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Autism's Gut/Brain Connection: Can the Microbiome Influence Neurodevelopment?

Paul Rokuskie:
In the fall of 2012 a series of guidelines on the management of autism-related medical conditions was published in the journal Pediatrics. Unfortunately, these guidelines have not been widely followed. To help increase the use of these autism related medical guidelines research is being conducted into many autism-related gastrointestinal issues. Recently two major research projects spanning three years each have received funding, one focused on intestinal bacteria, the other on chronic constipation. The goal is to advance our understanding of autism's gut-brain connection. You're listening to ReachMD. I'm Paul Rokuskie, your host, and with me today is Dr. Pat Levitt, Simms/Mann Chair in Developmental Neurogenetics, Children's Hospital Los Angeles, and Dr. James Versalovic, Pathologist in Chief and Head Department of Pathology, Texas Children's Hospital. Welcome, Dr. Levitt and Dr. Versalovic.

Dr. Pat Levitt:
Thank you.

Dr. James Versalovic:
Thank you very much.

Paul Rokuskie:
So Dr. Levitt, can you tell us a little bit about your professional background?

Dr. Pat Levitt:
I'm a developmental neuroscientist, Ph.D., and the research programs that I'm involved with are really focused mostly on trying to understand the role of genes and environment together that contribute to the development of circuits that are vulnerable in disorders like autism and schizophrenia and other psychiatric disorders, and we also look at clinical populations to try to understand individual differences among children who have the same diagnosis but may present in different ways.

Paul Rokuskie:
So Dr. Versalovic, tell us a little bit about your professional background.

Dr. James Versalovic:
I'm a physician scientist so I have an M.D. and a Ph.D. My medical specialty is pathology and so we're pathologists and we're actively involved in determining the diagnosis of children here at Texas Children's Hospital who have a variety of disorders, and my main focus in my biomedical research program has been gastrointestinal disorders in children and in this case how the intestine may be linked with the brain and the gut-brain access. So we're very interested in how the microbiome can influence diseases in children.

Paul Rokuskie:
So Dr. Versalovic, Can you tell us about the research you and your team have been working on?

Dr. James Versalovic:
So in our Texas Children's Microbiome Center based in Texas Children's Hospital we have a team of scientists who are actively working on understanding the human microbiome with an emphasis on intestine and by understanding the various microbes, mainly bacteria, that are present in the intestinal tract we're interested in how these differences in these bacterial communities can influence the immune system and the nervous system and signaling within the human body, and so beyond composition we're very interested in function and how these microbes coexist with humans living together as one system to hopefully promote health and prevent disease, and if we have disease how can we affect disease and reduce symptoms, maybe possibly in the future cure disease by changing the function of the

microbiome.

Paul Rokuskie:
So what is the methodology of your new microbiome study?

Dr. James Versalovic:
Well, in our new study we are interested in bacterial composition and function in children with autism spectrum disorders, and so in kids with autism we know that many have gastrointestinal symptoms, GI symptoms if you will, and often that's constipation, sometimes it may be just abdominal pain, diarrhea. We are trying to understand how the microbiome in the intestine may be contributing to these GI disorders in children with autism and by understanding the composition and the function of the microbiome in autism we're hoping that we can treat these symptoms and hopefully affect autism itself because we think the gut and brain are linked together. So we're really going to be studying the microbes themselves and the metabolites or the chemical compounds that are produced by these microbes that get into the blood stream, get into the body, affect the nervous system.

Paul Rokuskie:
So what are the outcomes of this research that you hope to find?

Dr. James Versalovic:
Well, first of all, we need to understand the differences in children with autism that have GI symptoms and disorders versus those that may just have autism without the GI disorders and begin to understand diseases in children with greater resolution. So we talk about stratification where we can separate patients by understanding the whole system more, microbe and man in this case, and by doing that hopefully we can gain some insights into why some patients respond to different treatments differently in different says, and so ultimately we want to be able to change the function and composition of the microbiome to reduce the symptoms, for example reduce the constipation, reduce the abdominal pain. Hopefully then also enhancing the quality of life for these children and ultimately maybe affecting autism itself, and if the brain and gut are linked together can we not only affect the GI function, can we begin to make an impact on brain function too, because we know these chemical compounds are providing signals from gut to the brain.

Paul Rokuskie:
So what are some of the possible applications of your research in the probiotics field?

Dr. James Versalovic:
Well, my laboratory has been involved in probiotics research for a number of years and we know that there are these first generation probiotics that are commonly recognized such as lactobacillus and bifidobacterium that may be present in yogurts and fermented foods and anyone going into a grocery store can read on a label and see these organisms that may be present, but we'd like to develop the second or next generation probiotics and by finding new probiotics based on the microbiome research in this project our goal is then to take these possible new microbes that have beneficial properties, develop new probiotics that can then be used in the context of autism, and these probiotics may reduce GI symptoms, may cure GI symptoms such as constipation, abdominal pain, but may also impact the disorder itself, these autism spectrum disorders in a deeper way, in a broader way again by affecting the gut-brain communication. So we are hoping to identify new candidate probiotics for autism, tailor made for autism.

Paul Rokuskie:
If you're just joining us you're listening to ReachMD. I'm your host, Paul Rokuskie, and I'm speaking with Dr. Pat Levitt and Dr. James Versalovic. We're talking about gut-brain studies and their impact on autism spectrum disorder research. So Dr. Levitt, we'd like to turn to you now. Can you tell us about the research you and your team have been working on?

