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Canadian Study: Is there a Digestive Link to Autism?

By Kulani Mahikoa

A newly formed multidisciplinary research team at the University of Western Ontario in London, Canada, will study the involvement of a number of environmental factors, particularly those involving diet and the digestive system, in the causes and symptoms of autism spectrum disorders.

The research group's goal is to find the basic processes underlying the cause of autism. Headed by Dr. Derrick MacFabe, the Kilee Patchell-Evans Autism Research Group (Web site: http://www.ssc.uwo.ca/psychology/autism.htm) hopes to uncover the workings of specific brain areas that may be responsible for autistic behavior. The group's long-term goal is to develop screening methods to identify infants who may be "at risk" for autism and possibly to devise treatment strategies to prevent autism or lessen its severity.

"Many studies report abnormalities of the digestive system in autistic patients, including episodes of diarrhea or constipation," says MacFabe. Furthermore, many caregivers report that some patients' symptoms are worsened by certain dietary factors, particularly milk or wheat products.

"The gut-brain link to autism is an emerging field that has only recently been explored," he continues. "Gut-brain effects may result from alterations in the diverse populations of bacteria which normally inhabit the human digestive tract. Normally these bacteria produce largely beneficial compounds such as essential vitamins and substances found to be important in normal brain development, immune function or protection against some forms of cancer. However, in certain instances, alterations in the composition of these bacterial populations caused by a variety of conditions may lead to overproduction of some of these compounds. Alternatively, some persons may be relatively unable to break down these compounds due to inherited or acquired disorders."

MacFabe adds, "Autism is clearly a disorder of behavior; therefore, the detailed analysis of complex movement, both in human autism and in experimental animal models of the disorder, is absolutely essential. The development of a suitable animal model will allow researchers to ethically and rapidly examine possible environmental risk factors, and to discover the basic processes by which these agents affect brain and behavior." Ultimately, MacFabe notes, the research team hopes that their findings will lead to novel treatment interventions.

The researchers also are examining the effects of gut metabolic compounds at the behavioral, electrical and biochemical levels. They have found that some of these bacterially produced compounds, known as short-chain fatty acids, when injected in small amounts into the brains of experimental rodents, immediately produce bouts of hyperactivity and repetitive behavior resembling those seen in autism spectrum disorders. The animals also display brain electrical changes resembling some types of human epilepsy, which often co-exists with autism. Repeated exposure to these compounds increases the severity and duration of these effects, suggesting that these compounds exert permanent effects on brain and behavior, according to MacFabe. "Moreover, brain tissue from these animals, when examined microscopically, reveals an inflammatory process resembling that found in brain tissue donated from deceased persons with autism," he says. The main brain changes appear to involve the glia, the non-neural component of the brain. These cells, thought to be the "scaffolding" of the nervous system, have been found to play a previously underappreciated role in the working of the nervous system.

Glia are now known to be involved in diverse processes, such as the maintenance of a stable environment for nerve cells, learning and memory, and the rapid transmission of information throughout the brain. They are important throughout the life cycle in orchestrating the orderly development of the nervous system, and also in brain cell rewiring or repair during learning or following brain injury.

Thus, abnormalities found in experimental animals may lead to problems in information processing, brain electrical activity and the orderly production of movement, and provide a link to some environmental risk factors in human autism, such as those involving the diet or digestive tract. The group is further expanding this preliminary work to examine the effect of these compounds on early brain development and social behavior.

Another aspect of the research team's work will be to assess environmental factors or genetic sensitivity in large populations of those with autism and their families. With the assistance of Dr. Jeanette Holden, director of the Autism Spectrum Disorders — Canadian-American Research Consortium (Web site: http://www.asdcarc.com/), the group will have access to a patient registry of more than 7,000 participants.

MacFabe cautions that this work is in its infancy and is currently limited to rodent studies. However, the observed effects of these bacterial compounds may provide an important framework in linking digestive and dietary factors to the brain, immune and behavioral effects found in human autism spectrum disorders, he says.

The Kilee Patchell-Evans Autism Research Group was started by Derrick MacFabe and prominent businessman David Patchell-Evans, president and CEO of GoodLife Fitness Clubs, Inc. Patchell-Evans is also the father of Kilee, a child with autism, for whom the group was named. Patchell-Evans and the Autism Canada Foundation (Web site: http://www.autismcanada.org/home.htm) provided donations of $1.2 million to fund the group. Researchers participating include University of Western Ontario psychology chair Dr. Kaus-Peter Ossenkopp, and Drs. Donald Peter Cain, Martin Kavaliers, Elizabeth Hampson and Fred Possmayer, research scientists specializing in the effects of a variety of compounds on brain development, function and complex behavior. In addition, strong collaborative alliances have been formed with other academic institutions in Canada and the United States. A paper outlining the group's work (MacFabe et al., "Neurobiological Effects of Intraventricular Propionic Acid in Rats: Possible Role of Short Chain Fatty Acids on the Pathogenesis and Characteristics of Autism Spectrum Disorders," Behavioural Brain Research) *is in press.*