All You Need is Lobe

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**SPEAKERS**

Noah Guiberson, Devon Collins, Leslie Sibener, emily costa

**Noah Guiberson** 00:00

Please put your hands together for Noah Guiberson! Oh, hello, welcome. Welcome everyone. Thank you so much for coming out to a special Brain Awareness Week edition of Facts Machine. My name is Noah Guiberson and I am 1/3 of Facts Machine, a show by and for people who are curious about everything, but especially the things that make them laugh. Now, as you may already know, our theme for tonight's show is neuroscience. And this is very exciting for me because I am a neuroscientist. Yes, I'm very proud. But sometimes I wonder, Am I really a neuroscientist? When I tell my friends and family that I'm a neuroscientist, their questions always presume that I know something about cognition or human behavior. And I feel compelled to backpedal and tell them things like okay, well, technically what I am is a biochemist who studies like proteins that are in the brain. And maybe that's not fair. To me, neuroscience is, you know, a big tent. And there's a lot of ways to study really important questions about the brain. But I can't help but feel a little jealous when other neuroscientists get to do cool shit like this. If you don't know what this is, this beautiful technique is called Brain bow, essentially, by expressing like random different ratios of red, green and blue fluorescent proteins in the nervous system. It allows you to distinguish tightly packed individual neurons from their neighbors. And this had a major impact on the effort to map connections between neurons in the brain. And God, it would be cool not just to know how to do this, but just like to have a reason to. And since I don't know I, I'm feeling a little self conscious about my neuroscience bonafide, so I've invited two real neuroscientists to join us for tonight's show, Leslie Sibener and Dr. Devin Collins will be out here in just a moment. And finally, you know, when you put on a show like this, you never know what the energy the audience is going to be. So I figured I'm out here first, why not do something so vulnerable? So unironic, so heartbreakingly earnest, that you can't help but root for us. Please welcome to stage Rose McCathran. (Noah sings the following to the tune of "Somewhere Over the Rainbow" from The Wizard of Oz.) Do I know how to brainbow? I do not. All I know how to do is 10 kinds of Western Blot. If knew how to brainbow, I'd be cool. And then I'd have somewhere to go after graduate school. Some day I'll graduate from school and hopefully you get asked to do a cool talk. Maybe I'll learn a sweet technique so my CV is not so weak and I'll get a post-doc. I don't know how to brainbow. Is that fine? Folks get jobs without brainbow, right? Then why...can't...I? (Singing concludes.) Please everyone, welcome to the stage, Em Costa, Leslie Sibener, and Dr. Devon Collins. Welcome everyone once again to Facts Machine: All You Need is Lobe. My name is Noah Guiberson and I am joined by two neuroscientists and science communicators, Lesley Sibener and Dr. Devin Collins. I'm also joined as always by Emily Costa, who is not a neuroscientist at all. Instead Em is inexplicably a lung scientist. So well welcome to the stage everyone. I mean, Em of course you've been here many times but Leslie and Devon, welcome. And I'm so glad you could join us. Leslie, when I ask you first, I'm really concerned that I'm not a real neuroscientist, and I'm sorry if you mainly do western blot neuroscience as well. But you should all be concerned for this answer. What? What do you do?

**Leslie Sibener** 05:35

Hello, this is excellent, I'm so excited to be here with everybody. I am truly wowed by the vision of everybody on stage and beautiful singing. But what I do is I do something called Systems Neuroscience. And so neuroscience can kind of be divided into this different hierarchy where you have cellular molecular neuroscience, which it sounds like maybe that's what you're up to with your western blots.

**Noah Guiberson** 05:59

Yeah, I think I feel like cellular molecular neuroscience might be like a pejorative term, I, I did not mean it that way, I might just be very, very self conscious, but I'll take your word for it. Um,

**Leslie Sibener** 06:10

And then what I do is I do systems neuroscience, looking at specifically motor learning. So that's the process of how you're able to learn very dexterous skills, with your hands or with your legs, or all these different things. And specifically, I work with mice. And so I use this technique called two photon calcium imaging...

**Noah Guiberson** 06:29

Give it up for two photons!

**Leslie Sibener** 06:32

Thank you, thank you. And so I basically am able to take these videos that look like lightning flashing in the brain, and you got hundreds of cells at one time. And then you're able to do all this lovely computational type neuroscience by taking all the activity from the individual neuron sets at one time, and seeing how that activity changes as you learn a motor skill. So I teach mice how to play with this little joystick with their forepaw. And they're very cute. They get very good at it. And yeah, that's, that's what I do.

**Noah Guiberson** 07:04

Amazing. So, Dr. Devin Collins, you are the only person on this stage who has actually gotten their PhD. Yeah. So I'm gonna be sort of emphasizing Dr. all night because we love it. Dr. Devin Collins, PhD. Would you tell us a little bit about the research that got you that doctor in neuroscience PhD?

**Devon Collins** 07:33

Yeah. First though, I just want to like a tip of the hat because I've done calcium imaging and it fucking sucks.

**Noah Guiberson** 07:39

Give it up for calcium!

**Devon Collins** 07:42

It is so hard.

**Noah Guiberson** 07:43

That is the technique that you have to drink on tonight, anytime calcium imaging is mentioned. Fortunately, I think I missed that, because I think that's the probably the last time.

**Devon Collins** 07:53

So God, my PhD feels like forever in a day ago. So I'm a behavioral pharmacologist and I was I, when I started my PhD, it was kind of at the peak of the current opioid epidemic. So I was really interested in prescription pills and like, what's different about them, if anything, so I spent a lot of time getting mice and rats high. We like so my lab is really good at a lot of like different behavioral assays, and one of them is called intravenous self administration. And so what we would do is we, it's a little gruesome, but stick with me, not super gruesome. We'd stick a catheter into a mouse's jugular, and we teach them to like administer drugs to themselves, just like a human would do. And so we hooked them up to a little bag of oxycodone or heroin or some other opioid or maybe even cocaine, and they press a little lever, they're given the choice between the drug and saline. And my job was to kind of figure out like, Okay, what's their pattern of administration, if they have like, genetic differences, so we use a lot of like transgenic mice, you know, figuring out like how those different mouse strains self administer, to think about like individual differences in mice, but then, you know, translate those to humans, hopefully. I did a lot of stuff. Some of it worked, some of it didn't but a lot of drugs and a lot of...

