2018 Summary of Advances Nominations: January – April 2018

Question 1 (Screening and Diagnosis)	
David Mandell	Sacrey LR, Zwaigenbaum L, Bryson S, Brian J, Smith IM, Roberts W, Szatmari P, Vaillancourt T, Roncadin C, Garon N. **Parent and clinician agreement regarding early behavioral signs in 12- and 18-month-old infants at-risk of autism spectrum disorder.** Autism Res. 2018 Mar;11(3):539-547. doi: 10.1002/aur.1920. Epub 2018 Jan 22. [PMID: 29356441]
	Even expert clinicians using standardized measures in a high-risk sample miss important infant and toddler behaviors that could assist in making a diagnosis of autism. The study findings suggest that we need better strategies for eliciting and incorporating parent feedback into the screening and diagnostic process.
Question 2 (Underlying Biology)	
David Amaral	Avino TA, Barger N, Vargas MV, Carlson EL, Amaral DG, Bauman MD, Schumann CM. **Neuron numbers increase in the human amygdala from birth to adulthood, but not in autism.** Proc Natl Acad Sci U S A. 2018 Apr 3;115(14):3710-3715. doi:10.1073/pnas.1801912115. Epub 2018 Mar 20. [PMID: 29559529]
	The authors report the results of a stereological analysis of the number of neurons in amygdala nuclei of 52 human postmortem brains ranging from 2 to 48 years of age [24 neurotypical and 28 autism spectrum disorder (ASD)]. In neurotypical development, the number of mature neurons in the basal and accessory basal nuclei increases from childhood to adulthood, coinciding with a decrease of immature neurons within the paralaminar nucleus. Individuals with ASD, in contrast, show an initial excess of amygdala neurons during childhood, followed by a reduction in adulthood across nuclei. This suggests that there is a dysregulation of neuronal maturation in the amygdala, a structure commonly implicated in the neuropathology of ASD.
*Joshua Gordon***	Karalunas SL, Hawkey E, Gustafsson H, Miller M, Langhorst M, Cordova M, Fair D, Nigg JT. **Overlapping and Distinct Cognitive Impairments in Attention-Deficit/Hyperactivity and Autism Spectrum Disorder without Intellectual Disability.** J Abnorm Child Psychol. 2018 Feb 15. doi: 10.1007/s10802-017-0394-2. [Epub ahead of print] [PMID: 29450820]
	The current study, supported by NIMH, examined shared and distinct cognitive impairments in children (ages 7-15 years) with ADHD and ASD, a using both continuous symptom measures and empirically-defined categorical groups (ADHD, n=509; ASD, n=97; and TD controls, n=301). The findings showed that certain cognitive impairments in ASD (i.e., processing speed, working memory, and response inhibition) were independent of ADHD symptoms; while select impairments in ADHD were independent of

	ASD symptoms. Moreover, differences in reaction time on cognitive measures were distinct in that children with ASD showed consistently slower reaction times on fasts tasks, indicating a preference for accuracy over speed, relative to children with ADHD and controls. The study's findings indicate a phenotypic model in which certain cognitive impairments reflect shared liability between ASD and ADHD children, but are not attributable to comorbid symptom profiles between the two disorders.
Question 3 (Risk Factors)	
Alison Singer *Joshua Gordon***	Gandal MJ, Haney JR, Parikshak NN, Leppa V, Ramaswami G, Hartl C, Schork AJ, Appadurai V, Buil A, Werge TM, Liu C, White KP; CommonMind Consortium; PsychENCODE Consortium; iPSYCH-BROAD Working Group, Horvath S, Geschwind DH. **Shared molecular neuropathology across major psychiatric disorders parallels polygenic overlap.** Science. 2018 Feb 9;359(6376):693-697. doi:10.1126/science.aad6469. [PMID: 29439242]
	This study showed that autism, schizophrenia and bipolar disorder share some similarities in the patterns of gene expression in the brain. These findings were only possible by looking at brain tissue of individuals affected with these conditions and comparing gene transcription. While the profiles were not exact, the patterns looked similar enough that it's highly probable they share a similar genetic etiology. Such similarities were not seen between autism and major depression or alcoholism. This provides even more understanding on why schizophrenia, bipolar disorder and autism overlap in terms of some symptoms.
	In this NIMH-funded study, a team of investigators examined gene expression in postmortem brains of people who had been diagnosed with autism spectrum disorder (ASD) (n=50), schizophrenia (n=159), bipolar disorder (n=94), major depressive disorder (n=87), or alcoholism (n=17), and matched controls (n=293). The results revealed for the first time that disorders with a large overlap in genetic risk factors also had a large overlap in patterns of gene expression, shared dysfunction in similar molecular pathways, and similar impacts on synapse and neuro-immune functions for individuals with autism, schizophrenia, and bipolar disorder. This study also highlights the significant benefits of team-oriented scientific collaboration in that the data were drawn from the PsychENCODE consortium, a data-sharing collaboration of NIMH grantees.
Linda Birnbaum	Kalkbrenner AE, Windham GC, Zheng C, McConnell R, Lee NL, Schauer JJ, Thayer B, Pandey J, Volk HE. **Air Toxics in Relation to Autism Diagnosis, Phenotype, and Severity in a U.S. Family-Based Study.** Environ Health Perspect. 2018 Mar 12;126(3):037004. [PMID: 29553459]
	This publication represents an advance for studying air pollution as a risk factor for autism on multiple fronts, both in the design and the exposures assessed. Firstly, the authors addressed unmeasured family-level confounding by using a multiplex family (two or more siblings with an ASD diagnosis)-based design with continuous measures of ASD-related traits and

