Brain Science Podcast Episode 48

Transcribed by Diane Jacobs
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(Music)

INTRODUCTION

*This is the **Brain Science Podcast** - the podcast for everyone who has a brain - and I'm your host, Dr. Ginger Campbell. On the Brain Science Podcast we explore how recent discoveries in neuroscience are unraveling the mysteries of how our brains make us who we are. For more information including show notes, links to previous episodes, and information about how to subscribe, please go to the website brainsciencepodcast.com. We also have a discussion forum at brainscienceforum.com and you can send me email at docartemis@gmail.com.*

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Welcome to the ***Brain Science Podcast***. This is Episode 48. Today I'm going to be talking with Dr. Gary Lynch who's the coauthor of the new book called *Big Brain: The Origins and Future of Human Intelligence*. This is our second episode about brain evolution. If you haven't had a chance to listen to episode 47 yet, you don't necessarily need it before this episode but you'll probably want to go back for the background information.

Big Brain is a book aimed at general audiences, and today in particular with Dr. Lynch we're going to talk about two rather radical hypotheses that he has presented in this book. One is the idea that the olfactory lobes provided a template for the rest of the development of the mammalian cortex and in particular the primate cortex. Also Dr. Lynch proposes that rather than selection pressures leading to our having big brains, we actually got big brains as a result of our ancestors beginning to walk upright which allowed our brains to get larger. Dr. Lynch has spent more than 20 years studying memory at the level of the synapse. As a part of his work he has been involved in developing computer simulations for how the brain and the cortex work. I think it's because brain evolution is not his primary specialty that he brings a fresh perspective to looking at the evidence about brain evolution. In this discussion we're going to talk about the evidence for and against his unusual hypotheses. I found it very interesting and I think you will too.

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INTERVIEW

GC: Gary, I really appreciate your coming on the ***Brain Science Podcast*** today.

GL: I'm glad to be here. I really am.

GC: Thanks. Can you tell us a little bit about your background?

GL: Sure. I am actually a neuroscientist working on synaptic mechanisms that encode memory. I suppose that's what I'm really fairly well-known for, a phenomenon called long term potentiation, and over the years we've worked the idea that this is the substrate of memory encoding. What we've really been doing is chasing down the basic cellular mechanisms by which this synaptic change happens to the point of mapping where it occurs in the brain during learning. So what you got there is for the first time you actually visualize what we used to call engrams, that is to say memory traces, seeing the actual synaptic modifications one by one that are happening that have been learned.

Now, as work proceeded - and that's been going on for more than twenty years, the question that actually came up, how does all this work together to produce what we experience as memory? And how is it possible to ever retrieve memory? And those questions are really questions of what are known as network level physiology, or network modeling. And so that did lead me into modeling - that did lead me into computer simulations and *that* led me into the material that's in the book. OK?

(laughter) I hope that helps.

GC: So, how did you get interested in the issue of brain size?

GL: It goes way back for me, very far back. It's a sort of an astonishing thing to say, but we don't really have a "theory of the cortex." We really don't have a theory of what constitutes maybe 85% of the human brain. So, I've always been interested in that and my interest became ever more acute as we began to creep up the kind of questions from the much more cell biological level.

So as I cast about to try to find ways to come up with a sort of global theory about how cortex works, I ran into this extraordinary phenomenon of brain size and cortical size. The fact is, that if you look at a human, it's probably fair to say that the most striking single physical aspect that separates the human being from other animals is the colossal size of the brain. And that colossal size of the brain is due to the enormous expansion of the cortex.

So right there was some sharp, clear-cut clue as to what it is that gives us this fantastic memory power, that gives us this fantastic cognitive power - I thought it had something to do with size. So that led me into a whole series of investigations on, a) how did the brain get large, and b) what is the meaning of size.

GC: And your co-author, Dr. Granger, he's also involved in doing the computer simulations?

GL: Yeah - he's the guy - we set out in the beginning to - this is now back in the late eighties and early nineties.. we set out to actually simulate - to make simulacra of real brain biological networks. In other words these are not exactly what people call neural network models - those are sort of very artificial little neurons and everything - what we did was just make the thing as it actually sits in the brain. So we would wire up our model the way the brain, the cortical networks are wired up. And we would put learning rules in there that were based on my work with the synaptic plasticity, or cell biological rules. And we put those into those cortical networks, and to our amazement the networks did some rather extraordinary things. In other words, oddly enough we weren't trying to solve a problem, in other words we weren't using a neural network to try and figure out how language gets built.. we simply wanted to know what a network does when you run it this way. And we found some rather remarkable things.

And, those things, again, came to size. And it led us ultimately to a rather radical hypothesis about a way that the association cortex, which is the greater part of human cortex - the way the association cortex operates and the way it ever got to be so big.

GC: Right.

GL: And Rick did that - Rick was the guy - he and I did all that modeling work.

GC: OK, I'm going to give you time to talk about your hypothesis in a few minutes but we need to do some preliminary stuff to get to there... and one question that I always ask people that are in this area is, how are our brains really different from computers - since you're doing simulation obviously you're probably even more aware of the differences.

GL: Right.

GC: And you don't have to go into all of them but what do you think are the key differences?

