BRAIN SCIENCE PODCAST

with Ginger Campbell, MD

Episode #54:
Michael Merzenich on Neuroplasticity

Aired February 13, 2009

"If there's an aspect of this that's important, I think it is the lesson that most changes that are occurring in brains when brains are losing functionality are reversible. Or, from a child perspective, most of the limitations that are recorded in the brain of a child in fact are improvable." -Dr. Michael Merzenich

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"Whatever you struggle with in a sense as it stems from your neurology, the inherent plasticity of brain gives you a basis for improvement. This is a way underutilized and under-appreciated resource that we all have." -Dr. Michael Merzenich

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Welcome to year 3 of the *Brain Science Podcast*, the show for everyone who has a brain. I'm your host Dr. Ginger Campbell. On the *Brain Science Podcast*, we discuss some of the latest books in neuroscience and I interview scientists, philosophers, and other leading thinkers. Our goal is to explore how neuroscience is unraveling the mystery of how our brains make us who we are. Please visit our website at brainsciencepodcast.com or send me e-mail at docartemis@gmail.com.

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This is episode 54 of the *Brain Science Podcast*. Today I am talking with Dr. Michael Merzenich, who was one of the pioneers in the field of neuroplasticity. He will share some of the highlights of his long career with us and give us some practical advice about how we can continue to tap our brain's plasticity, whatever our age.

Before I get into the interview, I want to thank those of you who are supporting the *Brain*

Science Podcast with your donations. And I also want to apologize to those of you whose e-mails I have not yet answered. I still haven't gotten caught up, but rest assured, I read all of your e-mails.

Now let's get on into the interview.

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Ginger Campbell: I want to welcome my guest today to the *Brain Science Podcast*- it's Dr. Michael Merzenich. Well I've talked about your work a lot on my podcast so it's a great privilege to have you on the show today.

Michael Merzenich: Well it's nice to talk to you Ginger.

Ginger Campbell: The discovery of neuroplasticity is one of the most exciting recent developments in neuroscience, and since you are one of the pioneers in this area, I was hoping that maybe we could start by looking back at the early part of your career and working our way forward.

Michael Merzenich: Sure.

Ginger Campbell: How did you first get interested in neuroscience?

Michael Merzenich: Well it really came from an interest as a young student in issues in philosophy and psychology. Originally I became interested in studying, you could say, the great issues of philosophy and the brain. As a sort of joke I called myself an applied philosopher when I was young, but really what I meant was that as a neuroscientist, my interest was in these more complex issues of the origin of the abilities as they're explained by the brain and, you know, how we can explain ourselves in a sense, on the basis of our neurology.

Ginger Campbell: That's interesting. That's kind of how I got into this podcast.

Michael Merzenich: Yeah, well. These are among the greatest of human questions, of course. So what we're all about and how that's explained or not explained by what we understand about our brains.

Ginger Campbell: I know that you did you PhD work under Vernon Mountcastle and I was wondering if you could explain to my listeners why Dr. Mountcastle's work is so important.

Michael Merzenich: Well he was a great lion of neuroscience. He actually discovered basic features of the organization of the cerebral cortex. He was one of the first persons to really define what's called the cortical column, which is the basic processing unit of the cerebral cortex. This is very elementary to our science. A lot of our science has been based upon these early discoveries of his. But he was also one of the first neuroscientists that attempted to explain aspects of perception, of feeling, in neurological terms, and that's specifically why I decided that as a young scientist to go work with him.

So he was trying to explain the very elemental basis of, you could say, a perceptual moment- what constituted the basis of awareness, or what really accounted for your ability to distinguish one thing that you felt or that you say from another. These very elemental aspects of perception he was trying to explain in neurological terms, and this was my meat. This was the kind of thing I was interested in as a young scientist, and he was a wonderful, wonderful mentor. And in fact he is, to this day, a wonderful source of wisdom for me.

Ginger Campbell: And what did you study for your PhD thesis?

Michael Merzenich: Well I actually studied aspects of sensation that come from the skin, and I did a combination of experiments in psychology and behavioral measurement and physiological measurement in the brain, and this is exactly what I was interested in, in a sense, was try to account for dimensions of behavior by dimensions of response so that I could record in the brains, in this case in animals.

Ginger Campbell: When did you get interested in neuroplasticity? I know it wasn't called

that back then, but...

Michael Merzenich: Well, actually when I was a young scientist, most people viewed the brain as being rigid in its organization and not plastic beyond an early period in early development and childhood. But there was a background interest and background current of experiment and thought that was being pursued in that period by people from the physiological side of neuroscience who call themselves physiological psychologists. They were doing relatively convincing experiments across the epoch of the time that I was being trained, documenting aspects of plasticity, primarily in the hearing cortex and in the motor cortex. And to make a long story short, I pursued those interests, primarily in reading- didn't do too many experiments that related to them in my young career- but then I became interested in the cochlear implant.

And the cochlear implant is a hearing substitution device. The cochlear implant provides very compelling evidence of the power of plasticity in the older or adult brain, and that certainly re-stimulated my interest in plasticity in general. Then I began to do experiments in animals in the 1970s which demonstrated the power of plasticity in the adult brain. Basically I began to see the possibilities- the explanatory possibilities- that this provided for us and began to see how this must be in play, powerfully in play, in the development of our human abilities and that it was in place, in play, throughout life.

Ginger Campbell: Let's back up to the cochlear implant for a few minutes.

Michael Merzenich: Sure.

Ginger Campbell: Can you tell us a little bit more about that work? And I'm particularly interested in why scientists at that time were convinced that a cochlear implant couldn't work?

Michael Merzenich: Well they had a lot of reasons for that. [laughs] One reason was that they believed that the inner ear was so fragile that surgery on it was just an impossibility, that any attempt to introduce a mechanical device into the inner ear would result in its utter

destruction. Cochlear implant is a electrical stimulation device which is designed to excite or shock the auditory nerve- the hearing nerve- in a person that basically has lost hearing because the sensory organ itself has been damaged or lost through pathology or through injury or whatever. They're deaf because the hearing organism is severely damaged or degenerated, and yet we know that in most of those individuals the hearing nerve is intact.

