

2016 Summary of Advances Nominations: January – July 2016

Question 1 (Screening and Diagnosis)	
David Mandell	<p>McPheeters ML, Weitlauf A, Vehorn A, Taylor C, Sathe NA, Krishnaswami S, Fonnesebeck C, Warren ZE. <b>Screening for Autism Spectrum Disorder in Young Children: A Systematic Evidence Review for the U.S. Preventive Services Task Force [Internet]</b>. U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016 Feb. Report No.: 13-05185-EF-1. [PMID: <a href="#">26985520</a>]</p> <p><i>While I think that there's strong disagreement in the autism community with the recommendations of the taskforce, it speaks to the need for large scale population based studies that rigorously examine screening and treatment in combination on child outcomes.</i></p>
Bruce Cuthbert NIMH (Also nominated in 2015)	<p>Miller M, Iosif AM, Young GS, Hill M, Phelps Hanzel E, Hutman T, Johnson S, Ozonoff S. <b>School-age outcomes of infants at risk for autism spectrum disorder</b>. Autism Research. 2016 Jun. [PMID: <a href="#">26451968</a>]</p> <p><i>This study examined the long-term outcomes of younger siblings of children already diagnosed with ASD. As children with a higher than average risk for autism, it is important understand the extent to which their later school-age outcomes or developmental deficits may be associated with a higher risk for ASD; or signs of other neurodevelopmental disorders. In their follow-up study of (N=79) younger siblings of children (ages 5.5 – 9 years) with ASD and (N=60) typically developing children, the researchers found that even though they had not developed autism, the siblings of children with ASD showed higher risks for a range of adverse developmental outcomes such as lower language skills, higher parent reported ratings of psychopathology, learning problems, as well as mood and anxiety problems.</i></p>
Question 2 (Underlying Biology)	
Bruce Cuthbert NIMH	<p>Dean III DC, Travers BG, Adluru N, Tromp DP, Destiche DJ, Samsin D, Prigge MB, Zielinski BA, Fletcher PT, Anderson JS, Froehlich AL. <b>Investigating the Microstructural Correlation of White Matter in Autism Spectrum Disorder</b>. Brain connectivity. 2016 Jun. [<a href="#">27158271</a>]</p> <p><i>This study examined the nature of interrelated connections in the white matter microstructure that is a significant factor in synchronized brain functions. In comparing children with ASD (N=92) to typically developing children (N=43), the researchers found evidence of less-correlated coherence in the white matter microstructure of the ASD sample relative to the typically developing group. This study contributes to efforts to better understand how structural neural differences, specifically how disrupted brain connectivity in the white matter microstructure of the brain may be an underlying feature of the neural structure of individuals with ASD. Further investigations into how the neural networks and connections are affected in ASD can lead to new knowledge about the etiology and pathophysiology of the disorder.</i></p>
Bruce Cuthbert NIMH	<p>Falahpour M, Thompson WK, Abbott AE, Jahedi A, Mulvey ME, Datko M, Liu TT, Müller RA. <b>Underconnected, But Not Broken? Dynamic Functional Connectivity MRI Shows Underconnectivity in Autism Is Linked to Increased</b></p>