**emily costa** 09:25

So you did a PhD.

**Noah Guiberson** 09:29

Also, I wanted to mention so you may notice that you saw in the picture today, Rob Frawley is was not able to join us tonight. He is a very busy science educator for Biobus...anybody know Biobus? Wonderful organization taking a bus full of awesome like microscopes and samples to schools all around the city and I think in other cities to net sometimes, right? It's a wonderful wonderful organization you should volunteer and/or donate lots of money at www.biobus.org. And I just wanted to ask them and so, of course, Rob is a extremely busy science educator. He's a lead community scientist at Biobus so of course, he was too busy to come here tonight. Do you? Where do you work and what is your title?

**Devon Collins** 10:12

So I work for an organization called Biobus. Oh, and my title, get this: lead community scientist.

**Noah Guiberson** 10:20

Whoa. I'm starting to think Rob wasn't really busy tonight. It is almost 10 o'clock. What children was he teaching? We're gonna have to investigate that. But in the meantime, to share tonight's first story about neurosci- Oh, wait, sorry, I'm forgetting someone. Em,

**emily costa** 10:42

Hello!

**Noah Guiberson** 10:43

Why did you choose the wrong graduate program?

**emily costa** 10:47

The wrong program?

**Noah Guiberson** 10:49

Yeah. Well, I mean, field of study.

**emily costa** 10:52

Someone had to do it.

**Noah Guiberson** 10:55

Why don't you tell us a little something about the lungs. Or I'm sorry, what you study with the lungs?

**emily costa** 11:00

Oh, so to really liven the mood, I study lung cancer.

**Noah Guiberson** 11:03

Give it-- no, kidding.

**emily costa** 11:06

Yeah, let's not, let's not do that. But yeah, I study lung cancer, non small cell lung cancer, and a very specific subset of it, where patients have mutations to three genes. We don't really understand how these mutant genes operate together. But we do know that clinically, these patients have really aggressive disease. So what I'm trying to do is model these mutant genes and study them and understand them and hopefully, maybe find a way to target them with therapy. That's what I'm up to.

**Noah Guiberson** 11:37

I am, of course, completely fucking kidding. That is amazing. And the lungs are extraordinary. But we are going to keep ragging on the lungs on it. So for real to share tonight's first story about neuroscience, please welcome to the mic, Leslie Seidner.

**Leslie Sibener** 11:58

That's me. Hello. Okay, so I'm so so excited to be here with all of you today, especially during Brain Awareness Week, great week of the whole year. And so we're gonna start off, I want to ask everybody in this room, we can see this picture of, you know, a crusty lecture hall at some undescribed and described University. And I want to ask you, do you see anything that's missing from this picture? If you do, just like shout it out? Please? I'll give you like 10 seconds. Okay, besides people think, besides people. For me, I am a left handed individual. And so whenever I walk into a room like this, I always am looking for a left handed desk for myself. And so they're usually situated on the aisle. As you can see, they do not exist here. It this is a very tough room. I have taken tests when I was an undergrad in rooms just like this, and it was horrendous. And so as a lefty, there are all of these truly annoying things that you have to put up with all the time. This world was not made for lefties. It's a righties world and I just exist in it.

**Noah Guiberson** 13:07

Give it up for righties!

**Leslie Sibener** 13:12

But you know, I'm not alone in this affliction in the world. roughly 10% of the population are lefties. Are there any lefties in the crowd? Please raise your hand. Yes, thank you. Thank you. Thank you instant kinship. Thank you. And so just to give you a little bit of background, we're going to do some etymology or what I like to say left homology credible. Thank you. And so left handed as we use it today is actually derived from the word lift from Old English, which actually means weak and you know, I'm not that weak, I can do pull up so not bragging. And then in other languages, it evolved also with very negative connotations and French gauche meaning awkward clumsier in this day and age. dreadfully you know unfashionable. But the oldest one that I really like, is sinister, which comes from Latin, which means unlucky, but as we know, this has really taken on a horrible horrible meaning in in this days world and so it's, you know, evil and very, very wicked. But what's hilarious is that sinister is actually still commonly used all the time every single day. You're especially in the medical field. So being left handed is technically called sinister reality. So that's tough.

**Noah Guiberson** 14:31

That I think we talked about this that the, the, like Coat of Arms of Australia, it's like because in heraldry they use like sinister to me like on the left side and dexterous me on the right side. So the coat of arms on Australia of Australia has a sinister emu.

**Leslie Sibener** 14:45

I mean, that's it's pretty Yeah, I mean, I, you know, I love being lefty, this is this is building to that. But along with all these words, so much stigma has arisen that there are all these different common day phrases that are really anti left handed is what I'll say. So we have two left feet, which is being extremely clumsy, as you know, left handed back in the 19 century actually, was referred to as homosexuals. Born from the left hand really intense, an illegitimate child, left footers. Back in the holy wars, religious wars, Catholics or Protestants were called left voters depending on what majority area you were residing in. And the left hand path is obviously the devil's path or black magics. Because if you really think about it, right, he's got all of these really great things associated with them. And really, the original right hand man is Jesus. Jesus, in many, many famous depictions of God, and Jesus in paintings, this is a lovely painting by Alaska's. But you can see Jesus depicted on the right hand of God. So you know, Lefty is we have like the devil on the left side of God. So that's me. And because of all of his bad reputation about being left handed, there's a long history of left to right hand conversion throughout the world. Even to this day and age, as recently as in 2007, a study done in Taiwan showed that 53% of left handed individuals were actually converted to being right handed. That's really tough. But this type of conversion can actually lead to things like dyslexia, stuttering, and a lot of emotional distress. And I think the most famous depiction of this that maybe some people have seen here is from The King's Speech, King George's sixth was born, a left hander was converted to being righty. And as now a Oscar winning stutter, evolved from that individual. Thank you, Colin Firth. And so you know, even though there's this really bad reputation, there's also some really fabulous, influential, powerful lefties in the world, which I'm proud to be a member of. So we have Leonardo da Vinci, people like Mozart, Barack Obama, Marie Curie, and so many other fantastic people, you can just like screw, like, look at all of these things and see that these people, sorry about that. All these people, they're fantastic. If you're able to screw them, you're really lucky. And so really, now we're, that was really a long tangent, because I never got to just rant about being a lefty and how unfair everything is. But to my delight, in 2020, there was something that came to my attention that combined three very important aspects of my identity being a left handed individual being a woman, and being a neuroscientist. And that was in a paper called human olfaction. Without apparent olfactory bulbs, this came from the Weizmann Institute. And so how in, in this study, I'm going to talk to you about it. But first, I'm going to give you a little bit like olfaction, one on one. So olfaction is your ability to smell. And so this all starts with different smells out in the world or in New York, maybe there's some you know, hot garbage, some fresh urine. Maybe if you're lucky, there's actually like freshly baked bagels. And as you inhale, these odorants flood inside your nasal cavity and your nasal cavity is lined with the olfactory epithelium. And in that epithelium, there are the ends of olfactory receptor neurons that when they come in contact with these odorants, they become activated depending on if there's a match between the odorant and the specific type of olfactory receptor neurons there, millions of them. And so then this is where all this smell information jumps into your brain from your nose, they get activated, these olfactory receptor neurons get activated, send action potentials into your brain and get to the olfactory bulb. So this is what this paper is studying. And so in the human, if you take an MRI scan of the human brain, you can see the olfactory bill really just looks like these two dangly balls.