Well there was a religious belief on one side of the clinical hearing community and the research community that if you introduced any instrument into the inner ear, it would result in ultimate final loss of that surviving nerve. And we quickly demonstrated in the early 1970s that that just wasn't true- that we could introduce practical devices into the inner ear and it had no very significant impact on the survival of the nerve itself, so we could shock it and in fact it could put up with that and tolerate that. So that was one reason people didn't believe it.

The second reason was that people did not believe that you could provide adequate control of stimulation in the inner ear- control on a level that would really provide a basis of simulating that incredibly complicated normal input that represents complex signal like oral speech. So they were very skeptical about generating a faithful enough representation in simulation of that complexly coded information that the normal inner ear delivers to the brain. For them to be effective that simulation had to be acceptably sophisticated.

Now on the other hand we were optimistic because we knew that in communication science people had demonstrated that you could reduce the information in speech very substantially. And the speech might not sound perfectly normal, but it was still understandable, still intelligible. Interestingly at that time juncture we weren't really counting on brain plasticity to contribute to the improvement of what a person heard. It turns out that the brain makes really amazing adjustments to the cochlear implant once it's in place. And even though you don't initially understand what you're hearing, not so long after most people understand everything. And the reason they do is because of the remarkable plasticity of the brain, that is to say, the way we represent information to the brain is in fact not very good. We are quite limited in relation to that real sophisticated information that the normal ear delivers to the brain, but the brain doesn't care- it makes beautiful plastic adjustments and it gets the most out of that information and as a consequence the speech for most cochlear implant users is completely

intelligible. They understand pretty much everything that people say to them, and have high normal uses of it.

Ginger Campbell: So you think that in retrospect the plasticity is a very important component of why it works?

Michael Merzenich: Absolutely. The engineers that work on this device have mostly credited themselves with the miracle, but actually it's God or Mother Nature or whoever invented cortical plasticity.

Ginger Campbell: So in a person that's got a cochlear implant, that's put in the inner ear?

Michael Merzenich: Right.

Ginger Campbell: Are the bones of the middle ear still intact in a person who's using a cochlear implant?

Michael Merzenich: No and they don't matter because basically you're bypassing all of that normal sound transmission system and you're receiving the sound and you're encoding it as a pattern of electrical stimulation, and you're shocking the nerve to generate a pattern input to the brain that's a simulation of the normal pattern that would be represented if all of that transmission machinery was in place. So basically you're providing an artificial way to provide coded information to the brain about the complex sounds of speech. You can only do that crudely. In the intact ear there are more than 30,000 nerve fibers that are providing information about sounds from the ear to the brain, and you know you can stimulate 10 or 15 or 20 channels of information with an electrical device- those are practical limits. It's a little bit like playing Chopin with your forearms, you know, it's crude.

And of course the brain initially struggles to interpret it with any significant accuracy, and most people initially don't understand what they're hearing very well. They describe the speech as robotic or as very noisy or very difficult to interpret, and 3 or 4 or 5 months later, the majority of people have acquired relatively high levels of speech understanding, and they

understand pretty much everything that's said to them, they understand what they hear over the telephone or when their back is tuned to somebody, and they describe what they hear as being pretty normal- "Sounds like it sounded like when my hearing was intact many years ago." And we know that they're doing this with very different, very much altered patterns of activation of the nerve and activation in the brain, and what makes all that possible is the plasticity of their brain. The brain basically is reinterpreting the speech. It's processing it in ways that provide them with a new basis for interpreting and understanding it. So there are powerful resources that they've had all along, you could say, that substantially account for the miracle of understanding.

Ginger Campbell: Could you use a cochlear implant in somebody who was congenitally deaf?

Michael Merzenich: Yes, and there the problems are a little bit more complicated. The biggest benefits come when that child is very young, and in fact the greatest success comes with implantation of children at a relatively young age, and the reason for that is because the auditory cortex doesn't just sit there without uses in a person that's born deaf. Basically it's subsumed by inputs that come primarily from vision, and in fact if a person learns American Sign Language (which most deaf individuals do in American culture or their equivalent sign languages in another culture) it's actually very heavily engaged in representing that language in the brain as if you're hearing. Instead of hearing that same cortex is used very beautifully to represent hearing by vision. For those reasons and for complicated reasons in older and older ages, it's more and more difficult to, you could say, re-establish this cortex as hearing cortex. So ultimately it's more and more complicated and more and more difficult to make this complete translation... conversion of the functional uses of these broad regions of cortex for the second purpose or hearing purpose. But those effects are very strong in young brains.

Ginger Campbell: And that's consistent with what we now know about the competitive nature of neuroplasticity.

Michael Merzenich: Exactly, exactly right.

Ginger Campbell: Would you like to talk a little bit about your work with animals? Did you work mainly with monkeys?

Michael Merzenich: Well initially we did many experiments in monkey, and then gradually we made a transition more and more to studies in rats, because we discovered that we could answer most of the questions that we're interested in in rats. And because the human methods themselves became more and more effective, instead of doing those second order experiments in monkeys, which is always difficult to do, we do now most of our second order experiments directly in humans. We can leap across, you could say, from rats to humans. So our current strategy, and the strategy for a number of years now, has been predominantly using the rat model and on the basis of things we could only learn in a real brain- if we can't learn it directly from the brain of a human, then we can do these basic things and then extend them to studies in humans.

Ginger Campbell: Would you explain what you mean by second order studies?

Michael Merzenich: Well I mean commonly, issues that relate to fundamental processor mechanisms can only be conducted using at least moderately invasive procedures where we actually record from the brain. And then we document aspects of the consequences of what we're doing physically, anatomically, chemically in the brain. And to be precise enough to really interpret what's happening in the brain as you learn.