GL: Well one enormous difference is that the brain is a giant probabilistic machine. The last thing on earth you want when you build a computer is to have a probabilistic machine - in other words, I'm sending this trace in here... and maybe this time, this chip will turn on and maybe this time it won't turn on by some set of rules of probability. But the brain does work that way, and that's a key to understanding it, a key to understanding how it operates. But it clearly separates it from any kind of hard-wired machine.

The simplest example is two neurons communicating with each other with a synapse between them. I activate neuron A and I wait for a response in neuron B. About two thirds of the time that synapse will not function, OK? So I stimulate neuron A three times - only one of those three times will the neuron operate. Can you imagine running a machine, a computer like that?

Another way in which brains - that we argue in the book - that brains are very different, is that, we believe that the cortex, the association areas of the cortex, are organized in a very random fashion - not truly random because you're never going to have true randomness in biology, but they are very low order in terms of their organization, and they are almost random. And again, computers are the things that are built hard-wired in diagram.. randomness is not really it but there is a phenomenon in computers that has some similarity to what we are talking about and this is so-called random access memory. But in general computers are things that are wired up, every one's the same, every one operates exactly the same.

Brains, according to us, have both the probabilistic aspect and in terms of their basic wiring patterns, a great deal of randomness.

GC: So then how can we do computer simulations that can really help us understand how real brains work?

GL: By putting in random connections.. (laughter) so you simulate - you take a computer and you say, "I want you to simulate a system in which all of your elements are randomly connected." We give it rules. We say.. you know.. "We want a probability of connection between any two elements," but basically all the elements in our models are randomly connected. And we put in probabilistic elements at the synapses in the model. OK? So even though the model itself is built on the computer the software reflects these real brain properties.

Again, I want to emphasize the point that this little enterprise that Rick Granger and I were doing was rather idiosyncratic. I don't know of other people who do this actually simulating the wet ware of the brain in software.

GC: Are you familiar with the work that Jeff Hawkins is doing in his attempts to model the cortex?

GL: Yes. Yes I am.

GC: He's already been on the show and talked about what he's doing, so can you offer any comparison between your work and his?

GL: Yeah - again, our work is much more concerned with not asking the question how brain solves a problem. We don't actually ask that question at all.

GC: Oh. OK.

GL: We ask the question, "What emerges when you throw all these brain properties together?" without any prejudgment or expectation at all - we say, put all these properties together. You look at the enormous complexity of even a single synapse but you look at the complexity of a network - it's just too much to hold in your head to ask, "What's it doing?" So you build a model, and you throw it all in there, and you turn the model on, and you say, "What comes out?"

You see?

GC: Yeah..

GL: We're not trying to ask a question how the brain solves a problem - we're asking, "What is the emergent phenomenon that comes out of this phenomenon, out of this network, with these rules?"

GC: It just goes to show that what question you ask makes a big difference, doesn't it?

GL: Oh, it totally does, and I suppose a lot of people would say, well, that's kind of crazy because we have all these great things that we know the brain does and we don't know how they do it so let's find out how brain does things and we'll find our way. But that simply isn't my interest.

To give you a simple example, we have established a set of timing rules whereby synapses change their strength by x amount. OK? Why do they change, what is the meaning that they change their strength of the synapses, of the connections by say, 40%, which is what they do.. Why isn't it 400%? or 10%? What is that particular value mean, if you see what I mean..

GC: ..Yeah..

GL: It's much closer to the kind of problems physicists deal with when they ask a question - what is the meaning of that constant? OK? What does that constant do and what is it doing in there, and so the only way you know they can get at that often times again is with mathematical modeling. Well, we're just doing that for brain. We want to know why these val... brain cells in the human cortex, in the average cortex might have 20,000 synapses. Well, what is the meaning of 20,000 rather than 5000? Rather than 50,000? What property emerges from that?

GC: OK.. So did the two kinds of circuits that you talk about in your book, the point-to-point mapping and the random access circuits - were those things that you put in as rules in your simulation or did they come out of your simulation?

GL: You're right - we put those into the simulation. Those are anatomical observations. In other words if you look at the - and again this is where I said we're getting into - now I want to stress when we are getting into interpretation and speculation - but my reading of the anatomy and we're not the only ones but it's a minority reading - my reading of the anatomy says that vast stretches of the cortex have - from the anatomy as I'm saying - reading of that anatomy is that vast stretches of the cortex have what we call random access designs, and so, when we build models, we put that design in them.

GC: Could you explain for my listeners what the point-to-point mapping and the random access circuits are, why that's important?

GL: Well, yeah... you can see it in a minute if you just consider that.. you know.. everybody that's had a college course in neuroscience or psychology is aware that we have these homunculi in our cortex. So there's a map of the entire body up there. There's an area of the cortex that represents the hand and then an area that represents the wrist and then the forearm - all those areas are actually sitting adjacent to each other pretty much in the same form that they actually are in the body. This means that the fingers are projecting, in order, to an area of the cortex, and right next to that area is an area that the wrist is projecting to. OK, so that's point to point.

GC: Right.

GL: It's called topographic. It's like you have a map - you have a grid map here and you just superimpose that grid map on the wall. It's just one point to one point.