	<p><b>Intra-Individual Variability Across Time.</b> Brain connectivity. 2016 Apr 22. [PMID: 26973154]</p> <p><i>While functional connectivity is an important target of investigation into the pathophysiology of autism, prior functional connectivity MRI (fcMRI) studies have relied on static points of time when trying to identify areas of underconnectivity that may be associated with the cognitive or social deficits characteristic of autism. The current study represents an important advance for the field of neuroimaging in autism, in that it comparatively examines the temporal variation in functional connectivity between a sample of ASD and typically developing individuals. Moreover, the study's focus on the temporal dynamics of neural connectivity showed evidence of greater variability across time in connectivity rather than indications that functional connections are completely broken or altered in ASD.</i></p>
<p>Cathy Spong NICHD</p>	<p>Nordahl CW, Mello M, Shen AM, Shen MD, Vismara LA, Li D, Harrington K, Tanase C, Goodlin-Jones B, Rogers S, Abbeduto L, Amaral DG. <b>Methods for acquiring MRI data in children with autism spectrum disorder and intellectual impairment without the use of sedation.</b> Journal of neurodevelopmental disorders. 2016 May 5;8(1):1. [PMID: 27158271]</p> <p><i>Magnetic resonance imaging (MRI) has been used to gain insight into the neurobiological underpinning of ASD. The majority of studies, however, have involved individuals with IQs in the normal range (IQ &gt;85). CDC's prevalence data indicate that among the children with ASD, 54% of them were classified as having IQ scores in the borderline to intellectual disability range (IQ &lt;85). This study fills a critical need in demonstrating feasibility in acquiring high-quality images without the use of sedation in children with ASD and intellectual impairment.</i></p>
<p>Walter Koroshetz NINDS</p>	<p>Orefice LL, Zimmerman AL, Chirila AM, Sleboda SJ, Head JP, Ginty DD. <b>Peripheral Mechanosensory Neuron Dysfunction Underlies Tactile and Behavioral Deficits in Mouse Models of ASDs.</b> Cell. 2016 Jun 9. [PMID: 27293187]</p> <p><i>This paper identifies a critical role for ASD genes Mecp2 and Gabrb3 in somatosensory neurons for development of ASD tactile and behavioral deficits. Deletion of Mecp2 or Gabrb3 in peripheral somatosensory neurons in mice caused impaired presynaptic inhibition, mechanosensory dysfunction, and tactile deficits. The tactile impairments due to deletion of these genes during development, but not in adulthood, led to social interaction deficits and anxiety-like behaviors. Restoring Mecp2 expression in Mecp2-null mice rescued the tactile sensitivity and behavioral deficits. These data strongly indicate a role for mechanosensory processing dysfunction in anxiety-like behaviors and social interaction deficits in mouse models of ASD. This novel finding is potentially groundbreaking for autism and related neurodevelopmental disorders, elucidating an essential role for peripheral sensory systems in brain development and complex behaviors.</i></p>
<p>James Battey NIDCD</p>	<p>Tager-Flusberg H. <b>Risk factors associated with language in autism spectrum disorder: Clues to underlying mechanisms.</b> Journal of Speech, Language, and Hearing Research. 2016 Feb 1;59(1):143-54. [PMID: 26502110]</p>

	<p><i>Language impairment affects the majority of children with autism spectrum disorder (ASD). This article focuses on risk factors associated with ASD, with particular emphasis on language. Many of the risk markers for ASD are also found in studies of risk for specific language impairment, including demographic, behavioral, and neural factors.</i></p>
<p>Walter Koroshetz NINDS</p>	<p>Yi F, Danko T, Botelho SC, Patzke C, Pak C, Wernig M, Südhof TC. <b>Autism-associated SHANK3 haploinsufficiency causes Ih channelopathy in human neurons.</b> Science. 2016 May 6;352(6286):aaf2669. [PMID: 26966193]</p> <p><i>Mutations of the SHANK3 gene are associated with ASDs, and its deletion is thought to cause major symptoms of Phelan McDermid Syndrome. SHANK3 is a scaffolding protein expressed in most cells and is particularly enriched postsynaptically at excitatory synapses. Researchers in this study found that heterozygous and homozygous SHANK3 mutations were associated with severely and specifically impaired Ih (hyperpolarization-activated cation) channels in human neurons. The mutations also altered neuronal morphology and synaptic connectivity, which was reduced with chronic pharmacological blockage of the Ih channels. The study also suggests that the SHANK3 protein is involved in organization of the Ih channels. This paper sheds light on the specific pathogenic mechanisms underlying synaptic dysfunction impairments caused by SHANK3 mutations, and may provide a rationale for future pharmacological intervention.</i></p>
<p><b>Question 3 (Risk Factors)</b></p>	
<p>Ruth Etzel</p>	<p>Avella-Garcia CB, Julvez J, Fortuny J, Rebordosa C, García-Esteban R, Galán IR, Tardón A, Rodríguez-Bernal CL, Iñiguez C, Andiarena A, Santa-Marina L. <b>Acetaminophen use in pregnancy and neurodevelopment: attention function and autism spectrum symptoms.</b> International Journal of Epidemiology. 2016 Jun 28;dyw115. [PMID: 27353198]</p> <p><i>Why this is useful and should be followed by other studies: May provide clues to primary prevention.</i></p>
<p>David Amaral</p>	<p>Eriksson JM, Lundström S, Lichtenstein P, Bejerot S, Eriksson E. <b>Effect of co-twin gender on neurodevelopmental symptoms: a twin register study.</b> Mol Autism. 2016 Jan 19;7:8. [PMID: 26793297]</p> <p><i>Simon Baron-Cohen and others have hypothesized that exposure to elevated levels of prenatal testosterone is associated with elevated traits of ASD. Assuming that testosterone levels from a dizygotic male twin fetus may lead to enhanced testosterone exposure of its co-twins, the prenatal testosterone hypothesis was tested by comparing same-sex with opposite-sex dizygotic twins with respect to neurodevelopmental symptoms. This is a very large twin study in Sweden carried out through record review of 8156 dizygotic twin pairs. The outcome, having a male co-twin, resulted in less risk of ASD was contrary to the prenatal testosterone, "extreme male brain" hypothesis. Having a female co-twin increased the risk of ADHD.</i></p>
<p>Alison Singer</p>	<p>Jokiranta-Olkonemi E, Cheslack-Postava K, Sucksdorff D, Suominen A, Gyllenberg D, Chudal R, Leivonen S, Gissler M, Brown AS, Sourander A. <b>Risk of Psychiatric and Neurodevelopmental Disorders Among Siblings of Probands With Autism Spectrum Disorders.</b> JAMA psychiatry. 2016 Jun 1;73(6):622-9. [PMID: 27145529]</p>