	severity as well as diagnosis. Secondly, the number of air toxics assessed for association with risk of diagnosis was larger than previous (155 air toxics), going well beyond the most well studied air pollutant associated with autism, PM2.5. Lastly, since air pollution represents a mixture and risk associated with a specific air toxic may be confounded by exposure to other air pollutants, a subset of chemicals was examined using two-pollutant models. Using this novel study design and this wider range of air toxic exposures, the authors were able to identify novel air pollutants associated with both risk for and severity of autism diagnosis.
Question 4 (Treatments and Interventions)	
David Mandell	Nevill RE, Lecavalier L, Stratis EA. **Meta-analysis of parent-mediated interventions for young children with autism spectrum disorder.** Autism. 2018 Feb;22(2):84-98. doi: 10.1177/1362361316677838. Epub 2016 Nov 14. [PMID: 29490483]
	This paper shows that the effects associated with parent-mediated intervention, while statistically significant, are small. Given that the intervention strategies that are being taught are the same as those demonstrated to have larger effects in clinician-mediated interventions, it suggests that either we are not good at teaching parents to implement these interventions, or that it is too much of a burden to place on parents, and we should consider clinician-implemented interventions as a more effective alternative.
Question 5 (Services)	
David Mandell	Kennedy-Hendricks A, Epstein AJ, Mandell DS, Candon MK, Marcus SC, Xie M, Barry CL. **Effects of State Autism Mandate Age Caps on Health Service Use and Spending Among Adolescents.** J Am Acad Child Adolesc Psychiatry. 2018 Feb;57(2):125-131. doi: 10.1016/j.jaac.2017.10.019. Epub 2017 Dec 5. [PMID: 29413145]
	Eleven states place age caps on their autism insurance mandates. This study shows that those age caps matter, and they reduce access to care for adolescents in those states relative to other states. Another important finding is that service use went down, on average, in all states, suggesting that there continue to be gaps in the healthcare system for adolescents with ASD, even when coverage for care is not an issue.
David Mandell	Rubenstein E, Daniels J, Schieve LA, Christensen DL, Van Naarden Braun K, Rice CE, Bakian AV, Durkin MS, Rosenberg SA, Kirby RS, Lee LC. **Trends in Special Education Eligibility Among Children With Autism Spectrum Disorder, 2002-2010.** Public Health Rep. 2018 Jan/Feb;133(1):85-92. doi: 10.1177/0033354917739582. Epub 2017 Dec 19. [PMID: 29257937]
	A third of children who meet research criteria for autism aren't in the autism category of special education. It is likely that this results in less specific and perhaps poorer educational care. The study begs the question of why these kids aren't in the autism category, how being in a different

	category affects the services they receive, and how the health care and education systems should be sharing information and supporting each other in making sure kids with autism are identified and receive appropriate care.
Alison Singer	Zerbo O, Modaressi S, Goddard K, Lewis E, Fireman BH, Daley MF, Irving SA, Jackson LA, Donahue JG, Qian L, Getahun D, DeStefano F, McNeil MM, Klein NP. **Vaccination Patterns in Children After Autism Spectrum Disorder Diagnosis and in Their Younger Siblings.** JAMA Pediatr. 2018 Mar 26. doi: 10.1001/jamapediatrics.2018.0082. [Epub ahead of print] [PMID: 29582071]
	In a matched cohort study of 3729 children with autism spectrum disorder and 592,907 children without autism spectrum disorder, the study found that children with autism spectrum disorder were less likely to be fully vaccinated for vaccines recommended between ages 4 and 6 years. The younger siblings of children with autism were also less likely to be fully vaccinated for vaccines recommended at any age. *This means that children with autism spectrum disorder and their younger siblings are at increased risk of vaccine-preventable diseases.*
Question 6 (Lifespan Issues)	
There were no nominations covering Question 6 topics from January - April 2018.	
Question 7 (Infrastructure and Surveillance)	
There were no nominations covering Question 7 topics from January - April 2018.	