

2016 Summary of Advances Nominations

Question 1 (Screening and Diagnosis)
<p>McPheeters ML, Weitlauf A, Vehorn A, Taylor C, Sathe NA, Krishnaswami S, Fennesbeck C, Warren ZE. Screening for Autism Spectrum Disorder in Young Children: A Systematic Evidence Review for the U.S. Preventive Services Task Force [Internet]. 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: 26985520]</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>
<p>Miller M, Iosif AM, Young GS, Hill M, Phelps Hanzel E, Hutman T, Johnson S, Ozonoff S. School-age outcomes of infants at risk for autism spectrum disorder. Autism Research. 2016 Jun. [PMID: 26451968]</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>
<p>McCormick C, Hepburn S, Young GS, Rogers SJ. Sensory symptoms in children with autism spectrum disorder, other developmental disorders and typical development: A longitudinal study. Autism. 2016 Jul;20(5):572-9. [PMID: 26395236]</p>
<p><i>This article is important because the role of sensory symptoms in forming adaptive skills is often overlooked in the rush to make kids "table ready." This can lead to situations where kids end up just learning to pretend to not be in pain and to tolerate being hurt on a regular basis, rather than to address the issue head-on. That's been changing over the past couple of years. This study is a good first step. It's a little flawed because parents filled out sensory symptom reports (the kids weren't really old enough yet) which means they may have missed something an adolescent study might have been able to self-report. I'd love to see follow-up eventually.</i></p>
<p>Xiao X, Fang H, Wu J, Xiao C, Xiao T, Qian L, Liang F, Xiao Z, Chu KK, Ke X. Diagnostic model generated by MRI-derived brain features in toddlers with autism spectrum disorder. Autism Res. 2016 Nov 22. [PMID: 27874271]</p>
<p><i>Although the pathophysiologic mechanisms of ASD are incompletely understood, the neuroanatomical features are considered valuable predictors for discriminating ASD from others. This study generated predictive neuroimaging models for toddlers (18-37 months of age) with ASD, which has had relatively little scientific study. The researchers conducted MRI scans on 85 toddlers with ASD or developmental delay and applied three data-mining approaches to generate and compare three diagnostic models. They also compared performance metrics of regional cortical thickness-based diagnostic models with those of cortical volume- and surface area-based models. They found that their thickness-based classification predictive model using random forest classifier showed higher accuracy, specificity, and</i></p>

sensitivity as compared to volume- and surface area-based classifications. Taken together with previous findings, average regional cortical thickness is the best predictive feature of ASD in toddlers, adolescents, and adults, and this points to the importance of understanding the genetic pathological mechanisms related to cortical thickness development in ASD.

Jones EJ, Venema K, Earl R, Lowy R, Barnes K, Estes A, Dawson G, Webb SJ. **Reduced engagement with social stimuli in 6-month-old infants with later autism spectrum disorder: a longitudinal prospective study of infants at high familial risk.** J Neurodev Disord. 2016 Mar 15;8:7. [PMID: 26981158]

To our knowledge, this study identifies the earliest brain-based biomarker of risk for ASD. In a prospective study, infant siblings of children with ASD were followed longitudinally and assessed at 6, 12, and 24 months of age. At 6 months of age, high risk infants who developed ASD showed reduced neural sensitivity to faces based on event-related brain potential measures, as well as reduced habituation (reflecting memory encoding) to faces. This study demonstrates that differences in the development of social brain circuitry reflecting reduced engagement with social stimuli are present by six months of age before behavioral symptoms of autism are evident.

Question 2 (Underlying Biology)

Dean III DC, Travers BG, Adluru N, Tromp DP, Destiche DJ, Samsin D, Prigge MB, Zielinski BA, Fletcher PT, Anderson JS, Froehlich AL. **Investigating the Microstructural Correlation of White Matter in Autism Spectrum Disorder.** Brain connectivity. 2016 Jun. [PMID: 27021440]

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.

Falahpour M, Thompson WK, Abbott AE, Jahedi A, Mulvey ME, Datko M, Liu TT, Müller RA. **Underconnected, But Not Broken? Dynamic Functional Connectivity MRI Shows Underconnectivity in Autism Is Linked to Increased Intra-Individual Variability Across Time.** Brain connectivity. 2016 Apr 22. [PMID: 26973154]

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.

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. **Methods for acquiring MRI data in children with autism spectrum**

disorder and intellectual impairment without the use of sedation. Journal of neurodevelopmental disorders. 2016 May 5;8(1):1. [[PMID: 27158271](#)]

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 >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 <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.

Orefice LL, Zimmerman AL, Chirila AM, Sleboda SJ, Head JP, Ginty DD. **Peripheral Mechanosensory Neuron Dysfunction Underlies Tactile and Behavioral Deficits in Mouse Models of ASDs.** Cell. 2016 Jun 9. [[PMID: 27293187](#)]

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.