	<p><i>Psychiatric and neurodevelopmental disorders cluster among siblings of probands with ASD. For etiologic research, these findings provide further evidence that several psychiatric and neurodevelopmental disorders have common risk factors. For families, these findings provide important information about watching for early warning signs of psychiatric disorder among siblings of probands with ASD.</i></p>
<p><b>Question 4 (Treatments and Interventions)</b></p>	
Larry Wexler	<p>Camargo SP, Rispoli M, Ganz J, Hong ER, Davis H, Mason R. <b>Behaviorally Based Interventions for Teaching Social Interaction Skills to Children with ASD in Inclusive Settings: A Meta-analysis.</b> Journal of Behavioral Education. 2016 Jun 1;25(2):223-48. [<a href="https://doi.org/10.1007/s10864-015-9240-1">doi: 10.1007/s10864-015-9240-1</a>]</p> <p><i>In this article, Camargo and colleagues investigated the overall effectiveness and differential effects of behavioral interventions on the acquisition of social skills by children with autism in general education. The omnibus results were large with a narrow confidence interval, indicating that the behavioral interventions analyzed were effective for teaching social skills to children with autism. We chose this study because its focus on effective interventions in inclusive settings will likely be of interest to practitioners of children with autism.</i></p>
David Mandell	<p>Chang YC, Shire SY, Shih W, Gelfand C, Kasari C. <b>Preschool Deployment of Evidence-Based Social Communication Intervention: JASPER in the Classroom.</b> J Autism Dev Disord. 2016 Jun;46(6):2211-23. [<a href="https://pubmed.ncbi.nlm.nih.gov/26936161/">PMID: 26936161</a>]</p> <p><i>One of the few true effectiveness trials of preschool intervention for children with autism</i></p>
Larry Wexler	<p>Corbett BA, Key AP, Qualls L, Fecteau S, Newsom C, Coke C, Yoder P. <b>Improvement in social competence using a randomized trial of a theatre intervention for children with autism spectrum disorder.</b> Journal of autism and developmental disorders. 2016 Feb 1;46(2):658-72. [<a href="https://pubmed.ncbi.nlm.nih.gov/26419766/">PMID: 26419766</a>]</p> <p><i>Corbett and colleagues conducted a randomized trial to investigate the efficacy of theater as a medium to teach social skills to children with autism. The peer-mediated intervention showed positive effects on communication, social interaction, and memory of faces. We found this work to be novel and an interesting contribution to the literature on social skills interventions for children with autism.</i></p>
Larry Wexler	<p>Hampton LH, Kaiser AP. <b>Intervention effects on spoken-language outcomes for children with autism: a systematic review and meta-analysis.</b> Journal of Intellectual Disability Research. 2016 May 1;60(5):444-63. [<a href="https://pubmed.ncbi.nlm.nih.gov/27120988/">PMID: 27120988</a>]</p> <p><i>The study by Hampton and Kaiser investigated whether early intervention has an effect on the spoken-language of children with autism. This meta-analysis analyzed 26 group studies with more than 1700 participants with autism and found that early intervention did have a significant impact on the language outcomes of children with autism, particularly when implemented by parents and clinicians simultaneously. We felt this study was important because it provides empirical support for early intervention and the inclusion of parents in the treatment of language delays and disorders.</i></p>
Larry Wexler	<p>Kasari C, Dean M, Kretzmann M, Shih W, Orlich F, Whitney R, Landa R, Lord C, King B. <b>Children with autism spectrum disorder and social skills groups at</b></p>

