual empirical scientific processes, 'cause it's really about an individual's experience. What we can say is that the biological mechanisms that we think are important for seeing color for example, seem to be very highly similar from one individual to the next whether it be human beings, or other animals. And so we think that the physiological process looks very similar on the front end, but once you're at the level of perception or understanding or experience, that's something that's a little bit tougher

00:13:47 “Strange” Vision

to nail down with the sorts of scientific approaches that we approach biological vision let's say. - You mentioned that there are five different cone types essentially, the cones being the cells that absorb light of different wavelengths. I often wondered when I had my dog, what he saw and how his vision differs from our vision. And certainly, there are animals that can see things that we can't see. - Right? - What are some of the more outrageous examples of that? - I've seen things. - And same things in the extreme. - Right. - Dogs I'm guessing see reds more as oranges, is that right? 'Cause they don't have the same array of of neurons that we have for seeing color. - Right, so the first thing is, it's not really five types of colons, there are really three types of colons. And if you look at the way that color vision is thought to work, you can sort of see that it has to be three different signals. There are a couple of other types of pigments. One is really mostly for dim light vision. When you're walking around in a moonless night and you're seeing things with very low light that's the rod cell that uses its own pigment. And then there's another class of pigments we'll probably talk about a little bit later, this melanopsin pigment. - I thought you were referring to like ultraviolet and infrared and things like that. - Right, so in the case of a typical, well, let's put it this way. In human beings, most of us have three cone types and we can see colors that stem from that. In most mammals including your dog or your cat, there really are only two cone types and that limits the kind of vision that they can have in the domain of wavelength or color as you would say. So really, a dog sees the world kind of like a particular kind of color blind human might see the world, because instead of having three channels to compare and contrast they only have two channels and that makes it much more difficult to figure out exactly which wavelength you're looking at. - Do colorblind people suffer much as a consequence of being colorblind? - Well, it's like so many other disabilities. The world is built for people of the most common type. So in some cases, the expectation can be there that somebody can see something that they won't be able to if they're missing one of their cone types let's say. So in those moments, that can be a real problem. If there's a lack of contrast to their visual system, they will be blind to that. In general, it's a fairly modest visual limitation as things go. For example, if not being able to see acutely can be much more damaging, not being able to read fine print for example. - Yeah, I suppose if I had to give up the ability to see certain colors or give up the ability to see clearly, I could certainly trade out color for clarity. - Right, of course, color is very meaningful to us as human beings, so we would hate to give it up. But obviously, dogs and cats and all kinds of other mammals do perfectly well in the world. - Yeah, because we take care of them.

00:16:56 How You Orient In Time

I spent most of my time taking care of that dog. - He took care of me too. Let's talk about that odd photopigment. Photopigment of course being the thing that absorbs light of a particular wavelength, and let's talk about these specialized ganglion cells that communicate certain types of information from eye to the brain that are so important for so many things. What I'm referring to here of course is, your co-discovery of the so-called intrinsically photosensitive cells, the neurons in the eye that do so many of the things that don't actually have to do with perception, but have to do with important biological functions. What I would love for you to do is explain to me why once I heard you say we have a bit of fly eye in our eye. - Yeah. - And you showed this slide of a giant fly from a horror movie. - Yeah. - Trying to attack this woman. - Yeah. - And maybe it was an eye also. So what does it mean that we have a bit of a fly eye in our eye? - Yeah, so this last pigment is a really peculiar one. One can think about it as really the initial sensitive element in a system that's designed to tell your brain about how bright things are in your world. And the thing that's really peculiar about this pigment, is that it's in the wrong place in a sense. When you think about the structure of the retina, you think about a layer cake essentially. You've got this thin membrane at the back of your eye, but it's actually a stack of thin layers and the outermost of those layers is where these photoreceptors you were talking about earlier are sitting. That's where the film of your camera is essentially, that's where the photons do their magic with the photo pigments and turn it into a neural signal. - I like that I've never really thought of the photoreceptors is the film of the camera, but that makes sense. - Or like the sensitive chip on CCD chip in your cell phone. It's the surface on which the light pattern is imaged by the optics of the eye, and now you've got an array of sensors that's capturing that information and creating a bitmap essentially, but now it's in neural signals distributed across the surface of the retina. So all of that was known to be going on 150 years ago, a couple of types of photoreceptors cones and rods. If you look a little bit more closely, three types of cones, that's where the transformation from electromagnetic radiation to neural signals was thought to take place. But it turns out that this last photopigment is in the other end of the retina, the innermost part of the retina, that's where the so-called ganglion cells are. Those are the cells that talk to the brain, the ones that actually can communicate directly what information comes to them from the photoreceptors. And here you've got a case where actually, some of the output neurons that we didn't think had any business being directly sensitive to light were actually making this photopigment, absorbing light, and converting that to neural signals and sending it to the brain. So that made it pretty surprising and unexpected, but there are many surprising things about these cells. - So, and what is the relationship to the fly eye? - Right, so the link there is, that if you ask how the photopigment now communicates downstream from the initial absorption event to get to the electrical signal, that's a complex cellular process involves many chemical steps. And if you look at how photoreceptors in our eyes work, you can see what that cascade is, how that chain works. If you look in the eyes of flies or other insects or other invertebrates, there's a very similar kind of chain. But the specifics of how the signals get from the absorption event by the pigment to the electrical response that the nervous system can understand, are characteristically different between fuzzy furry creatures like us and insects for example like the fly. - I see. - So these funny extra photoreceptors that are in the wrong layer doing something completely different are actually using a chemical cascade that looks much more like what you would see in a fly photoreceptor, than what you would see in a human photoreceptor, a rod or a cone for example. So it sounds like it's a very primitive aspect of biology that we maintain. - Exactly right, exactly. - And despite the fact that dogs can't see as many colors as we can and cats can't see as many colors as we can, we have all this extravagant stuff for seeing color and then you got this other pigment sitting in the wrong not wrong, but in a different part of the eye sending processing light very differently. - Right. - And sending that information into the brain. So, what do these cells do? Presumably, they're there for a reason. - They are, and the interesting thing is that, one cell type like this carrying one kind of signal which I would call a brightness signal essentially, can do many things in the brain. - When you say brightness signal you mean that, like right now, I have these cells do I have these cells? Of course. - You do. - I'm joking, I hope I have these cells in my eye. And they're paying attention to how bright it is overall, but they're not paying attention for instance to the edge of area or what else is going on in the room. - Right, so it's the difference between knowing what the objects are on the table and knowing whether it's bright enough to be daylight right now. So why does your nervous system need to know whether it's daylight right now? Well, one thing that needs to know that is your circadian clock. If you travel across time zones to Europe, now your internal clock thinks it's California time, but the rotation of the earth is for different part of the planet. The rising and setting of the sun is not at all what your body is anticipating. So you've got an internal representation of the rotation of the earth in your own brain, that's your circadian system it's keeping time. But now you've played a trick on your nervous system, you put yourself in a different place where the sun is rising at the quote wrong time. Well, that's not good for you, right? So you got to get back on track. One of the things this system does, is sends a oh, it's daylight now signal to the brain, which compares with its internal clock. And if that's not right, it tweaks the clock gradually until you get over your jet lag and you feel back on track again. - So the jet lag case makes a lot of sense to me, but presumably, these elements didn't evolve for jet lag. - Right. - So, what are they doing on a day-to-day basis? - Right, well one way to think about this is that, the clock that you have in not just your brain, in all the cells, almost all of the cells of your body, they're all oscillating, they're all. - They got local little clocks in them. - They got local little clocks in themselves, they're all clocks. They need to be synchronized appropriately, and the whole thing has to be built in biological machinery. This is actually a beautiful story about how gene expression can control gene expression, and if you set it up right, you can set up a little thing that just sort of hums along at a particular frequency. In our case it's humming along at 24 hours, 'cause that's how our earth rotates and it's all built into our biology. So this is great, but the reality is, that the clock can only be so good. I mean, we're talking about biology here. It's not precision engineering, and so it can be a little bit off. - Well, also it's in our brain, so it doesn't have access to any regular unerring signal? - Well, if in the absence of the rising and setting of the sun it doesn't, if you put someone in a cave, their biological clock will keep time to within a handful of minutes of 24 hours, that's no problem for one day. But if this went on without any correction, eventually you'd be out of phase and this is actually one of the things that blind patients often complain about. If they've got retinal blindness is insomnia. [indistinct] Exactly, they're not synchronized, their clock is there, but they're drifting out of phase because their clock's only good to 24.2 hours or 23.8 hours little by little if they're drifting. So you need a synchronization signal. So even if you never across time zones and of course we didn't back on the Savannah we stayed within walking distance of where we were, you still need a synchronizer, 'cause otherwise, you have nothing to actually confirm