Tager-Flusberg H. **Risk factors associated with language in autism spectrum disorder: Clues to underlying mechanisms.** Journal of Speech, Language, and Hearing Research. 2016 Feb 1;59(1):143-54. [[PMID: 26502110](#)]

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.

Yi F, Danko T, Botelho SC, Patzke C, Pak C, Wernig M, Südhof TC. **Autism-associated SHANK3 haploinsufficiency causes Ih channelopathy in human neurons.** Science. 2016 May 6;352(6286):aaf2669. [[PMID: 26966193](#)]

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.

Marchetto MC, Belinson H, Tian Y, Freitas BC, Fu C, Vadodaria KC, Beltrao-Braga PC, Trujillo CA, Mendes AP, Padmanabhan K, Nunez Y, Ou J, Ghosh H, Wright R, Brennand KJ, Pierce K, Eichenfield L,

Pramparo T, Eyler LT, Barnes CC, Courchesne E, Geschwind DH, Gage FH, Wynshaw-Boris A, Muotri AR. **Altered proliferation and networks in neural cells derived from idiopathic autistic individuals.** Mol Psychiatry. 2016 Jul 5. [Epub ahead of print] [[PMID: 27378147](#)]

Using fibroblasts from ASD individuals with early brain overgrowth and non-ASD controls with normal brain development, the present study generated human cells models in the form of induced pluripotent stems cells (iPSCs), neural progenitor cells (NPCs) and neurons. Results demonstrated that ASD-derived NPCs showed increased cell proliferation, while ASD-derived neurons displayed abnormal neurogenesis and reduced synaptogenesis leading to functional defects in neuronal networks. Moreover, defects in neuronal networks could be rescued by insulin growth factor 1 (IGF-1), a drug that is currently in clinical trials for ASD. These findings point to potential new innovations to develop future human cell models of other ASD endophenotypes and further examine cellular mechanisms that underlie the etiology and pathophysiology of ASD.

Green SA, Hernandez L, Bookheimer SY, Dapretto M. **Salience Network Connectivity in Autism Is Related to Brain and Behavioral Markers of Sensory Overresponsivity.** J Am Acad Child Adolesc Psychiatry. 2016 Jul;55(7):618-626.e1. [[PMID: 27343889](#)]

Though sensory processing impairments are common among individuals with ASD, their underlying biological mechanisms are poorly understood and for which there is no evidence-based intervention. Using Functional Magnetic Resonance Imaging, this study demonstrates that specific patterns of resting-state connectivity are related to both brain and behavioral markers of sensory overresponsivity in ASD. These findings have important Implications for intervention.

Libertus K, Greif ML, Needham AW, Pelphrey K. **Infants' observation of tool-use events over the first year of life.** J Exp Child Psychol. 2016 Dec;152:123-135. [[PMID: 27522041](#)]

This study examined the eye-gaze patterns of infants while observing naturalistic tool-use by an adult caregiver or actor. The findings revealed that during infant development there were significant changes in infants' eye-gaze patterns, particularly from 7 to 10 months of age, from an initial attention solely on facial gaze, toward a more dynamic integrated focus on both the actor's face and the tool or object of use. These findings shed new light on normative developmental processes among infants, which can help inform how eye-gaze and attentional biases develop differentially among children at-risk for ASD.

Shen MD, Li DD, Keown CL, Lee A, Johnson RT, Angkustsiri K, Rogers SJ, Müller RA, Amaral DG, Nordahl CW. **Functional Connectivity of the Amygdala Is Disrupted in Preschool-Aged Children With Autism Spectrum Disorder.** J Am Acad Child Adolesc Psychiatry. 2016 Sep;55(9):817-24. [[PMID: 27566123](#)]

The present study examined the extent to which functional connectivity of the amygdala is altered in preschool-age children with ASD. The findings showed that among children with ASD, there was evidence of significantly weaker connectivity between the amygdala and brain regions critical for social communication, as well as those implicated in repetitive behaviors (bilateral medial prefrontal cortex, temporal lobes, and striatum). Weakened functional connectivity was also associated with severity of ASD symptoms. These findings signal an advance in our understanding of the neurobiological mechanisms of ASD and hold promise for future studies that can further our knowledge of the early developmental changes in neural connectivity that are associated with deficits in ASD.

Torres EB, Denisova K. **Motor noise is rich signal in autism research and pharmacological treatments.** Sci Rep. 2016 Nov 21;6:37422. [[PMID: 27869148](#)]

This article argues that neuromotor problems, or problems controlling bodily movements, are at the core of autism. The authors statistically analyzed fMRI data of over 1,000 people. They examined involuntary head movements as the participants tried to sit still during the fMRI. The results demonstrate that people with autism experienced more involuntary movements than others and those with autism taking psychotropic medication moved even more. This has implications for diagnosis criteria, interventions, and medical treatments for autism.