The random access networks, which are certainly real - so for example, if you go into the olfactory cortex you find none of that point to point stuff. In fact the olfactory system - some of the things that launched all this - the olfactory system in fact throws it away rather aggressively. It is point to point design starting from the nose to the first stage of the olfactory system but beyond that it throws it away - it takes all the organization and it's as though it throws it all up in the air and makes it random. Everything goes to wherever it wants to go, and nothing is point to point.

And what we're arguing is, that basic olfactory design actually set a template for the evolution of the association regions of the cortex. OK.. so now why - what do you get with the point to point? Well, it's pretty straightforward. If this area of your cortex lights up suddenly you know that in a spatial map something happened in this region. OK?

GC: Right.

GL: If you have - your retina is a map of the external world there's something in the visual cortex on grid square x 1 y 3 lights up. The brain knows that there's something happening at 11 o'clock. There's spatial information tells you where things are and it tells you a lot more than that.

But what do you get with a random design? And what you get there is the ability to associate anything with anything else. See what I mean?

GC: Yeah.

GL: The great challenge to consciousness, the great challenge to the cognitive world is the ability, if I come up with a string of letters that you've never seen before, nonetheless you can associate those with letters as a new word. You go to a foreign language and you see oh, here's these letters, I've never seen these combinations of letters before. But I can associate these letters into a single object, into a single word. That ability to associate anything with anything else, that is in our argument a key ingredient of what we experience as cognition. Consciousness.

GC: And that would also be a suggestion to solving what they call the binding problem of how we remember things, all the elements of things, their sight smell touch altogether?

GL: Exactly. When you see a person's face what you have as a memory of that face is a composite of many many different angles of that face. But you also have characteristic gestures that the person makes. Blinks of the eye, facial grimaces, etc. All that stuff goes into your memory of this person and all of that stuff has been associated somehow in the brain.

Now it's very hard, and it's always been a giant problem in neuroscience, to imagine, and it's one of the reasons why the binding problem became so popular - how do you do that in a point-to-point topographic system? If all the information is carefully filed away in different spatial locations, how do you put it together? That's the problem, and what we're saying is, the way you do it is pretty much the way the olfactory system does, you take all that information from all those different areas and you throw it into a random design, all the axons just kind of cross randomly with each other. And as we have shown in our simulations, a system like that can associate anything with anything else.

GC: OK, so that gets us that basic idea - do you want to talk a little bit about evolution, so how we got from...

GL: Right... what I just told you is our hypothesis. It's based on I think very solid neuroanatomy that researchers have done, but it is hypothesis and speculative and probably controversial.

GC: Right. And we're going to come back to some of the pros and cons of your hypothesis after we give the listeners a little bit more background. What I wanted to give the listeners was a bit about what we know about early vertebrate brains, what we know about the early mammals and then come on up to the primates. Because you started it out with the early vertebrates and what was going on with them and olfaction. Do you want to start - do you think that's a good place to start?

GL: Sure.

GC: There was one question that I wanted to ask you before we went into the early vertebrates - since we don't have any brain fossils, how do we know what early brains were like?

GL: Well, as it happens the brain case is actually quite well-suited in the fossils - what they do is they basically fill it with latex, and then they can extract this thing out almost like a balloon and it actually prints in pretty good on the latex from the bone structures the different subdivisions of the brain. You get surprisingly good information for example, about where the cerebellum is located, where the olfactory bulbs are located, even things like where's the olfactory cortex. You can often times get that information from the case that's surrounding the brain.

GC: So, is that how we know for example how the hag fish which is a current species, is that how we know its brain is similar to what we know early vertebrate brains were like?

GL: That's right. (music) That's right. Incidentally this is not an era in which the government is interested in paying for evolutionary anatomy.

GC: Ha ha - That's a big surprise.

GL: (Laughter) Yeah. This is not - this kind of intellectual topic hasn't got, you know, there isn't even a dime of research going for any of that anymore.

There's two ways you know - one, you can make endocranial cast of the fossil brains today and you can get some pretty good information on that. There's a fellow at UCLA who wrote a marvelous book - the fellow's name is Harry Jerison, he wrote a book about all these endocranial casts. People do that kind of research.

But the other way you do it is by what is called the comparative method. In other words, we have hag fish today, we have lampreys today, we have fish of different types, OK, and we can look across these brains and we can say, well, what's in common between them? And then, from that you can begin to deduce what the final last ancestor - there was a common ancestor - all these different animals - what their brain must have looked like. So that's the sort of standard evolutionary practice. You kind of take the current animals - in other words we take bodies - you look at a gorilla's and a chimpanzee and a human, and you can actually make a pretty fair guess what did the last ancestor, the common ancestor of chimps, gorillas and humans look like. And now they go back and they find bones and they go, yeah that's actually pretty close to what we guessed it would look like.

There are those two routes - there's the comparative neuroanatomy route and then there is some actual evolutionary work done on fossil brains, on the endocranial casts of fossil brains.

GC: Are we ready to talk about the early vertebrates?

GL: Sure. What we wanted to get into the book was the story of how brains came to be the way they are today, and in particular how the human brain's come to be the way it is today. And what we are arguing in there is actually not at all a new argument but it is a controversial argument for the last I guess a century now.

What we're essentially saying is that the earliest vertebrate brains were dominated by olfaction and that these early brains, that is to say the cortical area, the prototype of the cortex, that area was dominated by olfaction so that this sort of random design was there from the very beginning, the design that we argue is in the human cortex and the association regions where most scientists think all the big stuff goes on.