**Noah Guiberson** 19:06

Yeah. Caught me, caught me laughing at that.

**Leslie Sibener** 19:12

And, and so they're very, very apparent, easily identifiable. And so in this study, classic science, they were not trying to do anything with olfaction they were just scanning individuals for another random study. And so this accidental discovery, they scanned a left handed woman and found that something was missing like the dangly balls weren't there. And so then they're like, Wow, that's really bizarre because this individual she didn't report any effects to her ability to smell she you know, existed her entire life thinking I can smell everything the same as anyone didn't even think there was an issue and there wasn't. And so what they ended up doing is they ended up searching for more and more left handed women because we're awesome. Um, and on before they even Got to the 20th individual to scan they found a second lefty woman who had no olfactory bowl but had no recollection of any issues with her ability to smell. That's, that's crazy. And so what they ended up doing is they dove into this research by comparing now an individual who had normal and tactile factory bulb, the two lefties who did not have olfactory bulbs, and then an individual who had something called Congenital anosmia. And so this individual was born without an olfactory bulb, and cannot smell so being an asthmatic on there are many innocent people in the world. And they unfortunately cannot delight in the sense that permeate through the world. And so then, what they ended up doing is they were first just looking at different areas of the brain and seeing Okay, does this area of the brain look normal, even though there's no olfactory bulb, so a few main areas that are associated with olfaction, we have the olfactory bulb, this is from a different view. And that you can see that they basically send the projections through the olfactory track, and they get to the cortex. There are many different areas associated with olfaction. But one is the Piriform cortex. And they saw that the anatomy of the boltless women were exactly the same, there was no difference, while the Nazarick individual, the person who could not smell her, she did not have an olfactory track. And then they looked at representation, which is basically putting them not in an MRI, but an fMRI or a functional MRI scanner, and gave them things to smell to see if their brains lit up in the same areas. And in the same way. And sure enough, the women who did not have olfactory bulbs still had different cortical areas that were lighting up to smells. Even though they did not, they didn't have the olfactory bulb, which is as you remember, like the first sight in the brain where you're supposed to have all of this olfaction information coming in. And so then my personal favorite behavioral tests they did, they did something called sniffing sticks. It's not even not even G just ended an apostrophe, but sniffing sticks. And using this behavioral test specifically for your sense of smell, you get this readout called TDI, and that has three different components to it. One is threshold. So how much of a smell do you have to be given before you say, Oh, I think I smell something. And then there is identification, which is saying, Okay, I'm giving you this smell, what is it? And then discrimination, I give you many smells, and you have to tell me, which each smell actually is. And so you know, unsurprisingly at this point, the two individuals who had no factory bulbs had, you know, the same scores as the regular person who had the olfactory bulbs intact. And so in this graph, you can see the three of them floating up there at the top with high TDI scores. And then the individual with congenital anosmia is actually like way down. And this makes sense, like, that person can't smell anything. Of course, they can't have, you know, any high scores in this type of test. And so really, what they did next is they looked for just more scans of left handed women to see okay, is this just like a crazy phenomenon that we stumbled upon? Or is this a real thing that's happening. And what they did is they went and looked into the Human Connectome Project, which is has lots of lots of brain scans that they were able to access and look at. And basically looking at that data, they found that there were more left handed women who did not have olfactory bulbs, but whose olfaction was not impacted. And so extrapolating from that data, they estimate that roughly 4.25% of left handed women are able to smell without olfactory bulbs, and that's about Yeah, 32 point 9 million individuals in the world who just don't have this area of the brain, but are, you know, going about life, totally normal. And so they had some ideas about how that might happen. They have some thoughts that maybe the olfactory bulb migrated or was reshaped in some way. They thought that maybe it was just too small to be seen on the scan. But I don't think that that's really possibility. Compensation. There are many other sensory modalities that we use in our everyday life to just get around. So maybe there was some other way that they were figuring out the smells and having experiences that they truly believe were smells, or there's some sort of unique coding mechanism that makes them able to smell without having the olfactory bulb, but my personal favorites, I think that we're just all witches like left handed. We're crazy. You just do cool stuff. And so personally, for me as a neuroscientist, I am just like desperate and clamoring to get my own brain scanned to know if I have this or not, do I have no factory? Well, I don't know. I think I can smell fine, like I really do. But unfortunately The sad tale is that in so many human MRI studies which I have reached out to people, my friends who are running these studies, I say, Please let me in your study, I desperately want to get a scan of my brain. And they always turn me away because left handers are excluded from the Yeah. Anyway, we're just so left out all the time.

**Noah Guiberson** 25:34

Keep it going for Leslie Seidner. Now, for the second neuroscience story of the night, please welcome to the mic, Dr. Devin Collins, PhD.