Parikshak NN, Swarup V, Belgard TG, Irimia M, Ramaswami G, Gandal MJ, Hartl C, Leppa V, Ubieta LT, Huang J, Lowe JK, Blencowe BJ, Horvath S, Geschwind DH. **Genome-wide changes in lncRNA, splicing, and regional gene expression patterns in autism.** Nature. 2016 Dec 15;540(7633):423-427. [[PMID: 27919067](#)]

This study used post-mortem genome-wide transcriptome analysis to explore molecular convergence in ASD. The analyses revealed ASD-associated dysregulation of primate specific long non-coding RNAs (lncRNA) and downregulation of alternative splicing of activity dependent neuron specific exomes, and also suggest SOX5 contributes to a reduction in regional differences in gene expression. They also found highly overlapping expression patterns shared by individuals with the 15q duplication syndrome and idiopathic ASD, which may represent an evolving adaptive or maladaptive response to primary insult. Co-expression network analysis revealed that individuals with ASD show age-related changes in the trajectory of microglial and synaptic function over the first two decades, reflecting an early alteration in developmental trajectory that becomes more evident in late childhood. The findings illustrate how diverse genetic perturbations can lead to phenotypic convergence at multiple biological levels in a complex neuropsychiatric disorder.

Study uses the largest cohort of brain tissue samples from people with autism to identify ways the genes act despite the "cause" of autism. This includes those with known rare mutations (dup15) vs. those with unknown genetic cause. The analysis reveals that there are age related changes in microglia and synaptic function of genes across the lifespan, that these genes affect development of synaptic connections, points to a neurobiological mechanism for early intervention as a key strategy, and that different causes of autism converge on the same pathways.

Tao J, Wu H, Coronado AA, de Laitre E, Osterweil EK, Zhang Y, Bear MF. **Negative Allosteric Modulation of mGluR5 Partially Corrects Pathophysiology in a Mouse Model of Rett Syndrome.** J Neurosci. 2016 Nov 23;36(47):11946-11958. [[PMID: 27881780](#)]

This paper shows a mechanistic link between MECP2 gene mutations, which cause Rett syndrome, and FMRP/mGluR5 abnormalities, which cause Fragile X. Investigators showed abnormal mGluR5- and protein-synthesis-dependent synaptic plasticity in a mouse model of Rett syndrome (Mecp2 knockout). Genome-wide profiling revealed significant overlap in ribosome-bound mRNAs overexpressed in the Mecp2 knockout mice and FMRP mRNA targets. mGluR5 negative allosteric modulator (NAM) treatment, which has been shown to ameliorate Fragile X phenotypes in Fmr1 knockout mice, reduced the level of overexpressed ribosome-associated transcripts and ameliorated some of the Rett syndrome phenotype. This paper demonstrates a potential mechanistic link between Fragile X and Rett pathophysiology via co-regulation of a subset of genes relevant to synaptic function. NIH is currently funding a phase 2 trial of a mGluR5 NAM in 3-6-year-old children with fragile X syndrome to determine whether treatment improves development of language learning.

D'Mello AM, Moore DM, Crocetti D, Mostofsky SH, Stoodley CJ. **Cerebellar gray matter differentiates children with early language delay in autism.** Autism Res. 2016 Nov;9(11):1191-1204. [PMID: [27868392](#)]

This paper examines the relationships between gray matter (GM), age of first word/phrase, and core ASD symptoms using voxel-based morphometry to examine whole brain GM differences in 8-13 year old children with autism and 35 age-matched typically developing controls. Composite age of first word/phrase negatively correlated with GM throughout the cerebellum. ASD children had reduced GM in right cerebellar Crus I/II when compared to typically developing children. Early language delay children had reduced GM relative to both non-early language delay and typically developing groups. Relationship between GM patterns and ADOS scores differed for early language delay versus non-early language delay groups. These findings highlight the importance of specific cerebellar networks in both ASD and early language development, and suggest that bilateral disruption in cerebellar regions that interconnect with fronto-parietal networks could impact language acquisition in ASD.

Question 3 (Risk Factors)

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, Sunyer J. **Acetaminophen use in pregnancy and neurodevelopment: attention function and autism spectrum symptoms.** Int J Epidemiol. 2016 Jun 28. pii: dyw115. [Epub ahead of print] [PMID: [27353198](#)]

Why this is useful and should be followed by other studies: May provide clues to primary prevention. Highlights a potential preventable exposure.

Eriksson JM, Lundström S, Lichtenstein P, Bejerot S, Eriksson E. **Effect of co-twin gender on neurodevelopmental symptoms: a twin register study.** Mol Autism. 2016 Jan 19;7:8. [PMID: [26793297](#)]

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.

Jokiranta-Olkonieni E, Cheslack-Postava K, Sucksdorff D, Suominen A, Gyllenberg D, Chudal R, Leivonen S, Gissler M, Brown AS, Sourander A. **Risk of Psychiatric and Neurodevelopmental Disorders Among Siblings of Proband With Autism Spectrum Disorders.** JAMA psychiatry. 2016 Jun 1;73(6):622-9. [PMID: [27145529](#)]

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.