00:25:45 Body Rhythms, Pineal function, Light & Melatonin, Blueblockers

when the rising and the setting of the sun is, that's what you're trying to synchronize yourself to. - I'm fascinated by the circadian clock and the fact that all the cells of our body have essentially a 24-hour-ish clock in them. - Right. - We hear a lot about these circadian rhythms and circadian clocks the fact that we need light input from these special neurons in order to set the clock. But I've never really heard it described how the clock itself works and how the clock signals to all the rest of the body when the liver should be doing one thing and the stomach should be doing another. I know you've done some work on the clock. So if you would just maybe briefly describe where the clock is, what it does, and some of the top contour of how it tells the cells of the body what to do. - Right, so the first thing to say is that, as you said, the clock is all over the place. Most of the tissues in your body have clocks. - We probably have what, millions of clocks in our body. - Yeah, I would say that's probably fair. If you have millions of cell types, you might have millions of clocks. The role of the central pacemaker for the circadian system is to coordinate all of these. And there's a little nucleus, a little collection of nerve cells in your brain it's called the suprachiasmatic nucleus the SCN, and it is sitting in a funny place for the rest of the structures in the nervous system that get direct retinal input. It's sitting in the hypothalamus, which you can think about as sort of the great coordinator of drives and. - The source of all our pleasures and all our problems. - Right. - Or most our problems. - Yes, it really is. But it's sort of deep in your brain things that drive you to do things. If you're freezing cold, you put on a coat, you shiver, all these things are coordinated by hypothalamus. So this pathway that we're talking about from the retina and from these peculiar cells that are encoding light intensity, are sending signals directly into a center that's surrounded by all of these centers that control autonomic nervous system and your hormonal systems. So this is a part of your visual system that doesn't really reach the level of consciousness, it's not something you think about, it's happening under the radar kind of all the time and the signal is working its way into this central clock coordinating center. Now what happens then is not that well understood, but it's clear that this is a neural center that has the same ability to communicate with other parts of your brain as any other neural center. And clearly, there are circuits that involve connections between neurons that are conventional. But in addition, it's quite clear that there are also sort of humeral effects that things are being oozing out of the cells in the center and maybe into the circulation or just diffusing through the brain to some extent that can also affect neurons elsewhere. But the hypothalamus uses everything to control the rest of the body. And that's true, the supracosmetic nucleus this circadian center as well, it can get its fingers into the autonomic nervous system, the humeral system and of course, up to the centers of the brain that organize coordinated rational behavior. So if I understand correctly, we have this group of cells, the suprachiasmatic nucleus, it's got a 24-hour rhythm, that rhythm is more or less matched to what's going on in our external world by the specialized set of neurons in our eye. But then the master clock itself the SCN, releases things in the blood humeral signals that go out various places in the body. And you said to the autonomic system which is regulating more or less how alert or calm we are, as well as our thinking and our cognition. So I'd love to talk to you about the autonomic part, presumably that's through melatonin, it's through adrenaline how is it that this clock is impacting how the autonomic system, how alert or calm we feel? - Right, so there are pathways by which the suprachiasmatic nucleus can access both the parasympathetic and sympathetic nervous system. - Just so people know the sympathetic nervous system is the one that tends to make us more alert, and the parasympathetic nervous system is the portion of the autonomic nervous system makes us feel more calm. - Right. - In broadcasting. Right, to first approximation, right? So, this is both of these systems are within the grasp of the circadian system through hypothalamic circuits. One of the circuits that will be I think, of particular interest to some of your listeners is a pathway that involves this sympathetic branch of the autonomic nervous system the fight or flight system that is actually through a very circuitous route innervating the pineal gland which is sitting in the middle of your brain. - The so-called third eye. - Right, so this is. - We'll have to get back to why it's called the third eye, because, yeah. - That's an interesting thing. - You can't call something the third eye and just. - Just leave it there. - Just leave it there. - Right. - Right. - Anyway, this is the major source of melatonin in your body. - So light comes in to my eye. - Yes. - Passed off to the suprachiasmatic nucleus essentially, not the light itself, but the signal representing the light. - Sure. - Then the SCN, the suprachiasmatic nucleus can impact the melatonin system. - Right. - Via the pineal? - Right, the way this is seen is that, if you were to measure your melatonin level over the course of the day, if you could do this hour by hour, you'd see that it's really low during the day, very high at night. But if you get up in the middle of the night and go to the bathroom and turn on the bright full fluorescent light, your melatonin level is slammed to the floor. Light is directly impacting your hormonal levels through this mechanism that we just described. So this is one of the routes by which light can act on your hormonal status through pathways that are completely beyond what you normally would think about, right? You're thinking about the things in the bathroom. Oh, there's the toothbrush, there's the tube of toothpaste. But meanwhile, this other system is just counting photons and saying oh wow, there's a lot of photons right now let's shut down the melatonin release. - This is one of the main reasons why I've encouraged people to avoid bright light exposure in the middle of the night. Not just blue light, but bright light of any wavelength, because there's this myth out there that blue light because it's the optimal signal for activating this pathway and shutting down melatonin, is the only wavelength of light that can shut it down. But am I correct in thinking that if a light is bright enough. - Right. - It doesn't matter if it's blue light, green light, purple light, even red light. - Right. - You're going to slam melatonin down to the ground which is not a good thing to happen in the middle of the night. - Right. - Correct? Right, yeah, any light will affect the system to some extent, the blue light is somewhat more effective, but don't fool yourself into thinking that if you use red light that means you're avoiding the effect, it's certainly still there. And certainly, if it's very bright, it'll be more effective in driving the system than dim blue light would be. - Interesting, a lot of people wear blue blockers. - Right. - And in a kind of odd twist of misinformation out there, a lot of people wear blue blockers during the middle of the day, which basically makes no sense because during the middle of the day is when you want to get a lot of bright light and including blue light into your eyes, correct? - Absolutely, and not just for the reasons we've been talking about in terms of circadian effects, there are major effects of light on mood. And seasonal affective disorder apparently, is essentially a reflection of this same system in reverse. If you're living in the northern climes and you're not getting that much light during the middle of the winter in Stockholm, you might be prone to depression and phototherapy might be just the ticket for you and that's because there's a direct effect of light on mood, there's an example where if you don't have enough light it's a problem. So I think you're exactly right. It's not about is like good or bad for you, it's about what kind of light and when that makes the difference. Yeah, the general rule of thumb that I've been living by, is to get as much bright light in my eyes ideally from sunlight anytime I want to be alert. - Right. - And doing exactly the opposite when I want to be asleep. - Yeah. - We're getting drowsy. - And there are aspects of this that spin out

00:34:45 Spending Times Outdoors Improves Eyesight

way beyond the conversation we're having now to things like this. It turns out that the incidence of myopia. - Nearsightedness. - Nearsightedness, right. Is strongly related to the amount of time that kids spend outdoors. - In what direction of effect? - The more they spend time outdoors, the less nearsightedness they have. - So this is not because they're viewing things at a distance, or because they're getting a lot of blue light, sunlight? - It's a great question, it is not fully resolved what the epidemiological, what the basis of that epidemiological finding is, one possibility is the amount of light which would make me think about this melanopsin system again. But it might very well be a question of accommodation that is the process by which you focus on near or far things if you're never outdoors, everything is nearby. If you're outdoors, you're focusing far, so this is. - Or unless you are on your phone? - Right, exactly. - There's a tremendous amount of interest these days in watches and things that count steps. I'm beginning to realize that we should probably have a device that can count photons during the day. - Right. - And can also count photons at night and tell us hey, you're getting too many photons, you're going to shut down your melatonin at night, or you're not getting enough photons, today you didn't get enough bright light, whether or not it's from artificial light or from sunlight. I guess that, where would you put? I guess you put on the top of your head or you'd probably want it someplace outward facing? - Right, probably what you need is as many photons over as much of the retina as possible to recruit as much of the system as possible. - In thinking about other effects

00:36:20 Sensation, Mood, & Self-Image

of this non-image forming pathway that involves these special cells in the eye and the SCN, you had a paper a few years ago looking at retinal input to an area of the brain which has a fancy name the peri-habenular, but names don't necessarily matter that had some important effects on mood and other aspects of light. Maybe you could tell us a little bit about what is the peri-habenular? - Oh, wow, so that's a fancy term, but I think the way to think about this, is a chunk of the brain that is sitting as part of a bigger chunk that's really the linker between peripheral sensory input of all kinds, virtually all kinds, whether it's auditory input or tactile input or visual input to the region of your brain the cortex that allows you to think about these things and make plans around them and to integrate them and that kind of thing. So, we've known about a pathway that gets from the retina through this sort of linker center which it's called the thalamus, and then. [indistinct] Exactly, but you want to arrive at the destination. Right now you're at grand central and now you can do your thing 'cause you're up at the cortex. So this is the standard pattern. You have sensory input coming from the periphery, you've got these peripheral elements that are doing the initial stages of. - The eye, the ear, the nose. - Your skin of your fingertips, right? The taste buds on your tongue they're taking this raw information in and they're doing some pre-processing maybe or the early circuits are. But eventually, most of these signals have to pass through the gateway to the cortex which is the thalamus. And we've known for years, for decades, many decades, what the major throughput pathway from the retina to the cortex is and where it ends up. It ends up in the visual cortex. You pat the back of your head that's where the receiving center is for the main pathway from retina to cortex. But wait a minute, there's more. There's this little side pathway that goes through a different part of that linking thalamus center. [indistinct]

