"Examining the Causes of Autism" with David G. Amaral

Transcript of Cerebrum Podcast

Guest: David G. Amaral, Ph.D., is a Distinguished Professor in the Department of Psychiatry and Behavioral Sciences at UC Davis. He is also the Beneto Foundation Chair and Research Director of the MIND Institute, which is dedicated to studying autism and other neurodevelopmental disorders. As research director, he coordinates a multidisciplinary analysis of children with autism called the Autism Phenome Project to define clinically significant subtypes of autism. More recently, Amaral has become Director of Autism BrainNet, a collaborative effort to solicit postmortem brain tissue to facilitate autism research. In April of 2015, Amaral became editor-in-chief of *Autism Research*, the journal of the International Society for Autism Research. In 2016, he was appointed to the Interagency Autism Coordinating Committee by the Secretary of Health and Human Services. Amaral received a joint Ph.D. in neuroscience and psychology from the University of Rochester and conducted postdoctoral research at the Department of Anatomy and Neurobiology at Washington University. He also conducted research at the Salk Institute for Biological Studies and served as an adjunct professor in the Department of Psychiatry at UC San Diego.

Host: Bill Glovin serves as editor of *Cerebrum* and the *Cerebrum Anthology: Emerging Issues in Brain Science*. He is also executive editor of the Dana Press and *Brain in the News*. Prior to joining the Dana Foundation, Mr. Glovin was senior editor of *Rutgers Magazine* and editor of *Rutgers Focus*. He has served as managing editor of *New Jersey Success*, editor of *New Jersey Business* magazine, and as a staff writer at *The Record* newspaper in Hackensack, NJ. Mr. Glovin has won 20 writing awards from the Society of Professional Journalists of New Jersey and the Council for Advancement and Support of Education. He has a B.A. in Journalism from George Washington University.

Bill Glovin: Why do the numbers of infants with autism keep going up? How important is early diagnosis? Is gene modification an option? What are some of the ways pregnant mothers might reduce the risk of having an autistic child? What can brain imaging reveal to us about autism?

These are just some of the issues we discuss in this month's *Cerebrum* podcast with David Amaral, one of the nation's foremost researchers on autism. Hi, I'm Bill Glovin, editor of *Cerebrum* and welcome.

These *Cerebrum* podcasts are still relatively new and we hope you find them somewhat enlightening. The idea is to ask the authors of our *Cerebrum* articles to elaborate on some of the research they've discussed in their articles. *Cerebrum* is the research based publication of the Dana Foundation, and you can subscribe to it free of charge by going to Dana.org.

Each month we focus in on a particular area in neuroscience. Mostly we focus on research but occasionally we'll also address public policy issues. All our articles are

written by neuroscientists. Last month it was Pain and Imaging. Next month it will be Telemedicine as it relates to psychiatric and neuro disorders.

But this month it's autism, and we are very, very fortunate to have David Amaral as our guest. David, who is founding research director of The MIND Institute at UC Davis, and a distinguished professor of psychiatry and neuroscience, had the time to write thanks to a sabbatical this past fall.

I first approached David about writing for us a few years ago after hearing him interview the actress Sigourney Weaver about her role in a film called, "Snowflake" in which she plays a high functioning autistic woman. That took place in the annual Brain Wave Series that the Rubin Museum in New York, and it was a wonderful and enlightening program.

David did a great job there and also on his article, which very specifically examines the causes of autism. You can link to the article at Dana.org.

Welcome David, and let's get the hardest question out of the way first. Would your wife mind if you became best friends with Sigourney Weaver?

David Amaral: She said she would have to punch her out if that happened, so I think probably not a good idea.

Bill Glovin: Okay. What inspired you to make autism your research area?

David Amaral: It was something of an accident, actually. I was initially interested in the parts of the brain that are involved in social behavior. Prior to that I'd worked with a number of collaborators on trying to identify brain systems involved in memory. And we did that effectively by studying people who had amnesia. My job in that collaboration was to try to identify what parts of the brain were damaged in those amnesiac patients.