Julvez J, Méndez M, Fernandez-Barres S, Romaguera D, Vioque J, Llop S, Ibarluzea J, Guxens M, Avella-Garcia C, Tardón A, Riaño I, Andiarena A, Robinson O, Arijia V, Esnaola M, Ballester F, Sunyer J. **Maternal Consumption of Seafood in Pregnancy and Child Neuropsychological Development: A**

Longitudinal Study Based on a Population With High Consumption Levels. Am J Epidemiol. 2016 Feb 1;183(3):169-82. [PMID: 26740026]

This is a large cohort study from a high-powered epidemiological institute in Spain, where seafood consumption is very high. Results suggest some protection from autism-spectrum traits by consumption of large fatty fish during pregnancy.

Bennett D, Bellinger DC, Birnbaum LS, Bradman A, Chen A, Cory-Slechta DA, Engel SM, Fallin MD, Halladay A, Hauser R, Hertz-Picciotto I, Kwiatkowski CF, Lanphear BP, Marquez E, Marty M, McPartland J, Newschaffer CJ, Payne-Sturges D, Patisaul HB, Perera FP, Ritz B, Sass J, Schantz SL, Webster TF, Whyatt RM, Woodruff TJ, Zoeller RT, Anderko L, Campbell C, Conry JA, DeNicola N, Gould RM, Hirtz D, Huffling K, Landrigan PJ, Lavin A, Miller M, Mitchell MA, Rubin L, Schettler T, Tran HL, Acosta A, Brody C, Miller E, Miller P, Swanson M, Witherspoon NO; American College of Obstetricians and Gynecologists (ACOG); Child Neurology Society; Endocrine Society; International Neurotoxicology Association; International Society for Children's Health and the Environment; International Society for Environmental Epidemiology; National Council of Asian Pacific Islander Physicians; National Hispanic Medical Association; National Medical Association. **Project TENDR: Targeting Environmental Neuro-Developmental Risks. The TENDR Consensus Statement.** Environ Health Perspect. 2016 Jul 1;124(7):A118-22. [PMID: 27479987]

This represents the consensus of many scientists and health professionals and should be read by IACC.

Zerbo O, Qian Y, Yoshida C, Fireman BH, Klein NP, Croen LA. **Association Between Influenza Infection and Vaccination During Pregnancy and Risk of Autism Spectrum Disorder.** JAMA Pediatr. 2017 Jan 2;171(1):e163609. [PMID: 27893896]

The authors found no association between ASD risk and influenza infection during pregnancy or influenza vaccination during the second to third trimester of pregnancy. However, there was a suggestion of increased ASD risk among children whose mothers received influenza vaccinations early in pregnancy, although the association was insignificant after statistical correction for multiple comparisons.

Dunaway KW, Islam MS, Coulson RL, Lopez SJ, Vogel Ciernia A, Chu RG, Yasui DH, Pessah IN, Lott P, Mordaunt C, Meguro-Horike M, Horike SI, Korf I, LaSalle JM. **Cumulative Impact of Polychlorinated Biphenyl and Large Chromosomal Duplications on DNA Methylation, Chromatin, and Expression of Autism Candidate Genes.** Cell Rep. 2016 Dec 13;17(11):3035-3048. [PMID: 27974215]

No justification provided.

Question 4 (Treatments and Interventions)

Camargo SP, Rispoli M, Ganz J, Hong ER, Davis H, Mason R. **Behaviorally Based Interventions for Teaching Social Interaction Skills to Children with ASD in Inclusive Settings: A Meta-analysis.** Journal of Behavioral Education. 2016 Jun 1;25(2):223-48. [doi: 10.1007/s10864-015-9240-1]

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.

<p>Chang YC, Shire SY, Shih W, Gelfand C, Kasari C. Preschool Deployment of Evidence-Based Social Communication Intervention: JASPER in the Classroom. J Autism Dev Disord. 2016 Jun;46(6):2211-23. [PMID: 26936161]</p>
<p><i>One of the few true effectiveness trials of preschool intervention for children with autism</i></p>
<p>Corbett BA, Key AP, Qualls L, Fecteau S, Newsom C, Coke C, Yoder P. Improvement in social competence using a randomized trial of a theatre intervention for children with autism spectrum disorder. Journal of autism and developmental disorders. 2016 Feb 1;46(2):658-72. [PMID: 26419766]</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>
<p>Hampton LH, Kaiser AP. Intervention effects on spoken-language outcomes for children with autism: a systematic review and meta-analysis. Journal of Intellectual Disability Research. 2016 May 1;60(5):444-63. [PMID: 27120988]</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>
<p>Kasari C, Dean M, Kretzmann M, Shih W, Orlich F, Whitney R, Landa R, Lord C, King B. Children with autism spectrum disorder and social skills groups at school: a randomized trial comparing intervention approach and peer composition. 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>
<p>Murza KA, Schwartz JB, Hahs-Vaughn DL, Nye C. Joint attention interventions for children with autism spectrum disorder: a systematic review and meta-analysis. International Journal of Language & 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>
<p>Park SY, Cervesi C, Galling B, Molteni S, Walyszada F, Ameis SH, Gerhard T, Olfson M, Correll CU. Antipsychotic Use Trends in Youth With Autism Spectrum Disorder and/or Intellectual Disability: A Meta-Analysis. J Am Acad Child Adolesc Psychiatry. 2016 Jun;55(6):456-468.e4. [PMID: 27238064]</p>

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.

