



INSAR 2016 Summer Institute Session VI: The Broader Autism Phenotype

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Course Materials

The purpose of these materials is to help provide an introduction to the Summer Institute session on the Broader Autism Phenotype (BAP). The materials were designed to prepare trainees who are unfamiliar with BAP research with the general background to get the most educational benefit from Dr. Constantino's presentation. Toward this objective, we have prepared the following: (1) learning objectives for this session; (2) some key terms and concepts to become familiar with parent and family-led intervention research; (3) some broad review articles that are recommended reading. These materials could be considered "prerequisites" in preparing for Dr. Constantino's presentation.

In collaboration with Dr. Constantino, these materials were developed by the trainee group for this session: Joshua Page (Washington University in St. Louis, jbpage@wustl.edu), Lauren Friedman (Washington University in St. Louis, friedmanl@wustl.edu), Alyzeh Haider (Washington University in St. Louis, haidera@wustl.edu), and Kristina Cottle (University of Utah, Kristina.Cottle@utah.edu). Feel free to contact us with questions/comments.

Register for this course and other sessions in this series by creating an account at <http://eweb.autism-insar.org/eweb/>

Learning Objectives

The Summer Institute for Autism Research was established in direct response to requests from early career researchers (graduate students, postdocs, etc.), who asked INSAR for greater training opportunities in multidisciplinary topics. In designing the Summer Institute, the priorities were: (1) to provide a multidisciplinary training platform for young scientists from various backgrounds; (2) allow international participation; and (3) make it freely available. Thus, the second Summer Institute covers broad topics (which are geared to researchers outside the respective topic areas), is offered over a free web platform, and allows researchers from around the world to connect with the presenter. The overarching goal of the Summer Institute is to expose junior scientists to topics they are not currently engaged in, with the hope that basic scientists and clinical scientists could learn from each other to ultimately advance the understanding of autism spectrum disorders.

The current session, **The Broader Autism Phenotype**, is lead by Dr. John N. Constantino and a team of trainees who worked in tandem to prepare these materials and the web presentation. The learning objectives for attendees of this session include:

1. Participants will appreciate the implications of the Broader Autism Phenotype (BAP) in understanding the biological causes of ASD
2. Participants will understand how variation in sub clinical autistic traits influences normal human social development and the course of non-ASD-related disorders of behavior and development
3. Participants will recognize challenges and complexities of ASD diagnosis incurred by the reality of the distribution of ASD traits in families and populations.

Glossary / Key Concepts

Endophenotype: An internal phenotype that meets the following criteria: must be associated with the disease of interest, heritable, familial (co-segregated with illness), state independent, trait dependent, and present in some unaffected relatives. Autism endophenotypes can be grouped into the following categories: biochemical, morphological, immunological, behavioral, neurophysiological/neuroanatomical, and neuropsychological. Social responsiveness is an example of an Autism endophenotype.

Reciprocal Social Behavior: Refers to the extent to which a child engages in emotionally appropriate turn-taking social interaction with others. Continuous measures of reciprocal social behavior may be useful for characterizing the broader autism phenotype and may enhance the statistical power of genetic studies of autism. By definition, autism is characterized by deficits in reciprocal social behavior, with accompanying delays in the development of language, and by the emergence of stereotypic patterns of odd behavior or behavior that reflects a restricted range of interests.

Social Reciprocity Scale (SRS): A 65-item questionnaire that measures variation in reciprocal social behavior as a continuous variable by parent/teacher report. Once completed, a summary score is generated that serves as an index of severity along the continuum of deficits in reciprocal social behavior in the population. The SRS may feasibly be used in large-scale genetic-epidemiologic studies and as a clinical measure of symptoms across the autistic spectrum.

Neurofibromatosis Type 1 (NF1): A genetic disorder characterized by the development of multiple benign tumors of nerve and skin, called neurofibromas, and abnormal skin coloration. The disorder is caused by mutations in the NF1 gene, on the long arm (q) of chromosome 17, which codes for a tumor suppressor gene called neurofibromin. Difficulties in social functioning are a prominent feature of NF1, and the condition has been associated with increased risk of ASD.

Female Protective Effect: Reduced phenotypic expression of inherited autism susceptibility among females. The female protective effect in autism spectrum disorder is not mediated by a single common locus on the X chromosome.

Associative/Assortative Mating: In human genetics, this refers to a form of nonrandom mating in which pair bonds are established on the basis of observable characteristics. An example of assortative mating is the selection of a mate based on physical traits. In this form of selection, individuals with similar genotypes and/or phenotypes mate more frequently than would be expected under random mating patterns.

Monogenic/Polygenic Disorders: Monogenic disorders are caused by the mutation of a single gene, while polygenic disorders are caused by the combined action of more than one gene. According to the literature, ASD is a complex polygenic disorder, with risk deriving from genetic variations in multiple genes.

Recommended Reading

Constantino, John N. "The quantitative nature of autistic social impairment." *Pediatric Research* 69 (2011): 55R-62R.

<http://www.ncbi.nlm.nih.gov/pubmed/21289537>

Constantino, John N., and Tony Charman. "Diagnosis of autism spectrum disorder: reconciling the syndrome, its diverse origins, and variation in expression." *The Lancet Neurology* (2015).

<http://www.ncbi.nlm.nih.gov/pubmed/26497771>

Gaugler, Trent, et al. "Most genetic risk for autism resides with common variation." *Nature genetics* 46.8 (2016): 881-885.

<http://www.ncbi.nlm.nih.gov/pubmed/25038753>

Gockley, Jake, et al. "The female protective effect in autism spectrum disorder is not mediated by a single genetic locus." *Molecular autism* 6.1 (2015): 1.

<http://www.ncbi.nlm.nih.gov/pubmed/25973162>

Vissers, Lisenka ELM, Christian Gilissen, and Joris A. Veltman. "Genetic studies in intellectual disability and related disorders." *Nature Reviews Genetics* (2015).

<http://www.ncbi.nlm.nih.gov/pubmed/26503795>