The common model is that we study the consequences of a particular environmental or genetic history of the brain, and we see that the brain is degraded in its operations, and then we're trying to define how we can, in that brain, in that animal, in that individual, drive improvements in its operations. We need to get to the details, and we can't get to the details in the same way in a human experiment as we can in an animal experiment, but once we know the lay of the land, we can use the human experiment in a confirmatory way, and we commonly do that. So, for example, we might actually see the processes or mechanisms that tell us how to improve some physical or chemical aspect of the operation of a brain, and then carry that to a human experiment with a secondary measure that tells us that the same thing is likely happening in the human brain.

Ginger Campbell: So that's like using an fMRI to determine how the map has changed, compared to using actual electrodes in the neurons.

Michael Merzenich: Yeah. An example of this, Ginger, is that currently we do experiments in which we've demonstrated that most of the things that occur in an aging brain, most of the changes that occur- many, many changes can be recorded in an old brain in an animal. So we have a list of 25, 30 things that change physically, chemically, functionally in the brain, none of them for the better. And then we exercise the brain- we train the brain in different ways- and it turns out that virtually every one of these things, every one of these physical, functional, chemical aspects, are reversible.

In a rat, we can take a rat that's near the end of life and we can drive it functionally so that it looks like a rat that's a young adult. Commonly we can drive them back so that they look like they're 3-6 months of age, when the rat dies at about 3 years of age normally. So we're going to have these really striking reversals of ability. Well now we can go to a human model, and we can look in an older human at the ability to reverse these dimensions of function. Now we can't measure all of these things directly, but we can assay them in various ways indirectly. An example would be that if we improve in the rat the conduction speeds in pathways in the brain, we can set up a specific experiment on a appropriate pathway in the human brain and we can actually determine whether or not we perturb its speed when we do the thing that was effective and working in a rat. But we do many experiments of this class in which we're trying to confirm in humans that we're driving the changes in humans that we can drive in the brain of an animal. Always the measurement in humans is less direct.

Ginger Campbell: Right.

Michael Merzenich: We can never be as specific or direct or as close to the real mechanism or process as we are in the animal. So a real deep knowledge of this has come critically out of these animal experiments increasingly out of experiments in rodents, and that's where most of the insights we have that have led us to improving human performance have come from.

Ginger Campbell: What do you think the most important discoveries of your work with animals have been?

Michael Merzenich: If there's an aspect of this that's important, I think it is the lesson that most changes that are occurring in brains when brains are losing functionality are reversible. Or, from a child perspective, most of the limitations that are recorded in the brain of a child in fact are improvable. We tend to think of the losses that occur, for example, in aging as reflecting inexorable changes that are occurring in a worn-out machine. And in fact that's just not the case. Almost every dimension of the way things are changing negatively as you get older are in fact reflecting processes that are fundamentally two-way processes- they can be better or stronger, they can be faster, or they can slow down and weaken. They're reversible processes.

Or when we look at- we set up a model of a pathology in which we're going to have progressive loss. We might have a model of something like, let's say, Parkinson's Disease. We're going to have progress loss across time in all kinds of complicated ways, and we try to track all of those changes and say, "Ah we're losing this ability to control our movement cognitively" or mentally or to remember, or whatever. Most of what's being reflected as being lost is reflecting aspects of loss that are reversible. Not everything. There's real pathology, there are real changes that occur that are resistant, but most of the aspects of loss in fact are reflecting processes that are adjusting to the pathology and are reversible to a substantial extent. So it provides new insight into how to attack the loss of function or limitations of function in child and adult populations. And it's medicine, Ginger, it's not just loosey-goosey soft-science "let's train and get better" kind of stuff. The more we understand it, the more we understand how to control plasticity to drive targeted changes that drive specific benefits on a more sophisticated and complete level than is generally achieved with drugs. It's medicine.

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Ginger Campbell: The *Brain Science Podcast* is part of the new Promed Network founded by Jamie Davis of *MedicCast* and *The Nursing Show*. If you are looking for medically-oriented podcasts, be sure to check out Promed Network at promednetwork.com. Jamie's site

complements the site I started at sciencepodcasters.org. Sciencepodcasters.org is the place to go to find science podcasts from a wide variety of fields.

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Ginger Campbell: I just want to go back to some of the historical stuff for just a minute.

Michael Merzenich: Sure.

Ginger Campbell: Then we'll come back up to the present because it sounds like you've got a lot of exciting stuff going on. When you were working early on when the idea of plasticity was still not widely accepted...

Michael Merzenich: Right.

Ginger Campbell: What was your experience with your colleagues like?

Michael Merzenich: [laughs] Well, initially it was really interesting because it was so contrary to the dominant view that the introduction of it from our perspective was- the response was almost hostile. People were very disbelieving, you could say, and that commonly resulted in almost an insulting response. It illustrates something that happens in science that happens in life in general, and it's that people develop almost religious perspectives about what they're supposed to believe about even silly things like the brain. There was a dogmatic belief that the brain beyond early life- that the fundamental connections in the brain were established in early life and every neuron knew what to do at a relatively young age, and that beyond that point it simply wasn't physically or chemically changing in this kind of way. And the demonstration that it was changing in fact on a large scale, and that that change occurred across life, basically to the end of life, was not very palatable to the mainstream of science.

I might say across this period there were always a group of scientists coming from the sub-discipline of psychology- from physiological psychology- that had also argued that the brain was plastic. Those were partners in crime, you could say, and were held in equal disrepute by

the mainstream of neural science and medicine. But it's really interesting that now, you know, you could say everyone believes in plasticity and now there are 10,000 discoverers of it.

Ginger Campbell: [laughs]

Michael Merzenich: But in historic period I would talk about these experiments that demonstrated the fact of plasticity on a large scale in brains and people would be insulting about it, or I'd receive back reviews from papers in the early period that were very insulting, as if I was inventing it- inventing results or distorting them in some way. You know the ups and downs of religious scientific belief can be astounding just as they are in society.

Ginger Campbell: Yeah, a little bit over a year ago I interviewed Dr. Edward Taub. He happens to have been at the medical school I went to...

Michael Merzenich: Mm hm.

