

IACC Strategic Plan for Autism Research 2010 Update for Question 4

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

Several notable studies and reviews on the efficacy of specific interventions for improving outcomes of individuals with ASD were published in 2010:

- A 2010 study showed that medications, such as risperidone, are most effective for reducing irritability and aggression when they are combined with intensive behavioral intervention (Frazier et al., 2010).
- A randomized controlled trial demonstrated the efficacy of a comprehensive early intensive behavioral intervention, based on the Early Start Denver Model, which integrated developmental approaches with principles of ABA for improving IQ, language, and adaptive behavior, and reducing severity of autism diagnosis, in toddlers with ASD (Dawson et al., 2010).
- Positive benefits from social skills training for improving social interaction and peer relationships were reported (Frankel, Myatt, Sugar et al., 2010).
- A systematic review concluded that modified cognitive behavioral interventions are efficacious for reducing anxiety in individuals with Asperger syndrome (Lang et al., 2010).
- An environmental scan of interventions for children, youth, and adults with ASD performed on behalf of the Centers for Medicare & Medicaid Services (Young, Mandell, et al., 2010), examined interventions for children, youth, and adults with ASD (<http://www.impaqint.com/files/4-content/1-6-publications/1-6-2-project-reports/finalasdreport.pdf>). The scan included services to address the core impairments associated with ASD and other support services such as behavioral interventions, peer training, and supported employment. For children, 15 interventions met the “evidence-based” criteria established, while the other 16 interventions studied met only the criteria for emerging or unestablished interventions. Far less evidence was available on services and supports for transitioning youth and adults, underscoring the need for more research in this area.

- **What gap areas have emerged since last year?**

Recent data (e.g. Pinto et al., 2010) indicate that several rare and highly-penetrant gene variants and copy number variations (e.g. NLGN3, NLGN4, NRXN1, SHANK 2 and 3, PTCHD1, maternally-inherited 15q11-q13, among others) are involved in ASD. There is a great need for translational research that can take advantage of these new genetic findings to (1) identify subgroups of individuals with ASD who respond well to specific medication and intervention approaches, (2) inform which signaling pathways are affected in ASD, (3) develop animal models to explore the down-stream effects of these genetic variants on brain function, and (4) discover targets for development of therapeutics. In order to develop effective medical and behavioral interventions, there is a continuing need for autism intervention networks which can provide platforms for conducting clinical trials and comparative effectiveness

research using genetic and other biomarkers for specific subtypes, other individual characteristics, and their relationship to response to specific treatments for people with ASD.

In a 2010 presentation to the IACC, data were presented from the Autism Treatment Network, a system of 14 academic health centers throughout the US and Canada that provide care to over 5,000 individuals with ASD, which showed that 65% of individuals with ASD experience sleep disturbances and 14% of those with sleep problems also have seizures. Gastrointestinal (GI) problems were also reported in 50%, and those with gastrointestinal problems were more likely to have sleep disturbances, behavioral problems, and a lower health related quality of life. Other health issues identified include seizures, food sensitivities, anxiety and depression. Recent consensus statements and expert reviews indicate that assessment and treatment of such conditions can lead to improvement in behavior and quality of life (Buie et al., 2010a, b; Cury, 2010), and represent a critical unmet need and great opportunity for improving overall health and quality of life of individuals with ASD.

When designing clinical trials the tremendous amount of heterogeneity present in those diagnosed with ASD must be taken into consideration. Therefore, it is essential not to apply treatments across the broad spectrum, which would tend to dilute results, but instead to identify sub-groups of those who have documented medical histories or laboratory data indicating they might respond favorably to a particular targeted treatment utilizing a more personalized treatment approach. In addition, it will be necessary to develop multifaceted treatment modalities (as opposed to single-treatment designs) due to the complexity of the medical co-morbidities that can occur. Treatment of just one condition might not be as successful in improving behavior as the successful treatment of several co-occurring conditions. Clinical trial methodologies must be developed that can accurately assess effectiveness of multiple treatment regimens.