Then we moved on to animal models to try and figure out the circuitry of memory. So, when I became interested in the neurobiology of social behavior, I wanted to start defining the social brain, which even now is much more vaguely understood than other sensory systems like vision or even memory.

Just at the time I moved to UC Davis and we were doing quite a few studies in non-human primates. But, we really didn't have a good sense of what parts of the brain are involved in social behavior, and I thought maybe if we were able to identify a human model of social impairment that would give us some clues, particularly if we could find out what parts of the brain are impaired in those patients.

And quite naively, initially I thought of autism, but I knew very little of autism. So, I started to look around in the literature to determine what was known about the neuropathology of autism, and realized that it was really a new field, that there had been very little done. In fact, the first neuro pathological study was done by Tom Kemper and Margaret Bauman, and that was only done in the mid-1980s.

So, my first impetus to get into the field of autism was to try and better define the neuropathology of autism, and started that in the late 1990s.

Bill Glovin: I'm not clear on the data from the Center for Disease Control and Prevention. At the Rubin event, you said that 1 in 48 children are born with some degree of autism. Their website says 1 in 68. The number seems to be a moving target. Is that because autism is difficult to diagnose?

David Amaral: Well it's difficult to diagnose and it's difficult to do epidemiological studies. The Center for Disease Control has had a long-term program where they try and monitor how many people have autism. But because autism is diagnosed in a number of different ways, it can be diagnosed in the school system, it can be diagnosed by psychologists or psychiatrists affiliated with medical institutions; we don't have a national database of all of the patients in our country. Because of that when an organization like the CDC tries to go out to examine prevalence it really is time consuming, expensive, and complicated.

So, if you look at the CDC data, for example, it seems that state to state to state the number varies quite a bit. It's all in the same general ball park, but the detail numbers are different. And that's probably because the numbers that are most accurate are in states that have a lot of providers of care for people with neurodevelopmental disorders. And the states where the data are less accurate have less developed health care for neurodevelopmental disorders.

But I think what is true is that the number of people that have been diagnosed with autism have certainly been increasing over the last 40 or 50 years.

Bill Glovin: A few weeks ago researchers at the University of North Carolina said they were able to predict with an 80 percent accuracy rate using an MRI scan, which babies who had an older sibling with autism would be later diagnosed with the disorder. How important is this advance?

David Amaral: Yeah, that's really a fundamental advance, and it's fundamental because at the moment we don't have a biomarker for autism. Autism is generally diagnosed when a child's best is joined to the behavioral sciences symptoms, and even the best clinicians don't feel comfortable confirming the diagnosis until a child is about two years of age.

And nationally, the diagnosis is done closer to four years of age. And again, that's because of a lack of an adequate number of providers to be able to do the diagnosis. So, to have a biomarker, particularly, the key thing about that study was that they employed an infant sibling strategy.

What that means is that if you think about the numbers that we're talking about a minute ago, the chance that any child in the United States is going to have autism is between 1 and 2 percent in the general public. But if a family has a child with autism, the likelihood that their next child is going to have autism goes up to 25 percent.

So, if you're looking for an early marker of autism, what you would want to do is recruit families that have one child with autism at the time when they're having their second child. And then monitor that second child really closely. And so typical infant sibling studies will start monitoring children at three months of age, and the families will come back into the institutions where these studies are being done every three to six months.

And we have here at the MIND Institute a scientist whose name is Sally Ozonoff, who's been doing this for a very long time, and is recognized as one of the foremost clinical scientists trying to identify early behavioral science of autism. And what Sally has shown is that even at 12 months, it's very difficult to identify anything behaviorally that would be diagnostic of a child going on to have autism.

Everybody hopes that we'll be able to come up with a biological marker that a child either has high risk, for example in the siblings, or children in general would be able to, for example, have a blood test or some other clinical test as soon as either the parents or the clinicians have some concerns about the developmental course of the child.

As I said, there's very little evidence at this point that there are biological markers that will allow us to do that. This study was one of the first really solid indications that something is going on in the brain, even before the child shows any behavioral signs and symptoms of autism.