Srinivasan SM, Eigsti IM, Neelly L, Bhat AN. **The effects of embodied rhythm and robotic interventions on the spontaneous and responsive social attention patterns of children with Autism Spectrum Disorder (ASD): A pilot randomized controlled trial.** Res Autism Spectr Disord. 2016 Jul;27:54-72. [PMID: 27453721]

This pilot study examined a novel form of a robotic movement intervention, as well as a rhythm-based therapy, each designed to facilitate and improve social interaction and engagement between young children with ASD and their social partners. Children who participated in either the rhythm-based therapy or the robotic movement intervention showed greater improvements in social attention, relative to children in the standard-of-care comparison group. However, children in the rhythm group showed greater attention to objects and social partners than those in the robotic movement group. And over the course of the 8-week intervention trial, children in the robotic movement group displayed increased inattention to the activities. These preliminary findings suggest the potential utility for larger prospective studies of rhythmic-based interventions that focus on whole-body imitation, and interpersonal synchrony-based activities that may enhance social attention in young children with ASD.

Almirall D, DiStefano C, Chang YC, Shire S, Kaiser A, Lu X, Nahum-Shani I, Landa R, Mathy P, Kasari C. **Longitudinal Effects of Adaptive Interventions With a Speech-Generating Device in Minimally Verbal Children With ASD.** J Clin Child Adolesc Psychol. 2016 Jul-Aug;45(4):442-56. [PMID: 26954267]

In the first of its kind study, this investigation compared growth in communications outcomes among (N=61) minimally-verbal school-age children with ASD (ages 5-8), who participated in three adaptive interventions using a multiple-assignment randomized trial (SMART) design. The three interventions consisted of joint attention, symbolic play, engagement and regulation (JASP), enhanced milieu teaching (EMT), and provision of a speech-generating device (SGD). The adaptive intervention design consisted of different combinations of the 3 interventions. The results showed that the combination of JASP+EMT+SGD led to the greatest gains in spontaneous communication utterances and joint attention among minimally-verbal children with ASD.

Anderson A, Locke J, Kretzmann M, Kasari C; AIR-B Network. **Social network analysis of children with autism spectrum disorder: Predictors of fragmentation and connectivity in elementary school classrooms.** Autism. 2016 Aug;20(6):700-9. [PMID: 26567264]

The study utilized an innovative social network analytic method to determine how the social networks of children with ASD in general education classrooms change, in comparison to the social connectivity of peers who do not have ASD. The study found that for girls with ASD, higher IQ was associated with stronger social connectedness with peers. However, for boys with ASD, increased social connectedness was associated with smaller classroom size. These relationships have important implications for how researchers and service providers design and implement interventions and services aimed at facilitating the social integration of children with ASD into general or mainstream classroom environments.

Yang D, Pelphrey KA, Sukhodolsky DG, Crowley MJ, Dayan E, Dvornek NC, Venkataraman A, Duncan J, Staib L, Ventola P. **Brain responses to biological motion predict treatment outcome in young children with autism.** Transl Psychiatry. 2016 Nov 15;6(11):e948. [PMID: 27845779]

This study found that functional MRIs (fMRI) could predict which children will benefit from Pivotal Response Treatment (PRT), one of a few evidence-based interventions for the condition, with near-perfect accuracy. Although more research is needed, the current research provides an important first step toward establishing objective biomarkers that can accurately predict treatment outcome in young children with autism.

Gordon I, Jack A, Pretzsch CM, Vander Wyk B, Leckman JF, Feldman R, Pelphrey KA. **Intranasal Oxytocin Enhances Connectivity in the Neural Circuitry Supporting Social Motivation and Social Perception in Children with Autism.** *Sci Rep.* 2016 Nov 15;6:35054. [[PMID: 27845765](#)]

Researchers found that by administering oxytocin as a nasal spray before social experiences, children had stronger responses to the social information. The findings suggest that use of oxytocin treatment before behavioral therapy could help reinforce the reward system in the brain that motivates social behaviors. Oxytocin treatment could be a way to enhance behavioral methods that are specifically tailored to provide positive social experiences and rewards.