- Like a local train. - Yeah. - From grand central to. - It's in a weird part of the neighborhood, right? It's a completely different, it's like a little trunk line that branches off and goes out into the hinterlands and it's going to the part of this linker center that's talking to a completely different part of cortex way up front, frontal lobe, which is much more involved in things like planning, or self-image or. - Self-image literally, how one. - Views oneself, do you feel good about yourself, or what's your plan for next Thursday. It's a very high level center in the highest level of your nervous system and this is the region that is getting input from this pathway which is mostly worked out in its function by [indistinct] Tara's Lab. I know you had him on the podcast. - We didn't talk about this path. - This pathway at all right. So Dale Fernandez and [indistinct] and the folks that work with them, were able to show that this pathway doesn't just exist and get you to a weird place. But if you activate it at kind of the wrong time of day, animals can become depressed. And if you silence it under the right circumstances, then weird lighting cycles that would normally make them act sort of depressed, no longer have that effect. - So it sounds to me like there's this pathway from eye to this unusual train route through the structure we call the thalamus, then up to the front of the brain that relates to things of self-perception, kind of higher level functions. I find that really interesting, because most of what I think about when I think about these fancy, well, or these primitive rather, neurons that don't pay attention to the shapes of things, but instead to brightness I think of well, it regulates melatonin and circadian clock, mood, hunger, the really kind of vegetative stuff if you will. - Right. - And this is interesting because I think a lot of people experience depression not just people that live in Scandinavia in the middle of winter, and we are very much divorced from our normal interactions with light. It also makes me realize that these intrinsically photosensitive cells that set the clock et cetera, are involved in a lot of things.

00:41:03 Sense of Balance

They seem to regulate a dozen or more different basic functions. I want to ask you about a different aspect of the visual system now, which is the one that relates to our sense of balance. So I love boats but I hate being on them. I love the ocean from shore, because I get incredibly seasick, it's awful. I think I'm going to get seasick if I think about it too much. [laughs] And once I went on a boat trip, I came back and I actually got motion sick or wasn't seasick 'cause I was rafting. So there's a system that somehow gets messed up. They always tell us if you're feeling sick to look at the horizon et cetera, et cetera. - Right. - So what is the link between our visual system and our balance system and why does it make us nauseous sometimes when the world is moving in a way that we're not accustomed to? - Right. - I realize this is a big question, because it involves eye movement, et cetera. - Right. - But let's maybe just walk in at the simplest layers of vision, vestibular, so-called balance system and then maybe we can piece the system together for people so that they can understand, and then also we should give them some tools for adjusting their nausea when their vestibular system is out of whack. - Cool, so the first thing to think about is that the vestibular system is designed to allow you to see how your or detect sense how you're moving in the world, through the world. It's a funny one because it's about your movement in relationship to the world in a sense, and yet it's sort of interoceptive in the sense that it is really in the end sensing the movement of your own body. - Okay, so interoception we should probably delineate for people is when you're focusing on your internal state as opposed to something outside you. - Right. - It's a gravity sensing system. - Well, it's partly a gravity sensing system in the sense that gravity is a force that's acting on you as if you were moving through the world in the opposite direction. - All right, now you got to explain that. You got to explain that to me. - Okay, so basically the idea is that, if we leave gravity inside, we're just sitting in a car, in the passenger seat and the driver hits the accelerator and you start moving forward, you sense that. If your eyes were closed, you'd sense it. If your ears were plugged in, your eyes would close, you'd still know it. - Yeah, many people take off on the plane like this they're dreading the flight and they know when the plane is taking off. - Sure, that's your vestibular system talking, because anything that jostles you out of the current position you're in right now will be detected by the vestibular system pretty much. So this is a complicated system, but it's basically in your inner ear very close to where you're hearing. - That they put it there. And I don't know. - And I don't really know, they're sort of derived. [indistinct] - Now I'm just kidding. To steal our friend Russ Van Gelder's explanation, we weren't consulted the design phase and no one. - That's a great [indistinct]. - But it's interesting it's in the ear. - Yeah. - Right? - Yeah, it's deep in there and it's served by the same nerve actually that serves the hearing system. One way to think about it is both the hearing system and this vestibular self-motion sensing system are really detecting the signal in the same way they're hairy cells and they're exciting. [indistinct] - Yeah, sort of they got little cilia sticking up off the surfaces. And depending on which way you bend those, the cells will either be inhibited or excited, they're not even neurons but then they talk to neurons with a neuron-like process and off you go. Now you've got an auditory signal if you're sensing things bouncing around in your cochlea which is. - Sound waves. - Sympathetically the bouncing of your eardrum which is symmetrically the sound waves in the world. But in the case of the vestibular apparatus, evolution has built a system that detects the motion of say fluid going by those hairs. And if you put a sensor like that in a tube that's fluid filled, now you've got a sensor that will be activated when you rotate that tube around the axis that passes through the middle of it, those we're just listening won't be able. [indistinct] - I was thinking of it as three hula hoops. - Right, three hoops. - One standing up, one lying down on the ground. - Right. - The other one the other way. - Three directions, the people who fly will talk about roll pitch and you all that kind of thing. So three axes of encoding just like in the. [indistinct] - Sort of the yes, the no and then I always say it's the puppy head tilt. - Yeah, that puppy tilt. - That's the other one. So the point is that, your brain is eventually going to be able to unpack what these sensors are telling you about how you just rotated your head in very much the way that the three types of cones we were talking about before are reading the incoming photons in the wavelength domain differently, and if. - Red, green, blue. - Yeah, you can compare and trust you get red, green, blue. So same basic idea if you have three sensors and you array them properly, now you can tell if you're rotating your head left or right, up or down that's the sensory signal coming back into your brain confirming that you've just made a movement that you will. - But what about on the plane? Because when I'm on the plane, I'm completely stationary the plane's moving. - Right. - But my head hasn't moved. - Right. - So I'm just moving forward, gravity is constant. - Exactly. - How do I know I'm accelerating? - So what's happening now is your brain is sensing the motion, and the brain is smart enough also to ask itself, did I will that movement or did that come from the outside? So now in terms of sort of understanding what the the vestibular signal means, it's got to be embedded in the context of what you tried to do, or what your other sensory systems are telling you about what's happening. - I see, so it's very interesting. But it's not conscious or at least if it's conscious, it's very not conscious, it's definitely very fast, right? The moment that plane starts moving, I know that I didn't get up out of my chair and run forward. - Right. - But I'm not really thinking about getting up out of my chair I just know. - I guess the way i think about it is that, the nervous system is quote, aware at many levels when it gets all the way up to the cortex and we're thinking about it, you're talking about it, that's cortical. But the lower levels of the brain that don't require you to actually actively think about it they're just doing their thing are also made aware, right? A lot of this is happening under the surface of what you're thinking, these are reflexes. - Okay, so we've got this gravity sensing system? - Right. - I'm nodding for those that are listening for a yes movement of the head, a no movement of the head or the tilting of the head from side to side. - Right. - And then you said that knowledge about whether or not activation of that system comes from my own movements, or something acting upon me like the plane moving. - Right. - Has to be combined with other signals. And so, how is the visual information or information about the visual world combined with balance information? - Right, so yeah. I guess maybe the best way to think about how these two systems work together, is to think about what happens when you suddenly rotate your head to the left. When you suddenly rotate your head to the left, your eyes are actually rotating to the right. Automatically, you do this in complete darkness. If you had an infrared camera and watched yourself in complete darkness, you can't see anything. Rotating your head to the left, your eyes would rotate to the right. That's your vestibular system saying, I'm going to try to compensate for the head rotation. So my eyes are still looking in the same place. Why is that useful, well, if it's always doing that, then the image of the world on your retina will be pretty stable most of the time and that actually helps vision. - Have they built this into cameras for image stabilization 'cause when I move, when I take a picture with my phone, it's blurry, it's not clear? - Well actually, you might want to get a better phone, because now what they have is software in the better apps that will do a kind of image stabilization post-hoc by doing a registration of the images that are bouncing around, they say the edge of the house was here, so let's get that aligned in each of your images. So you may not be aware if you're using a good new phone that if you walk around a landscape and hold your phone, that there's all this image stabilization going on. But it's built into standard cinematic technology now, because if we tried to do a handheld camera, things would be bouncing around, things would be unwatchable, you wouldn't be able to really understand what's going on in the scene. So the brain works really hard to mostly stabilize the image of the world on your retina and of course you're moving through the world so you can't stabilize everything. But the more you can stabilize most of the time, the better you can see. And that's why when we're scanning a scene looking around at things, we're making very rapid eye movements for very short periods of time and then we just rest, but we're not the only ones that do that. If you ever watch a hummingbird, it does exactly the same thing at a feeder, right? [indistinct] It is with its body. It's going to make a quick movement, 00:50:43 Why Pigeons Bob Their Heads, Motion Sickness

