



## INSAR 2016 Summer Institute Session IV: Sex Differences in ASD

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### Course Materials

The purpose of these materials is to help provide an introduction to the Summer Institute session on sex differences in ASD. The materials were designed to prepare trainees who are unfamiliar with research on sex differences with the general background to get the most educational benefit from Dr. Mandy's presentation. Toward this objective, we have prepared the following: (1) learning objectives for this session; (2) key terms and concepts related to methods and concepts in ASC sex differences research; (3) some broad review and research articles that are recommended reading. These materials could be considered "prerequisites" in preparing for Dr. Mandy's presentation. We have additionally prepared materials to support further reading on this topic if trainees are interested.

In collaboration with Dr. Mandy, these materials were developed by Marika C. Coffman (clinical psychology doctoral student at Virginia Tech; [marika@vt.edu](mailto:marika@vt.edu)), Laura Hull (doctoral student at University College London; [laura.hull.14@ucl.ac.uk](mailto:laura.hull.14@ucl.ac.uk)), Laura C. Anderson (clinical psychology doctoral student at the University of Maryland; [lander10@umd.edu](mailto:lander10@umd.edu)), and Ligia Antezana (clinical psychology doctoral student at Virginia Tech; [ligia@vt.edu](mailto:ligia@vt.edu)). Feel free to contact us with questions/comments.

## **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, Sex Differences in ASD, is led by Dr. William Mandy and a team of trainees who worked in tandem to prepare these materials and the web presentation. The aim of this seminar is to develop participants' understanding of sex differences in autism spectrum condition (ASC). Specifically, it aims to help participants learn about the following:

1. The existence of current diagnostic biases against females with ASC
2. Gender differences in how ASC manifests, with a specific emphasis on the female autism phenotype
3. Factors that contribute to under-recognition of females with ASC
4. Methodological challenges to research on the female autism phenotype, and how these can be overcome
5. Clinical implications, including the impact on girls and women of having ASC, and of current diagnostic biases against females.

## **Recommended Readings**

Dworzynski, K., Ronald, A., Bolton, P., & Happé, F. (2012). How different are girls and boys above and below the diagnostic threshold for autism spectrum disorders? *Journal of the American Academy of Child and Adolescent Psychiatry*, 51(8), 788–97.

Gould, J., & Ashton-Smith, J. (2011). Missed diagnosis or misdiagnosis? Girls and women on the autism spectrum. *Good Autism Practice (GAP)*, 12(1), 34–41.

Lai, M.-C., Lombardo, M. V., Pasco, G., Ruigrok, A. N. V., Wheelwright, S. J., Sadek, S. A., ... Baron-Cohen, S. (2011). A behavioral comparison of male and female adults with high functioning autism spectrum conditions. *PLoS One*, 6(6), e20835.

Mandy, W., Chilvers, R., Chowdhury, U., Salter, G., Seigal, A., & Skuse, D. (2012). Sex differences in autism spectrum disorder: evidence from a large sample of children and adolescents. *Journal of Autism and Developmental Disorders*, 42(7), 1304–13.

## **Future Readings/More Information**

Holliday-Willey, L. (1999). *Pretending to be normal*. London: Jessica Kingsley Ltd.

Hiller, R. M., Young, R. L., & Weber, N. (2014). Sex differences in autism spectrum disorder based on DSM-5 criteria: evidence from clinician and teacher reporting. *Journal of Abnormal Child Psychology*, 42(8), 1381–93. <http://doi.org/10.1007/s10802-014-9881-x>

Kreiser, N. L., & White, S. W. (2014). ASD in females: are we overstating the gender difference in diagnosis? *Clinical Child and Family Psychology Review*, 17(1), 67–84. <http://doi.org/10.1007/s10567-013-0148-9>

Lai, M.-C., Lombardo, M. V, Auyeung, B., Chakrabarti, B., & Baron-Cohen, S. (2015). Sex/gender differences and autism: setting the scene for future research. *Journal of the American Academy of Child and Adolescent Psychiatry*, 54(1), 11–24. <http://doi.org/10.1016/j.jaac.2014.10.003>

Mandy, W., & Lai, M.-C. (2016). Annual Research Review: The role of the environment in the developmental psychopathology of autism spectrum condition. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, 57(3), 271–92. <http://doi.org/10.1111/jcpp.12501>

<http://autisminpink.net/>

## **Glossary of Terms**

**DSM-5:** This manual describes the diagnostic criteria for neurodevelopmental, psychiatric and mental disorders including Autism Spectrum Disorder (ASD). Previous versions of the DSM included a category called Pervasive Developmental Disorders, which encompassed Autistic Disorder, Pervasive Developmental Disorder-Not Otherwise Specified, (PDD-NOS), Asperger's Syndrome, Rett's Syndrome, and Childhood Disintegrative Disorder. Individuals with diagnoses of Autistic Disorder, PDD-NOS, or Asperger's Syndrome based on DSM-IV were all considered part of the autism spectrum. In contrast, DSM-5 combines these subtypes of autism into one diagnosis: ASD. Diagnosing ASD using DSM-V criteria requires an evaluation of an individual's behavior in the following domains: 1) Social communication and social interaction and 2) restricted, repetitive patterns of behavior or interests. To make a diagnosis, these behaviors must occur in early in development, cause significant functional impairment, and not be fully explained by the individual's general intellectual ability.