Pickles A, Le Couteur A, Leadbitter K, Salomone E, Cole-Fletcher R, Tobin H, Gammer I, Lowry J, Vamvakas G, Byford S, Aldred C, Slonims V, McConachie H, Howlin P, Parr JR, Charman T, Green J. **Parent-mediated social communication therapy for young children with autism (PACT): long-term follow-up of a randomised controlled trial.** *Lancet.* 2016 Nov 19;388(10059):2501-2509. [[PMID: 27793431](#)]

*This is one of the first studies to examine the longer term benefit of low-intensity parent-delivered early intervention for young children with autism. Children with autism (aged 2 years to 4 years and 11 months) were randomly assigned to a parent-mediated communication-focused (Preschool Autism Communication Trial [PACT]) intervention or treatment as usual at three specialist centers in the UK. 152 children were recruited. 77 were assigned to PACT and 75 to treatment as usual. At the 13-month endpoint, there was a significant benefit was noted for parent-child dyadic social communication (but not language or cognitive abilities). Six years after the intervention, children whose parents were trained using the PACT model showed improved parent-child interaction skills, and fewer were considered to have “severe” autism as compared to the comparison group. Results were published on 25 October in *The Lancet*.*

Cihak DF, Moore EJ, Wright RE, McMahon DD, Gibbons MM, Smith CS. **Evaluating augmented reality to complete a chain task for elementary students with Autism.** *Journal of Special Education Technology.* 2016 May; 31(2), 99-108. [[doi: 10.1177/0162643416651724](#)]

In this article, Cihak and colleagues examined the effects of augmented reality to teach a chain task to three elementary-age students with autism spectrum disorders (ASDs). Augmented reality blends digital information within the real world. This study used a marker-based augmented reality picture prompt to trigger a video model clip of a student brushing her teeth. All students learned how to brush their teeth independently and maintained the skill 9 weeks later with the introduction of augmented reality. We found this work to be novel and an interesting contribution to the literature on chain task completion for children with autism.

Flores MM, Schweck KB, Hinton V. **Teaching language skills to preschool students with developmental delays and Autism Spectrum Disorder using Language for Learning.** *Rural Special Education Quarterly.* 2016 Apr; 35(1), 3-12. [Link not available]

Flores, Schweck, and Hinton investigated the effects of Language for Learning (LL) on the language of students with developmental delays (DD) and Autism Spectrum Disorder (ASD) in a rural preschool

classroom. Four preschool students with DD and ASD participated in 12 weeks of instruction, resulting in improved language skills. We included this study because it extends the literature regarding direct instruction for students with DD and ASD and adds the rural setting component.

Garbacz SA, McIntyre LL. **Conjoint Behavioral Consultation for children with Autism Spectrum Disorder.** Sch Psychol Q. 2016 Dec;31(4):450-466. [PMID: 25688808]

Garbacz and McIntyre examined the efficacy of Conjoint Behavioral Consultation (CBC) for children with Autism Spectrum Disorder (ASD) in early elementary school. In addition, the parent–teacher relationship, parent and teacher competence in problem solving, and CBC acceptability were examined. Participants included 3 children with ASD in early elementary school, and their parents and teachers. Findings suggested (a) CBC was efficacious for treating children’s social behavior in classrooms, (b) 2 of 3 parent–teacher dyads reported improvements in the parent–teacher relationship, (c) all parents and teacher reported increases in their problem-solving competences, and (d) CBC was highly acceptable to parents and teachers. We felt this study was important because it provides support for parent/teacher relationships and the inclusion of parents in the consultation.

Thiemann-Bourque K, Brady N, McGuff S, Stump K, Naylor A. **Picture Exchange Communication System and Pals: A Peer-Mediated Augmentative and Alternative Communication Intervention for Minimally Verbal Preschoolers With Autism.** J Speech Lang Hear Res. 2016 Oct 1;59(5):1133-1145. [PMID: 27679841]

The study by Thiemann-Bourque and colleagues investigated the effectiveness of a social intervention that integrates peer-mediated approaches and the Picture Exchange Communication System (PECS). Effects were evaluated using a series of A-B designs replicated across 4 children with severe autism and limited verbal skills. Seven peers without disabilities were trained to use PECS and facilitative social skills. Measures of changes included rates of communication behaviors, modes, functions, and engagement. Outcomes revealed an intervention effect for 1 child with autism, and this effect was replicated across 3 other children. All children improved in peer-directed communication, with greater increases for 2 children during snack time. For each child with autism, the primary communication behavior was to initiate with picture symbols to request; the peer’s primary communication was to respond. Two children increased communicative functions to comment and to share, and all 4 children showed improved social engagement. All peers increased their communication with the children with autism. We found that these findings add to the limited research on the benefits of teaching typically developing peers to be responsive listeners to preschoolers with autism by learning to use PECS.

Yakubova G, Zeleke WA. **A Problem-Solving Intervention Using iPads to Improve Transition-Related Task Performance of Students With Autism Spectrum Disorder.** Journal of Special Education Technology. 2016; 31(2), 77-86. [Link not available]

In this study, Yakubova and Zeleke examined the effectiveness of teaching problem-solving to improve transition-related task performance of three students with autism spectrum disorder (ASD) using a multiple probe across students design. Target behaviors included various transition-related tasks individualized for each student based on their individual educational and transition goals. Following a multicomponent intervention utilizing point-of-view video modeling paired with practice sessions and a self-operated cue sheet, all students were able to improve their problem-solving performance. Additionally, students generalized the skills to a second untrained setting. We felt this study was important because it adds to the limited literature on teaching problem solving to students with ASD, particularly transition-age students.