Ginger Campbell: for I guess over 20 years although I didn't realize he was there until I read about it in a book. But he expressed the same kind of frustration. In fact he said he was very frustrated because he did clinical experiments that he thought were very rigorous and met all the requirements for good clinical research that were essentially ignored...

Michael Merzenich: Right.

Ginger Campbell: until there was things like fMRI data to support it. I think he also mentioned that some of the work you did, he felt, confirmed what he was seeing.

Michael Merzenich: Right. And still, you know, and we begin to appreciate the clinical extensions of this science, which we begin to see rich with, you know, in a rich way in the 1980s. I thought, "Well this will roll into neurology and psychiatry," and I actually went out of my way to give several talks to neurological societies and psychiatric societies in that period and say, "Look- this is going to open things up for you. There are possibilities of treatment here that should be on your front burner, that you should be pursuing aggressively. There are

non-pharmacological strategies to help people on a wide scale by employing brain plasticity to drive brains in positive and improving directions, and you should be studying this."

And those talks were a great hit, you know, they were always in a sense found to be provocative and enjoyable and many people afterward told me how much they liked it, but nobody did anything or, you could say, very few scientists did very much to pursue those possibilities. And the actual translation of this into forms of treatment or therapy that could actually help people has been incredibly slow. Now there's a groundswell.

Ginger Campbell: Yeah.

Michael Merzenich: And now we're seeing intense research across the world in hundreds of places in which people are attempting to drive this into the world for the benefit of human populations. But it's slow to come, and it's very frustrating and Ed Taub certainly is an individual that... struggle and struggle and struggle to get people to use things that he knows would very greatly benefit very large numbers- millions of individuals in need of help. It's been very frustrating not to be taken more seriously with more intensity.

Ginger Campbell: The reason I bring this up is that I have a lot of listeners. My listeners range across the age span but I have quite a few students that listen and I'd like to give them a taste of both the pluses and the minuses of doing research. If they're the next person who comes up with an original idea, about how much tenacity is really required?

Michael Merzenich: Yeah, right. Well I don't want any young person to think that I ever had anything but fun being a scientist even when it is discouraging, and sometimes the rate of progress *is* discouraging and, you know, what a wonderful profession it is and what a privilege it is to in a sense be paid by the public to have this great fun that I've enjoyed and to know that it can have a very powerful, positive human impact, that that can be something that can be achieved in a research career in science and in medicine and I strongly encourage young people, but you have to keep your spirits up at times because there can be negative aspects, and it is a little bit of a roller coaster from the point-of-view of what people do and do not accept in science.

Ginger Campbell: In your career you've had more opportunities, I guess, than the average to make a big impact on patients' lives. I was thinking in particular, also, about your work with dyslexia. I guess that came out of your experience with working with hearing to begin with?

Michael Merzenich: It did, and actually the initial inspiration for that came from studies that were conducted in monkeys. And we were studying aspects of hearing and plasticity in monkeys and we began to realize that hearing processes in monkeys were highly plastic and that we could evaluate the performance of a monkey- these are little New World monkeys from South America. And we'd look at the ability of the monkey to make distinctions about complex stimuli, you could say like speech-like stimuli, and the monkey could be very poor at it initially, and we began to realize that we could dramatically improve the monkey's ability to operate as an accurate receiver of sound by training them appropriately intensely. And we also began to understand that the processes that we were observing were reversible and we could drive the ability of that monkey basically in a way that degraded its capacities to understand what it was hearing or interpret what it was hearing.

In other words, we began to understand that we could probably take you and train you appropriately over a period of a month or two and degrade your ability to understand what I'm saying, or we could turn around that training and probably substantially refine your ability to interpret with high accuracy, especially under difficult conditions, what it is that I'm saying, and understanding that your ability to operate in a domain-like language was fundamentally plastic. That it was subject to substantial refinement if you were less than perfect at it immediately opened up the possibility that we could probably train a child that wasn't very good at it to be better. And we know that a lot of children aren't very good at it, and among those are children, many children, that struggle to learn to read.

Ginger Campbell: I remember when I was in medical school, I got taught a very simple idea of what dyslexia was that didn't involve the auditory component at all.

Michael Merzenich: Right.

Ginger Campbell: Is that pretty well accepted now, that it's as much about hearing as it is about the visual?

Michael Merzenich: Right. The fundamental problem... if you could say there's a core problem that limits reading performance- and all dyslexics aren't identical, but the most common problem is a problem in phonemic reception accuracy. The phonemes are the sound parts of words that bear meaning in words, and the problem stems from the fact that the brain has not created the normal representation of the sound parts of words. So now we're going to try to make a translation of the sound parts of words in terms of their letter forms, and that only makes sense if the brain has done this sorting in the normal way, which basically allows the child to appropriately assign a letter, which is a form of representation of the sound, to it.

In the abnormal form of brain operations that apply in the dyslexic, that translation makes no sense. They do not have normal processing of those sound parts of words, and they are not sorted in the same way in the brain. So that translation makes no sense so it's fraught with error and the child struggles to make those relationships- to draw those relationships. We also know that these children commonly have a problem in how they process information serially in fast time. That also is strongly related to their having created this defective representation of sound inputs in their earlier language listening history. So we now know that it's a very large body of evidence which demonstrates that in most children, the core problem is a problem that really stems from language listening, which frustrates this assignment of the letter representational forms to sound.

Ginger Campbell: So you have to learn to listen right before you can learn how to read.

Michael Merzenich: It's only when you're sorting information appropriately does this translation of- I mean after all, reading is simply based upon the translation of what you hear in a written form. And if what you hear is not represented in the brain in the normal way, it's a very bad representational system. It really doesn't represent what you hear. So unless you correct that- unless you correct the listening, you cannot really generate a [? 0:29:08] reader. I mean you can do it only by using alternative strategies for reading, but you can't use a phonological approach to reading. You have to use a whole-word or other approach- then you

can be successful. But you can't use the classical efficient approaches to learn to read. So you have to correct the listening to correct the reading.