Dr. Pat Levitt:
Several years ago we did two studies that I think led us to where we are now. One was to look at children with autism spectrum disorders and their medical comorbidities. Every child with an autism spectrum disorder also typically will be diagnosed with a GI problem or an asthma problem, immune problems, and other kinds of medical issues that we typically don't think about as being a core component of the spectrum disorder. GI disorders are present, I think there's some consensus, there's about 40 percent of children diagnosed with autism spectrum disorder have a GI condition that can be diagnosed by a pediatric gastroenterologist. We did a genetic study and showed that there were certain genetic risk factors that we identified previously just in autism that seemed to be even more represented in children with autism and diagnosed GI conditions. So we became interested in trying to understand in more depth what might be unique about children who have both autism and a diagnosed GI condition.

It turns out from a study we did where we recruited children into the study in contrast to depending upon medical histories that you can find in hospital charts that children with autism and GI problems typically have more severe language impairment which is part of the core that's used for diagnosis, core symptoms. They tend to have more obsessive compulsive types of behavior, their social

communication tends to be impacted greater, and the other thing that we found which was a surprise is that we looked at a measure of oxidative stress which is a sign of problems with organ function. You can measure somebody's markers in blood or in urine and they're used very commonly in other disorders like stroke or aging, obesity, etcetera. So we looked at it in autism and saw that there's an elevation of these markers and there's a subset of children who are even higher in terms of their oxidative stress status compared to people who even have a stroke.

So that was a red flag for us in terms of then trying to design a study where we would recruit children and then follow them over the course of a year and try to do two things. One which you just heard about is to try to understand the symptomology better and trying to figure out whether we can predict children who respond well to GI treatment and those who don't. There's always a subgroup of children who don't seem to respond very well. We know that that has an impact on their ability to be compliant for their autism treatment.

So this study that we're doing at Children's Hospital Los Angeles as part of the Boone Fetter Clinic where our children and families with autism spectrum disorder come in, we're collaborating with a group at the Center for Autism and Neurodevelopmental Disorders at the University of California Irvine which is in Orange County to recruit children and follow them for a year, bringing them in every three months to see how well they're doing in terms of their GI treatment that is being administered by their pediatric gastroenterologist, and then doing a large number of measures to see how well their social communication, language, other behaviors that are associated with autism, are they improving or not.

At the same time we're measuring this oxidative stress marker because what we know from other studies that has not been looked at in autism yet is if their clinical conditions, if someone's clinical conditions get better then their oxidative stress improves as well and this marker gets better. If they don't respond then typically that marker stays high. So we're going to follow children over the course of a year, measure that marker, and correlate that with how well they're doing in terms of both their response to GI treatments from our pediatric gastroenterology specialists, as well as determining whether there are certain features of autism spectrum disorder that seem to improve more than others when a child's GI conditions get better, and that's the study in a nutshell.

Paul Rokuskie:
So you talked about oxidative stress a little bit there, how does that impact children with both autism spectrum disorder and constipation?

Dr. Pat Levitt:
So we found in the initial study that we published two years ago that if you look at this oxidative stress in children with autism spectrum disorder or with GI only and they don't have autism spectrum disorder this marker is elevated. It's in the children who have both where this combination seems to really play havoc with their systems, and Dr. Versalovic noted before that these children are medically complicated, the different systems talk to each other, the gut and the brain talk to each other, the brain also talks to the gut and we think that when both of those systems are disrupted in terms of functioning well that this condition of oxidative stress which essentially creates problems for the GI system and the brain to function at a highly efficient level, it puts a stress on the system, and we see this elevated more in children who have both conditions than when we look at children who have either one or the other.

Paul Rokuskie:
So Dr. Levitt, where can our listeners go to get more information about what you're working on?

Dr. Pat Levitt:
There's an email contact. The email is tummytroubles, t-u-m-m-y, troubles, one word, at CHLA.usc.edu. They can go to the Children's Hospital Los Angeles website and they'll be able to navigate to find information about the study itself which is described in some detail and the families that are going to participate in this are because of the nature of the study where children have to come back every few months it's going to be, the families are going to be located in southern California.

Paul Rokuskie:
So Dr. Versalovic, can you tell us where our listeners can go to get more information about the research you're working on?

Dr. James Versalovic:
We have a specific email address for any queries, questions about this project, and that is autismgi@bcm.edu, BCM for Baylor College of Medicine and Texas Children's Hospital where this study will be based will also be providing information on our main website and we're working on advancing that content. We also have a specific person, Dr. Ruth Ann Luna, L-U-N-A, and her email address is raluna@bcm.edu and we will be coordinating local efforts here based at Texas Children's Hospital, anyone can contact the Department of Pathology. In addition we have collaborative sites at the University of Texas Southwestern and Dallas, and Nationwide Children's in Columbus but if any individual is interested in those sites in Dallas, Texas and Columbus, Ohio they can certainly just email autismgi@bcm.edu and we'll provide that contact information for anyone interested.

Paul Rokuskie:
So I want to thank both of you for joining me today for this program.

Dr. James Versalovic:
Certainly.

Dr. Pat Levitt:
My pleasure.

Paul Rokuskie:
My thanks again to my guests, Dr. Pat Levitt, Simms/Mann Chair in Developmental Neurogenetics, Children's Hospital Los Angeles, and Dr. James Versalovic, Pathologist in Chief and Head of Department of Pathology, Texas Children's Hospital. We've been discussing autism spectrum disorder. Be sure to visit our website at ReachMD.com featuring podcasts of this and other series. I've been your host, Paul Rokuskie, and thank you for listening.