So I think it's a very optimistic study, and again, it indicates as I tried to say in my article, that most of the data thus far suggests that whatever is causing autism—and there's probably many things that cause autism, both genetic and environmental—that they're happening very early on to the child, and that there's very little evidence that autism even in children that have the regressive form of autism where they look sort of typical for the first couple of years in life and then regress into autism, even those children it looks like the biological underpinnings of the disorder started very, very early on.

Bill Glovin: Brain imaging obviously has changed the playing field in a lot of areas. But in autism how important is brain imaging? What can it tell us? Is there a lot of research that is yet to be uncovered with it?

David Amaral: I'll tell you about one of the studies that we participated in. We carried out an imaging study very much like the study that was just reported in *Nature* by the Ibus Network. In 2013 we reported that children, again, these were infant siblings, children that were to go on to have a diagnosis of autism had increased cerebral spinal fluid between their brains and their skulls. We called this increase extra-axial fluid, just meaning that it's around the perimeter of the brain.

Interestingly, what we found was that the more of this extra-axial fluid the children had, the more serious their autism was when it was diagnosed at 24 and 36 months. That paper was and the first author was a graduate student in my lab whose name is Mark Shen. In that paper we found not only that the children that had this increased cerebral spinal fluid, their brains were actually larger, as well. But it was a relatively small study. It did get published as I said in *Brain* in 2013.

But we then formed a collaboration with Dr. Joe Piven, who led the Ibus Group in this most recent *Nature* paper. And we asked them to allow us to examine their data with them to see whether we could reproduce this finding of increased extra axial fluid. And as it turns out we have found that in their population, which is a much larger population of children with autism that we did again see this increased extra axial fluid. That will be published in the next two weeks, actually, in a paper that will be coming out in *Biological Psychiatry*.

Again, it indicates that we see this increased extra axial fluid as early as 6 months. What's interesting again is that it strengthens the idea that the brain changes are happening very early on. And it also highlights the fact that some alteration in cerebral spinal fluid may be either contributing to the etiology of autism, or might be a sign of some underlying process that deregulates the circulation of cerebral spinal fluid.

In the old days we used to think that cerebral spinal fluid was just a cushion for the brain, that it was like a shock absorber. But, we now know that cerebral spinal fluid carries many substances, some good and some actually toxic metabolites, and clears the brain of those toxic metabolites, in the normal course of its production and circulation.

Now we don't know what the repercussions of this increased extra axial fluid is in these very young children who go on to have autism, but it highlights another area of research that was brought to the fore through imaging very young children.

I should say that there aren't that many studies out there that examine very young children who have a high risk of autism. In fact, the 2013 paper that I mentioned was I think the first paper that was published that had a population of children that actually did have a diagnosis of autism and were imaged as young as 6 months, and this idea of this paper that we've been talking about, the more recent *Nature* paper that touted its potential for predicting autism, was a much larger sample.

But there just aren't a lot of studies like that, that have been done thus far. I think more should be done, and we hope to be able to pursue those kinds of things in the future.

Bill Glovin: What would make it so difficult?

David Amaral: Well, it's costly. For the more recent *Nature* paper, it was a network of sites across the country. It was I believe six or seven sites. And again, even though the rate of children that will ultimately have a diagnosis of autism is 25 percent, that means that every three out of the four children that you image with all the costs and everything else of re-diagnosing the child and monitoring the child behaviorally, and carrying out the MRIs, and these are longitudinal studies so it's not a single MRI, but it's multiple MRIs. So, the child typically is imaged three or four times.

But still, well only one of those children out of the four will have autism. So, it's a very complex, expensive process. And for that reason, not many groups have actually attempted to do it. It's the same issue that when children with autism get older, most of the studies if you look in the literature, have tried to identify neuro pathological changes

or alterations in the brain of people with autism. Up until recently, virtually all of those studies were done with older people, and older people that were on the higher end of the autism spectrum.