Ginger Campbell: And that's how Fast ForWord™ works?

Michael Merzenich: That's exactly what it's designed to do- is to correct the listening.

Ginger Campbell: Do you want to talk about that just briefly?

Michael Merzenich: Well, it focuses on these fundamental core resources just like we would approach the training of a monkey to approach the facility with which it resolves the details of what it hears in order to make it a more efficient and more accurate processor of complex things arriving in hearing in high speed. So too can we train any child to be better in the accuracy and in the speed at which it receives and interprets information in his brain through listening. You can improve any normal child, but you can also improve children that are substantially impaired in those abilities and drive most of them to a normal performance level without too many hours of intensive exercise. And you can demonstrate that through such progressive training they can achieve relatively normal or more normal phonological processing that enables reading. So you see big impacts with relatively short amount of time spent in training, both in language accuracy, language reception, and language usage and in reading.

Ginger Campbell: Once the child has reached normal do they have to keep doing the exercises or is the effect...

Michael Merzenich: No there's a very high retention in ability and it's been measured in several scientific ways. Let me just say that the average gain in language abilities for a child that sits of the left side of the normal distribution below the 50th percentile- the average gain in control gain is about a standard deviation, so that would mean that if the child is at the 16th percentile, let's say, which would mean that they would be on the edge of eligibility for services as a kid that needs special help- special needs kid in most states- that kid on the average is driven to about the normal median.

Ginger Campbell: That's pretty impressive.

Michael Merzenich: And that occurs with about 20 to 25 hours of training.

Ginger Campbell: Over how much time would that usually be done in?

Michael Merzenich: Well usually it's done 50 minutes a day, so it would be about 25 to 30 days spent, an hour a day- 50 minutes a day. And then the second thing that's seen is that if the child is behind in reading, the gain that occurs with the signal listening program translates to an improvement of reading of about 1 1/2 to 2 years. In other words, if I train the child and now I make the child as an accurate listener- a more accurate listener- on the average what you'll see is close to a year's worth of gain in their reading abilities immediately after training. But then if you wait 3 or 4 months in which they're actually reading now with their recovered listening, you see most of a second year gain. So in other words if the kid is in the 5th grade and they're reading at the level of let's say a 3rd grader, most children approach that 5th grade reading level as a consequence of training. They gain those 2 years lost. So these are relatively substantial gains that are seen on the average in these controlled studies.

Ginger Campbell: Wow. So I've read that Fast ForWord™ also seems to help children in autism. How does that work?

Michael Merzenich: Well again, the most common or the most consistent deficit that applies in autism- it's on of the DSMIV criteria for identifying autism- is a language impairment. And in fact, commonly children that have problems that give them the inherited weakness that would result in autism are on a continuum with children that are merely language impaired. In other words, if I have a child that has let's say fragile X syndrome because of genetic impairment, in the child that's more severe they might be identified as autistic but they might have an identical twin that's a little less severe, and that twin will be merely language-impaired, you could say.

Ginger Campbell: Mm.

Michael Merzenich: So autism is on a continuum with language impairment and there's lots of studies that show that autism neurologically is related to language impairment. You could say that something more complicated happens in the brain that results in a whole series of other complex problems for the child that are beyond merely struggling to interpret language...

Ginger Campbell: Mm hm.

Michael Merzenich: and the things that come from that. I don't want to dismiss language impairment as being important, but I think you have to understand what I'm saying. In any event, if the child has a language age of about 4 or greater, Fast ForWord has demonstrated to be very useful for most children. If the child's language development is more primitive, then it has no measured benefit for language per se.

Ginger Campbell: Mm hm.

Michael Merzenich: I did a controlled study- not a controlled study- I did a study in which I just looked longitudinally. historically when Fast ForWord™ was first developed, at a series of I think 17 autistic children. Not completely sure of the number but it was of that order. About half the children were autistic, about half of them were pervasively developmentally disorder with language impairment- so-called PDDNOS (not otherwise specified). And to make a long story short, I saw language gains on a language battery that averaged about 1 1/2 standard deviations. So big effects. But those were selected children that all had some level of language ability when they started.

Ginger Campbell: Mm hm.

Michael Merzenich: They were probably also selected by the therapist that trained them as being likely to benefit, but I would say probably about 25,000 or 30,000 maybe 35,000 children have been trained who are autistic with Fast ForWord™ now. I have people come up to me all the time and tell me that it saved their autistic child's bacon. And whenever it's been

looked at at all in a controlled way or in these longitudinal studies it's been demonstrated to be beneficial in most children- not all but in most children, but most beneficial in children that are above a certain language age.

Ginger Campbell: Did you redesign Fast ForWord™ to be more helpful to autistic children or do they still do the original version?

Michael Merzenich: Well the original version has gone through a series of iterations so it's better and better and better and easier and easier to get started and also Scientific Learning created programs that were designed to help the children to some extent before they initiated Fast ForWord™. But it hasn't been redesigned as much as it should be, and actually it's on my agenda as something that we have to do in the very near future. I'm just done working on an agreement with Scientific Learning to get permission from them to allow me to do that.

Ginger Campbell: Alright, because you're not directly part of that company.

Michael Merzenich: Well, I'm an advisor to them on their research programs, and I communicate with them regularly and try to help them regularly.

Ginger Campbell: But it's a little bit different from your relationship with Posit Science.

Michael Merzenich: It is.

[music]

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[music]

Ginger Campbell: So is there anything else you'd like to talk about before we talk about Posit Science and what you're doing there?

Michael Merzenich: Well I guess we can talk about Posit Science and talk about what it means for your brain to be plastic in a general sense. You know, I mean this is a pretty wonderful asset because it means that whatever you struggle with in a sense as it stems from your neurology, the inherent plasticity of brain gives you a basis for improvement. One of the things that we're really struck by in all of our animal experiments is first of all the dimensions of plasticity and brains of any age- we've been studying plasticity in animals near the end of life for a while now, for example, and once the animal's learning machinery is reinvigorated appropriately, we can generate large-scale changes in these old brains. We can do it in all kinds of specifically targeted ways to improve this ability or that ability or this function or that function.