Young KR, Radley KC, Jenson WR, West RP, Clare SK. **Peer-facilitated discrete trial training for children with autism spectrum disorder.** Sch Psychol Q. 2016 Dec;31(4):507-521. [PMID: 27929320]

Young and colleagues conducted two different studies in this article to evaluate the feasibility and efficacy of peer-mediated, school-based discrete trial training (DTT) for students with autism spectrum disorder (ASD). In the first study, 6 typically developing elementary-age students were trained to use DTT procedures to teach target academic skills to 3 students with ASD who had been educated in a self-contained setting. A multiple probe-across-tutors design was applied to evaluate the accuracy with which the tutors implemented the DTT protocol. Results of the study indicated that training was effective in increasing the integrity of implementation of the DTT protocol. In addition, improvements in integrity were maintained following termination of training. To assess the effectiveness of the ability of previously untrained tutors to teach new, target behaviors to different children with ASD, a second study was conducted. Five of the 6 tutors taught 2 or 3 skills in a multiple probe fashion to children with ASD whom they had not previously tutored. Results suggest that peer tutors effectively generalized skills, as shown by participants with ASD who demonstrated rapid improvements in level and trend of target behaviors. Substantial increases in duration of engagement were noted, suggesting that peer-mediated DTT may result in meaningful improvements in both academic skills and inclusion with peers. We felt this study was important because it utilized typical peers to teach academic skills to their peers with ASD.

Question 5 (Services)

Nguyen CT, Krakowiak P, Hansen R, Hertz-Picciotto I, Angkustsiri K. **Sociodemographic Disparities in Intervention Service Utilization in Families of Children with Autism Spectrum Disorder.** J Autism Dev Disord. 2016 Dec;46(12):3729-3738. [PMID: 27639855]

This article is significant because the sample size is much larger than a lot of the other autism healthcare disparities studies I've seen about diagnosis and things like race, education, etc. It also covers not just race but issues like whether someone has public insurance – Which will be very important in fighting for autistic people and families while the Republicans reshape healthcare.

Mandell DS, Barry CL, Marcus SC, Xie M, Shea K, Mullan K, Epstein AJ. **Effects of Autism Spectrum Disorder Insurance Mandates on the Treated Prevalence of Autism Spectrum Disorder.** JAMA Pediatr. 2016 Sep 1;170(9):887-93. [PMID: 27399053]

This is the first to use national data to examine the effects of the state autism insurance mandates using such a rigorous design. It shows that more kids with autism are identified in mandate states, but the increase is not what insurance companies feared or what advocates hoped for.

Leslie DL, Iskandarani K, Dick AW, Mandell DS, Yu H, Velott D, Agbese E, Stein BD. **The Effects of Medicaid Home and Community-based Services Waivers on Unmet Needs Among Children With Autism Spectrum Disorder.** Med Care. 2017 Jan;55(1):57-63. [PMID: 27547947]

This is one of the first to show that a state level policy affects parent-reported experience of service need. It also represents a nice model of merging data about state policies with service data to examine policy outcomes. Finally, it shows that particular characteristics of the waivers, not just the waiver itself, is important in improving child and parent experience, which leads to more specific policy recommendations for states.

Kiely B, Migdal TR, Vettam S, Adesman A. **Prevalence and Correlates of Elopement in a Nationally Representative Sample of Children with Developmental Disabilities in the United States.** PLoS One. 2016 Feb 4;11(2):e0148337. [PMID: 26845701]

No justification provided.

Question 6 (Lifespan Issues)

Koegel LK, Ashbaugh K, Navab A, Koegel RL. **Improving Empathic Communication Skills in Adults with Autism Spectrum Disorder**. Journal of autism and developmental disorders. 2016 Mar 1;46(3):921-33. [PMID: 26520148]

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 that focused on expression of empathy in conversation, found post-intervention, notable gains in the communication skills.

Wehman P, Schall CM, McDonough J, Graham C, Brooke V, Riehle JE, Brooke A, Ham W, Lau S, Allen J, Avellone L. **Effects of an employer-based intervention on employment outcomes for youth with significant support needs due to autism**. Autism. 2016 May 5. [PMID: 27154907]

One of the first randomized trials showing huge effect sizes in improving employment outcomes for young adults with autism

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 under-represented 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.

Hirvikoski T, Mittendorfer-Rutz E, Boman M, Larsson H, Lichtenstein P, Bölte S. **Premature mortality in autism spectrum disorder**. Br J Psychiatry. 2016 Mar;208(3):232-8. [PMID: 26541693]

This is the study that the Autistica people spoke about, which found much higher rates of death from epilepsy among adults with ASD with an intellectual disability, and much higher rates of death from suicide for adults with ASD without an intellectual disability. It has been available online for a while, but it looks like it was published in print in 2016, making it appropriate for the 2016 summary of advances.