**Devon Collins** 25:56

All right, y'all, I am a man of the future. So I have my notes on my phone. But since there are people looking at me, I forgotten how to use it. All right, cool. All right. So Oh, that's my face. I have less hair now. But that's okay. All right. Oh, no, no, no, no, wait, okay. Okay. All right. So, um, I've got a couple jobs, not only in my neuroscience, a neuroscience researcher, and a lead community science scientists at Bio Bus. And my other life. I am a neuroscience teacher at a school that's actually like, down the street, here on the Lower East Side. And at the beginning of every semester, what I do is kind of an embarrassingly like, brief overview of select neuroscience history topics. I talked about people like Phineas Gage, give it up for Phineas Gage. Phineas Gage, I talked about Paul Broca. I talked about the OG like Ramon Iike Hall. Yeah, yeah. But what I realized and getting ready for tonight is that I somewhat shamefully leave out pharmacology history. And in my other life, being a behavioral pharmacologist, that's that kind of sucks. So I thought I would make it up to, to all the behavioral pharmacologists out there, by telling you a little bit about the history of a drug that has occupied a huge portion of my own professional life. And it's like weighed heavy on human history. So here's what we're gonna do. We're going to talk about heroin. So you can't talk about the history of heroin without talking about the story of this humble flower. Papaver somniferum. Did I say that right? Yes. Or more commonly known as the opium poppy, and poppies have given us a lot of cool things, or at least interesting things, one of them being the delicious, delicious lemon poppy seed muffin. But also, something not so cool. But also really useful is opium.

**Noah Guiberson** 28:00

A little Column A, little Column B... Column A little column B, it's

**Devon Collins** 28:02

Yeah little Column A, little Column B, it's great, you know. So what you see on the right is a milky latex. It's technically a latex, coming from the seed pod of, of the opium poppy. And humans really love opium and we have like, thought about it for a really long time. Opium like preparations show up and like ancient Greek manuscripts. Speaking of the Greeks, Homer kind of put in in the Odyssey, there's a drug called Nepenthe A, and it means the drug of like anti sorrow, or the drug of forgetfulness, or bliss. And Helen gives a mixture of wine and depend day to OTCs his men when he pieces out, and they're really sad about it. And then, of course, of course, keeping with our like, Wizard of Oz.

**Noah Guiberson** 28:55

Secret theme.

**Leslie Sibener** 28:56

Not so secret theme.

**emily costa** 28:57

Increasingly less secret.

**Devon Collins** 28:58

So forget Dorothy's nice sleep aid given to her very graciously by the Wicked Witch of the West field of poppies. So humans really, really fucking love opium. And it turns out that it's because there's some really fun magic ingredients in opium. One of them being morphine, it's like the chief active ingredient in opium, so it's doing like the lion's share of the work. But there are a couple of other things. There's codeine, which you've probably heard of, but what you might not have heard of, is this other thing called thi vein, which is like naturally occurring in opium but it's not as fun as codeine and morphine. It's not great for getting you high, but it is really good at giving you convulsions at the right dose so if you're into that the veins for you. But if not, don't worry, it's it's actually not that useless. We can chemically convert it and some really like useful painkillers like oxycodone, and something called Naloxone which is used to reverse opioid overdoses. So the ban is, is not a jerk. It's just misunderstood. So, so much like the vein actually opium and its derivatives have kind of a dark side, I did a search for literally a Google search for evil Poppy. And that's what came up. The internet will always provide, um, so

**emily costa** 30:24

I was going to say that's sinister, but I know better now. Yeah.

**Devon Collins** 30:29

So if you're like me and you, well, maybe you're not like me, I don't know. But there have been a lot of folks who have been really interested in that dark side. And one of the most important as we're talking about heroin, is this guy, Charles Romley. Adler, right. And he was a chemist working at St. Mary's College, in London in the 1870s. And he was really interested in the problem of of morphine addiction. And so he really didn't like dislike this problem of addiction. So he was looking for alternatives to morphine. I'm not funny, okay. No, he was looking for alternatives to morphine that would be safe and non addictive. Spoiler alert, he didn't find it. But he did come up with something really interesting. So it turns out that not only C bein is a really great starting point for making new opioid drugs. So he started with morphine. And he stumbled upon this process called acetylation. Basically, he boiled anhydrous is great, excuse me, anhydrous morphine with a compound called acetic anhydride. What do you see is these little these little groups on this morphine backbone. Those are acetyl groups. And so he named it diacetylmorphine, really great name. He made this new compound. And he was really interested in seeing what it did. So he sent it to a colleague of his name, FM peers. And he injected this into young dogs and rabbits. And I'm not going to read this whole thing. But I have a couple of highlights here that I want to share with you. So the effects of diacetylmorphine and these rabbits and dogs was great prostration sleepiness, a slight tendency to vomiting but only in some cases. And my personal favorite, a diminution of the temperature of the rectum about four degrees. I just, I love that it's about four degrees. Wait.

**Noah Guiberson** 32:27

Yeah, great question Celsius or Fahrenheit.

**Devon Collins** 32:31

That makes a big difference. I mean, these were men of science. I don't know. So, so they, they they ended up what they ended up with was, instead of a drug that was like, less potent or are ostensibly safer than morphine, they ended up with something that's about two times stronger than morphine. So they didn't find what they were looking for. So they largely like abandoned, they abandoned diacetylmorphine. And it kind of disappeared until about 23 years later, in Germany, another chemist named Felix Hoffman working for Bayer was looking for ways to isolate or make codeine out of opium, and maybe a couple of other things. And little known fact, or maybe you know, this, I don't know. He is the guy who also invented aspirin, which is acetyl salicylic acid. So he really loved putting acetyl groups on things. And so it's no wonder that he stumbled upon the same method for acetal ating morphine, that Wright had come up with about a quarter of a century earlier. The Bayer group, they also kind of found like it was about two times more potent than morphine. It wasn't what they were, you know what, it definitely wasn't codeine, and it wasn't, definitely wasn't like less addictive than morphine. But they didn't care. They slapped a brand name on it, and gave us the name heroin. And they said--

**Noah Guiberson** 34:06

Wait a minute. They were looking for a less addictive drug than opium. And they created heroin. They wouldn't let me graduate if I brought that in. Like--

**Devon Collins** 34:20

It was a different time, man. Yeah, they didn't they didn't have western blots. They didn't.

**Noah Guiberson** 34:25

How can you even do science without Western blots and two photon calcium imaging?

**Devon Collins** 34:34

so they marketed the shit out of heroin. And you can actually see like, a couple of their ads here one on the left is like this, like just a little insert, you know for like getting information about heroin, and you can see aspirin there too. But they also had this read they like they were just really into marketing in Spanish language. until like, for kids like for cough syrup and like Spanish speaking countries. It's like, I found like five of these things. And they're all worse than, like, each one is worse than the last. But I just want to point out this kid's eyes. Like he, he does not care about his coffee.