This is a way underutilized and underappreciated resource that we all have. I think most of us feel as if we're progressing in a neurological condition, that we're progressing in life and we're losing functionality. Most of us think that we're in a downhill, more-or-less hopeless and unavoidable slide, and that is just not true. A hell of a lot can be done to reverse or slow down that slide. And one of the challenges of all of this for us, and this is certainly a challenge in Posit Science, is to help people with more tools to help them do that. But also one of my challenges is to help educate people about how to do that and how to approach that. The brain plasticity science provides a basis of good advice to almost anybody in this situation, and so, you know, there's a whole educational process that has to occur to help people understand it, and I really appreciate what you've been trying to do to achieve that, Ginger.

Ginger Campbell: Thank you. So are there some basic principles that a person who wants to tap their plasticity needs to know?

Michael Merzenich: Well there are, of course, but it's a little complicated. One thing I can tell you is that commonly people that are struggling, basically you have withdrawn from life and engagement in serious learning or serious brain change, and they have to reinvigorate their mechanisms and processes that control learning. You have to find things that you can

work on and improve at that are rewarding to you. You have to look at a life of continuous learning. I don't mean just reading and watching interesting new TV programs, I mean new learning. I mean really engage your brain to acquire new ability. And what you learn has to be serious. You get almost nothing out of exercise or activities in which you're not really focused or engaged, that don't really matter to you. If they don't matter to you, they don't matter to your brain and nothing will change as a consequence of your activities, and so forth. And then your physical status, your physical well-being, physical activity counts for a lot also from the point-of-view of your brain health. You have to keep that up. So there are principles. It's hard to summarize them in simple ways, but I say a life of continuous learning that's important for you and your brain are really important sides of it.

Ginger Campbell: Being engaged in the world around you in as many ways as possible?

Michael Merzenich: Wake up and smell the roses. And start acting on it and pick a few and try to figure out how they work.

Ginger Campbell: When I interviewed Dr. Elkhonon Goldberg he told me that one of the things he does is he makes it a point of doing things- in particular he mentioned computer things that are somewhat difficult that he could get his graduate students or whatever to do for him- that he makes a point of doing at least some of those himself for that very reason.

Michael Merzenich: Right. Well one of the things we do is we disengage and we seek a life of ease, and we seek a life that's not challenging, that never really demands anything of us or very little of us. We think that's the happy elder life, and that's a big mistake. Rather than trying to struggle with continuously trying to get across town, we buy the device that tells us where we're at at every second so we can do it in a brainless way.

Ginger Campbell: [laughs]

Michael Merzenich: Rather than go out and do something actively, we try to figure out how to bring it in front of us in some way so that we don't have to move off of our butt. And then all of the interactions that would come from actually being there and seeing it and witnessing it

or being a part of it are lost. In all kinds of ways we do things that are designed to destimulate and to reduce our capacity to operate in the world, and certainly reduce the way in which we're growing in the world, and that disengage our brains. And that's a mistake. We should be trying to increase and reinvigorate our brains, not disengage them.

Ginger Campbell: It seems as if the whole brain fitness movement has turned into a fad and there's a lot of different programs that you can get on the internet and...

Michael Merzenich: Right.

Ginger Campbell: I know that one of the things that Posit Science tries to do is it tries to scientifically validate your programs. Do you want to talk a little bit about that?

Michael Merzenich: Well that's a commitment to what we're doing here, and we're not distributing anything that we haven't demonstrated works. And the claims that we make are meant to be almost like medical claims. They're based upon having done controlled studies- and I mean controlled studies in a sort of gold-standard way- and we're trying to have those controlled studies be conducted by people outside of our immediate company because, well first of all we want to know in an objective way that what we're doing works, and where it's constructed to be continuously improvable, we're trying to define where we're at from the point-of-view of how we can help people at any given point in time and then we're working immediately on the next iterative version of what we're doing so that not too far in the future we can provide something substantially better and stronger.

Ginger Campbell: So you started that with a program that is hearing centered.

Michael Merzenich: That's right- hearing and language, you could say, because the operations and receiving information from listening in a human life and your use of language are incredibly powerful contributors to your operations in a life, and they're subject to really strong deterioration in the average older life and we can improve them very substantially by intensively training them.

Ginger Campbell: It's making me wonder whether my lack of- what I call my lack of- aptitude for foreign language is actually a hearing issue. [laughs]

Michael Merzenich: Well, it is in part a hearing issue because one of the first things you need to do to acquire proficiency in a second language is to operate in accurate listening so that you can interpret those complex sounds changing in real time. And that's commonly a hang-up. It commonly really delays and often frustrates the development of the ability to operate in a second language. It's not that you couldn't learn to read it on some level, but actually operating it as a correct oral user of the language, a receiver of the language, is very very frustrating for many individuals. And even when they learn it they learn it in a kind of baby talk form and when they hear it at real speed, it's impossible for them to deal with.

In a sense that's what happens in an old brain. Old brains are pretty good as long as everybody talks deliberately and slowly. They make a few errors then. You can demonstrate that if you just deliver words one at a time in a random way to a person of above about 60, and they miss about 5% of them, a surprisingly large number. But when they hear words in a continuous [slow? lull? 0:42:47] they have enough information from the context so that that doesn't really matter very much. But, if you just speed up that speech by 25%- so now the normal speech rate is 25% faster than normal- you can reach a condition in which a substantial percentage of people over 60 understand almost nothing, okay. So you don't have to challenge them very much before they have a complete breakdown. Now a 20 or 30 or 40 year old at a 25% compression of speech hears everything. You just aren't resolving the information with the same precision in detail in time or in frequency on the same level as you were when you were younger, but that's substantially improvable.

You can improve those abilities dramatically in most older individuals, and that improvement results in a very substantial increase in accuracy in interpreting what you hear. And then when you improve its accuracy at speed, you're basically providing much more powerful fed-forward information to the memory operations or the cognitive operations of your brain from listening.