And why is that? Well, it's because again, taking an MRI, many listeners may have already had an MRI and they know that you have to stay perfectly still. And every scan can take 10 minutes. And if you have a child that is nonverbal and not very compliant in the past, the only choice would've been that you would have to anesthetize the child. And obviously that's not the kind of thing that we want to do in a research setting. And we don't want to do it over and over again.

Our team here at the MIND Institute has developed strategies for either imaging the children at night when they go to sleep. So we have a program here called the Autism Phenome Project, where we've imaged over 300 children. The first time that we image these children is when they actually already have a diagnosis of autism.

We bring them into the MIND Institute in between two and three-and-a-half years of age, just after they've been diagnosed. And we do our first scan, and actually the first, second, and third scans, which is separated by a year, by having the child come into the imaging center, and we have set it up so that they can go to sleep. And then when they go to sleep we pop them in the MRI, do the scan, and we've had absolutely excellent results.

But lately we have some children who are now in the age range between 8 and 12. Again, we want to continue imaging the brain because a lot of the thinking now is that you're not going to see ... Because the brain is developing over this period of time that what may actually characterize autism is not so much a static image of the brain, but a change in its developmental trajectory.

So, we've brought these children back, and again, now you can imagine you have a child that has an IQ of 40, nonverbal, and how are you going to, again ... And now sleeping doesn't work because they are too aware of their surroundings and so we have to come up with a different way of scanning them.

Again, this team now is led by Dr. Christine Wu Nordahl, and we have dedicated staff that are working with her. And we actually go through a two-week process where we train the child to feel comfortable having an MRI. And we do it by understanding their motivations. For example, which videos do they like to watch?

And we ultimately, through success of approximation, bring the child to feel comfortable laying in the scanner, and believe it or not, we have had nearly a 100 percent success with children at all parts of the spectrum all the way from the most impaired to the most highly functioning children that we have in our program.

We're now just beginning to understand the differences in children who have autism—that may have different phenotypic characteristics. But again, I guess I tell you this story

because just to recount how difficult in a sense to carry out imaging studies in a population that has a number of challenges like those who have autism.

Bill Glovin: Yeah, we recently did an article on the Mind of a Terrorist, and we were talking about imaging and how difficult it was to find a terrorist to image.

David Amaral: Right.

Bill Glovin: So I can understand the difficulties, but this sounds remarkable. Referencing the program at the Rubin, again, with Sigourney Weaver, I think in the Q & A section you said that there were two large studies that have shown that taking prenatal vitamins in the three months prior to pregnancy dramatically decreases the likelihood of autism. How come that was left out of the article?

David Amaral: The article was focusing on the causes of autism. And I think there are a number of things that people have proposed might reduce risk. I think that's a whole other topic. At the Rubin, I didn't want it to be all doom and gloom. I certainly wanted to highlight that there were some positive things coming out of the research.

I think in terms of what somebody could do in order to, which is relatively easy, straight forward and safe, is to consider if they're anticipating a pregnancy to get on prenatal vitamins, particularly it probably is the case that it's folic acid that may be helping to prevent some aspect of whatever's causing autism.

There was a little bit of a controversy a year ago, and actually after the Rubin talk, a group began to indicate that you might actually be held to have too much folic acid, that those data haven't been published, yet. They were presented at a meeting, the International Meeting for Autism Research. But I think standard prenatal vitamins are still thought to be protective.

There is at this point, given that we're still struggling to understand the causes of autism there's very little else that we could suggest that will certainly reduce the risk like the prenatal vitamins.

Bill Glovin: You write that measles during pregnancy has a cause and effect in terms of autism, but that vaccinations make measles mostly a non-issue and that flu and other infections have not been linked to autism. Is there anything else during pregnancy, such as any drugs, for example, that you suspect could have a connection?

David Amaral: Well, so I did indicate in the article that there is some concern about SSRIs, serotonin reuptake inhibiters.

Bill Glovin: Right.