**Noah Guiberson** 35:16

Does that look likea bottle of Jagermeister a little bit?

**Devon Collins** 35:18

It's kind of--it does k--yhat's what it looks like! Oh, yes. All right.

**Noah Guiberson** 35:23

Should I be proud of that? Alright.

**Devon Collins** 35:27

We can share our show.

**Noah Guiberson** 35:29

Hey...cigarette after the show.

**Devon Collins** 35:31

Alright. So um, so that is basically that's how we got heroin, right? But why is it? Why is it a lousy substitute for morphine? All right. So like many other drugs, like us, like all other drugs, when morphine or heroin or opium enters the body, goes through a couple different processes, you got to absorb it, it's got to move through the body to different places get where it's going. And it has metabolized, and maybe you found my favorite part of this. It's like the boys, yeah. And this guy's got triangle poops.

**Noah Guiberson** 36:12

I don't see anything wrong with this. It's amazing.

**Devon Collins** 36:14

So. So the basically, right--

**Noah Guiberson** 36:20

I'm sorry, I can't help myself, doo doo or do not, there is no triangle. Thank you.

**Devon Collins** 36:28

So basically, the takeaway is that the drugs got to get to where it's going. And it's got to, you know, it's subject to a couple of different processes. So one of the places are in stencil to be the most important place that morphine and heroin and other drugs go is the brain. And you can see here, this is actually this is, when I don't want to go too far into it. This is showing you the binding sites for morphine and other opioid drugs in the brain. And they're kind of concentrated in these little areas that you'll see in a second are really important for the way that we process pleasure, among other things. And the thing about heroin is that it's really fucking good at getting into your brain. So it turns out those little acetyl groups help it bypass this natural barrier that exists between your blood and your brain. And it's aptly named the blood brain barrier. And it's formed by these different cells in around brain capillaries that cover and form these really tight junctions in between, in between themselves, and are in between each other. Yes. So that they blocked things from leaking into the blood from the brain that shouldn't go into the blood. And vice versa, they keep things from the blood that shouldn't be in the brain, your brain is really important. It's a very privileged space. And you can actually see that right here. And this really cool fluorescent microscope image. The green is all of these different. They're called astrocytes that wrap themselves around the capillary, which is this like black space here. So that's where the blood would be. And then inside is on the other side of that is brain tissue. So it's really forms a barrier that you can literally see. And the thing about those two acetyl groups on the heroin is that it helps pull, it makes it really what's called lipophilic. It loves fat, and your cell membranes are made of fat. And so it just goes right through. Whereas morphine would have a little bit of a tougher time, also gets actively pumped in. But we won't talk about that. So what I've got here to kind of illustrate that is it actually these really old papers, not really old, but they're like, not super new. So on the left, what you're looking at is the concentration of in the blood of heroin and its metabolites after an IV injection, and on the right is the amount in the brain. And what ends up happening and it's a little different than morphine is heroin gets into the brain really, really fast. And in almost instantly, within a couple of minutes, it's converted into a couple of things. This chemical in the middle here called Six mono acetyl morphine, so it takes one of the acetyl groups off, and it actually turns into morphine itself. So instead of just getting a little bit of morphine, you get a shit ton of morphine hammering away on the brain after just a couple of minutes. So it gets in there within the first like three to 15 minutes, then you start building up this huge amount of mono acetyl morphine, which is really active. And then over time, you get a steady amount of morphine building up. So you end up getting more and morphine than you would with just morphine alone. And that has some really important effects on this neurotransmitter system here called dopamine, which has a ton of different functions in the brain, including movement and habit formation, motivation and reward and planning and a place called the free frontal cortex. It's really important for things like oh, my gifts are gone. Oh no. It's really important for things like, like pleasurable things like eating positive social interaction, listening to things like music. Michelle was listening to music and like Just absolutely bopping out. Or some time with your special person, something like that. And dopamine is really important for kind of teaching your brain about what's good. So you get a little bump of dopamine when something great happens, your brain knows we should do that, again, that was really cool. Drugs, however, especially heroin and morphine, just take that and like ramp it the fuck up. So you end up getting this like unnatural dopamine curve. And it kind of disrupts all of that biology. So that hammering away with the with the morphine really disrupts all that brain biology. So the last thing I want to talk to you about is just what does that look like for behavior. So this is a paper by actually, this person, creek here with with Vincent Dole and Marie nice wonder Creek was my PhD advisor, oh, they actually were really interested in the problem of opioid addiction as well in the 1960s, with the heroin epidemic in New York. And so they looked at the typical pattern of heroin injection in users in New York. And they found that across the day, they were injecting multiple times to kind of titrate and keep that amount of heroin and morphine in the system at kind of a constant level. And it was an up and down that really causes those those problems with the brain and the changes in function. Here they are right there. This is Vincent dome, or a nice wonder and the late maraging Creek, who was my thesis advisor, and I don't want to leave you on a bummer. They didn't just like, you know, look at people injecting drugs, they also figured out a solution. By finding a couple of other chemicals, they went through an old library of chemicals that were actually was actually seized after the Second World War. So Germany gave us methadone as well as and as well as Bayer's heroin. They found methadone. And methadone is really cool, because what it does is it kind of flattens out that curve. So it gets rid of drug craving it and it makes it easier to manage the symptoms of a heroin addiction among others, than just you know, talk therapy alone or just trying to quit cold turkey. So I hope that you have seen that heroin has a really sordid history, and that the puppy has given us a lot of things. And just looking around at a couple of different chemicals and kind of flicking around and finding out can lead to some tragedy but also lead to some great things. So yeah, thanks.

**Noah Guiberson** 42:43

Keep it going for Devin Collins. So for a third and final neuroscience story tonight, please welcome a breath of fresh air. The Wind Beneath My lungs. Lung scientist Em Costa

**emily costa** 43:12

Yeah, yeah, I heard what you said before.

**Noah Guiberson** 43:16

What's that? Interesting.

