

The Autism Treatment Network and Autism Intervention Research Network on Physical Health: Future Directions

Autism spectrum disorders (ASDs) represent complex neurodevelopmental disorders with multiple etiologies.¹ The resulting variability of behavioral, medical, and developmental concerns that affect individuals with ASDs has made it extremely difficult to predict which treatments work best for which individuals. Developing effective treatments and improving care for individuals with ASDs throughout the life span remain urgent priorities. Comprehensive coordinated care for individuals with ASDs will require further advances in our knowledge of medical and behavioral interventions and a health care system that can deliver them consistently.

Over the past 7 years, the Autism Speaks Autism Treatment Network (ATN) and more recently the Autism Intervention Research Network on Physical Health (AIR-P) have significantly increased understanding of the prevalence, nature, and treatment of medical conditions in children with ASDs, such as gastrointestinal conditions, sleep disorders, metabolic disorders, and seizures. The network has pioneered in standardizing the clinical evaluation of children with ASDs, based on a comprehensive, multidisciplinary model of care. The network has also developed key partnerships that have helped the field move from limited consensus toward evidence-based autism-specific guidelines in key areas of medical concern, and has acquired the infrastructure and expertise to develop more targeted treatment studies that can help move the most effective therapies through the research pipeline and into the hands of consumers. The ATN has led in the application of quality improvement methods to autism care and in systematic efforts to bring the experience and lessons of the network to broader communities of professionals and parents. This effort, led by Autism Speaks, has allowed strong synergy among research, clinical, and family communities. Key areas of continued growth for the research activities of network include (1) ongoing enhancement of research infrastructure, including increased availability of biological samples; (2) expansion of the research agenda to include more focused research on epilepsy, psychiatric comorbidities, endocrine issues, biomedical interventions, challenging behaviors, and emergent issues in adolescence; (3) attracting and nurturing new investigators; and (4) increasing use of the network for collaborative multisite studies.

The network will also continue to grow in its impact on the care that children with ASDs and other neurodevelopmental disabilities receive. Key parts of this growth may involve a larger number of network sites; other efforts will expand the reach of the network by improving care, disseminating practices widely, and finding ways to affect the care of much larger numbers of children and youth with ASDs. The high

AUTHORS: James M. Perrin, MD,^a Daniel L. Coury, MD,^b Nancy Jones, PhD,^c and Clara Lajonchere, PhD^e

^a*Department of Pediatrics, Harvard Medical School, MassGeneral Hospital for Children, Boston, Massachusetts;* ^b*Nationwide Children's Hospital; Ohio State University School of Medicine, Columbus, Ohio;* and ^c*Autism Speaks, Los Angeles, California*

KEY WORD

autism spectrum disorder

ABBREVIATIONS

AIR-P—Autism Intervention Research Network on Physical Health

ASD—autism spectrum disorder

ATN—Autism Treatment Network

CER—comparative effectiveness research

CTSAs—Clinical Translational Science programs

This manuscript has been read and approved by all authors.

The statements, findings, conclusions, and recommendation are those of the author(s) and do not necessarily reflect the view of Maternal and Child Health Bureau, Health Resources and Services Administration, or the US Department of Health and Human Services.

Accepted for publication Aug 8, 2012

www.pediatrics.org/cgi/doi/10.1542/peds.2012-0900S

doi:10.1542/peds.2012-0900S

Address correspondence to James M. Perrin, MD, Department of Pediatrics, Harvard Medical School, MassGeneral Hospital for Children, 100 Cambridge St, #1542, Boston, MA 02114. E-mail: jperrin@partners.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2012 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

prevalence of ASDs and other neurodevelopmental disabilities makes essential the active involvement of primary care clinicians in the ongoing management of children and youth with neurodevelopmental disabilities. Active partnerships with federally funded programs, such as University Centers of Excellence in Developmental Disabilities and the associated Leadership Education in Neurodevelopmental Disabilities Programs, as well as the training programs in developmental-behavioral pediatrics, will also serve as key vehicles for dissemination. The changes in health care organization and financing arising from the implementation of the Affordable Care Act can also strengthen care delivery for children with ASDs and other neurodevelopmental disorders. Both research and program development will also extend to the transition to adulthood of young people with ASDs, a period of vulnerability for most adolescents with chronic conditions.^{2,3}