David Amaral: Inhibitors that are anti-depressants. It was interesting that while I was doing the research for the article it became clear that it wasn't so much the SSRIs, but the fact that the mother was suffering from depression. So, this is a case where if you just looked at

the risk of having depression during pregnancy, or you looked at the risk of taking SSRIs because you do have depression, it turned out that the risk wasn't any greater.

I think that's an example of where, you know, it depends on how you ask the question. And if you don't have the appropriate control group, the unmedicated mothers who had depression, then you may actually come to the wrong answer.

I'm not a neuro toxicologist, but when I listen to talks by neuro toxicologists, I do get concerned that there is so little testing on many of the compounds that people are taking, even other kinds of supplements and things like that, that there's safety during pregnancy. I think the take home message is that they're very few other kinds of drugs that have really been studied with any kind of comprehensiveness.

I mean one example is that I have a colleague here, Judy Van de Water, who has found that a subset of women (and I mention this in the article) have unusual antibodies. And these antibodies are directed at proteins in the fetal brain. And she's proposed that if it is the case that these antibodies may be interacting with the developing fetal brain, and altered in some way, that ultimately leads to autism. And so she calls this “paternal antibody type of autism.”

These are unusual antibodies that we don't know how they are generated. They may be generated to something else and cross react with the brain, but they're certainly there. But, if you just even watch television for a little while you'll see that there are more and more antibodies that are being used for treatment of arthritis, or eczema, or all kinds of things, and I think at this point we know almost nothing about whether these antibodies might cross the placenta during pregnancy, and whether they'd get into the fetal brain.

This is a whole area that I think is opening up because we are developing a new class of antibody pharmaco therapeutics. Yet, again I think the only thing to do at this point is probably be cautious in taking them during pregnancy. But we have very little understanding about how antibodies get transported from the mother, through the placenta, and into the fetus, and into the fetal brain.

So, I think there's a huge amount of research to be done, and I think it's increasingly important that given that we're coming up with more and more things that people can ingest or treatments that we take more seriously the fact that while they'll have positive benefits, certainly that they potentially could have deleterious effects.

I mean Thalidomide was, I mentioned in the article this, as well, a drug that was used in Europe for anti-nausea during pregnancy. That drug not only caused profound birth defects but also increased the percentage of children that went on to have a diagnosis of autism.

It's not clear why there are so many causes of autism. One would hope that, ultimately, we'll come to a final common pathway that we'll understand what parts of the brain are altered that lead to the autism. That might lead us to an understanding why all of these various challenges are affecting that pathway. But at this point we're still not there, yet.

Bill Glovin: With that in mind, we recently published an article titled, "Drinking Water and the Developing Brain" and in it the author writes about a demonstrated link between developmental neuro toxins and genetics and autism. And at the Rubin(referencing that again) you said there are 60,000 chemicals in the environment that remain untested.

David Amaral: Right.

Bill Glovin: Which is consistent what she was writing about. Do you recommend a mother only drink bottled water? And what are the potential environmental factors that need to be avoided?

David Amaral: Yeah, so this question comes up often. I think it's a good question, and I think on the one hand expectant mothers, or mothers, or women who are thinking of becoming pregnant, I think should exercise as much caution as they're able to do. Since there's indications that things like pesticides might be increasing risk. All these things that environmental epidemiologists have told us about certainly increase risk but a very small amount.

The hope, or I guess the expectation is that once we understand all of this, that if you were simply to add up the risks, you would find that they would be sufficient to cause autism in some individuals and not others. And again, it gets complicated because the same kind of risks may cause autism in one child, one pregnancy and not in another. And that's probably because one child has a certain complement of genes, whereas the other doesn't. And that they might have a complement of genes that puts them at risk for being affected by environmental factors.

To get back to your question I think using appropriate caution and trying to limit as much as possible any environmental factors that could potentially put somebody at risk. So, to answer your question, if you are living in a place where you know that there's high levels of contaminants in the water system, I would certainly say that during pregnancy it would be wise to try and limit exposure to that.

You can eat organic foods rather than eating foods that might have higher levels of environmental intoxicants. But, it's just being reasonable and reasonably cautious, I think at this point, is what people recommend.