But the fundamental principle of that is actually incredibly archaic and goes back 500 and some odd million years to the very first vertebrate brains. We have tried to establish that point, and it's just an anatomical story. We try to establish that point and then we ask this question: why did brains get large? When we go from fish forward there's really good evidence that there was no pressure for increase in size of brain for over two hundred million years. It's amazing to think of this, but for over 200 million years, actually closer to three hundred million years the brain, as we evolved frogs, amphibians, reptiles, the brain really doesn't increase in size. I mean there are individual groups in which it grew large but I'm talking about brains in a class of animals. It didn't happen. And Harry Jerison was the first guy to point this out.

That's rather astonishing. Hundreds of millions of years go by and this thing is pretty static. Now suddenly, maybe a hundred and eighty, two hundred million years ago this grows very large. And the dinosaurs, birds, some dinosaurs that go to birds and into mammals. We asked the question "Why did that happen?" And oddly enough that question has never been really thoroughly addressed, we come up with some arguments about it. But suddenly the brain increases in size by about 3 fold, in both the protobirds and the protomammals - it suddenly gets to be 3 times larger. We trace that story into the earliest mammals, we argue that again, the thing that was driving the increase in brain size, we argue, was probably olfaction. Olfaction and hearing. But olfaction primarily.

So that's kind of like a surprising statement to primates because we're such visual animals and we..

GC: So what was going on with vision?

GL: Well, see, the earliest mammals were not predominantly visual animals. They were probably mostly nocturnal, they were probably high latitude animals where there's a lot of darkness for long periods of the year. Their big evolutionary jump in the sensory systems (and Jerison again was the guy who first made this argument so far as I can tell) was probably - if you compare a mammal to a reptile to a bird, you find that one group has extraordinarily good vision, and actually pretty bad hearing and smell.

Birds don't have good olfactory sense. And neither do reptiles. And they're not particularly acute with audition. But if you look at early mammals, if you look at primitive mammals today, they're mammals that have fantastic sense of smell and very, very acute hearing. So, we're arguing that what happened was, there was this enormous expansion of the olfactory and auditory systems and the brain reflected that, and there was laid down the basic design of a very large olfactory system, and we chose the brains of these different animals, these early animals, you know, illustrating that point.

Now the argument we have becomes, OK, so now that's fine, now we've got the mammals in place and things go along just peachy fine.. Somewhere along here the brain jumps up again, but basically most mammals, to this day, have brains that are pretty much the same in size, you know, once you compensate for body size.

GC: Right.

GL: And then the story's OK, fine - now we have the primates appear, and the brain jumps again. Not a great deal, but some - it jumps again. And then finally of course the humans come along, and you get this colossal increase in brain size. And so each one of those steps the book tries to outline why did that happen, and most of the emphasis being on why did it happen in humans.

GC: The main theory that you present in the book is about how the specialized sensory areas arose in mammals, right? Can you kind of explain that and how it's different from the traditional explanation?

GL: Yeah - we're saying that what happened was when the neocortex began to expand OK, when the neocortex began to expand the actual first diagram for it was olfactory - that is not to say that the cortex was doing an olfactory function - but whatever functions it was doing it was doing with a basic olfactory design. And that's what we call random access. So, we're arguing that what we today call association cortical regions evolve *before* the primary sensory regions or at least at the same time as the primary sensory regions.

The traditional view is of the brain, of the mammal brain, certainly ours, is that what you had originally was these big primary point-to-point topographic sensory systems occupying the cortex. Then with evolution, according to this story, then with evolution what happens is, they start connecting these primary sensory areas and the areas in between them become these association regions. And then, as the brain gets bigger or rather, as evolutionary pressures continue, these association regions grow larger and larger and larger and larger. OK? That's the traditional view.

GC: And your view's the opposite.

GL: My view's the opposite. My view is the association cortex was there from the very beginning of the mammalian cortex and that in fact it may have preceded the pri- it certainly preceded the current form of the primary sensory areas. And so it was always there, and the primary areas were there - they may have come along at about the same time, they may have trailed a bit. But then they come in - the association region, the whole idea of association cortex, the whole machinery that you think of has the stuff that is supporting your cognitive operations was in fact there from the very beginning of the mammals. That's the argument.

It's a speculation.

GC: That's OK - you put out stuff that people can try to test in the future, right? But can you talk a little bit about the pros and cons for your theory?

GL: Well, for me the pro of it is, is it doesn't involve any kind of special selective evolutionary pressures to produce that cortex. That's a pro. It explains how that thing was there and how it got there and you don't have to start doing what everybody else does, which is to say, well, there was an evolutionary pressure for intelligence and so that drove the production of the association cortex, OK? To me that's a very very difficult argument to put any meat on.

GC: Yeah, because there's an awful lot of species doing quite well without being smart.

GL: (Laughter) Exactly right! And a whole lot of people running around that don't seem to need it.

GC: (Laughter)

GL: That's a general theme in the book, is that in fact, is that intelligence as far as evolution is concerned is one vastly overrated variable.

GC: What about the connections... to me it seemed like one of the most convincing parts of your theory is the whole way the olfactory cortex which you're saying is the template - goes to all these other key connections, the amygdala, the hippocampus, so forth, and so do the association areas, but not the other primary sensory areas.