and then it's going to be stable. And when you watch a pigeon walking on the sidewalk, it does this funny head bobbing thing. But what it's really doing, is racking its head back on its neck while its body goes forward so that the image of the visual world stays static. - Is that why they're doing it? - Yes, and you've seen the funny chicken videos on YouTube, right? - You take a chicken move it up and down the head stays in one place, it's all the same thing. All of these animals are trying hard to keep the image of the world stable on their retina as much of the time as they possibly can. And then when they've got to move, make it fast, make it quick and then stabilize again. - That's why the pigeons have their head back? - It is, yeah. - Wow. - Yeah. - I just need to pause there for a second and digest that, amazing. In case people aren't. Well, there's no reason why people would know what we're doing here, but essentially, what we're doing is we're building up from sensory light onto the eye, make color to what the brain does with the integration of that circadian clock, melatonin, et cetera. And now what we're doing is we're talking about multi-sensory or multimodal combining one sense vision with another sense balance. - Right. - And it turns out that pigeons know more about this than I do, because pigeons know to keep their head back as they walk forward. - Right. - All right, so that gets us to this issue of motion sickness. - Right. - And you don't have to go out on a boat. Anytime I go to New York, I sit in an Uber or in a cab in the back. And if I'm looking at my phone while the car is driving, I feel nauseous by time I arrive at my destination. - Right. - I always try and look out the front of the windshield, because I'm told that helps but it's a little tiny window. - Right. - And I end up feeling slightly less sick if I do that. So what's going on with the vision and the balance system that causes a kind of a nausea? And actually, if I keep talking about this. [indistinct] [laughs] I don't throw up easily, but for some reason motion sickness is a real thing for me. - It's a problem for a lot of people. I think the fundamental problem typically, when you get motion sick is what they call visual vestibular conflict. That is, you have two sensory systems that are talking to your brain about how you're moving through the world. And as long as they agree you're fine. So if you're driving, your body senses that you're moving forward. Your vestibular system is picking up this acceleration of the car, and your visual system is seeing the consequences of forward motion in the sweeping of the scene past you. Everything is honky-dory, right, no problem. But when you are headed forward but you're looking at your cell phone, what is your retina seeing? Your retina is seeing the stable image of the screen. There's absolutely no motion in that. - Or the motion is just or some other emotion like a movie. - If you're playing a game or you're watching a video, a football game, the motion is uncoupled with what's actually happening to your body. Your brain doesn't like that, your brain likes everything to be aligned. And if it's not, it's going to complain to you. - By making me feel nauseous. - By making you feel nauseous and maybe you'll change your behavior. So you're getting. - I'm getting punished. - Yeah, for setting it up. [indistinct] - Right. - By the vestibular? - You'll learn. - Visuals. [laughs] In time, I love it. I love the idea of reward signals and we've done a lot of discussion about this on this podcast of things like dopamine reward and things, but also punishment signals and I love this example. Well, maybe marching a little bit further along this pathway, visual input is combined with balance input. Where does that occur, and maybe 'cause I have some hint of where it occurs. You could tell us a little bit about this kind of mysterious little mini-brain that they call the cerebellum. - Cerebellum, yeah. So the way I tried to describe the cerebellum to my students is that, it serves sort of like the air traffic control system functions in air travel. So that it's a system that's very complicated and it's really dependent on great information. So it's taking in information about everything that's happening everywhere not only through your sensory systems, but it's listening into all the little centers elsewhere in your brain that are computing what you're going to be doing next and so forth. So it's just ravenous for that kind of information. - So it really is like a little mini-brain. - It is, it's got access to all those signals. and it really has an important role in coordinating and shaping movements, but if you suddenly eliminated the air traffic control system, planes could still take off and land but you might have some unhappy accidents in the process. So the cerebellum is kind of like that. It's not that you would be paralyzed if your cerebellum was gone because you still have motor neurons, you still have ways to talk to your muscles, you still have reflex centers, and it's not like you would have any sensory laws because you still have your cortex getting all of those beautiful signals that you can think about, but you wouldn't be coordinating things so well anymore. The timing between input and output might be off. Or if you were trying to practice a new athletic move like an overhead serve in tennis, you'd be just terrible at learning. All the sequences of muscle movements and the feedback from your sensory apparatus that would let you really hit that ball exactly where you wanted to after the nth rep, right? Now 1000th rep or something you get much better at it. So the cerebellum is all involved in things like motor learning and refining the precisions of movement so that they get you where you want to go if you reach for a glass of champagne that you don't knock it over or stop short. [indistinct] - People who have selective damage to the cerebellum. - Absolutely. - And I'm familiar with. Well, Korsakoff's is different, right? Isn't that a B vitamin deficiency in chronic alcoholics? - Right. - And they tend to walk kind of bow-legged and they can't coordinate their movements. That has some that not memory bodies but also a cerebellum? - I'm not sure about the cerebellar involvement there. But the typical thing would be a patient who has a cerebral or stroke or a tumor for example, might be not that steady on their feet if the dynamics of the situation you're standing on a street car with no handle pull to hold on to, they might not be as good at adjusting all the little movements of the car. There's a kind of tremor that can occur as they're reaching for things, because they reach a little too far and then they over correct and come back, things like that. So it's very common neurological phenomenon actually. Cerebellar ataxia is what the neurologists call it, and it can happen not just with cerebellar damage, but damage to the tracts that feed the information into the cerebellum. - Right, it is the private structure. - Exactly, or output from the cerebellum. - And so, the cerebellum is where a lot of visual and balance information is combined. - In a very key place in the cerebellum, which it's really one of the oldest parts. - In terms of flocculus. - The flocculus, right. It's a critical place in the cerebellum where visual and vestibular information comes together recording just the kinds of movements we were talking about. This image stabilizing network it's all happening there. And there's learning happening there as well. So that if your vestibular apparatus is a little bit damaged somehow, your visual system is actually talking to your cerebellum saying there's a problem here, there's an error, and your cerebellum is learning to do better by increasing the output of the vestibular system to compensate for whatever that loss was. So it's a little error correction system that's sort of typical of a cerebellar function and it can happen in many, many different domains. This is just one of the domains of sensory motor integration that takes place there. - So I should stay off my phone in the Ubers. if I'm on a boat, I should essentially look and as much as possible act as if I'm driving the machine. - Right. - That'd be weird if I was in the passenger seat pretending I was driving the machine. But i do always feel better if I'm sitting in the front seat passenger. - Right, so more of the visual world that you can see as if you were actually the one doing the motion I would think. - Let's stay in the inner ear for a minute as we continue to march around the nervous system. When you take off in the plane or when you land or sometimes in the middle of there, your ears get clogged or at least my ears get clogged, that's because of pressure buildup in the various tubes

01:00:03 Popping Ears

of the inner ear, et cetera, we'll get into this. But years ago, our good friend Harvey Karten, is a another world-class neuroanatomist gave a lecture and talked about how plugging your nose and blowing out versus plugging your nose and sucking in should be done at different times depending on whether or not you're taking off or landing. And I always see people trying to unpop their ears. - Right. - And when you do scuba diving you learn how to do this without necessarily I can do it by just kind of moving my jaw now 'cause I've done a little bit of diving. But what's the story there? We don't have to get into all the differences in atmospheric pressure, et cetera, but if I'm taking off and my ears are plugged, I've recently ascended, plane take off, my ears are plugged, do I plug my nose and blow out, or do I plug my nose and suck in? - Right, so the basic idea is that, if your ears feel bad because you're going into an area of higher pressure, so if they pressurize the cabin more than the pressure that you have on the surface of the planet, your eardrums will be bending in and they don't like that. If you push them more they'll hurt even more. - It's a good description that the pressure goes up then they're going to bend in. - Bend in and then reverse would be true if you go into an area of low pressure. So if you knew you started to drive up the mountain side the pressure's getting lower and lower outside, now the air behind your eardrum is ballooning out. - Yep. - Right? So it's just a question of are you trying to get more pressure or less pressure behind the eardrum and there's a little tube that does that and comes down into back your throat there. And if you force pressure up that tube, you're going to be putting more air pressure into the compartment. - To counter it. - If it's not enough and if you're sucking you're going the other way. In reality, I think as long as you open the passageway, I think the pressure differential is going to solve your problem. So I think you could actually blow in when you're not supposed to. - Okay, so you could just hold your nose and blow air out, or hold your nose and suck in the. - Right. - Effect either way is fine? - I think so. - Excellent, I just won $100 from Harvey Karten. [laughs] - Thank you very much, this is a lot. Harvey and I used to teach neuroanatomy together and I was like I don't think it matters, but thank you very much, I'll split that with you. - Okay. [laughs] - This is important stuff. But it's true you hear this. So it doesn't matter either way. - I'm no expert in this area. - Don't worry. - Don't quote me. - He's not going to, well, I'm going to quote you. But, okay, so we've talked about the inner ear,