Ginger Campbell: So hearing better helps you remember better?

Michael Merzenich: Hearing better helps you remember better. If you represent information in more detail- in a stronger, more powerful way- that information in a sense gets through. It's interpreted more accurately and it's interpreted at higher speed. You can measure all of those things in a brain and you can measure all of them in the performance abilities of an individual that's trained. You actually see improvements of the efficiency of the operations of their brain that reflect this more effective fed-forward information.

[music]

Ginger Campbell: Since the principle that you use in this seems to be sort of starting out hearing stuff slower and speeding it up, how does that translate into doing visual work?

Michael Merzenich: Well in vision, again, we start with a person making easy distinctions in relatively slow speed forms. You're alluding to the visual training program that we've created and have widely provided called InSight, and all of those start in a person making visual distinctions about what they see under relatively slow and non-time-challenged conditions.

And that's because if you look at the performance of an older person, as they operate in vision, the most striking limitations that they have relate to how they operate when they're sampling information- that speed. And the reason that that occurs is because basically as you get older, you spend more and more time looking at things directly in front of you in the center of gaze. You have less and less command of the visual field that's away from the center of gaze. Basically that's occurring because you're struggling just a little bit in making accurate distinctions about the things you're seeing in front of you without thinking. You're spending more and more time staring at the things in front of you, moving your eyes less and less, doing less and less sampling, and that means that your ability to process information that's coming in when the sampling rate is higher- that is to say that if your eyes were moving more rapidly- is more and more degraded because you're getting less and less information.

You can think of a young person- when they see something that's interesting that's in front of

them or off to the side, their eyes move to it and they bounce around on it 4 or 5 or 6 or 7 times a second. And they're getting a series of snapshots, providing the basis of a highly resolved reconstruction of what it is that they are seeing. An older person might move their eyes to it, but they just stare at it and they commonly do relatively little exploration of it if they move to it at all. And basically now we put them in a time challenged training exercise and challenge them to make distinctions about things that are happening all at speed, and they simply cannot do it. In fact it's just amazing for me to be behind the computer screen of a 70, 75, 80-year-old and watch what they can't see, because they can't see things that are so big and bold to me. I'm 66, although I might say I've spent a lot of time training myself on these visual training programs [laughs] and really can't improve anymore on them. But I cannot believe what they can't see.

When we improve these operations we can get those eyes to brighten up again. We can get them to move again, we do get them to move again. We can open them up so they see the whole world again. They no longer have those blinders on from primarily operating on things just in front of their nose. And we can get them to move the eyes rapidly to something that emerges, that's surprising in the screen, and bounce around it just like a young person. As a consequence of that they're getting much more complete information from it. They're reconstructing what they see more completely and they remember it better.

Ginger Campbell: Wow. What do you see as the biggest challenge coming up? I guess I may be skipping ahead.

Michael Merzenich: Well one of the things that we're doing now, Ginger, is we're focusing on people that have more problems than the problems that apply to the normally aging individual. And there are people that are in more trouble still. One class of those people are people that are approaching the onset of senile dementia, of forms of Alzheimer's Disease or its kin. What we're working on intensely are on strategies that are trying to reverse the functional abilities of the older person at risk for that end-of-life catastrophe, to strengthen them enough so that we delay the onset or its effective onset so that the person can live independently for a substantially longer period of time, maybe to the end of their natural life. So that's one of the areas of focus.

The second group of people that we're strongly focused on that are more substantially impaired are people that suffer from psychotic illness. Our main target there has been active schizophrenics, and we've developed complicated training programs that are designed to drive the cognitive performance abilities of people with schizophrenia as far in a normal-ward direction as possible. We have very strong effects- stronger effects than have been achieved with any medicine that I know of- that very substantially contribute to rehabilitating such an individual, to helping them re-establish themselves independently in the community again, and we've demonstrated that we were able to do that. So we're trying to now carry the evaluation of the use of those tools through a Food and Drug Administration review process, because we want the world to view that as medicine.

Ginger Campbell: Right.

Michael Merzenich: To think of that as something that should be prescribed to somebody, you could say, that is almost necessary (?) for them to have to be better, that represents a very inexpensive alternative way to think about how you would help such a person get better and maybe thrive again in a more natural life. And there's a whole series of related extensions of this in the psychotically ill population that we're trying to get to that relate to that.

Ginger Campbell: I've been recently getting quite a few e-mails from people that have been affected by head trauma. Do you think that there's any potential for this kind of work? I would guess there would be for people with head trauma.

Michael Merzenich: We've applied it in small studies. We have a study that's ongoing that's being conducted at Walter Reed Hospital in soldiers that have suffered from IED explosion exposures[1].

Ginger Campbell: Mm hm.

Michael Merzenich: Exposures where they have diffuse trauma. We've also given software

[1] IEDs improvised explosive devices

to the Easter Seals that have given it to a substantial number of returning Iraqi veterans who have been exposed to IED explosions primarily, and then measurements that we got back from those studies are very, very positive. We've also applied it in individuals that have diffuse brain injury from other reasons, for examples in individuals that have had brain infections, so an example for that would be AIDS dementia or loss of cognitive abilities that are impairing an individual to the extent to which they are at high risk for the onset of dementia and have lost their job and so forth. We've had good impacts there. Or in people that have had diffuse trauma that come from things like chemotherapy. Several studies have now been conducted in breast cancer survivors where the chemotherapy has had such a strong impact on their cognitive abilities that the individuals have significant impairment. We've been able to show that we can substantially reverse that and so forth.

So there are a whole range of uses of intense training strategies to drive the brain in strengthening their positive directions using this class of tools. Now it's complicated because the ideal strategies that apply to each one of these populations are a little bit differentiated from every other one. There are significant individual differences in how the ideal programs would be shaped for each of these populations. But there's also a lot of overlap because in almost all of these cases, we can use general principles of plasticity to drive the brain to represent information in higher fidelity, more accurately at high speed. So there's a lot of overlap. We don't have to reinvent the wheel every time we approach another one of these problems. But there also is a significant differentiation, and especially when you come to populations like people who have suffered from stroke where to some extent the individual losses that apply in one patient to another have to be dealt with.

