Questions Remain Regarding the Effectiveness of Many Commonly Used Autism Treatments

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Parents of newly diagnosed children with autism spectrum disorder (ASD) are faced with a dizzying array of treatments that promise to improve their child's autism symptoms, cognitive and language abilities, and health. Desperate to leave no stone unturned as they strive to help their child have the best possible future, many parents spend countless hours and large amounts of money on unproven therapies. Unfortunately, as the 2 systematic reviews published in this issue of *Pediatrics* describe, the scientific field has not done enough to provide definitive answers about the effectiveness of many commonly used treatments.

The first article, by Sathe et al[1] ("Nutritional and Dietary Interventions for Autism Spectrum Disorder: A Systematic Review"), provides a detailed review of studies on the effects of various supplements, including omega-3 fatty acids, digestive enzymes, methyl-B_{12}, levocarnitine, and gluten- or casein-free diets. The results of the existing studies were mixed, with some studies finding positive results and others finding no benefit. The available studies are small and short-term, precluding any definitive answer about whether nutritional supplements or dietary therapies are helpful for children with ASD. This is unfortunate in light of the fact that special diets and dietary supplements are the most commonly used complementary and alternative treatment by children and adolescents with ASD.[2]

The second article, by Weitlauf et al[3] ("Interventions Targeting Sensory Challenges in Autism Spectrum Disorder: A Systematic Review"), focuses on treatments for sensory symptoms, a common feature of ASD that now is considered 1 of the diagnostic symptoms of ASD, according to the American Psychiatric Association (*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*).[4] Children with ASD can exhibit sensory overresponsivity, underresponsivity, or both.[5] Sensory overresponsivity, which is characterized by heightened and unusual reactivity to sensory stimuli, can be disabling and is often associated with avoidance, aggression, anxiety, lower levels of social and adaptive behavior, and food selectivity.[6–8] Higher rates of sensory overresponsivity are also associated with sleep problems and chronic gastrointestinal symptoms.[9,10] Thus, an effective treatment of sensory challenges would have a significant impact on children's and families' quality of life. Based on the existing studies, Weitlauf et al[3] conclude that there is evidence that sensory integration–based intervention is associated with improvements in both sensory-related and motor skill outcomes in children with ASD. This is encouraging news. This form of therapy is typically delivered by an occupational therapist and involves special exercises designed to improve a child's responses to touch, sound, sight, and movement. The authors also note that there is promising evidence

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that massage can improve sensory challenges and ASD symptom severity. However, the authors' confidence in their conclusions about both types of therapy is low because of the small number and size of existing studies. The authors were not able to draw any firm conclusions about music therapy and auditory integration therapy, given the paucity of available data.

Looking ahead, it is crucial that researchers address this huge gap in our knowledge about the efficacy of treatments that parents are commonly using and paying for. To achieve this end, studies must be carefully designed with appropriate controls. Treatments should be manualized, with standardized protocols and measures of fidelity of implementation. Furthermore, a major challenge is the well-documented large placebo response in many ASD clinical trials, estimated to be of moderate effect size.[11] Evidence suggests that ≤30% of participants with ASD respond to placebo treatments. In a recent meta-analysis of 25 trials of pharmacological and dietary interventions, it was found that factors such as type of rater, the geographic location of the trial, and presence of adjunctive treatments contributed to the placebo effect. Remarkably, 47% of the improvement in the active treatment group could be attributable to the placebo effect.[11] This phenomenon underscores the need for careful assessments of statistical power in designing ASD clinical trials.

There is a need for standardized, objective, quantitative, and reliable outcome measures that can be aggregated across autism clinical trials. The authors of the systematic reviews published in this issue of *Pediatrics* were unable to compare or combine results across trials because of the variability in both the types of outcomes and how they were measured. Many existing autism assessment tools were designed for screening and diagnosis and are not sensitive to assessing change in autism symptoms in response to a treatment. The measurement of treatment response is particularly complex in ASD. ASD is heterogeneous, involving symptoms that vary depending on an individual's symptom profile, gender, cognitive and language abilities, and development level. Ideally, outcome measures should be linked to the treatment's hypothesized mechanism. Current efforts are focusing on developing outcome measures for autism clinical trials that are linked indirectly or directly to underlying biology, such as patterns of attention and neural circuitry.[12–14] Such measures can help determine whether the treatment is influencing the hypothesized treatment mechanism and potentially predict treatment response.[15] They can also serve as an early efficacy signal that can detect response to treatment before changes in more distal measures such as motor skills and social behavior are evident.[14] Fortunately, large-scale efforts are under way that are aimed at improving our ability to reliably measure treatment response in ASD clinical trials, including validating biomarkers that can be used to stratify participants and more sensitively and reliably assess outcomes.[16,17]

Progress is being made to develop novel treatments that promise better outcomes for people with ASD. We must press forward by testing these treatments in the most rigorous fashion and be careful to limit our conclusions until definitive trials are conducted. Practitioners, policymakers, and parents who are striving to help their children with ASD are depending on the autism research community to conduct research that will provide the answers they need.

ABBREVIATION

ASD: autism spectrum disorder

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