But having said that we know women that have interacted with the MIND Institute or have supported our research who have done everything during their pregnancies—ate organic food, stayed away from fish with high levels of mercury, did everything right. I mean, they were very knowledgeable and they did everything they possibly could do to limit the risk. And nonetheless had children with autism.

So, I think one message would be, yes, do everything that you can but don't blame yourself if you end for having a child with autism. It's unlikely that it's something that you did that contributed to the risk for that child. And support research because there's a huge amount that we yet need to know about what are the causes of autism.

My article was just really sort of scratching the surface of what's known out there. But it also highlights that there is a huge amount more that we need to know to understand the link between environmental risk and whether a child is going to have autism or not.

Bill Glovin: Speaking of causes, one fascinating part of the article I thought was in the post-natal section when you talk about a Romanian study where social isolation is suspected in fostering some features of autism. Has there been anything else that might indicate a social component?

David Amaral: Well, so that's an interesting line of literature and thinking. These articles that actually show the linkage, so earlier articles show the linkage between the very brutal upbringing that these Romanian orphanage children had, where there was just terrible social isolation, terrible sensory stimulation, and a lot of those children came to the orphanages because they had some problem initially, either some developmental problem or other problem initially.

But, certainly the person who examined them early on was a guy named Michael Rutter, who's a very distinguished child psychologist from Great Britain. What he said was, yes, they have some surface characteristics or some behavioral characteristics that reminds you of a child with autism. But they also had some distinguishing features, as well. They tended to get better over time and other features that I mentioned in the article that made him think that this was, he called it sort of "an autistic like condition." But it wasn't real autism.

My take on it is that there is obviously parts of the brain that are controlling social behavior. And that as I said earlier, the kinds of things that alter those brain systems that lead to, that altered social behavior in autism, I think, generally speaking, happen early on. But, if a child were to undergo the horrible conditions that these children in the orphanages sustained, you can perturb those brain regions, as well.

Is that real autism? Well, I don't think so because it doesn't normally happen in the normal human condition. Is it affecting the same parts of the brain? Maybe some of them, but again, because they were behavioral differences it really didn't produce an autism that a current diagnostician would say is real autism.

So, social impairments are not only characteristic of autism, they're certainly a big feature of autism, but actually the word autism was first used in describing schizophrenia. And as one of the symptoms of schizophrenia, there's social withdrawal and people talked about autistic behavior in schizophrenia before even autism was formally diagnosed, or formally described in the 1940s.

So, you can alter the parts of the brain that are going to lead to autism, and get some impairment of social behavior. But I don't think that's a typical way that children nowadays that we're diagnosing with autism come. And so that is really the only post-natal influence that I know of.

I did mention the vaccines, and I know that many, many families are concerned that vaccines might be causing autism. But again, going back to the beginning of our discussion, most of the data that I'm aware of suggest that the things that are causing autism whether they're genetic mutations or alterations in brain development, happen long before a child is getting the vaccines that most families are concerned of, things like the measles, mumps, and rubella vaccine that start at 12 months of age.

Bill Glovin: Mm-hmm (affirmative).

David Amaral: And again, I tried to emphasize in the article that again most readers probably are not old enough to remember the time when there were German measles epidemics. The last one was in 1964 as I mentioned in the article.

When those were happening tens of thousands of children were born ... Well first of all tens of thousands that died, and then tens of thousands of other children were born with neuro developmental disorders. And seven percent of the children who were born to women who were exposed who had German measles during their pregnancies had autism, seven percent. I mean it's a huge number.

And so, while I know that vaccines can prevent cases of autism I have not seen any data that indicates that post-natal vaccines is a cause of autism.

Bill Glovin: Hmm, many of our articles talk about genetics as our best chance to defeat various neurobiological disorders. What are your thoughts on tinkering with the DNA of embryos to reduce the risk of mental disorders such as autism?

David Amaral: Well, Bill.

Bill Glovin: That's an easy one, right?

