

IACC Strategic Plan for Autism Research 2010 Update for Question 1- When Should I be Concerned?

What is new in the research area and what have we learned this past year?

Research from two important studies over the past year has pointed to the importance of factors that place children at increased risk for ASDs. Findings indicate the role of underlying genetic disorders and prenatal risk factors that when present, may warrant screening and early follow up and in some instances, more specific medical work up. First, an evidence-based review of a large clinical series of patients with ASD and with other developmental disorders concluded that chromosomal microarray resulted in considerably higher diagnostic sensitivity for genetic testing than did G-banded karyotyping, particularly for submicroscopic deletions and duplications (Miller et al., 2010). Second, a study by Johnson et al., found that very preterm birth (<26 weeks gestational age) was associated with a much higher risk of developing ASD, with a prevalence of 8% diagnosed by age 11. While early gestational age has been identified as a risk factor for ASD, previous studies have lacked the power to examine children born at such vulnerable gestational ages.

Evidence is also accumulating on the developmental trajectory for autism. A 2010 prospective study showed little deviation between children who eventually developed autism and typically developing children up to age 6 months, after which time measurable differences emerged (Ozonoff et al., 2010). Importantly, while a decrease in developmental trajectory of skills was found in the majority of children, it was not identified by most parents, suggesting current limitations in the use of parent-identified early markers of ASD in the first year of life.

Two important studies highlighted work on the barriers to early screening and diagnosis. Evaluation of the implementation of the AAP recommendations for developmental surveillance was conducted in 17 diverse pediatric practices and demonstrated reasonable success in implementing ongoing screening (85% of practices screened patients at recommended screening ages), but that pediatric practices experienced challenges in referral for medical subspecialty care and early intervention (King et al., 2010). A second study (Norris and Lecavalier, 2010) evaluated the diagnostic sensitivity of the various parent/care-giver autism Level 2 screening scales for children older than 3 years—beyond the AAP-recommended screening ages—and concluded that even in this older age group, while some tests performed well, overall, more scientific evidence is needed for these instruments.

What gaps have emerged since last year?

Recent data (Shattuck et al., 2009; CDC 2009) show that girls are diagnosed with ASD at a later age than are boys. Examination of the 2009 autism portfolio analysis of currently funded research shows that studies in girls and minority racial/ethnic/socioeconomically disadvantaged populations remains a gap area. While the authors speculate on reasons for this disparity, including different clinical manifestations of ASD by gender and cultural differences in accepted or anticipated behaviors in girls relative to boys, gender should be included as an important disparity factor in studies examining barriers to early screening and diagnosis.

There are important ethical, legal and social issues implications resulting from the study by Miller et al., particularly relating to screening for genetic and other markers for autism and other developmental disorders. There is a diverse range of opinions in the autism community on early screening for autism ranging from strong support for developing biologic prenatal screening methods to concerns that such efforts may lead to selected terminations of fetuses showing genetic or other biomarkers of increased risk. It is imperative that autism research proceed with the appropriate precautions and safeguards and that the concerns of the autism community are reflected in this process. At this point, the state of the science is focused on improving early screening in the first years of life to identify risk for an ASD in order to initiate early intervention to reduce or prevent the development of disabling symptoms and promote positive skill development.

The study by King et al. highlights the need for a clearer understanding of the challenges and barriers to screening and referral. Studies are needed to determine the factors that lead to implementing screening and referral programs that successfully serve children with ASD and their families. Studies should include factors relating to the clinical practice, availability and collaboration among community-based services, and information needs of parents, other caregivers, and early educators.

There is a lack of reliable and valid screening and diagnostic tests for use in international, resource-poor settings. Early screening and diagnosis when coupled with inexpensive, parent-guided interventions is an important potential prevention strategy in such settings.

Research is needed to identify effective methods for screening especially children at higher risk for ASDs, such as the extremely preterm children studied by Johnson et al.

What new research opportunities and research objectives have emerged?

- Conduct at least one study to determine the positive predictive value and clinical utility (e.g., prediction of co-morbid conditions, family planning) of chromosomal microarray genetic testing for detecting genetic diagnoses for ASD in a clinical setting, by 2010.
- Conduct at least five studies of the ethical, legal, and social implications (ELSI) of autism research, including at least one study regarding the potential impact of future pre-natal genetic testing and at least one study regarding the need and clinical utility of genetic testing and genetic counseling as part of a standard diagnostic ASD assessment. Ensure the inclusion of both individuals on the autism spectrum and family members as distinct stakeholder groups in these studies,
- Currently funded research projects are identifying screening techniques in individuals at high risk for autism but for these to have clinical utility it will be necessary to develop a standardized, coordinated method to validate them in multi-center studies.
- Conduct at least two studies which aim to develop predictive risk profiles indicating the need for heightened surveillance and screening to identify children with an ASD by 2012.
- Conduct research to identify effective methods to promote early screening of individuals at higher risk for ASDs as early as practicable using evidence-based screening techniques. [Note: this need is also stated in the Combating Autism Act of 2006.]

- *Revise Short-Term Objective C to better define the screening and referral system and the targeted health disparities: Conduct at least three studies to identify barriers to implementation of and access to screening, diagnosis, referral and early intervention services among diverse populations, as defined by socio-economic status, race, ethnicity, and gender of the child.*
- *Revise Short-Term Objective B to include 'gender' as a population qualifier and 'resource-poor international settings'.*

New References

Centers for Disease Control and Prevention. Prevalence of autism spectrum disorders – Autism and Developmental Disabilities Monitoring Network, United States, 2006. *MMWR* 2009;58(SS10):1-20.

Johnson S et al. Autism spectrum disorders in extremely preterm children. *J Pediatr.* 2010 Apr;156(4):525-31.e2. Epub 2010 Jan 13.

King TM et al. Implementing developmental screening and referrals: lessons learned from a national project. *Pediatrics.* 2010 Feb;125(2):350-60. Epub 2010 Jan 25.

Miller DT 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 May 14;86(5):749-64.

Norris M, Lecavalier L. Screening accuracy of Level 2 autism spectrum disorder rating scales: A review of selected instruments. *Autism.* 2010 Jul;14(4):263-84.

Ozonoff F et al. A prospective study of the emergence of early behavioral signs of autism. *J Am Acad Child Adolesc Psychiatry.* 2010 Mar;49(3):256-66.e1-2.

Shattuck PT et al. Timing of identification among children with an autism spectrum disorder: Findings from a population-based surveillance study. *J Am Acad Child Adolesc Psychiatry.* 2009 May;48(5):474-483.