GL: Right. Thank you for pointing that out. That is to me a very strong pro for the book, for the hypothesis. And that is an anatomical fact so far as we understand the anatomy. What I'm hedging on so far as understanding the anatomy and putting these caveats in there, what I'm trying to say is that there is no market today for neuroanatomists to be working this kind of stuff out. So most of what we know about this stuff was worked out years ago. So there's great great realms of ignorance and darkness about how the association cortex is wired up and were it goes. We can only deal with the data that are out there.

(Music)

Astoundingly enough, given that all of us would agree that its absolutely essential to understand human nature and human beings, there are very few people who study it. So that's why the hemming and hawing when I say well to the extent we know. It's based on a limited literature. But that literature certainly strongly suggests that the association regions are going to these different sub fields, these different subcortical areas, and those happen to be exactly the areas as you said that the olfactory system goes to. So for me, it is a pro for the idea. Those connections were there from the very beginning. So there was never a problem. You don't have to explain how this happened.

GC: It's interesting because I did an episode on smell several months ago and we talked about - well actually I was interviewing Rachel Herz who wrote a book about smell, and one of the things we talked about was how smell's the only sense that goes straight to the cortex and it goes to the amygdala and it goes all these other places, but we never really thought about what the implications of that was or why that would be, in fact looking at it from the other direction it seems kind of weird but looking at it from the way you're looking at it it starts to come, to me it starts to make some sense.

GL: It's a very striking thing. It is a very very striking feature. And I mean we think of the hippocampus as the magic memory coding machine and if you look at almost any mammal outside the primates you're going to find that the massive input to the hippocampus is from the olfactory system.

We consider the dorsal medial nucleus of the thalamus, which is the primary source of input to the frontal cortex, you know, the frontal cortex is magical, right? You look in other mammals, that is staying away from the primates, but you look at a rat, and the main sensory input to the dorsal medial nucleus is olfactory. And our olfactory system is projecting directly to the frontal cortex. So the distance from the air to the hippocampus is maybe one to three synapses. The distance from the eyeball to the hippocampus is many many more synapses. The olfactory system has privileged access to the amygdala, which is a region that we all agree is regulating emotion. So, emotion, memory, planning.. frontal cortex is planning, amygdala is emotion, hippocampus is the encoding of memory.. olfactory system has privileged access to all of these relative to the other sensory systems, and I'm saying that reflects the original design of the mammalian brain. That reflects the way it was set up. And so then you build an association system which is there from the beginning, and it has privileged access to those same areas. So what it is, is, that is actually how vision and hearing and all that , that's how we're getting all that information into these necessary regions that sort of generate behaviour is through these association regions that are using the old olfactory paradigm.

GC: Right. And if the primary sensory regions had really come first they should be connected.

GL: Right. That's right.

GC: Yeah.. You already said that obviously the climate right now is not favorable for funding any research in this area but if the climate was different how would you test this hypothesis?

GL: Oh I think the whole thing would fall out if someone were to come along and start a massive program on the anatomy and physiology of the association cortex and picking any animal you'd like. Now there is something further we'd have to discuss about this in terms of its relevance to humans and that's - we could get to that if you'd like. Really it lies in the claim that the olfactory cortex has a design, which we do know, and the association cortices are going to be a reflection of that design - not the same exact design but be very close to that design. And if that's the case then I don't see how else anyone could explain this - it is asking too much of the imagination to think that this thing happened twice. That an essential olfactory design was then reinvented by the neocortex.

GC: OK, so, just for the sake of the listeners, this is going to be all totally new to them.. can you recap exactly what is happening that's so important in the olfactory system?

GL: It goes back to this business I mentioned - the olfactory system deals with something you have to deal with constantly in the cognitive world and are not aware of it. The cognitive world has to deal with the idea there's an object out there in front of me that has 4 wheels and 2 doors and windshield wipers, OK? That's an object, a visual object. And I have in my mind the word, "car." Those two things have to be associated. One's auditory and one's visual. There is literally an endless amount of that stuff that you have to do ALL the TIME. And in fact, when you're really good at it, people go, wow, how did you come up with that association? You notice, they can follow you in that association no matter how bizarre it is, right?

GC: Right.

GL: You've got some obscure Roman emperor and the invention of algorithms or something and you put this all together in your head and everybody goes "right!" but you put it together in the head and those things have nothing superficially to do with each other.

What I'm saying is if you look at the olfactory system that system can do the following thing: it can take any two primary chemicals, that have odors, that did not exist - let's take two odors the perfume industry came up with in the last ten years, and you take those two odors and you mix them together and you make a new odor - your olfactory system will instantly encode that and recognize that for years to come. Two chemicals that have actually nothing to do with each other - maybe one's a floral chemical and maybe one is some kind of earthy chemical. These odors have nothing to do with each other structurally or any other sense. And yet your brain, your olfactory system will take these two disparate signals and merge them into one unitary perception.

And what I'm suggesting to you, that little trick, which is essential for survival, - I mean think about rats. Rats come into the world, most of odors they have to deal with didn't exist in the past - there was no way you could have hard-wired in the representations of any of these odors. Now instead and the odors are always composite, so instead you build a system that can associate anything with anything else. That's the basic trick that the olfactory system can do. If you go into that system you find that the plasticity rules for making those assemblies are the same plasticity rules that all the neuroscientists now believe is the basis for rapid encoding of commonplace memory.