01:02:35 Midbrain & Blindsight

we've talked about the cerebellum. I want to talk about an area of the brain that is rarely discussed which is the midbrain. - Yeah. - And for those that don't know, the midbrain is an area beneath the cortex. I guess we never really defined cortex was kind of the outer layers or are the outer layers of the at least mammalian brain or human brain. But the midbrain is super interesting, because it controls a lot of unconscious stuff, reflexes, et cetera. And then there's this phenomenon even called blind sight. So could you please tell us about the midbrain about what it does, and what in the world is sight? - Yeah, so there's a lot of pieces there. I think the first thing to say is, if you imagine the nervous system in your mind's eye, you see this big honking brain and then there's this little wand that dangles down into your vertical column the spinal cord and that's kind of your visual impression. What you have to imagine is starting in the spinal cord and working your way up into this big magnificent brain and what you would do as you enter the skull, is get into a little place where the spinal cord kind of thickens out. It still has that sort of long, skinny trunk-like feeling. - It's more like a paddle or a spoon shape. - Right, it starts to spread out a little bit and that's 'cause your evolutionists packed more interesting goodies in there for processing information and generating movement. So beyond that is this tween brain we were talking about. This linker brain with diencephalon really means the between brain. - Oh, I thought you said tween. - Well, it is, yes. - No, no, no, between. Between. - Between. [indistinct] - You said tween. - Yeah, it's the between, it's the between brain is what the name means. It's the linker from the spinal cord in the periphery up to these grand centers of the cortex. But this midbrain you're talking about is the last bit of this enlarged sort of spinal cordy thing in your skull, which is really the brain stem is what we call it. The last bit of that before you get to this relay up to the cortex is the midbrain. And there's a really important visual center there, it's called the superior colliculus. There's a similar center in the brains of other vertebrate animals a frog for example or a lizard, would have this is called the optic tectum there but it's a center, then in these non-mammalian vertebrates, is really the main visual center. They don't really have what we would call a visual cortex although there's something sort of like that. But this is where most of the action is in terms of interpreting visual input and organizing behavior around that. You can sort of think about this region of the brain stem as a reflex center that can reorient the animal's gaze or body or maybe even attention to particular regions of space out there around the animal and that could be for all kinds of reasons. It might be a predator just showed up in one corner of the forest and you pick that up and you're trying to avoid it. - Or just any movement. - Any movement, right? It might be that suddenly something splats on the page when you're reading a novel and your eye reflexively looks at it. You don't have to think about that, that's a reflex. - What if you throw me a ball but I'm not expecting it? - Right. - And I just reach up try and grab it touch it or not. Is that handled by the midbrain? - Well, that's probably not the midbrain although by itself, because it's going to involve all these limb movements, this movement of your arm and body. - What about ducking if something's suddenly thrown in your head? - Sure, right, things like that will certainly have a brainstem component, a midbrain component, something looms and you duck. It may not be the superior colliculus we're talking about now, it might be another part of the visual midbrain. But these are centers that emerged early in the evolution of brains like ours to handle complicated visual events that have significance for the animal in terms of space, where is it in space? And in fact, this same center actually gets input from all kinds of other sensory systems that take information from the external world from particular locations and where you might want to either avoid or approach things according to their significance to you. So you get input from the touch system, you get input from the auditory system. I work for a while in rattlesnakes, they get input from a part of their warm sensors on their face, they're in these little pits on the face. - To work on baby rattlesnakes, right? - They were adults. - Oh, I wasn't trying to diminish the danger. I thought for some reason they were little ones. - No. - Why in the world would you work on rattlesnakes? - Well, because they have a version of an extra receptive sensory system that is they're looking out into the world using a completely different set of sensors. They're using the same sensors that would feel the warmth on your face if you stood in front of a bonfire. Except, evolution has given them this very nice specialized system that lets them image where the heat's coming from. You can sort of do that anyway, right? If you walk around the fire, you can feel where the fire is from the heat hitting your face. - Is that the primary way in which they detect prey? - It's one of one of the major ways. And in fact, they use vision as well and they bring these two systems together in the same place in this tectum regions brain stem, midbrain. - What's the tongue jutting about when the snakes? - That I don't know. That may be old factory, they're maybe. - They're sniffing the air with their tongue? - Yeah, there may be, 'cause. - On our drive you told me that flies actually taste things with their feet. - They do, yeah. - That's so weird. - Yeah, they have taste receptors and lots of funny places. I want to pause here just for one second before we get back into the midbrain. I think what's so interesting in all seriousness about taste receptors on feet, heat sensors, tongues shutting out of snakes and vision and all this integration is that, it really speaks to the fact that all these sensory neurons are trying to gather information and stuff it into a system that can make meaningful decisions and actions. And that it really doesn't matter whether or not it's coming from eyes or ears or nose or bottoms of feet, because in the end, it's just electricity flowing in. And so it sounds like it's placed on each animal, it always feels weird to call fly an animal. But they are creatures, they are animals. It's placed in different locations on different animals depending on the particular needs of that animal. - Right, but how much more powerful if the nervous systems can also cross-correlate across sensory systems? So if you've got a weak signal from one sensory system, you're not quite sure there's something there. And a weak signal from an another sensory system that's telling you the same locations is a little bit interesting. There might be something there if you've got those two together you've got corroboration. Your brain now says it's much more likely that that's going to be something worth paying attention to. - Right, so maybe I'm feeling some heat on one side of my face and I also smell something baking in the oven. - Right. - So now there's, it's neither is particularly strong, but as you said, there's some corroboration. - Right. And that corroboration is occurring in the midbrain. - Right, and then if you throw things into conflict, now the brain is confused and that may be where your emotion sickness comes from. So it is great to have, as a brain, it's great to have as many sources of information as you can have, just like if you're a spy or a journalist, you don't want as much information as you can get about what's out there, but if things conflict, that's problematic, right? Your sources are giving you different information about what's going on.

01:10:44 Why Tilted Motion Feels Good

Now you've got a problem on your hands, what do you publish? - The midbrain is so fascinating. I don't want to eject us from the midbrain and go back to the vestibular system, but I do have a question that I forgot to ask about the vestibular system which is, why is it that for many people including me, despite my motion sickness in cabs, that there's a sense of pleasure in moving through space and getting tilted relative to the gravitational pull of the earth? For me growing up it was skateboarding, but people like to corner in cars, corner on bikes, maybe for some people it's done running or dance. But what is it about moving through space and getting tilted a lot of surfers around here. Getting tilted that can tap into some of the pleasure centers. Do we have any idea why that would feel like? - I have no clue. - Is there dopaminergic input to this system? - Well, the dopaminergic system gets a lot of places. It's pretty much to some extent everywhere in the cortex a lot more in the frontal lobe of course, but that's just for starters. There's basically dopaminergic innervation most places in the central nervous system. So there's the potential for dopamine urging involvement but I really have no clue about the tilting phenomenon. - People pay money to go on roller coasters. - Right, well, I think that may be as much about the thrill as anything. - Sure. And the falling reflex is very robust in all of us when the visual world's going up very fast it usually means that we're falling. - Right. - But some people like that, some people don't. - Right. And kids tolerate a lot more sort of vestibular craziness spinning around until they've dropped. - And I've friends, it always you worries me a little bit that they throw their kids. I'm not recommending anyone do this. When they're little like throwing the kids really far back and forth, some kids seem to love it. - Yeah, yeah, our son loved being shaken up and down very vigorously, that's the only thing that would calm him down sometimes. - Interesting, yeah, so I'm guessing we can guess that maybe there's some activation of the reward systems from. - Yeah. - Being moving through space. - Well, if you think about how rewarding it is to be able to move through space and how unhappy people are who are used to that who suddenly aren't able to do that, there is a sense of agency, right? If you can choose to move through the world and to tilt, that's not only you're moving through the world, but you're doing it with a certain amount of finesse, maybe that's what it is. You can feel like you're the master of your own movement in a way that you wouldn't if you're going straight. I'm just blowing smoke here, right? - Yeah, well, we can speculate, that's fine.

01:13:24 Reflexes vs. Deliberate Actions

I couldn't help but ask the question. Okay, so if we move ourselves pun intended back into the midbrain, the midbrain is combining all these different signals for reflexive action.

