A NEW THERAPY TO REDUCE ANXIETY, IrrITABILITY AND GASTROINTESTINAL ISSUES IN AUTISTIC INDIVIDUALS

Gastrointestinal (GI) issues are extremely common in autistic individuals. In fact, recent research suggests that up to 80 percent of autistic children present with at least one GI issue. The most common issues are constipation, diarrhea, bloating and abdominal discomfort.

The reason why children with autism present with higher rates of GI abnormalities is still under investigation. Many studies have analyzed the gut microbiome of individuals with autism spectrum disorder (ASD) and compared the results with the non-ASD population. Although many differences are seen, recent research has shown that there is a significant difference in gut microbial metabolites in ASD individuals compared to non-ASD individuals. The gut microbiome is comprised of bacteria, viruses, fungi and other microorganisms. When these organisms break down, they produce metabolites. While metabolites can have local effects in the GI tract, they can also be absorbed into the body’s systemic circulation where they can affect a person’s immune system, metabolism and organs. They can even cross the blood-brain barrier and affect the brain and cognitive function.

One specific gut metabolite that has been shown to be elevated in children with autism is 4-ethylphenyl sulfate (4EPS). When present at elevated levels, this metabolite can be toxic and has been associated with anxiety and chronic kidney disease. It also has the ability to cross the blood-brain barrier and alter the activity of brain cells.

In experiments with mice, a therapeutic known as AB-2004 has been shown to reduce the levels of 4EPS. It does this by binding to 4EPS as it passes through the GI tract, and it is then excreted in the stool. Results from these experiments showed a reduction in anxiety-like behaviors and lower levels of 4EPS.
The next step in research is to take this therapeutic to a human clinical trial to see if the same effects are seen in individuals with autism. A research group from Axial Therapeutics (Woburn, MA) and the California Institute of Technology carried out this clinical trial. The goal was to determine if AB-2004 was safe and tolerable, if it decreased 4EPS levels, and if its administration resulted in any behavior changes in study participants.

**Study**
This study was a human pilot study. It was open-labelled, which means that the participants knew about the therapeutic they were taking, and there were no placebo controls. A total of 30 adolescents with GI symptoms and a confirmed diagnosis of ASD were enrolled in the study. Each participant was given the therapeutic AB-2004 three times a day for eight weeks. Urine, blood and stool samples were collected at the beginning and the end of the trial. Behavior was also assessed at the beginning and the end of the trial, as well as four weeks after the trial ended.

**Results**

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<th>Well Tolerated</th>
<th>Over 76% Improvement</th>
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<td>AB-2004 was well tolerated by all participants, and there were no adverse effects.</td>
<td>Over 76 percent of participants improved in GI symptoms after the eight-week trial of AB-2004.</td>
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<th>Reduced Levels of 4EPS</th>
<th>Anxiety &amp; Irritability</th>
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<td>There were reduced levels of 4EPS in the urine and blood samples collected at the end of the eight-week trial.</td>
<td>Exploratory behavior analysis showed a reduction in anxiety and irritability after eight weeks of trial. While the decreased anxiety continued after the drug removal, the irritability did return.</td>
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Discussion
Research has shown a direct relationship between GI discomfort and troubling behaviors, such as self-injury, aggressiveness, poor sleep and irritability, especially in nonverbal autistic children. Given the fact that the gut and the brain have a strong communication system known as the “gut-brain axis,” these findings make sense. Elevated levels of the metabolite 4EPS could be one explanation for some autistic behaviors.

This clinical trial shows that there could be medications that aid with gastrointestinal issues, anxiety and irritability in autistic individuals. While we recognize that these are not considered core symptoms of autism, they are commonly seen in autistic individuals and are related to the spectrum of challenges such individuals experience. Future studies are needed with a larger group of participants to confirm that the use of AB-2004 is safe, and to further investigate brain function when AB-2004 is administered. The next step, which is to repeat the experiment with a double-blind placebo-controlled trial, is currently under way. We look forward to seeing the results of this trial.

Written by Autism Advocate Parenting Magazine

To find out more about a clinical trial that is researching AB-2004, please visit this website: www.TheAutismStudy.com

References