EXTENDING RESEARCH TO IMPROVE CARE FOR CHILDREN AND ADOLESCENTS WITH ASDs

Much recent research has helped expand knowledge of the biologic and genetic basis of ASDs, including defining new and novel mechanisms that can lead to new treatments for ASDs and its complications. The ATN and AIR-P provide an excellent platform for carrying out research, including clinical trials conducted in real-world settings with a diverse and well-characterized population of young people with ASDs. Several strategies can help growth in clinical research, including complementing the strong network phenotypic and clinical information with biological data, maximizing use of newer investigative strategies, such as comparative effectiveness research, and applying methods from health services and patient-centered outcome research to the care of children with ASDs.

Incorporating Biologic Data

Identifying biomarkers and biologic profiles for individuals with ASD can markedly expand the value of the comprehensive ATN phenotypic data. The availability of biospecimens and a centralized repository are critical for facilitating the development and application of modern molecular-based research, including gene expression and genomics, proteomics, and metabolomics. Recent advances in high-throughput assays in these areas highlight the potential utility of molecular-based approaches linked with phenotypic data to serve as predictors of treatment response.⁴ The identification of biomarkers derived from blood plasma, saliva, or urine could provide insights into targeted treatment strategies designed to improve or reverse autistic symptoms. The ATN currently collects behavioral and phenotypic data on children in the registry and has recent funding from the National Institute of Mental Health to pilot collection of biospecimens at select ATN sites. The addition of biologic specimens on this well-characterized population could rapidly advance understanding of these disorders. Although the data currently collected in the registry reflect standard of care in assessment and increasingly in treatment, the collection of biologic data outside of routine laboratory testing would be considered as part of research activities. Clinicians increasingly report that results of chromosomal microarray influence the medical care they provide to their patients.⁵ The systematic collection of microarray data as part of the patient registry can help answer questions that may impact health care, policy, and research.

Microarray technologies can help identify etiologic subtypes and could ultimately allow a physician to better predict the response of an individual before the medication is prescribed.⁵ Using this genetic information in the

refinement of patient selection algorithms could help make personalized medicine a reality for individuals with ASD. Recent statements from key professional groups supporting the use of microarray data in the evaluation of children with unspecified causes of intellectual disability should help make this testing standard of care for children with autism.^{6,7}

Growth in network research should also leverage other important large-scale research initiatives such as the Clinical Translational Science programs (CTSAs), now in place at most US academic health centers, as well as most US-based ATN sites. The CTSAs provide additional resources to investigators by providing access to core laboratories, supporting collaborations among a diverse set of investigators to achieve common goals, and supporting opportunities for cross-institutional collaborations extending beyond those of the ATN. One common interest of the CTSAs and the ATN/AIR-P is the nurturing of younger investigators in areas of clinical research in autism and other neurodevelopmental disabilities. AIR-P internal requests for applications provide significant opportunities for junior investigators, including the development of a mentorship program across the network that matches junior investigators with senior researchers with shared areas of interest. The network has also developed a monthly research seminar series for investigators.

A Platform for Research

Given the extreme heterogeneity of ASDs and other neurodevelopmental disorders, effective treatments for individuals with ASDs will likely benefit from a personalized medicine approach that takes into account individual differences in etiologic and phenotypic characteristics. We recognize that current knowledge of the underlying genetics and

biology of autism and related disorders provides little direction to personalized approaches, but hopefully expanded research involving populations well-characterized in both behavioral and biologic ways will lead to better individualized treatments. Comparative effectiveness research (CER) offers research and analytic strategies that can account for clinical and social diversity in real-world populations. Parents and clinicians need more accurate, scientific evidence to help predict which treatments will work most effectively for which individuals. Although more medications and behavioral interventions are in the pipeline for individuals with ASDs and other neurodevelopmental disabilities, the vast majority of clinical trials to date only have compared specific treatments with placebo. Very few studies have carried out head-to-head comparisons of 2 or more treatments. CER studies can provide information about which individuals benefit most from which treatments. Given the early stage of development of CER in the field of autism, the ATN is uniquely positioned to serve as a platform to support these types of trials specifically in the areas of sleep and challenging behaviors. For example, studies using pharmacogenomics and clinical trials would allow clinicians to determine which medication in a certain class would be best for treating specific symptoms.^{8,9}

