

**EDITORIAL: Stephen M. Edelson, Ph.D.**

## Large-scale studies in autism: What do they show?

Over the past decade, many studies have documented substantial impairments in the gastrointestinal (GI), immunological, and metabolic systems of individuals with autism spectrum disorders (ASD). Although this is well known among researchers in the autism biomedical field, many other professionals have yet to acknowledge the high rate of these medical comorbidities.

The lack of awareness of medical symptoms associated with autism is partly due to the poor lines of communication among researchers, clinicians, and therapists in the autism and general medical communities.

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Another reason for it, which is the theme of this editorial, is that many professionals are unaware of the findings of large-scale research studies, which are a core component of scientific investigation.

Most of the research documenting gastrointestinal, immune, and metabolic impairments in ASD has involved small-to-moderate sample sizes. However, in the past few years, numerous large-scale studies have documented high rates of medical problems in individuals with autism as compared to the general population. Some of these medical problems have also been shown to be highly related to challenging behaviors. A brief summary of several of these studies is described below.

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 In a study of 300,000 children in the United States, children with ASD were 60% more likely to suffer from irritable bowel disease than neurotypical controls (*Journal of Autism and Developmental Disorders*, 2018).

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 A meta-analysis, which combines and re-analyzes the data from previously published studies, revealed that children with autism were four times more likely to experience gastrointestinal complaints as compared to controls (*Pediatrics*, 2014).

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 Based on 17 items on a questionnaire filled out by 131 parents of children with ASD, pediatric gastroenterologists were able to correctly identify GI problems in 84% of the children (*Journal of Autism and Developmental Disorders*, 2018).

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 A study involving 522 children with ASD and 703 controls revealed that the children with ASD were 75% more likely to suffer from sleep problems than controls (*Pediatrics*, 2019).

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 Researchers found a strong correlation between sleep problems and aggression in 1,045 children with ASD (*Research in Developmental Disabilities*, 2018).

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 A moderate-size study involving 81 children with ASD found that sleep problems were associated with aggression, irritability, inattention, and hyperactivity (*Journal of Autism and Developmental Disorders*, 2016).

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 A study examining the U.S. National Health Interview Survey database analyzed data from 1,868 children with ASD and 197,652 controls. Children with ASD were 7% more likely to suffer from food, respiratory, and skin allergies than controls (*JAMA Network Open*, 2018).

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 Researchers using the National Survey of Children's Health database studied the prevalence of obesity in autism. Obesity is related directly or indirectly to GI function, immunology, and metabolism. Analyzing data on 875,963 teenagers with ASD and 31,913,657 controls, the researchers found that the individuals with ASD were 7% more likely to be obese than controls (*Autism*, 2018).

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 A study examined the prevalence rate of obesity in 5,053 children with ASD who were between two and 17 years of age. Thirty-five percent of them were overweight, and 18% were obese (*Pediatrics*, 2015).

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 Another important component of scientific investigation is referred to as *converging operations*. This means that researchers study a phenomenon in many different ways, providing support to a hypothesis from a multitude of perspectives. Over the past decade, hundreds of studies have investigated medical problems associated with autism, using numerous sample sizes, experimental designs, and assessment measures. Such studies overwhelmingly indicate the presence of several common medical comorbidities in autism, and some of these comorbidities are related to challenging behaviors.

Given the frequent association of medical symptoms with autism, standardized diagnostic assessments (e.g., ADOS-2, ADI-R) and medical evaluations (conducted by pediatricians) should address these common

symptoms. If any medical comorbidity is suspected, standard practice should include a referral to a specialist.

Regarding treatment of medical comorbidities, there are many small-to-moderate studies published and underway. However, at this time, only two medical interventions

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are approved by the Food and Drug Administration (FDA), and they are both psychiatric drugs: risperidone (Risperdal) and aripiprazole (Abilify). There are no FDA-approved interventions to treat common medical problems in autism, such as GI, immune, or metabolic dysfunction. Physicians should consider, at the very least, prescribing treatments that have already been standardized for the general population.

One note: Based on many clinical reports, doctors should take caution regarding medication doses. Some individuals with ASD are sensitive to certain medications and, as a result, tend to overreact when given a recommended dose. The opposite effect can also occur, with individuals requiring more than the suggested dose in order to show a response. It would be advisable to start low and increase slowly when prescribing medications.

The fact that individuals with autism often suffer from medical comorbidities should no longer be considered questionable. Professional licensing organizations should require professional training (e.g., CME) about these medical conditions in order to ensure that providers offer patients with ASD optimal care. (Note: ARI offers, in joint providership with the Cleveland Clinic, complimentary AMA PRA Category 1 Credit™ to physicians and the general public.)

Finally, funding agencies should focus more of their attention on supporting research on GI, immunological, and metabolic problems in ASD. They should do this by financing multidisciplinary (i.e., medical, sensory, behavioral) studies.

In recent years, our knowledge about the role of comorbid medical problems in ASD has expanded rapidly. Now it is time for us to translate this knowledge into state-of-the-art research and more effective treatment options, so individuals with ASD can get the help they need.