David Amaral: That's probably above my pay grade. I've come to learn is that when we first started the MIND Institute, it was at the inducement of four families that have children with autism. As I was learning to become an autism researcher in those early days, what they told me is they wanted me to cure autism, that's what they wanted. And they wanted to do it as quickly as possible.

Sort of naively I thought, well, autism is the enemy and let's figure out what causes it and then we can figure out how to either eliminate that cause or treat the effects of that cause. So that was my early education. Now, I have friends who are autistic, and I realize that while there are many, many aspects of autism that are disabling and we certainly need to try and create or prevent those disabling aspects of autism; I've come to learn that there's actually many, many aspects of autism that are beneficial.

There's a colleague and now friend of mine, John Robeson, who is an adult with autism who sits on the inter agency coordinating committee with me. He talks quite candidly about the problems that he's had in his life making and sustaining social contact. He

talks about his anxiety problems. And certainly, there is issues and challenges that he's had to deal with.

But he's also talked about the fact that he sort of intuits electronic circuits, and in his early career he traveled with KISS, the rock group, and was able to work with them because he could actually fix their amplifiers even though he had no formal training in electrical engineering.

He just was able to understand, comprehend electronics and was able to not only fix things, but actually create things, and created a lot of their fancy gear that they used, and went on to then open an automotive repair shop and has written several books on the challenges and the benefits of being autistic.

So, when you say should we tamper with the DNA of a fetus to try and eliminate mental disabilities, I think we have to have a debate about whether if we remove the bad aspects of being autistic, whether we'd remove the good aspects, as well. I think we're nowhere close to being able to figure that out at this point in time.

The other aspect of that is that the genetics of autism are incredibly complicated. There are hundreds of genes, or over 100 genes now that have been shown to be associated with risk for autism. There's a prediction that, that may go up to a 1,000 or more. I think we just don't have an idea at this point in time how these genes, even the ones that are very clearly associated with autism, and if you have a mutation ...

I mean first of all there's very few genes that if you have a mutation in that gene you're definitely going to have autism. There's one called the CA-E8 gene that looks like, it's very, very rare, but it looks like if you have a mutation of that gene than you're very highly likely to have a diagnosis of autism.

But even with that gene we don't know how mutations of that gene lead to autism in the end. So, I think, I don't know, we're decades if not longer away from being able to tinker with DNA to try and modify both psychiatric disorders and mental disorders like autism.

And again, I think hopefully before we're technically able to do that, I would hope that we would have a ... This is where we need ethicists and philosophers and probably even people who come from a religious perspective, as well, who can debate the pros and cons of doing that type of tinkering.

Bill Glovin: Do you see a society that is more tolerant and accepting of autistic adults? And are there enough social services for them?

David Amaral: Well, so no. The answer to your first question is yes. I think autism even in the 20 or so years that I've been involved in it people felt ... The parents were thought of autism and any kind of mental disorder, neuro developmental disorder in children as sort of a scourge.

When I first got into the field in the late 1990s, many families were ashamed that they had a child who had a diagnosis of autism. And I think that is almost completely changed in the United States. I think now through advocacy groups, through self-advocates, people are incredibly more tolerant of the autistic community. And I think that's an absolutely wonderful thing.

So, there is a revolution going on right now of trying to incorporate people on the autism spectrum into ... Certainly in research more and more people with autism are getting involved in research. In the society that we established some years ago called the "International Society for Autism Research" there's many more people who are on the spectrum who are participating in that.

There's an effort nation-wide to find appropriate employment for people with autism. But this is just starting. And I think the answer to your second question, the amount of services available for people with autism and other neurodevelopmental disorders is nowhere near what is necessary in the United States. I do hope that both the government and private organizations will able to marshal increasingly more resources to be able to allow people to be able to have gainful employment.

But the other thing is that the long-term care of people with autism is an issue, as well. I know many, many families who their main worry is who's going to take care of my child after I die? And many of these children as they turn into adults still need a fair amount of support in order to go through daily life. And again, we don't have a nation-wide system to be able to provide for that support.

