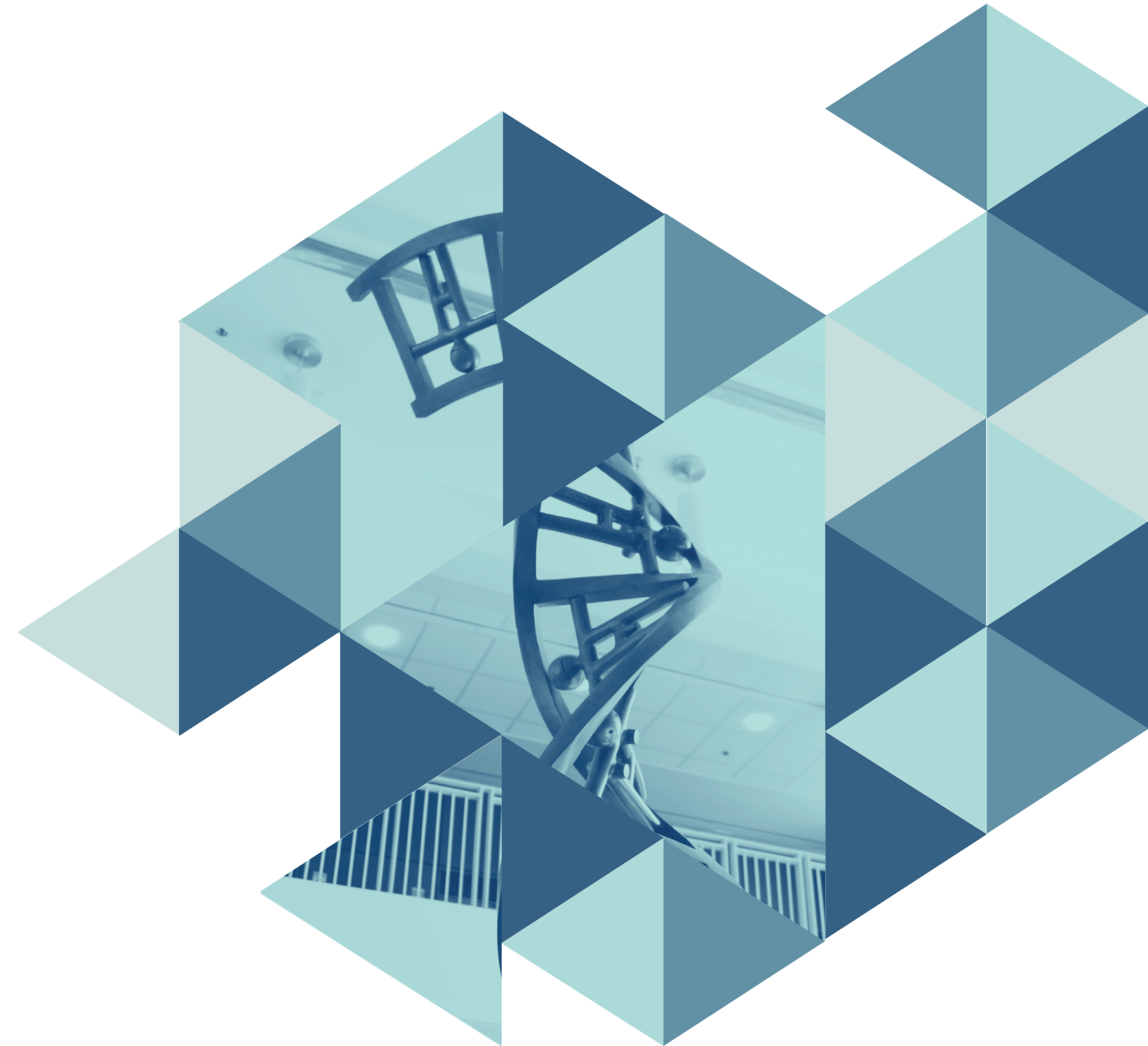


Introduction to Psychiatric Genetics

An Overview in Tourette Syndrome and
Obsessive-Compulsive Disorder

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History of Psychiatric Genetics