At what point does this become deliberate action? Because if I look at something I want and I want to pursue it, I'm going to go toward it and many times that's a deliberate decision. - Right, so this gets very slippery I think, because what you have to try to imagine is all these different parts of the brain working on the problem of staying alive and surviving in the world, they're working on the problem simultaneously, and there's not one right answer how to do that. But one way to think about it is that, you have high levels of your nervous system that are very well designed to override an otherwise automatic movement if it's inappropriate. So if you imagine you've been invited to tea with the queen and she hands you very fancy Wedgewood teacup very thin. - Wedgewood teacup? - Yes, with very hot tea in it and you're burning your hand, you probably will try to find a way to put that back down on the saucer rather than just dropping it on the floor because you're with the queen. You're trying to be appropriate to that. So you have ways of reining in automatic behaviors if they're going to be maladaptive. But you also want the reflex to work quickly if it's the only thing that's going to save you. The looming object coming at your head, you don't have time to think about that. So this is the interplay in these hierarchically organized centers of the nervous system at the lowest level. You've got the automatic sensors and centers and reflex arcs that will keep you safe even if you don't have time to think about it, and then you've got the higher center saying, well, maybe we could do this as well or maybe we shouldn't do that at all, right? So you have all these different levels operating simultaneously and you need bi-directional communication between high-level, cognitive centers, decision-making on the one hand, and these low-level very helpful reflexive centers, but they're a little bit rigid, a little hard-wired so they need some nuance. So they're both of these things are operating in tandem in real time, all the time in our brains and sometimes we listen more to one than the other. You've heard people in sports talking about messing up at the play 'cause they over thought it. Thinking too hard about it. That's partly you've already trained your cerebellum how to hit a fastball right down the middle. - Right, and if you start looking for something new or different, you're going to mess up your reflexive swing. - Right, if you're trying to think about the physics of the ball as it's coming at you, you've already missed, right? Because you're not using your, all those reps have built a kind of knowledge is what you want to rely on when you don't have enough time to contemplate. - This is important and a great segue

01:16:35 Basal Ganglia & the “2 Marshmallow Test” for what I'd like to discuss next which is the basal ganglia. This really interesting of the area of the brain that's involved in go-type commands and behaviors instructing us to do things and no-go preventing us from doing things. Because so much of motor learning and skill execution and not saying the wrong thing or sitting still in class or as you use with the tea with the queen example feeling discomfort involves suppressing behavior and sometimes it's activating behavior. - Right. - A tremendous amount of online attention is devoted to trying to get people motivated. This isn't the main focus of our podcast. We touch on some of the underlying neural circuits of motivation dopamine and so forth. But so much of what people struggle with out there are elements around failure to pay attention. - Right. - Or challenges in paying attention which is essentially like putting the blinders on and they're getting a soda straw view of the world and maintaining that for a about of work or something of that sort and trying to get into action. So of course, this is carried out by many neural circuits not just the basal ganglia. But what are the basal ganglia, and what are their primary roles in controlling go type behavior and no-go type behavior? - Yeah, so the basal ganglia are sitting deep in what you would call the forebrains or the highest levels of the brain. They are sort of cousins to the cerebral cortex which we talked about as sort of the highest level of your brain, the thing you're thinking with. - The cerebral cortex being the refined cousins and then you've got the. - Right. - The brute, yeah. - Yeah. That's probably totally unfair, but. - That's right, I like the basal ganglia. I can relate to the brutish parts of the brain. A little bit of hypothalamus, a little bit of basal ganglia, sure. - We need it all, we need it all. And this area of the brain has gotten a lot bigger as the cortex has gotten bigger and it's deeply intertwined with cortical function. The cortex can't really do what it needs to do without the help of the basal ganglia and vice versa. So they're really intertwined. And in a way you can think about this logically is saying, if you have the ability to withhold behavior or to execute it, how do you decide which to do? Well, the cortex is going to have to do that thinking for you. You have to be looking at all the contingencies of your situation to decide is this a crazy move, or is this a really smart investment right now or what? - I don't want to go out for a run in the morning, but I'm going to make myself go out for a run, or I'm having a great time out on a run and I know I need to get back but I kind of want to go another mile. - I mean, another great example is that, the marshmallow test for the little kids. They can get two marshmallows if they hold off just 30 seconds initially, they can have one right away. But if they can wait 30 seconds, they got two. So that's the no go because their cortex is saying, I would really like to have two more than having one. But they're not going to get the two unless they can not reach for the one. So they've got to hold off the action and that has to result from a cognitive process. So the cortex is involved in this in a major way. - Yeah, as I recall in that experiment, the kids used a variety of tools. Some would distract themselves. I particularly related to the kid that would just put himself right next to the marshmallows and then some of the kids covered their eyes, some of them would count or sing. Yeah, so that's all very cortical, right? Coming up with a novel strategy, simple example that we're using here. But of course, this is at play anytime someone decides they want to go watch a motivational speech or something just a Steve Jobs commencement speech just to get motivated to engage in their day. - Should I take this new job? It's got great benefits, but it's in a lousy part of the country. - Why do you think that some people have a harder time running these go no-go circuits and other people seem to have very low activation energy we would say, they could just, they have a task, they just lean into the task. - Right. - Whereas some people getting into task completion or things of that sort is very challenging for them? - Yeah, I think it's really just another, it's a special case of a very general phenomenon which is brains are complicated. And the brains we have are the result of genetics and experience, and my genes are different from your genes and my experiences are different from your experiences. So the things that would be easy or hard for us won't necessarily be aligned, they might just happen to be just because they are, but the point is that, you're dealt a certain set of cards, you have certain set of genes, you are handed a brain, you don't choose your brain it's handed to you. Then there's all this stuff you can do with it. You can learn to have new skills or to act differently or to show more restraint which is kind of relevant to what we're talking about here. Or maybe show less restraint if your problem is you're so buttoned down, you never have any fun in life and you should loosen up a little bit. - Thank you, I appreciate that. - Yeah. - Yeah. [laughs] David's always encouraging me to have a little more fun in life. [laughs] So basil ganglia they're kind of the disciplinarian or they're sort of the instructor conductor of sorts, right? Go, no-go, you be quiet, you start now. - I wish I knew more about the basal ganglia than I do. My sense is that, this system is key for implementing the plans that get cooked up in the cortex, but they also influence the plans that the cortex is dishing out because this is a major source of information to the cortex. So it becomes almost impossible to figure out where the computation begins and where it ends and who's doing what because these things are all interacting in a complex network, and it's all of it. It's the whole network, it's not one is the leader and the other is the follower. - Right, of course, yeah, these are all the structures that we're discussing are working in parallel. - Right. - And there's a lot of changing crosstalk. I have this somewhat sick habit David. Every day I try and do 21 no-gos. So if I want to reach for my phone, I try and not do it just to see if I can prevent myself from engaging in that behavior, if it was reflexive, if it's something I want to do a deliberate choice, then I certainly allow myself to do it. - Right. - I don't tend to have too much trouble with motivation with go type functions, mostly because I'm so busy that I'd wish I had more time for more goes so to speak. But do you think these circuits have genuine plasticity in them? - Absolutely, everybody knows how they've learned over time to wait for the two marshmallows, right? You don't have to have instant gratification all the time. You're willing to do a job sometimes it isn't your favorite job because it comes with the territory and you want the salary that comes at the end of the week or the end of the month, right? So we can defer gratification. We can choose not to say the thing that we know is going to inflame our partner and create a meltdown for the next week. We learn this control, but I think these are skills like any other you can get better at them if you practice them. So I think you're choosing to do that to spontaneously, is kind of a mental practice, it's a discipline, it's a way of building a skill that you want to have. - Yeah, I find it to be something that when I engage in a no-go type situation, then the next time and the next time that I find myself about to move reflexively, there's a little gap in consciousness