I always think whether autism is educating us about how to be a better society, and I think that it's not an either *or* situation. Sometimes I hear debates where people say, "Well we shouldn't be spending so much money on doing basic research about autism. We should be putting it all into finding support services."

Whenever I hear that argument I think this would be shooting ourselves in the foot, right? We need more resources for both because if we don't actually understand what's causing autism, we're never going to get to the point where we can have targeted treatment to decrease disability. So, we definitely need more funding to go into research into causes and outcomes of autism.

On the other hand, we also need more funding for the people that have autism right now so that they can get better job training and ongoing social services and social support services. So, what it's teaching us is that as a society we should be doing more for people who have these problems than not less.

Bill Glovin: I only have 16 to 17 more questions, but I think that's a great note to end on. So, I'm gonna let you off the hook 'cause you probably have a life and things you need to get to, so, is there anything that I've kind of left out that you'd like to say about anything?

David Amaral: I think you've done a good job, Bill. I think one thing that I would say is that understanding autism is really a partnership between families who have affected

individuals, and the scientists and clinicians that are trying to understand and treat this disorder.

So, for those who are listening to this podcast who might be family members, or even people who are affected by autism, I would encourage you to participate in research. And one easy way that anybody, or virtually any place in the country can participate in autism research at this point in time, is that if you have a family member, or if you yourself are affected by autism, you can join a national research project called SPARK, S-P-A-R-K.

This is a very ambitious project that is being funded by the Simons Foundation in New York. The goal of this project is to recruit 50,000 families or individuals with autism across the nation. And the cool thing about this is that it ... for these 50,000 families, and it's important that it be the individual affected by autism and their both biological parents because the study is first and foremost trying to understand more about the genetics of autism.

But the cool thing is that you can do this all from the comfort of your own home so that if you go to the SPARK website and maybe I can give you, Bill, a link to the website so you could post that, as well. But I'm sure people would be able to find it.

You go to the SPARK website. You can sign onto this project and what happens is there are questionnaires on the website that the family members can answer. And then the SPARK group will send a kit out to you in order to get a sample of your spit. There's actually DNA in your spit, and that's all you have to do. There's no blood sampling or anything else, so it's relatively straight forward.

You mail the kit back to SPARK and then you become part of this national database that will help us understand the genetics of autism. Plus, it will open up possibilities for future scientific research, so we'll be able to recontact these 50,000 families to do additional studies in the future.

It's these kinds of collaborations between families and scientists, and funding agencies like the Simons Foundation, that I think are really going to allow us to understand this very complicated disorder. So, my last plea would be to, for those affected by autism, please participate in research wherever you are. And link to the SPARK website and see if that's something that you feel comfortable collaborating with us.

And my institute is one of the sites, one of 23 sites around the country, but participating in any of the sites will help us achieve the goal of getting information on these 50,000 families. And I should say just to reassure people is that the information that comes into SPARK is all anonymized, so we respect the privacy of people who participate in SPARK, and at the same time, though, it's going to provide incredibly valuable information to help us understand what's going on to cause autism.

Bill Glovin: Hmm, that's great information. Interestingly in preparing to talk to you I was scouring the Simons Website and saw SPARK only yesterday.

David Amaral: Oh, good.

Bill Glovin: So, they do a great job, and -

David Amaral: Yes, they are terrific.

Bill Glovin: And they have some great publications. And I saw that you're affiliated with them, as well, and they have funded some MIND Institute research.

David Amaral: Yep.

Bill Glovin: Great, well thank you so much, David. It was really just an honor to really have you write for us, and you did an amazing job, and hopefully it'll do some good.

David Amaral: Thank you. I enjoyed working with you, and I hope people enjoy the article and this podcast.

Bill Glovin: And thanks again to David Amaral for that insightful discussion. He covered an amazing amount of important areas concerning something that is important to millions of people. To access David's article go to Dana.org.

And don't forget about Brain Awareness Week, which is coming up March 13th to the 19th. And to get information on events and how to get involved, again, you can go to Dana.org.

And I'm Bill Glovin and thanks for tuning in, and we'll see you next month. Bye.