GC: That's what you mean when you're talking about the random access networks - that's what's needed for that -

GL: That's right. Try to find a solution to that problem. You're an animal that's going into a totally novel environment, and there are going to be two chemical cues, and they have nothing to do with each other, they're two random chemical cues coming off the same object that you have to make a unitary representation to it. Try to figure out how to do that without a what we call a random access system. It's a really hard trick. We as humans now have vastly expanded association systems - I'm suggesting that rather than using odors what we're doing is the same trick for my Roman emperor and my algorithm.

GC: I just want to bring out this one thing because I don't think we've explicitly said it, that in the olfactory system the information starts out point-to-point and gets turned into random access information pretty early on.

GL: Right. Right. Exactly right. And that by the way is an anatomical reality.

GC: And so do we think what happens in the other systems - would it be more of a parallel thing, that the point-to-point for example for vision once the information comes through the thalamus - is the point-to-point going to go to the visual cortex and then...

GL: Right. The old original associational afferents from the thalamus are still there in the cortex. But it would appear that in the advanced cortices the way this thing now works is that you go to the point-to-point systems, several levels of that and then eventually you dump it into an association system in very much the same way that the olfactory system works.

GC: In lower animals, for example, vision is handled lower down, that point-to-point would have ended at the level of the thalamus?

GL: Yeah, exactly. It's always there - as you know, if you take a rat and damage its visual cortex it's not blind

GC: Right, but we are.

GL: Its old point-to-point systems are still working that are below the level of cortex. So for the rat to do any sort of association cortex it brings it up to the visual cortex and then it ships it out, very quickly, into a random access system. That's the argument. Now that argument stays an anatomical argument. That's something anyone can go out and test, but you know as I say there's no money in that field so you won't find a lot of guys doing it.

GC: So what happens to our brains when we get to the primates, it's all about the prefrontal cortex?

GL: Well see there's where we get into more trouble (laughter). It not as though I'm not in enough trouble already. Fortunately I have my business on synaptic plasticity you see and that's another world. So now here's where we get into a little bit more hot water.

All right: the primates have vastly expanded association regions - relative to the other parts, the primary regions. The human brain, most of that cortex is actually association cortex; there's vast - absolutely unbelievably vast territories to this thing that are association type cortex. All right, so the question is, so now, what does that mean? And how did it get there? Maybe the first question would be, how did that happen? And then maybe if you had a question or an idea about how it happened you might say what it means.

So that's what happens in the primates, the vast expansion of these things. Now, what we argue is, that what happened is the primate brain got large and the association regions got disproportionately large because that's the fundamental equation or rule for brains.

GC: How would we test that?

GL: Well we did test it in the book by saying, Does a human being have disproportionately large pri.. or, association cortex? There are some areas that we were able to find data on for six or seven species of primates, in some cases anthropoids, and now you can say OK now we can make a regression line against brain size. In other words does your brain have a disproportionately large frontal cortex as almost everyone believes, or it that exactly the right size frontal cortex you should have for the fact that you have this huge brain? Do you see a distinction?

GC: Yeah.

GL: What we're saying what happened is this: If you take a jockey and you expand that jockey to the size of a basketball player, what you would find is the arm length as proportionate to the body would be greater in the basketball player than in the jockey. That's called allometry. Children which are little people so I'm told, and look at the size of their heads compared to body - their head is much larger proportional to the body, right? than it is in adult. I mean we must look strange to kids because our heads are small relative to our bodies from their perspective. All right, that's an allometry. That's saying, when you change the size of the whole you change the size of the parts. But you don't change them equally, you change them disproportionately by some biological developmental rule.

So what we're arguing is, and we show graphs to this effect - this is one of the neater parts of the book - we're arguing that the frontal cortex of human beings and the association regions of the human brain are exactly the size they should be for a brain of our size. So the question is not how did the association regions get large, the question is how did the brain get large?

(Music)

GC: Right. And we don't really know the answer to that do we?

GL: Oh sure we do. I mean I wouldn't have the book go that far then leave the reader hanging. I mean, this is speculation, obviously, but you can't just it there like that after we put in all those graphs and equations and things... What we're saying is that if you took a chimpanzee brain and increased it to the size of a human brain, you would have a human brain.

Now that's not rigorously true but if you meant the size of the frontal cortex, the size of the association cortex, that monkey would have a frontal associational region the same size as yours. Now that's the kind of stuff that disturbs people for some reason. I mean we are brought up to believe in - what's the great word I heard McCain using the other day... "exceptionalism" of our species!

GC: (Laughter) Yeah..

GL: .. We're an exceptional nation of an exceptional species and we're all brought up to believe that. Now what I just said to you was No, that's not really true. What happened was your brain got big, and so again, the question of why did it get big? All right: There's two arguments. One is that what happened was, let's say - by the way, this jump in brain size in humans, this is one of the more startling things you'll ever come across. We plotted all the data that we could collect in the book about brain size and about Australopithecines and Homo erectus, Neanderthals and all the rest of it. We plotted all the data that we could find in the literature. And when we look at those plots there's something startling - this increase in brain size happened in a blink. I mean, I remember when I used to teach physical anthropology here I mean this kind of stuff in physical anthropology they used to have a curve, well here is Australopithecine about 5 and a half million years ago and sort of gradually bigger and bigger and that's still a blink in geological time until it turns into the splendiferous thing it is today in humans I mean but when we got all the data and we plotted it this act split the Australopithecines from the actually a little earlier from the chimps nothing happens for two or three million years to the brain, it just gets a little bit bigger...