**emily costa** 43:23

Hear that? That was 40 hertz, the audio frequency. And that sound along with a much more pleasant one. Could one day alleviate epilepsy by altering the music in our brains? So what what is my face? So what do I mean by music in our brains? Well, our brains make music, sort of, at the very least they have rhythm. You may have heard the phrase neurons that wire together fire together, and it's true. You're on set operate. Oh, it's like this is just off the rails if I'm already wrong. Okay. So what is it again? Neurons that fire together, wire together, fire together, neuroscientists, this is a real thing, right?

**Leslie Sibener** 44:12

It's the other way around. It's fire together wire together.

**emily costa** 44:15

Alright,

**Noah Guiberson** 44:16

Leave her alone! She's a lung scientist!

**emily costa** 44:20

(in unison with Noah) I'm a lung scientist! Thank you. We are sticklers for accuracy as a fax machine. Perfect. Neurons that fire together wire together. And it's true. Neurons that operate together in a network electrically fire together. And this coordinated firing in multiple networks results in repeating patterns or oscillations of electrical activity known as brain waves. So there are five kinds of brain waves. And they're named for their frequency. So we have delta theta, alpha, beta and gamma. And these waves are oscillating in our brains at various times and in various places. And we measure brainwaves using electroencephalography. And, yes, we're EEG through electrodes placed on a person's scalp or sometimes even inside of their brains. So brainwaves are associated with specific neural processes. And we think that synchronization of different brainwaves helps different parts of our brain communicate with each other. So for example, gamma and theta waves which both occur in the hippocampus and in the frontal neocortex have been observed to sync up, and we think that might have roles in cognition and memory. We've also noticed, and brace yourselves, that our brainwaves sync up to external stimuli that occur at similar frequencies. So for example, flickering lights, music or sounds, even rhythmic finger tapping. And this means that we can consciously expose ourselves to rhythmic stimuli to alter our brain activity. Okay, so this is, first of all, totally ridiculous. But it also has real potential to treat or at least reduce symptoms in patients with neurological diseases. And there have been lots of studies over the past few decades, exploring this potential. So I'll give you one example from a lab at MIT, looking at treating Alzheimer's with light that flickers in a game of frequency. So gamma waves are significantly reduced in the brains of Alzheimer's patients, and applying this light therapy and mouse models of Alzheimer's cleared protein aggregates or plaques that are a hallmark of Alzheimer's, restored memory and learning ability and literally prevented neuron death. And that's what's shown here. So these are images of mouse brains with different cell types and different colors. And the main thing to note is this black, oh, there she is, is this black gaping hole where brain should be. And it's only in the Alzheimer's mouse, but it's not present in the control normal mouse. And it's also not present in the Alzheimer's mouse that received light therapy for an hour a day. So just blinking lights, rescued neurons from dying. It's crazy that I mentioned epilepsy as a disease folks are studying this phenomenon in and there are numerous studies showing that brainwave syncing stimuli, particularly of an auditory nature, could reduce the number and frequency of seizures and epilepsy patients. So One such study came out last year from the epilepsy and cognition or ECOG. Lab at Dartmouth. They previously saw positive effects from playing that 40 hertz sound that you just heard for epilepsy patients. But the only problem was like you, the patients did not enjoy it. They were like, can we listen to anything else please? So in hopes of finding a more pleasant Sonic experience with the same therapeutic effects, the researchers turned to...MOZART!

**Noah Guiberson** 47:50

Somebody said Taylor Swift.

**emily costa** 47:51

Maybe not yet.

**Noah Guiberson** 47:53

Very much the Mozart of our age.

**Leslie Sibener** 47:54

Mozart's a lefty, it was on the slide.

**emily costa** 48:01

Yes, there we go. Perfect. Man, it's true. can't catch a break. But to poll the crowd has anybody here heard of the Mozart effect? Anybody? Hands up? Yes. And all the early Millennials just outed themselves. So yes, the Mozart effect was a really fun romp in pop pseudoscience that happened in the mid 90s. So the idea came from this one study where they played a Mozart piece, the Sonata for two pianos and D Major pay for 48. For some undergrads before they did a spatial reasoning test. The very and I want to emphasize very modest results of that study appeared in headlines as Mozart makes you and also your babies for some reason smarter promote, prompting the creation of Mozart self help books and mixtapes and headphones size to fit pregnant bellies, I presume, and prompting the governors of Georgia and Tennessee to spend upwards of $100,000 on Mozart CDs for school kids in their states. Turns out they can follow the science and from public education when it suits them. Maybe it's a branding thing. I don't know. I am making a lot of enemies tonight. So this fad, along with inconsistencies in the protocols and tech used in research about K 448. The Mozart piece and epilepsy, left the Mozart effect shrouded in skepticism for a number of years, until equipped with a fancier tech, bright young minds and an eclectic playlist, the ECOG lab revisited it. So here's what they did. They enrolled 16 human participants all with a drug resistant epilepsy and played each of them clips from the following playlist. Mozart, k 448. Other classical stuff, Wagner blissed yada yada, violent noise familiar with yada yada, yada yada, to listen to, it's truly changed the game, violent noise, which is like a high pitched frequency that increases with time, k 448. But with some frequencies filtered out, and then three songs from the participants preferred genre, with or without some lower frequencies artificially boosted. So the purpose of all these options along with the filtering and the boosting, was to pinpoint exactly what musical features produce the Mozart effect. And to see whether the the effect was actually unique to Mozart, k 48. So, as participants listened to the music, the researchers measured how frequently they experienced IEDs, which are these unique spikes that appear in EGS of epilepsy patients. And the idea was that a potentially therapeutic song would reduce the number of EDs IDs, excuse me. So to briefly examine the preferred genre thing a little further. So the options were country heavy metal and rock'n'roll, which like, okay, fine, but one of the two heavy metal songs wasn't Nickelback, which seems squarely at odds with their goal of finding enjoyable music. You know, like, you know, they admitted that from the grant proposal. They don't even show data collected during the Nickelback song. Here it is. Thank you, you're all very kind. I mean, if they're really looking for music people like why not include Africa? By Toto? That's right, I followed the assignment.