INCREASING PARTICIPATION OF FAMILIES

Autism Speaks has grown as an organization with strong leadership from families and consumers working together to enhance the lives of people with ASDs. The organization has encouraged consumer participation on many organizational committees, including scientific boards, and solicits feedback from families to ensure that their strategic priorities remain aligned with the needs of the community. It collaborates

with other consumer groups with similar policy interests. Within the ATN and AIR-P, parents have become effective partners, both at each site and across the network in helping to set research and program priorities, reviewing research findings, participating in quality improvement efforts, and helping to assess progress in the network. Partnerships between professionals and parents will lead to continued improvement and growth in the network, ensuring that the research has direct relevance to children and families with ASDs, and that findings and best practices are disseminated broadly to other families, practitioners, and policy makers.

Organizing and Financing Care for Children With ASDs and Other Neurodevelopmental Disorders

Many questions arise regarding the best ways to organize and finance care for individuals with ASDs, including their health care. As with health care for people with neurodevelopmental disabilities in general, that for young people with ASDs varies greatly from community to community and often reflects the experience and beliefs of particular practitioners without a systematic approach. What portion of care can take place in primary care settings and what requires subspecialty arrangements? What service arrangements lead to the most efficient use of limited resources while still ensuring children and families access to timely services? What are the best ways to ensure early identification and most appropriate referral? Current work from the network has addressed several opportunities to standardize clinical evaluation and treatment. Health services research methods, which examine organization and financing of services, can help address issues of personnel, team care, distribution of care and providers, and tradeoffs in different means of financing care.¹⁰ Methods now developing under the

aegis of the Patient Centered Outcomes Research Institute may also have substantial import for care for children and youth with ASDs.¹¹

EXPANDING NETWORK REACH

The ATN sites currently provide care to about 27 000 children and youth with ASDs, a small proportion of the more than 750 000 persons with ASDs <18 years old in the United States and more than 2 million children and adolescents with neurodevelopmental disorders in North America. What mechanisms exist for expanding the network and its influence on the care of much larger numbers of children? Unlike less prevalent conditions, such as cystic fibrosis (1 in 3500) or sickle cell disease (1 in 5000 in the United States), where children can receive the bulk of their care from specialty centers, autism care will require active involvement from community physicians and primary care professionals. Many primary care clinicians already provide much care to young people with autism, but improving that care and ensuring best access to multidisciplinary care as needed will require strengthening the relationships between primary care providers and subspecialty centers, as well as strengthening the financial base of care in general. Growing information technology capabilities offer some effective platforms for communication between primary care and subspecialty care providers (and with families). Providing high-quality multidisciplinary care for children with ASDs and other neurodevelopmental disabilities takes time, whether in primary care or subspecialty units, and methods of financing care should provide payment to support the time needed.

Growth in these collaborative efforts should link actively with other efforts to strengthen primary care, including several provisions of the Affordable Care Act that focus on the development

of team-based care in communities, emphasize chronic care management in primary care, strengthen the medical home, and include payment reform to enhance primary care. Previous experience with expanding primary care involvement in children's mental health care, such as with attention-deficit/hyperactivity disorder and depression, has documented the importance of enhancing the financial base of services so that primary care practitioners have the time needed to work actively with young people with complex conditions and their families.¹² Newer organizational structures, including patient navigators, colocated multidisciplinary personnel, and systems that provide backup to primary care providers, all

may help care for children with neurodevelopmental disorders. The collaboration between the ATN/AIR-P and the National Initiative on Children's Healthcare Quality will increasingly address the question of best practices in the involvement of primary care practitioners in the care of youth with ASDs. Efforts in this area will help characterize what collaborative models work best and the quality improvement techniques that will be most effective in implementing these practices more widely.

Recent successful efforts to improve payment for services for children with ASDs have focused in large part on behavioral interventions. Building on that success can help strengthen reimbursement for medical care across

the care spectrum of providers and conditions affecting children and youth with ASDs. Over the next few years, it will be critical to develop comprehensive views of what care networks for children with autism and other neurodevelopmental disabilities should look like and how they can integrate effectively with the larger system of care.