GC: Right..

GL: Isn't that fascinating?

GC: That's in Striedter's book too isn't it?

GL: Yeah he's got these jumps, but if you look at our data those are replots and recalculations, so it's as good as I can make it, but it looks like something happened about 2 million years ago and the brain popped up, and that is by the way the shift from the Australopithecines to the Homo *habalines* and the, ah.. Homo *erectus*.

Now the Homo *erectus* stays pretty level, not jumping up very high, and incidentally for this believe it or not there are a lot of data on Homo *erectus* brain sizes over the last couple million years. It doesn't do much for a million and a half years and then pop! there's a second jump in brain size. So that's geologically how it happened in time, that's what happened - so now what pushed that jump in brain size..? Remember according to my argument, our argument, that brain size increase automatically guarantees a disproportionately colossal association cortex that gave you the stuff of consciousness and cognition free, according to our argument. So what happened? Why did it get big?

Well, one group, and this is now almost universal, there's a whole field called evolutionary psychology, and you know these are very very bright guys, what they're arguing is that some place back when, there was this intense competition between human groups, human subgroups. And so, various aspects of intelligence, what we call intelligent behaviour became evolutionarily adaptive. Let's take language. And foresight. And planning. Numeracy. And dozens of other variables.

So what happened was the brain association regions that are related to those functions grew large. Now as you're growing all these different pieces, numeracy, literacy, the ability to throw a curve ball, all these other valuable cognitive traits - as you're growing each one of these of course the association regions grow very large. That's the hypothesis. OK, that's one hypothesis.

And one of the things I think in this book that is radical is we are eventually saying that's just about dead wrong. That never happened. That that pressure for these cognitive traits is not what made the association regions large and because the association regions grew large the whole brain grew large. It's the direction of causality.

GC: Right.

GL: The evolutionary guys are arguing that you added all these modules to the cortex and thereby necessarily expanded the size of the cortex. We're saying, no, the cortex just got large because the brain got large and that's it. Why did the brain get large? In our argument it's because we switched to bipedalism. And when we switched to bipedalism, we made big babies. And when you make big babies, in primates, you make big brains.

GC: And would you explain why bipedalism would allow us to have big babies?

GL: Yeah. It has to do with the birth canal, OK? And it has to do with the size of the lumbar region of the spinal cord - of the spine. Humans actually have more lumbar vertebrae than gorillas do. You need those extra lumbar vertebrae to sort of spring the shoulders up. There's a curve in the lower part of the back. Now if you look at how modern humans walk you'll also notice that what they're doing because they're bipedal they're not shuffling, they're not moving their legs side-by-side forward. What they're doing is swinging their legs on the hips. To do that you need to broaden the hips. You broaden the hips, now you've done two things - you've lengthened the uterus and you've broadened the birth canal. That's the argument. Now when you did that you removed limits on the size of the fetus, of the embryo.

GC: Up to a point.

GL: Up to a point. Exactly. But limitations that had always been there - it's the case that human females have very difficult births. Other primates don't, and that's because, we're arguing, that in fact their uterus in those animals is restricted by the demands of their knuckle-walking life style. That's the idea. That is bound to be the source of a lot of arguments. I mean, anybody wants to look at that I'm sure there's a lot of people that really, really don't like that idea.

GC: Yeah.. there is one thing that really does seem to be supported by the evidence and that is the fact that we walked before our brains got big, right?

GL: Right - it's the timing. It's the timing of the thing that's so important here. We know that in those three million years there were Australopithecines were evolving towards bipedalism. And it is, just as you say, that the bipedalism appeared just in advance of the time that the brain makes its big jump. It's first big jump. That's the argument. That's not a coincidence according to us. The one is that is in fact causal - bipedalism caused the increase in brain size by increasing the size of the baby.

GC: What about the second jump?

GL: Yeah that's a little harder for me to handle or anyone else. There's been and by the way we're in this business here, making explanations or at least they're hypotheses - there are no established hypotheses for this kind of thing. But the fact that what I think was an evolutionary adaptation and we know this happened, OK? We know this happened - there were evolutionary adaptations to make the birth process simpler, to increase the safety of the birth process. People who study this are all satisfied - I'm no expert at all obviously, but the people who do study it are satisfied that in the last half-million years a number of adjustments were made in the female pelvis for the purpose of birth. I think when they did that they removed yet another constraint on fetus size and head size and allowed another brain to happen.

What's really radical about this is that we're saying that the brain size increase was just a happy accident. That there wasn't selective evolutionary pressures for association regions or for big brains but that in fact the whole thing was just a happy byproduct of the fact that we are higher anthropoid apes, we are higher primates who went bipedal.

GC: Does that bring us to the fundamental question of, are we smart because our brains are big or smart because our brains are different?

GL: We're smart because our brains are big. Is the point of the book. Now, big again means proportions are different. But those proportions are different only because the brain's big.