**Noah Guiberson** 51:39

Secret, secret assignment

**emily costa** 51:40

If you say so. So here's what they learned. At least 30 seconds of listening to the original unfiltered Mozart, k 448. Reduced IDs by two thirds in participants. Wow, cool. Literally everything else did bubkis Mozart one, all other popular music since the 18th century, but especially Nickelback. So what gives What's so special about K 448? Well, the researchers analyzed the musical features of K 448, like harmonies, and tambor and they divided the piece into segments based on these features. So the boundaries between segments are the points where the music shifts, or changes direction. And that's shown in this image here, which is admittedly like way too high level for me to totally understand. But it shows how the segment's appear across the sound frequency spectrum. So you see these kind of clear sort of edges, like in that kind of pink gradient, that demarcates the boundaries between the segments. So to kind of look at this a little more myself, I picked a boundary that they identified, and I figured out where it happens in the sheet music. And sure enough, there's definitely a musical shift. So the green box over the boundary matches the green box and the sheet music. And you can clearly see that just by looking at the notes, one melody ends, and then you have the boundary and then another completely different melody begins. And the researchers noticed that whenever participants heard one of these boundaries, their frontal lobe started cranking out lots of theta brainwaves. And from prior studies, we know the same kind of relativity happens when we feel a positive emotional response to music. And when we are confronted with sudden changes in music and things like volume, tempo, or key changes. In both situations, we also pay more attention to the music. So the hypothesis is that when we listen to Mozart, K448, it sounds nice to us. It makes us happy. So we listen to it more closely. And then it catches us by surprise and defies your expectations. So we listen to it even more closely. And all of that translates to this heightened activity in our brains that might be therapeutic for patients with epilepsy. So there are still, of course, lots of questions to be answered. And we're a ways away from being prescribed playlists or light shows. But in light, not even intentional, laughing my own jokes. Of all the ways that music already helps us to connect to cope to express ourselves. It's kind of amazing to think that someday, it might even help us tune up our brains. Now, so hold Thank you. Thank you, thank you but hold your applause because our amazing pianists Rosemarie Catherine and Ryan Breck mocker will now grace us with an excerpt from Sonata for two pianos and D Major K448. And I encourage you to please feel free to groove along with your brain waves as you listen, but also feel equally free to clap and cheer and holler like they did in Mozart's day. By the way this stiff like proper listening to music silently? No, no, no, no, no. Get rowdy. That's how it's supposed to be and it's warranted. As mentioned, this sonata rips, so.

**Noah Guiberson** 52:31

Hell yeah.

**emily costa** 52:59

Keep it going for our incredible musical accompaniment. All right the moment we've all been waiting for: the trivia answers. Which one of the following statements about chicken intelligence is not true? A chickens can recognize more human faces than humans can be. This chicken social structure is called the pecking order. See, chickens are able to able to do basic arithmetic or D roosters will pretend to find food so that a hen will approach what did y'all put?

**Leslie Sibener** 57:08

A is not true.

**Noah Guiberson** 57:10

That is correct. A is not true. That would be insane that someone put that? Okay. That would be ridiculous.

**Devon Collins** 57:25

Could they count the number of faces that they can recognize?

**Noah Guiberson** 57:29

Good question. They can do arithmetic, basically addition and subtraction with numbers up to five. So it turns out the number of human faces they can recognize was like, like 700, which is still pretty fucking impressive. Like humans were like 1000s. So it was Yeah. Anyway, question

**emily costa** 57:49

Still pretty good! 700...

**Noah Guiberson** 57:50

What part of the brain is named after a mythological creature in Greek and Roman mythology with an equine head and a piscine tail?

**Devon Collins** 57:56

We guessed hippocampus?

**Noah Guiberson** 57:58

Of course you did! Because the answer is hippocampus. Everybody knows about the hippocampus, right? hippocampus basically comes from the Greek for horse and sea monster with hippocampus respectively, sometimes depicted drawing Poseidon's chariot. In the brain, this is a very important area for like learning and memory. It's one of the most famous areas the brain. Who's heard of the hippocampus? Give it up for the hippocampus! Question three, the human enteric, and by enteric that means gut, nervous system has roughly the same number of neurons as there are in the whole brain of a a mouse, be a rat, see a cat or d a horse?

**emily costa** 58:38

Well, our guts told us that the answer was C cat.

**Noah Guiberson** 58:45

That is correct. Your gut is very very smart to tell you that your gut has about 500 million neurons which is sort of on the order of the number of neurons in a cat's whole brain. Question for in The Wizard of Oz when the wizard awards scarecrow diploma what mathematical theorem does scarecrow misquote?

**Leslie Sibener** 59:06

Luckily, the Wizard of Oz is my favorite movie. I did not integrate it into the theme tonight. It just happened. And it's the Pythagoras theorem.

**Noah Guiberson** 59:14

That is absolutely right. When the wizard it's when scarecrow is like I'm so sad. I don't have a brain the wizard says I think it's something like you can correct me if I'm wrong here. Basically, it's like where I come from, which was I was basically the you know, like United States so like there were there are people who had no more brains than you and yet what they had that you don't is a degree or a diploma. And so he writes out him I think it was like a degree in like, intellectual ology, some something like that. And then as soon as he's handed it, Scarecrow says the sum of the square roots of any two sides when I saw Sully's triangle is equal to the square root of the remaining side, which is wrong. But in fact, just in case anyone's key and score which we are be. The real Pythagoras theorem is the sum of the squares of the legs of a right triangle is equal to the square of the hypotenuse. Question five. Yeah, how nutritious is zombies diet anyway? About how many calories are there in an average human brain?

**Devon Collins** 1:00:16

Little more than what you need in a day? 2500?

**Noah Guiberson** 1:00:19

Yes, that is correct. See 25 That's just true. There is a paper that was like, let's figure out how many calories it would be in all the organs. It's fascinating. And growth. Question six while to Dale chicks love chicken neuroscience here. I actually really, really do because it's one of the like, the really like classic neuroscience, model animals and one of the people who like along with Rita Levi Montalcini, very famous, extraordinary neuroscientist who worked on chickens with a person named Victor hamburger. And to Dale chick chicks know that objects removed from view still exist, but humans don't until about six months, what is this ability called?

**emily costa** 1:01:01

Object permanence!

**Noah Guiberson** 1:01:02

That is correct! Question seven, when glia were first discovered in 19th century, they were called Nervin kits, a German word meaning what?

**Leslie Sibener** 1:01:14

That would be nerve glue.

**Noah Guiberson** 1:01:16

That is correct. Nerve glue. They originally thought that glia were the stuff that sort of like stuck everything together. glia also, so nerve and kid is just basically German for like nerve putty, but it was sort of meant like nerve glue. And glia comes from the Greek word that means essentially glue. So that's interesting. Question eight. That's a final question for tonight. Aristotle believed that the heart was the seat of sensation and thought and that the brain played only a support role. What did Aristotle believed the brain did to help the heart?