	<p><b>school: a randomized trial comparing intervention approach and peer composition.</b> Journal of Child Psychology and Psychiatry. 2016 Feb 1;57(2):171-9. [PMID: 26391889]</p>
	<p><i>The study by Kasari and colleagues compared the efficacy of a didactic and activity-based intervention on the social skills of school-age children with autism. The didactic SKILLS based intervention was implemented with a homogenous group of students with autism while the activity-based ENGAGE intervention was implemented with a heterogeneous group of children with autism and their peers without disabilities. The children with autism in the didactic SKILLS based group had greater effects on measures of peer engagement and isolation than children in the activity-based ENGAGE group. We found this article to be an interesting contribution to the research base on social skills interventions for children with autism as it provides information on how to support children’s social skill development.</i></p>
Larry Wexler	<p>Murza KA, Schwartz JB, Hahs-Vaughn DL, Nye C. <b>Joint attention interventions for children with autism spectrum disorder: a systematic review and meta-analysis.</b> International Journal of Language &amp; Communication Disorders. 2016 May 1;51(3):236-51. [PMID: 26952136]</p>
	<p><i>In this article, Murza and colleagues conducted a meta-analysis of group studies that investigated joint attention in children with autism. The omnibus results were positive and indicated that joint attention interventions are effective for children with autism. We found that this article provides a thorough overview of the literature on joint attention interventions and to be a valuable addition to the research base on effective interventions for children with autism.</i></p>
David Mandell	<p>Park SY, Cervesi C, Galling B, Molteni S, Walyzada F, Ameis SH, Gerhard T, Olfson M, Correll CU. <b>Antipsychotic Use Trends in Youth With Autism Spectrum Disorder and/or Intellectual Disability: A Meta-Analysis.</b> J Am Acad Child Adolesc Psychiatry. 2016 Jun;55(6):456-468.e4. [PMID: 27238064]</p>
	<p><i>This carefully conducted meta-analysis shows that the proportion of children with ASD who are prescribed an antipsychotic is high and appears to be increasing. Given that these medications have significant side effects and often are prescribed to address behavioral problems, the results suggest the urgency of more broadly implementing behavioral interventions in communities.</i></p>
<p><b>Question 5 (Services)</b></p>	
<p>No articles were nominated in January-July 2016 for Question 5</p>	
<p><b>Question 6 (Lifespan Issues)</b></p>	
James Battey NIDCD	<p>Koegel LK, Ashbaugh K, Navab A, Koegel RL. <b>Improving Empathic Communication Skills in Adults with Autism Spectrum Disorder.</b> Journal of autism and developmental disorders. 2016 Mar 1;46(3):921-33. [PMID: 26520148]</p>
	<p><i>Many individuals diagnosed with Autism Spectrum Disorder (ASD) experience challenges with recognizing and describing emotions in others, which may result in difficulties with the verbal expression of empathy during communication. There is limited research on interventions for adults with ASD targeting these deficits. This study, which examined the effectiveness of an adult intervention</i></p>

	<i>that focused on expression of empathy in conversation, found post-intervention, notable gains in the communication skills.</i>
<i>David Mandell Julie Lounds Taylor</i>	Wehman P, Schall CM, McDonough J, Graham C, Brooke V, Riehle JE, Brooke A, Ham W, Lau S, Allen J, Avellone L. <b>Effects of an employer-based intervention on employment outcomes for youth with significant support needs due to autism.</b> Autism. 2016 May 5. [ <a href="#">PMID: 27154907</a> ]
	<i>One of the first randomized trials showing huge effect sizes in improving employment outcomes for young adults with autism</i>
	<i>This study has some limitations, but it is one of only a few RCTs focused on improving employment among youth with ASD. It is also important because it focused on youth with ASD who have an intellectual disability (who are typically underrepresented in this area of research). The authors found remarkable employment rates for youth who go through the extensive program relative to a control group. Findings suggest that given a long-term, internship-like experience, youth with ASD who have an intellectual disability are able to obtain and maintain employment at the site where they interned.</i>
<b>Question 7 (Infrastructure and Surveillance)</b>	
<i>David Mandell</i>	Christensen DL, Baio J, Braun KV, Bilder D, Charles J, Constantino JN, Daniels J, Durkin MS, Fitzgerald RT, Kurzius-Spencer M, Lee LC, Pettygrove S, Robinson C, Schulz E, Wells C, Wingate MS, Zahorodny W, Yeargin-Allsopp M. <b>Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2012.</b> MMWR Surveill Summ. 2016 Apr 1;65(3):1-23. [ <a href="#">PMID: 27031587</a> ]
	<i>The most comprehensive finding we have to date the rate of autism, using this surveillance strategy, has stabilized.</i>