You know, the old classic story about this sort of thing was that the Irish elk had these enormous antlers and everybody said what would possibly be the evolutionary value of having these colossal antlers on this elk? And then of course people came along and said well wait a minute well if you just take all elks and scale them by size the Irish elk has exactly the antlers it would have any elk would have that would be that big. It just happens to be a big elk.

That's the kind of thing - that kind of argument has gone on back and forth in evolutionary biology - how much of the features that you see in an animal are due to selective pressures as opposed to being secondary to some other change such as body size? So I guess that's probably in a way the most radical thing that's in the book is the statement or the argument that in fact although it's almost universally accepted there must been this colossal evolutionary pressure for intelligence and hence for a giant associational cortex which of course necessitated a giant brain - we're saying no.. I still don't see what would compel me to think that was the case.

GC: I think another thing that tends to support your interpretation in my mind is the fact that the more we do comparative anatomy say between us and chimps and even monkeys the more we realize that our brains have in common other than size - even Broca's area which is associated with speech is essentially present in monkeys..

GL: Yeah that's exactly right and the whole history of this field and that by the way is an area that's controversial most of these guys are still rebutting it but as I read the literature I'm pretty satisfied that the guys are saying they found the homologue of Broca's areas are right. And of course by the way those same guys are claiming that it's lateralized as it is in the human.

GC: Right..

GL:.. in the chimp. I mean it's astounding. And you ask them well what is that area doing and they say well it has to do with communication between the chimps but they're hand gesture communication. Your point's very well taken - that's exactly right. The more we learn about the chimp brain the more we see it as being similar to human. And again, this whole field has been one in which going all the way back to the original arguments between Thomas Huxley and the debates on is the human brain different than the chimp brain - all the way back to that until now, has been one long story of people saying, well that's not really different. Well now OK that really isn't different. On and on that story and that's I think where we arrived to day, I think that does tend to push the evidence in favor of the argument that there really wasn't a giant set of evolutionary pressures for intelligent behaviour that caused our brains to grow large. But you're going to have a hell of a time dissuading people of that idea because it's so gratifying. If in the end of the day the deity didn't make us special then at least evolution did.

GC: The reason I wanted you to come on the show and talk about this stuff is because I think it puts the things we're learning into a certain perspective that I wanted my listeners to be aware of when they hear about something like the fact that olfaction has all this privileged access they can think about, well, what are the implications of that.

GL: It takes you a long way. It is a different orientation to the thing. And I hope it also has the effect of saying well even though everybody would say, my god, it's obvious we got big brains because we had evolutionary pressure for intelligence for example, well actually go out and study why from a biological perspective you think that's true. Why is it that you know that you're telling me that would necssesitate that conclusion?

GC: We'd also have to be able to give a reason why whales and dolphins have big brains - what evolutionary pressure would they have had on them?

GL: Exactly right. And in all instances of this big brain phenomenon - that's what the book's called, Big Brain - all instances of big brain it's very very difficult - we could well be wrong, but at least we're calling attention to the fact that this is an absolutely fixed assumption in the minds of most people and I don't think there is any reason to take this as a scientific dogma. This is a nice hypothesis but I mean I wouldn't even classify it a a particularly strong hypothesis. Again as I say most of my world is cell biology. So maybe that's part of the problem. But that's what we're talking about and then we want to ask the question can we imagine what would have happen if the brain had been larger? And we get into all that kind of stuff.

GL: So you've been studying the synapse forever for twenty plus years and synapses and neurons are pretty much the same in all animals right?

GL: Yup. They are. The cortex is pretty much the same and there's big differences between say birds and mammals - there are quite clear differences you can point to but once you're in the mammals and once you're talking about something like the hippocampus.. studying the rat hippocampus I don't know anything that the human hippocampus has as a surprise.

GC: It's a good thing we have all these similarities for neuroscientists are trying to study.

LG: (Laugh) You better believe it.

GC: Eric Kandel wouldn't have his Nobel prize if aplesia didn't..

GL: (laughter).. have some similarities . Well I don't know I think Eric probably got the Nobel Prize for some of the stuff he did on the hippocampus too. But there are these marked similarities and and we can extrapolate I think with some degree of comfort from all the stuff we're learning on rats and look at it's working out we're now launching cognition enhancing drugs based on experiments that were done on rat synapses in vitro, so things are playing out.

GC: Well, Gary, I really appreciate you taking the time to talk with me today.. maybe you might want to come back on the show in the future and tell us more about your basic science work with the synapse and memory.

GL: Oh sure, it's been a lot of fun, it really has. I'm glad you had me on - it's been - I love talking about this stuff you can probably guess.

GC: I really like having the opportunity to give people like you a chance to talk about your ideas in detail because I'm sure you've had plenty of those sound bite type of interviews..

GL: Oh yeah. The LA Times did a very nice series on the lab and stuff we're doing - that was a nice bit but yeah, absolutely true - most of the time it's, "Will you tell me what you do in five minutes" and "What do you mean, transmitter?" (Laughter) .. this has been very pleasant.

GC: Well, I will end you the links to everything once it's up on the internet and I look forward to maybe getting to talk to you again in the future.

GL: OK. Thank you again.

GC: OK. Bye.

(Music)

Further reading:

1. The Evolution of the Brain and Intelligence (Harry Jerison, 1973)