The ATN and AIR-P have worked extensively to share knowledge and experience, as well as the outcomes of guideline development and research, with both professional and parent audiences. These efforts will continue to expand as part of the effort to influence and improve the care that young people with ASDs and their families receive.

REFERENCES

1. Abrahams BS, Geschwind DH. Connecting genes to brain in the autism spectrum disorders. *Arch Neurol*. 2010;67(4):395–399
2. Stein REK, Perrin JM, Iezzoni LI. Health care: access and medical support for youth and young adults with chronic health conditions and disabilities. In: Lollar D, ed. *Launching into Adulthood*. Baltimore, MD: Paul H Brookes Publishing; 2010:77–102
3. Seltzer MM, Floyd F, Song J, Greenberg J, Hong J. Midlife and aging parents of adults with intellectual and developmental disabilities: impacts of lifelong parenting. *Am J Intellect Dev Disabil*. 2011;116(6):479–499
4. Lit L, Sharp FR, Bertoglio K, et al. Gene expression in blood is associated with risperidone response in children with autism spectrum disorders [published online ahead of print June 7, 2011]. *Pharmacogenomics J*. doi:10.1038/tpj.2011.23
5. Correia CT, Almeida JP, Santos PE, et al. Pharmacogenetics of risperidone therapy in autism: association analysis of eight candidate genes with drug efficacy and adverse drug reactions. *Pharmacogenomics J*. 2010;10(5):418–430
6. Miller DT, Adam MP, Aradhya S, et al. Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. *Am J Hum Genet*. 2010;86(5):749–764
7. Shen Y, Dies KA, Holm IA, et al; Autism Consortium Clinical Genetics/DNA Diagnostics Collaboration. Clinical genetic testing for patients with autism spectrum disorders. *Pediatrics*. 2010;125(4). Available at: www.pediatrics.org/cgi/content/full/125/4/e727
8. McGrew SG, Peters BR, Crittendon JA, Veenstra-Vanderweele J. Diagnostic yield of chromosomal microarray analysis in an autism primary care practice: which guidelines to implement? *J Autism Dev Disord*. 2012;42(8):1582–1591
9. Owley T, Brune CW, Salt J, et al. A pharmacogenetic study of escitalopram in autism spectrum disorders. *Autism Res*. 2010;3(1):1–7
10. Perrin JM. How can quality improvement enhance the lives of children with disabilities? *Future Child*. 2012;22(1):149–168
11. Patient-Centered Outcomes Research. Available at: www.pcori.org/patient-centered-outcomes-research/. Accessed March 2, 2012.
12. American Academy of Pediatrics. Report of the Task Force on Mental Health. *Pediatrics*. 2010; 125(suppl 3):S69–S125

**The Autism Treatment Network and Autism Intervention Research Network on
Physical Health: Future Directions**

James M. Perrin, Daniel L. Coury, Nancy Jones and Clara Lajonchere

Pediatrics 2012;130;S198

DOI: 10.1542/peds.2012-0900S

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/130/Supplement_2/S198
References	This article cites 9 articles, 1 of which you can access for free at: http://pediatrics.aappublications.org/content/130/Supplement_2/S198#BIBL
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Developmental/Behavioral Pediatrics http://www.aappublications.org/cgi/collection/developmental_issues_sub Autism/ASD http://www.aappublications.org/cgi/collection/autism:asd_sub
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.aappublications.org/site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: http://www.aappublications.org/site/misc/reprints.xhtml

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®



PEDIATRICS[®]

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

The Autism Treatment Network and Autism Intervention Research Network on Physical Health: Future Directions

James M. Perrin, Daniel L. Coury, Nancy Jones and Clara Lajonchere

Pediatrics 2012;130;S198

DOI: 10.1542/peds.2012-0900S

The online version of this article, along with updated information and services, is
located on the World Wide Web at:

http://pediatrics.aappublications.org/content/130/Supplement_2/S198

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 345 Park Avenue, Itasca, Illinois, 60143. Copyright © 2012 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN[®]