01:24:40 Suppressing Reflexes: Cortex

that I can make a decision whether or not this is really the best use of my time. Because sometimes I wonder whether or not all this business around attention certainly there's the case of ADHD and clinical diagnosed ADHD. But all the issue around focus and attention is really that people just have not really learned how to short circuit a reflex. And so much of what makes us different than rattlesnakes, or well, actually they could be deliberate, but from the other animals and is our ability to suppress reflex. - Yeah, well, that's the cortex. Or let's say the forebrain. Cortex and basal ganglia are working together sitting on top of this lizard brain that's giving you all these great adaptive reflexes that help you survive. You just hope you don't get the surprising case where the thing that your reflex is telling you is actually exactly the wrong thing and you make a mistake, right? [indistinct] Right, so that's what the cortex is for. It's adding nuance and context and experience, past association and in human beings obviously, learning from others through communication. - Well, I was, you went right to it and it was where I was going to go. So let's talk about the cortex. We've worked our way up the so-called neuraxis as the aficionados will know, so we're in the cortex. This is the seat of our higher consciousness, self-image, planning and action. But as you mentioned, the cortex isn't just about that, it's got other regions that are involved in other things. So maybe we should staying with vision, let's talk a little bit about visual cortex. You told me an amazing story about visual cortex and it was somewhat of a sad story unfortunately about someone who had a stroke to visual cortex. Maybe if you would share that story because I think it illustrates many important principles about what the cortex does. - Right, so the visual cortex you could say the projection screen. The first place where this information streaming from the retina through this thalamus connecting linker gets played out for the highest level of your brain to see. It's a representation, it's a map of things going on in the visual world that's in your brain. And when we describe a scene to a friend, we're using this chunk of our brain to be able to put words which are coming from a different part of our cortex to the objects and movements and colors that we see in the world. So that's a key part of your visual experience when you can describe the things you're seeing, you're looking at your visual cortex, and this is. - Could I just ask a quick question? So right now because I'm looking at your face. - Right. - As we're talking, there are neurons in my brain more or less in the configuration of your face that are active as you move about. And what if I were to close my eyes and just imagine, I do this all the time by the way David. I close my eyes and i imagine David Berson's face. [laughs] I don't tend to do that as often, maybe I should. But you get the point, I'm now using visualization of what you look like by way of memory. - Right. - If we were to image the neurons in my brain, would the activity of neurons resemble the activity of neurons that's present when I open my eyes and look at your actual face? - This is a deep question, we don't really have a full. - It seems like. [indistinct] - Yes, except you're talking about looking in detail at the activity of neurons in a human brain and that's not as easy to do as it would be in some kind of animal model. But the bottom line is that, you have a spatial representation of the visual world late as a map of the visual world lay down on the surface of your cortex. The thing that's surprising is that, it's not one map, it's actually dozens of maps. - What do each of those maps do? - Well, we don't really have a full accounting there either, but it looks a little bit like the diversification of the output neurons of the retina, the ganglion cells we were talking about before. There are different types of ganglion cells that are encoding different kinds of information about the visual world, we talk about the ones that were encoding the brightness. but other ones are encoding motion or color these kinds of things, the same kinds of specializations in different representations of the visual world in the cortex seem to be true. It's a complex story, we don't have the whole picture yet, but it does look as if some parts of the brain are much more important for things like reaching for things in the space around you. And other parts of the cortex are really important for making associations between particular visual things you're looking at now and their significance. What is that object, what can it do for me, how can I use it? - What about the really specialized areas of cortex like neurons that respond to particular faces, or neurons that I don't know can help me understand where I am relative to some other specific object? - Right, so these are our properties of neurons that are extracted from detected by recording the activity of single neurons in some experimental system. What's going on when you actually perceive your grandmother's face, is a much more complicated question and it clearly involves hundreds and thousands and probably millions of neurons acting in a cooperative way. So you can pick out any one little element in this very complicated system and see that it's responding differentially to certain kinds of visual patterns and you think you're seeing a glimpse of some part of the process by which you recognize your grandmother's face. But that's a long way from a complete description and it certainly isn't going to be at the level of a magic single neuron that has the special stuff to recognize your grandmother, it's going to be in some pattern of activity across many, many cells resonating in some kind of special way that will represent the internal memory of your mother. - So it's really incredible? - Yeah. - I mean that every time we do this deep dive which we do from time to time, you and I we kind of like march into the nervous system and explore how different aspects of our life experiences is handled there and how it's organized. After so many decades of doing this, it still boggles my mind that the collection of neurons one through seven active in a particular sequence gives the memory of a particular face and run backwards seven through to one, it gives you a, it could be rattlesnake pit viper heat sensing organs. - Right. - You were talking about earlier. So it sounds, is it true that there's a lot of multi-purposing of the circuitry, like we can't say one area of the brain does A and another area of the brain does B. So areas can multitask or have multiple jobs. They can moonlight. - Right, but I think in my career, the hard problem has been to square that with the fact that things are specialized that there are specific genes expressed in specific neurons that make them make synaptic connections with only certain other neurons. And that particular synaptic arrangement actually results in the processing of information that's useful to the animal to survive, right? So it's not as if it's either a big undifferentiated network of cells and looking at any one is never going to tell you anything that's too extreme on the one hand, nor is it the case that everything is hardwired and every neuron has one function and this all happens in one place in the brain, it's way more complicated and interactive and interconnected than that. - So we're not hardwired or soft-wired? - Both. - We're sort of, I don't know what the analogy should be what substance would work best David? - No idea there, but the idea is that, it's always network activity. There's always many, many neurons involved and yet there's tremendous specificity in the neurons that might or might not be participating in any distributed function like that, right? So you have to get your mind around the fact that it's both very specific and very non-specific at the same time. It's a little tricky to do, but I think that's kind of where the truth lies. - Yeah, and so this example that you mentioned to me once before about a woman who had a stroke in visual cortex,

01:33:33 Neuroplasticity

I think it speaks to some of this. - Right. - Could you share with us that story? - Sure, so the point is that, all those of us who see have representations of the visual world in our visual cortex. What happens to somebody when they become blind because of problems in the eye, the retina perhaps? You have a big chunk of the cortex, this really valuable [indistinct] for neural processing that has come to expect input from the visual system and there isn't any anymore. So you might think about that as fallow land, right? It's just used by the nervous system and that would be a pity, but it turns out that it is in fact used. And the the case that you're talking about is of a woman who was blind from very early in her life and who had risen through the ranks to a very high level executive secretarial position in a major corporation. And she was extremely good at braille reading and she had a braille typewriter and that's how everything was done. And apparently, she had a stroke and was discovered at work, collapsed and brought her to the hospital. And apparently, the neurologist who saw her when she finally came to said, "I've got good news and bad news." Bad news is you've had a stroke, the good news is that it was in an area of your brain you're not even using it's your visual cortex and I know you're blind from birth so there shouldn't be any issue here." The problem was, she lost her ability to read braille. So what appears to have been the case and this has been confirmed in other ways by imaging experiments in humans is that, in people who are blind from very early in birth, the visual cortex gets repurposed as a center for processing tactile information. And especially if you train to be a good braille reader, you're actually reallocating somehow that real estate to your fingertips. A part of the cortex that should be listening to the eyes. So that's an extreme level of plasticity. But what it shows, is the visual cortex is kind of a general purpose processing machine, it's good at spatial information and the skin of your fingers is just another spatial sense and deprived of any other input the brain seems smart enough if you want to put it that way to rewire itself to use that real estate for something useful, in this case, reading braille. - Incredible, somewhat tragic, but incredible. At least in that case tragic, yeah. - Very informative. - Very informative. And of course it can go the other way too. - Right. - Where people can gain function in particular modalities

01:36:27 What is a Connectome?

like improved hearing or tactile function in the absence of vision. - Right. - Tell us about connectomes, we hear about genomes, proteomes, microbiomes, ohms, ohms, ohms these days. - Yeah. - What's a connectome and why is it valuable? - Yeah, so the connectome actually now has two meanings. So I'll only refer to one that is my passion right now. And that is really trying to understand the structure of nervous tissue at a scale that's very, very fine. - Smaller than a millimeter. - Way smaller than a millimeter, a nanometer or less, as that's 1,000 times smaller, or it's actually a million times smaller. So really, really tiny on the scale of individual synapses between individual neurons or even smaller like the individual synaptic vesicles containing little packets of neurotransmitter they're going to get it released to allow one neuron to communicate to the next. So very, very fine, but the notion here is that, you're doing this section after section at very fine scale. So in theory what you have is a complete description of a chunk of nervous tissue that is so complete that if you took enough time to identify where the boundaries of all the cells are, you could come up with a complete description of the synaptic wiring of that chunk of nervous tissue because you have a complete description of where all the cells are and where all the synapses between where all the cells are. So now you essentially have a wiring diagram of this complicated piece of tissue. So the omics part is the exhaustiveness of it rather than looking at a couple of synapses that are interesting to you from two different cell types. You're looking at all the synapses of all of the cell types which of course is this massive avalanche of data, right? - So in genetics, you have genetics and then you have genomics which is the idea of getting the whole genome. - All of it. - And we don't really have an analogous word for genetics, but it would be connectivity and [indistinct]. - Right. [indistinct] - Right, so it's wanting it all and of course it's crazy ambitious, but that's where it gets fun. Really it's a use of electron microscopy, a very high resolution microscopic imaging system on a new scale with way more payoff in terms of understanding the connectivity of the nervous system and it's just emerging, but I really think it's going to revolutionize the field because we're going to be able to query these circuits how do they actually do it, look at the hardware in a way that's never been possible before. - The the way that I describe this to people is if you were to take a chunk of kind of cooked but cold spaghetti. - Right. - And slice it up very thin you're trying to connect up each image of each slice of the edge of the spaghetti as figure out which ropes of spaghetti belong to which. - And have a complete description of where this piece of spaghetti touches that piece of spaghetti is there's something special there obviously. - Meat sauces and all the other cell types and the pesto where it all is around the spaghetti because those are the other cells, the blood vessels and the glial cells. And so, what's it good for? Maps are great, I always think of connectomics and genomics and proteomics, et cetera as necessary, but not sufficient. - Right. Right, so I mean in many cases what you do is you go out and probe the function and you understand how the brain does the function by finding neurons that seem to be firing in association with this function that you're observing. And little by little you're work your way in and now you want to know what the conductivity is maybe the anatomy could help you. But this connectomics approach or at least the serial electron microscopy reconstruction of neurons approach, really is allowing us to frame questions starting from the anatomy and saying, I see a synaptic circuit here, my prediction would be that these cell types would interact in a particular way, is that right? And then you can go and probe the physiology and you might be right or you might be wrong. But more often than not, it looks like the structure is pointing us in the right direction. So in my case, I'm using this to try to understand a circuit that is involved in this image stabilization network we're talking about, keeping things stable on the retina and this thing will only respond at certain speeds of motion. These cells in the circuit like slow motion they won't respond to fast motion, how does that come about? Well, I was able to probe the circuitry, I knew what my cells looked like, I could see which other cells were talking to it, I could categorize all the cells that might be the players here that are involved in this mechanism of tuning the thing for slow speeds, and then we said it looks like it's that cell type and we went and looked and the data bore that up. But the anatomy drove the search for the particular cell type because we could see it connected in the right place to the right cells. So creates the hypothesis that lets you go query the physiology, but it can go the other way as well. So it's always the synergy between these functional and structural approaches it gives you the most lift. But in many cases, the anatomy has been a little bit the weak sister in this. The structure trying to work out the diagram because we haven't had the methods. Now the methods exist and this whole field is expanding very quickly, because people want these circuit diagrams for the particular part of the nervous system that they're working on. If you don't know the cell types and the connections, how do you really understand how the machine works? - Yeah, what I love about is, we don't know what we don't know. - Right. - And scientists we don't ask questions, we pose hypotheses. Hypotheses being of course some prediction that you wager your time on basically. - Right. - And it either turns out to be true or not true, but if you don't know that a particular cell type is there, you could never in any configuration of life or a career or exploration of a nervous system wager a hypothesis because you didn't know it was there. So this allows you to say ah, there's a little interesting little connection between this cell that I know is interesting in another cell that's a little mysterious but interesting, I'm going to hypothesize that it's doing blank, blank and blank and go test that. And in the absence of these connectomes, you would never know that that cell was lurking there in the shadows. - Right, right, yeah. And if you're just trying to understand how information flows through this biological machine, you want to know where things are. Neurotransmitters are dumped out of the terminals of one cell and they diffuse across the space between the two cells which is kind of a liquidy space and they hit some receptors on the postsynaptic cell and they have some impact. Sometimes that's not through a regular synapse, sometimes it's through a neuromodulator like you often talk about on your podcast that are sort of. - Dopamine. - Dopamine, exactly. Oozing into the space between the cells and it may be acting at some distance far from where it was released, right? But if you don't know where the release is happening and where other things are that might respond to that release you're groping around in the dark. - Well, I love that you are doing this and I have to share with the listeners that, the first time I ever met David and every time I've ever met with him in-person at least at his laboratory at Brown, he was in his office, door closed, drawing neurons and their connections. [laughs] And this is somewhat unusual for somebody who's a endowed full professor or chairman of the department et cetera for many years to be doing the hands-on work. Typically, that's the stuff that's done by technicians or graduate students or postdocs. But I think it's fair to say that you really love looking at nervous systems and drawing the accurate renditions of how those nervous systems are organized and thinking about how they work. - Yeah, it's pure joy for me. I mean, I'm a very visual person, my wife is an artist, we look a lot of art together just the forms of things are gorgeous in their own right. But to know that the form is in a sense the function that the architecture of the connectivity is how the computation happens in the brain at some level even though we don't fully understand that in most contexts, gives me great joy 'cause I'm working on something that's both visually beautiful but also deeply beautiful in a sort of a higher sort of knowledge context,