Ginger Campbell: Right. So if an individual was interested in trying to use the programs that you're developing, would it be more appropriate for them to contact Posit Science directly or would it be appropriate for them to buy one of the programs, or what would you recommend?

Michael Merzenich: Well they can take either approach. They can try it- it's not going to be harmful for them to use it, I mean we know of no inherent dangers or problems with using it in that respect- or they can contact us in our research group here, and we might be interested

in helping them and guiding them in some sense or advising them in some sense, and we might be interested in helping them as being a source of information back to us on whether or not it does possibly impact in the condition that applies for them. So they're very welcome to contact us, but they're also very welcome to give it a try.

Ginger Campbell: The programs that you have that are aimed at the general public- do you have recommendations about what age a person should be before starting into those programs?

Michael Merzenich: Well I think that a person at any age can benefit from the use of this and to some extent it matters more on the conditions of whether you perceive a need or not. A 20-year-old can have a need in improving their visual or their listening operations, or the cognitive operations. And a 60-year-old can be doing just great, right? There are families in which there's an inherited weakness that can put a person at risk for early onset of something very bad happening like Alzheimer's Disease. At a relatively young age a person might think about doing things prophylactically to make them stronger, and this is one of those things that they can think about doing. It's to some extent individual. Basically the software is designed to find the performance level of an individual and drive them to a higher level. So it might find the performance level of the average 40-year-old to be quite a bit higher than the performance level of the average 70-year-old. It will find that. But then it will drive all of them as far as they can go in a positive or corrected direction, and almost everybody's improvable.

Ginger Campbell: And I got an e-mail recently that indicates you finally have a Mac version.

Michael Merzenich: Yeah, we do. Yeah, about time.

Ginger Campbell: One thing is that your programs are relatively expensive, so from the standpoint of, say, someone who's trying to sort out all these different things that are on the internet, is there any advice that you would offer?

Michael Merzenich: Well, the problem is is that most things that are applied and most

things that are out there are unproven from the point-of-view of their use.

Ginger Campbell: Yeah.

Michael Merzenich: The benefits that might ascribe. Going across the landscape, there are some things that are inexpensive but I think are obviously more useful or more likely to be useful than other things. So the problem is is that there's almost never a controlled study that demonstrates the utility. It's sort of surprising when a company that might have, let's say, 10 or 12 million dollars in revenue won't do a controlled study. [laughs] But that's the reality of it. There are even large players in this landscape that just haven't done scientific studies that determine whether what they do actually has any benefit or not.

Ginger Campbell: Because there's nothing like the FDA to force them to, I guess.

Michael Merzenich: Yeah, and I think that this has got to change. Of course it does make things more expensive. It's one of the things that contributes to expense. You know, if you run a controlled trial on one of these things, you're talking about the kind of expenses that apply in running controlled trials for drugs.

Ginger Campbell: Right.

Michael Merzenich: It's just costly as hell to do that, so it's not free. But on the other hand, how can you sell something and make promises to people about how it will make them better or stronger without having any real evidence, and ideally that's unequivocal evidence, that those statements about its efficacy, the benefits of it can come from it, are true. And what kind of value do you get by doing something in which there is no such support? So I think somehow we have to clear up this landscape. It's a mess of a landscape. And we have to have some kind of standards on it, because at this point no one can know what to believe. It's just a mess. And all I can say about what we do, is that we know it works. We're not distributing anything, we're not providing anything to anybody that we do not have good evidence that may be effective for the uses to which it's applied, except in these experimental cases we talked about a few minutes ago.

Ginger Campbell: Right. Well I really appreciate you taking the time to talk to me today, Dr. Merzenich. Is there anything else you'd like to share with my listeners before we close?

Michael Merzenich: Take your brain fitness seriously because it's all up to you, and remember that you have this great asset that you carry around within your skull- to be stronger, to be better. It's more or less up to you if you utilize it or if you allow yourself to deteriorate in ways that just aren't necessary or completely necessary. And keep up the good fight.

Ginger Campbell: Thank you.

Michael Merzenich: I enjoyed talking to you, Ginger.

Ginger Campbell: I did too. Thanks so much.

Michael Merzenich: You bet.

Ginger Campbell: Bye.

Michael Merzenich: Bye.

[music]

I want to thank Dr. Merzenich for coming on the *Brain Science Podcast*. Remember that you can find show notes and links at our website, brainsciencepodcast.com. The transcript of this episode should be available by the end of February. We now have two people working on transcripts, so I hope that we will have all the back episodes available by the end of 2009. If there's a particular episode that you need, please let me know.

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main support for this podcast comes from listener donations. Information about how you can help is also available at brainsciencepodcast.com.

Those of you who are regular subscribers will have gotten episode 25 of *Books and Ideas* in last month's feed. This episode was an interview with Dr. Paul Offit, author of *Autism's False Prophets*. I hope that you will share this episode with as many people as possible. If you are a podcaster, please feel free to put this episode into your podcast feed. This is only the second time that I have put an episode of *Books and Ideas* into the *Brain Science Podcast* feed, and I did it because I think that the subject of vaccine safety is one that is very important, especially since at least in the United States we're starting to see diseases arising and deaths arising from children not being vaccinated. I hope that more of you will subscribe to *Books and Ideas*. I'm going to be putting out the *Brain Science Podcast* around the second Friday of every month, and *Books and Ideas* on the fourth Friday of every month.

The next episode of the *Brain Science Podcast* is an interview with philosopher Patricia Churchland. Churchland is the author of several highly respected books, including *Neurophilosophy*. We will talk about the relationship between neuroscience and philosophy, and I will get her take on some of the issue I talked about back in episode 53, which was a discussion of the book Did My Neurons Make Me Do It? Until next month, please keep the e-mails coming and please keep telling your friends about the *Brain Science Podcast*. I look forward to talking to you again next month.

[music]

-transcribed by Jenine John