**ADOS:** Autism Diagnostic Observation Schedule. A semi-structured, observation-based assessment of social-communication and restricted or repetitive behaviors used to aid in the diagnosis of ASD. The ADOS consists for 5 different modules. The module for an assessment is chosen based on the individual's language ability and age. Importantly, the ADOS should not be used alone to diagnose ASD and must be combined with parent-report measures and clinical judgment.

**3Di:** Developmental, Dimensional, and Diagnostic Interview. A computerized, highly reliable interview used by trained clinicians for the evaluation of suspected cases of ASD in children from 3 years of age and older.

**Gender / Sex:** Sex refers to a person's biological status and is typically categorized as male, female, or intersex (i.e., atypical combinations of features that usually distinguish male from female). Indicators of biological sex include sex chromosomes, gonads, internal reproductive organs, and external genitalia. Gender refers to the attitudes, feelings, and behaviors that a given culture associates with a person's biological sex.

**Core symptoms of ASD:** The core symptoms of ASD include deficits in social communication and social interaction as well as restrictive, repetitive patterns of behavior or interests.

**ASC or ASD?:** The diagnostic term used by DSM-V is Autism Spectrum Disorders (ASD), which includes Autism, Asperger's Syndrome, Pervasive Developmental Disorder and other conditions. However, some individuals on the spectrum find the use of the term 'disorders' stigmatising. The term 'Autism Spectrum Conditions' (ASC) is therefore suggested as an alternative which acknowledges the range of abilities and experiences within the autism spectrum.

**Co-morbidity / co-occurring condition:** The presence of one or more disorders, or diseases, in addition to the primary disorder. The second disorder is typically independent of the primary disorder.

**Meta-analysis:** A meta-analysis is a statistical procedure for combining results from multiple different studies in order to better identify patterns among research studies. Meta-analyses lead to higher statistical power and lead to more robust conclusions than an individual study. They can be thought of as "doing research on previous research."

**Odds ratio:** Odds ratios can be used to describe the strength of the association between two variables. Odds ratios are used to compare the relative odds of the occurrence of the outcome of interest (e.g. disease or disorder), given exposure to the variable of interest (e.g. health characteristic, aspect of medical history). The odds ratio can also be used to determine whether a particular exposure is a risk factor for a particular outcome, and to compare the magnitude of various risk factors for that outcome.

- OR=1 Exposure does not affect odds of outcome
- OR>1 Exposure associated with higher odds of outcome
- OR<1 Exposure associated with lower odds of outcome

**Phenotype:** An observable characteristic or trait of an organism. For example, a clinical phenotype is the characteristic of cognitive, personality, behavior, and psychiatric patterns that are typical for a disorder.

**Cohort Study:** A longitudinal study that follows a group of individuals who share characteristics (e.g. were born at the same time), over an extended period of time. The ALSPAC study (Avon Longitudinal Study of Parents and Children) has followed over 14,000 children who were born in the Bristol area of the UK and their parents since 1991.

**Case Ascertainment:** How participants are identified for inclusion in an ASC study group. Active ascertainment involves testing the entire population for ASC and only including those who meet diagnostic criteria. Passive ascertainment involves asking for participants who already have an ASC diagnosis or are considered at risk.

**SCDC:** The Social and Communication Disorder Checklist (SCDC) is a measure of autism traits within the general population. Individuals who score highly on this scale have higher levels of social communication difficulties, including ASC.

**Internalising:** Behaviors in which an individual inwardly expresses their problems. Symptoms include anxiety, sadness, social withdrawal, and fearfulness. Examples of internalising disorders include depression, anxiety, obsessive-compulsive disorder, and eating disorders such as bulimia nervosa and anorexia nervosa. Higher levels of co-occurring internalising problems have been found in females with ASC compared to males with ASC.

**Externalizing:** Behaviors in which the individual outwardly expresses their problems toward their environment. Behaviors involve overactivity, poor impulse control, noncompliance, and aggression. Examples of externalizing disorders include attention-deficit/hyperactivity disorder, oppositional defiant disorder, conduct disorder, and intermittent explosive disorder. Co-occurring externalizing symptoms are common in ASC.

**Eating disorder:** Eating disorders are characterized by irregular eating habits and severe distress about body weight or shape. Eating disturbances may include inadequate or excessive food intake. Examples of eating disorders are anorexia nervosa, bulimia nervosa, and binge eating disorder.

**Anorexia nervosa:** Anorexia nervosa (AN) is an eating disorder characterized by refusal to maintain a healthy weight, an obsessive fear of gaining weight, and a distorted perception of their body. The DSM-5 describes two subtypes of anorexia nervosa: 1) binge-eating/purging type and 2) restricting type. The binge eating/purging subtype is characterized by eating large quantities of food followed by purging behaviors such as vomiting or misuse of laxatives, diuretics, and enemas. The restricting subtype is characterized by limiting the quantity of food intake through dieting, fasting, and excessive exercise. Severity of AN is characterized by an individual's body mass index (BMI) with lower BMI indicating greater severity.