01:45:20 How to Learn (More About the Brain)

what is it all about. - I love it, well, as a final question, I get asked very often about how people should learn about neuroscience, or how they should go about pursuing maybe an education in neuroscience if they're at that stage of their life or that's appropriate for their current trajectory. Do you have any advice to young people, old people, anything in between about how to learn about the nervous system more maybe in a more formal way? I mean obviously, we have our podcast, there are other sources of neuroscience information out there, but for the young person who thinks they want to understand the brain, they want to learn about the brain, what should we tell them? - Well, that's a great question. And there's so many sources out there. It's almost a question of how do you deal with this avalanche of information out there, I think your podcast is a great way for people to learn more about the nervous system in an accessible way. But there's so much stuff out there and it's not just that. I mean, the resources are becoming more and more available for average folks to participate in neuroscience research on some level. There's this famous Eyewire project of Sebastian. - Oh yeah, maybe you let us about Eyewire. - Yeah, so that's connectomics and that's a situation where a very clever scientist realized that the physical work of doing all this reconstruction of neurons from these electron micro-graphs, there's a lot of time involved. Many, many person hours have to go into that to come up with the map that you want of where the cells are, and he was very clever about setting up a context in which he could crowdsource this and people who were interested in getting a little experience looking at nervous tissue and participating in a research project could learn how to do this and do a little bit. - From their living room. - From their living room. - We'll put a link to Eyewire, it also is a great bridge between what we were just talking about connectomics and actually participating in research. - Right. - And you don't need a graduate mentor or anything like that. - Right. So more of this is coming and I'm actually interested in building more of this so that people who are interested, want to participate at some level don't necessarily have the time or resources to get involved in laboratory research can get exposed to it and participate and actually contribute, so I think that's one thing. I mean, just asking questions of the people around you who know a little bit more and have them point you in the right direction. Here's a book you might like to read, there's lots of great popular books out there that are accessible that will give you some more sense of the full range of what's out there in the neurosciences. - We can put some links to a few of those that we like. - Right. - On basic neuroscience. - Right. - Our good friend Dick Masland, the late Richard, people call him Dick Masland had a good book. I forget the title at the moment. It's sitting behind me somewhere over there on the shelf about vision and how nervous systems work. A pretty accessible book for the general public. - Right - Yeah. - Right, so that, and there's so many sources out there. I mean, Wikipedia is a great way. If you have a particular question about visual function, I would say by all means, head to Wikipedians and get the first look and follow the the references from there, or go to your library, or there's so many ways to get into it, it's such an exciting field now. There's so many, I mean, any particular realm that's special to you, your experience, your strengths, your passions, there's a field of neuroscience devoted to that. If you know somebody who's got a neurological problem or a psychiatric problem, there's a branch of neuroscience that is devoted to trying to understand that

01:49:04 Book Suggestion, my Berson Appreciation

and to solve these kinds of problems down the line. So feel the buzz, it's an exciting time to get involved. - Great, those are great resources that people can access from anywhere zero-cost as you need an internet connection. But aside from that, we'll put the links to some. And I'm remembering, Dick's book is called, "We Know It When We See It." - Right, one of my heroes. - Yeah, a wonderful colleague who unfortunately we lost a few years ago. But listen David, this has been wonderful. - It's been a blast. - We really appreciate you taking the time to do this as people probably realize by now you're an incredible wealth of knowledge about the entire nervous system, today we just hit this top contour of a number of different areas to give a flavor of the different ways that the nervous system works and is organized and how that's put together, how these areas are talking to one another. What I love about you is that you're such an incredible educator and I've taught so many students over the years. But also for me personally as friends, but also any time that I want to touch into the the beauty of the nervous system, I rarely lose touch with it. But anytime I want to touch into it and start thinking about new problems and ways that the nervous system is doing things that I hadn't thought about, I call you. So please forgive me for the calls past, present and future unless you change your number. And even if you do, I'll be calling.

01:50:20 Zero-Cost ways to Support the HLP, Guest Suggestions, Sponsors, Patreon, Thorne

- It's been such a blast Andy. This has been a great session and it's always fun talking to you. It always gets my brain racing, so thank you. - Thank you, thank you for joining me today for my discussion with Dr. David Berson. By now, you should have a much clearer understanding of how the brain is organized and how it works to do all the incredible things that it does. If you're enjoying and/or learning from this podcast, please subscribe to our YouTube channel. That's a terrific zero-cost way to support us. In addition, please subscribe to our podcast on Apple and Spotify. And on Apple, you have the opportunity to leave us up to a five-star review. As well if you'd like to make suggestions for future podcast episode topics, or future podcast episode guests, please put those in the comments section on our YouTube channel. Please also check out our sponsors mentioned at the beginning of each podcast. That's the best way to support us. And we have a Patreon, it's patreon.com/andrewhuberman. There you can support us at any level that you like. While today's discussion did not focus on supplements, many previous podcast episodes include discussions about supplements. And while supplements aren't necessary for everybody, many people derive benefit from them for things like sleep or focus or anxiety relief and so on. One issue with the supplement industry however, is that oftentimes the quality will really vary across brands. That's why we partnered with Thorne, T-H-O-R-N-E, because Thorne supplements are of the absolute highest standards in terms of the quality of the ingredients that include and the precision of the amounts of the ingredients they include, in other words, what's listed on the bottle, is what's actually found in the bottle, which is not true of many supplements out there that have been tested. If you'd like to see the supplements that I take, you can go to thorne.com/u/huberman, and there you can see the supplements that I take and you can get 20% off any of those supplements. And if you navigate deeper into the Thorne site through that portal thorne.com/u/huberman, you can also get 20% off any of the other supplements that Thorne happens to make. If you're not already following Huberman Lab on Instagram and Twitter, feel free to do so. Both places I regularly post short video posts, or text posts that give tools related to health and neuroscience and so forth. And most of the time, that information is non-overlapping with the information on the podcast. Again, it's just Huberman Lab on Instagram and Twitter. And last but not least, thank you for your interest in science.