Strang JF, Meagher H, Kenworthy L, de Vries AL, Menvielle E, Leibowitz S, Janssen A, Cohen-Kettenis P, Shumer DE, Edwards-Leeper L, Pleak RR, Spack N, Karasic DH, Schreier H, Balleur A, Tishelman A, Ehrensaft D, Rodnan L, Kushner ES, Mandel F, Caretto A, Lewis HC, Anthony LG. **Initial Clinical Guidelines for Co-Occurring Autism Spectrum Disorder and Gender Dysphoria or Incongruence in Adolescents**. J Clin Child Adolesc Psychol. 2016 Oct 24:1-11. [PMID: 27775428]

This article is potentially groundbreaking because it's become increasingly clear that a larger proportion of the autistic population is gender nonconforming, in contrast to the general population. Having clear guidance on how to respond to what can be a complex situation for both parents and their children is super important for professionals so they can respond appropriately. I also think this is important because suicide rates are high both in the autistic and trans communities. One of the factors contributing to Kayden Clarke's attempted suicide and death by police was that he was told he could not start transitioning until he was "cured of his Aspergers."

Roux AM, Rast JE, Anderson KA, and Shattuck PT. **National Autism Indicators Report: Vocational Rehabilitation.** Philadelphia, PA: Life Course Outcomes Research Program, A.J. Drexel Autism Institute, Drexel University, 2016. [<http://drexel.edu/autismoutcomes/publications-and-reports/publications/National-Autism-Indicators-Report-Vocational-Rehabilitation/#sthash.ZhrjVYEI.dpbs>]

This seems to be a pretty comprehensive view of what we can learn about Vocational Rehabilitation services from the VR dataset. Much of the information is not new and has been reported in other articles, but combining it all in a highy readable way seems to be an important contribution.

Fernandes LC, Gillberg CI, Cederlund M, Hagberg B, Gillberg C, Billstedt E. **Aspects of Sexuality in Adolescents and Adults Diagnosed with Autism Spectrum Disorders in Childhood.** J Autism Dev Disord. 2016 Sep;46(9):3155-65. [[PMID: 27401993](#)]

I have a few quibbles with the methodology of this paper, but it is addressing in some depth the sexuality of adults with ASD, which is an incredibly understudied topic. This is a cohort that has been followed from childhood has already been well-characterized, which I think is a nice strength of this paper and offsets the smaller sample size. The use of a self-report and parent-report sample alleviates to some extent the concerns of using one or the other.

Maisel ME, Stephenson KG, South M, Rodgers J, Freeston MH, Gaigg SB. **Modeling the cognitive mechanisms linking autism symptoms and anxiety in adults.** J Abnorm Psychol. 2016 Jul;125(5):692-703. [[PMID: 27196436](#)]

Comorbid psychiatric issues are a significant challenge for adults with ASD, but little research has been done to understand why these problems emerge. This study explores reasons why adults with ASD experience anxiety, linking anxiety symptoms to adverse reactions to emotional experiences while also having difficulty recognizing and understanding their emotions.

Woodman AC, Mailick MR, Greenberg JS. **Trajectories of internalizing and externalizing symptoms among adults with autism spectrum disorders.** Dev Psychopathol. 2016 May;28(2):565-81. [[PMID: 26612272](#)]

This is one of the largest studies of well-characterized adults with ASD, (n=259) and to date longitudinal data has been collected over 12 years at 7 time points. This is a reasonably thorough examination of changes in problem behaviors across adolescence and adulthood. Results suggested that there is a subgroup of adults with ASD who are at high and consistent risk for behavior problems (although the majority of the sample were improving in behavior problems over time. Findings also point to the importance of the family environment in predicting behavior problems.

Question 7 (Infrastructure and Surveillance)

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. **Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2012.** MMWR Surveill Summ. 2016 Apr 1;65(3):1-23. [[PMID: 27031587](#)]

Most comprehensive finding we have to date the rate of autism, using this surveillance strategy, has stabilized.

Hewitt A, Hall-Lande J, Hamre K, Esler AN, Punyko J, Reichle J, Gulaid AA. **Autism Spectrum Disorder (ASD) Prevalence in Somali and Non-Somali Children.** J Autism Dev Disord. 2016 Aug;46(8):2599-608. [PMID: [27106569](#)]

The current study presents results from an autism spectrum disorder (ASD) public health surveillance project conducted in Minneapolis. The study was designed to compare ASD prevalence in Somali children (ages 7–9) to that of non-Somali children. The study adapted methodology used by the Centers for Disease Control and Prevention’s Autism and Developmental Disabilities Monitoring Network. Results indicated that Somali (1 in 32) and White (1 in 36) children were about equally likely to be identified with ASD, but more likely to be identified with ASD than Black and Hispanic children. Somali children with ASD were significantly more likely to have an intellectual disability than children with ASD in all other racial and ethnic groups.