**Devon Collins** 1:01:49

So he thought that it was a radiator that cooled the blood.

**Noah Guiberson** 1:01:53

That is exactly right. The brain cools down the heart. That's what Aristotle thought it was like the whole purpose of the brain. He thought cognition and stuff happened here. But you shouldn't think that this was like something a lot of people thought in fact, a lot of people before during and after, like immediately after Aristotle's like preeminence. We're like this is wrong. This is just absolutely wrong. But I do want to break before we finish trivia I want to tell you that yes, radiator is also exactly the word that was in the the stuff that I Googled about this.

**Leslie Sibener** 1:02:25

He's a PhD so he knows these things.

**Devon Collins** 1:02:27

I deserve it.

**emily costa** 1:02:28

That's it.

**Noah Guiberson** 1:02:30

You know how like at the thesis defense when like they kick everyone else out? Is that where they tell you what Aristotle thought?

**Devon Collins** 1:02:35

That's where they tell you what Aristotle thought. Don't tell anyone though. They'll take my PhD away.

**Noah Guiberson** 1:02:41

Livestream watchers all around the world: please close your eyes and ears...just close all your...holes. Fuck. I do want to read you something Aristotle wrote in two things. Aristotle from The Parts of Animals: "Of course, the brain is not responsible for any of the sensations at all. The correct view that the seat and source of sensation is the region of the heart", and then in a different treatise it says, from Sense and Sensibilia: "The brain is the moistest and coldest of all the body." So that is the trivia let's find out how our team did...we already did they got a perfect score!

**emily costa** 1:03:38

Carried by our neuroscientists! Absolutely.

**Noah Guiberson** 1:03:40

Absolutely, hard to believe.

**emily costa** 1:03:43

But like the lungs, I supported them!

**Noah Guiberson** 1:03:44

You sure did.

**emily costa** 1:03:45

Thank you.

**Noah Guiberson** 1:03:46

I just want to before we get to the top scores I just want to say that here at fax machine there's no team who came in last place there's only the team that learned the most.

**emily costa** 1:04:00

The Facts Machine way!

**Noah Guiberson** 1:04:02

So please celebrate learning with me for the team the nerve children Thank you very much nurse children for playing I hope you enjoyed it. I hope you've learned a lot tonight that's that's what we're all about. Sorry. So in third place tide we have there is no triangle and flavortown This is great energy is exactly what I want to hear when I tell someone they're in third place that's that's when you know you're having a great trivia. We have a two way tie for second place with seven out of eight Stroke of Genius Heidelberger? This might be a conflict of interest with a perfect score, Rose and Ryan, our pianists. They can play trivia and the piano, we gotta give it up. Thank you all for coming out to celebrate Brain Awareness Week. I hope you will check out we check out all the amazing other neuroscience events this week that brainy br AI, NY for New York are putting on over the next week. It's gonna be a whole lot of fun. And if you enjoyed the show, we'll be back here actually, Saturday May 28 for marine biology show with Shark scientists, Jada l Kok and squid scientists Dr. Diana Lee PhD. There, there can only ever be one doctor. And the show is called C's get degrees. It isn't Robin that one. Oh yeah. Finally, if you want to learn more about the awesome stuff our guests are doing you can follow them at Lesley Seidner and at deep fried Devin on Twitter. And if you want to learn more about our show, you can follow us at fax machine pod or if you'd like to follow us individually you can find me at Arts and Sciences M underscore em cast and Rob at sweater vest SCI. So, you know, the question remains, how do you end a show like this? We want you know we want an audience to leave on a high note you know something special and we probably want to do something so vulnerable. So unironic so heartbreakingly earnest, that you can't help but stand and cheer. Thank you so much. So I'd like to ask Ryan to join me on stage one last time I'm so glad I studied neuro. A discipline most thorough. Cognition would explain. And my heart would be achin', while my bones are busy breakin', if I didn't have a brain. My half smile just belies and my stomach's butterflies, oh, how can I explain? Away my liver I'd be drinkin' if about lungs I was thinkin'...thank God I have the brain!

**emily costa** 1:07:36

Okay, you know what? That's it. Stop the music.

**Noah Guiberson** 1:07:38

What?

**emily costa** 1:07:39

Stop the music. Thank you. Thank you. Noah.

**Noah Guiberson** 1:07:42

What?

**emily costa** 1:07:42

This whole show. I just you know, I can't I can't keep it to myself anymore. I can't do it. Okay, right. Let's all agree: the spleen is garbage. We're on the same page with that one, right?

**Noah Guiberson** 1:07:52

The spleen is garbage yes.

**emily costa** 1:07:53

But but the lungs, Noah, the lungs! When you disparage the lungs...it just knocks the wind out of me, you know? Come on!

**Noah Guiberson** 1:08:04

Look--

**emily costa** 1:08:05

Thank you.

**Noah Guiberson** 1:08:05

Em, I'm sorry. I didn't, I didn't realize I was hurting your feelings. And to be honest, I don't really know anything about any other organs. No neuroscientists do.

**emily costa** 1:08:18

...really guys? Really?

**Noah Guiberson** 1:08:20

How does studying the lungs make you feel?

**emily costa** 1:08:24

Well, if you really want to know...

**Noah Guiberson** 1:08:26

Oh, oh she's singing.

**emily costa** 1:08:27

Oh I! Love alveoli! Their gas exchange inspires! Handling oxygen but never starting fires. A goal to which! We should aspire! And the brain needs lungs for thinkin', without air we'd be sinkin', our songs would go unsung. Maybe we'll collaborate and then we both can graduate so how's about we get a-lung?

**Noah Guiberson** 1:08:59

Hey, you know what? I like the sound of that!

**emily costa** 1:09:07

Maybe we'll collaborate and then we both can graduate, now we can get a-lung!

**Noah Guiberson** 1:09:13

Thank you all so much for coming out tonight! We couldn't do it without you. Please keep it going for Ryan Brechmacher! Keep it going for Rose McCathran! Thank you so much to Caveat, to the bar, and also most of all, to our guests, Leslie Sibener and Dr. Devin Collins. Thank you so much, thank you for coming. We will see you at the bar!