In April of 2010, an NIH-sponsored workshop (<http://www.nidcd.nih.gov/funding/programs/10autism/>) identified the urgent need for more research on children with ASD who have not developed functional verbal language by five years of age. Among the topics discussed was the development of new intervention approaches that directly teach spoken communication skills and Augmentative and Alternative Communication (AAC). More research is needed on the efficacy of novel service-provision, education, and treatment approaches that facilitate communication skills in people with ASD who are nonverbal and in individuals with challenges in verbal ability, including the need for evidence on the utility of AAC for specific subpopulations of persons with ASD. Potential areas of investigation include oral-motor skills, auditory/speech processing, social attention mechanisms, and impairments in intentional communication. In addition, research is needed on ways to improve access to AAC and the most appropriate means of AAC to utilize with specific subpopulations of individuals on the autism spectrum, including both individuals who are nonspeaking and individuals with speech which is partially or periodically limited. Comprehensive studies focusing on both adults and school-aged children on the autism spectrum should address the components of the most effective AAC approaches and factors which enhance or moderate improvements in communication, behavior and quality of life as a result of AAC usage.

Additional focus is needed to identify and address health disparities for people with ASD. While attention has been given to closing disparities in access to health care and health outcomes on the basis of race and income, little has been done to close this gap for people with developmental and intellectual disabilities, including autism. Recent legislative initiatives, including the Children's Health Insurance Program Reauthorization Act (CHIPRA) and the Affordable Care Act support this research, as well as the refinement of quality of life measures for children, and the development of quality of life measures for adults. Data generated from the National Core Indicators (<http://www2.hsri.org/nci/>) has revealed some data regarding quality of life specifically for people with ASD enrolled in state programs. Furthermore, a 2010 congressional briefing held as part of the Advancing Futures for Adults with Autism Initiative identified an urgent need for treatment research to address the needs of adults with ASD, particularly treatments focused on improving health, social relationships, adaptive behavior, communication, and cognitive functioning.

- **What new research opportunities and research objectives have emerged?**
 - Support funding mechanisms to encourage the use and testing of fidelity and outcomes of evidence-based medical treatment protocols for community physicians, including dental practitioners, by 2013.
 - Develop, evaluate, and disseminate an appropriately scaled (e.g. community-based) autism early intervention program for implementation in underserved, low resource, and low literacy populations in the U.S. and internationally (e.g. in low- and middle-income countries) by 2012.
 - Support at least 5 translational research studies that explore the impact of novel compounds for improving functioning in animal models of ASD by 2012.
 - Conduct 5 multi-site comparative effectiveness studies that address the relative effectiveness of different and/or combined pharmacological, nutritional, behavioral, service-provision, including parent or caregiver training approaches, for the treatment of medical and psychiatric co-morbidities by 2015.
 - Support at least 3 studies that utilize biomarker information to stratify individuals with ASD to predict optimal response to treatments by 2013.
 - Support at least 3 studies on service-provision models that enhance access to Augmentative and Alternative Communication (AAC) supports in both classroom and adult service-provision settings, such as residential service-provision and the impact of such access on quality of life, communication and behavior.
 - Support at least 3 studies on the efficacy of novel treatment approaches that facilitate communication skills in individuals who are nonverbal, including the components of effective ACC approaches for specific subpopulations of persons with ASD by 2012.

- Conduct at least one study assessing access to AAC for children and adults with ASD who have limited or partially limited speech and the impact on functional outcomes of access.
- Support at least 3 studies of the efficacy of widely used intervention models for which extensive published data are not available, such as TEACCH, DIR, and others commonly used by families by 2013.
- Support at least 2 studies that focus on the prevention of secondary disability in ASD, such as co-morbid medical and psychiatric conditions, quality of life, unemployment, isolation, homelessness, and involvement in the justice system, by 2013.
- Conduct at least one Community-Based Participatory Research (CBPR) study to identify disparities in access to health care and in health care outcomes, including secondary conditions, between individuals on the autism spectrum, other people with developmental disabilities and the non-disabled population by 2012.
- Conduct at least 3 studies that address areas of potential harm as a result of autism treatments, including pharmacological, behavioral, and other interventions, by 2012.

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