- Sir Francis Galton
 - Late 19th and early 20th century
 - Charles Darwin's half-cousin
 - Created statistical concept of correlation
 - First to apply statistical methods to study human differences
 - First to study inheritance of intelligence
 - Pioneered eugenics (whoops), also coined the term itself
 - Coined the phrase “nature vs. nurture”
 - He also devised the first weather map and proposed the existence of anticyclones
- Rough start with eugenics
 - The field of behavioral genetics has had a rough history with eugenics
- Promising findings for people with mental health issues
 - Instrumental in identification of disorder-causing variants
 - Helpful in pharmacogenomic approaches to treatment of psychiatric disorders

Psychiatric Disorders

- Greatly disturb thinking, moods, and behaviors
- Diagnosed by mental health professionals (e.g. psychiatrist)
- Described by ICD-10 and DSM-5
- Broad range of heritability (low to higher than some complex physiological disorders)

Neurodevelopmental and Obsessive-Compulsive Disorders

- Neurodevelopmental disorders
 - Intellectual disabilities
 - Communication disorders
 - Autism spectrum disorders
 - Attention Deficit / Hyperactivity Disorder
 - Specific learning disorder
 - Motor disorders
 - Tic disorders
 - **Tourette's Disorder**
- Obsessive-compulsive disorders
 - **Obsessive-compulsive disorder**
 - Body dysmorphic disorder
 - **Hoarding disorder**
 - Trichotillomania
 - Excoriation

Tourette's Disorder (Syndrome)

- Characterized by:
 - Multiple motor and at least one vocal tics present during illness, not necessarily concurrently
 - May wax and wane, but have persisted for more than 1 year since the first tic onset
 - Onset is before age 18 years
 - The disturbance is not attributable to the physiological effects of a substance or another medical condition
- Prevalence is 3-8 per 1,000 in school-aged children
- Males are more affected than females, ration between 2:1 and 4:1
- Course
 - Onset: 4-6 years of age
 - Peak severity: 10-12 years of age
 - Decline in severity: adolescence and adulthood
- Comorbidities:
 - ADHD
 - OCD
- Heritability: 80%

Obsessive-compulsive disorder

- Characterized by:
 - Obsessions and/or compulsions
 - Time consuming or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
 - Not attributable to the physiological effects of a substance or a medical condition
 - Not better explained by other mental disorder
- Prevalence is 1.2% in the US (12-month)
- Females affected slightly more in adulthood, males in childhood
- Course
 - Onset: teens and tweens, rarely after 35
 - Chronic if untreated
- Comorbidities:
 - Tic-related
- Heritability: 30%

Reproducibility issues in psychology

- Initial report by Nosek et al. in 2015 findings:
 - 35% of the replications yielded significant findings (at $p < 0.05$)
 - Mean effect size in the replications was half the magnitude reported in the original studies
- Reproducibility remains a concern in the field, we address it by:
 - Methodological triangulation (use of multiple tests and batteries to assess behavior)
 - Investigator triangulation (multiple investigators assess the results)
- Best estimates:
 - At least two investigators will review the results independently
 - Consensus is reached on final diagnosis

Plan of attack (consortium level)

- Clinical data
 - Collected and processed by lab's and collaborators' clinicians
 - Analyzed from psychiatric and epidemiological perspective
 - Handed to geneticists and statisticians for genetic studies
- Genetic data
 - DNA
 - Illumina Global Screening Array Microchip
 - CNV
 - GWAS
 - Whole Exome Sequencing
 - Rare mutations
 - RNA
 - Under consideration
- Data mining

Plan of attack (Franjo level)

- CNV (data mostly available)
 - Development of CNV pipeline to identify inherited and *de novo* CNVs in parent-proband trios
 - Analysis of over 1500 trios currently being genotyped
- GWAS (data mostly available)
 - Association analysis of SNPs associating with particular disorder phenotypes
 - Example: symmetry symptoms in Tourette's Syndrome
- Pedigree development (data available)
 - Development and description of a large Costa Rican pedigree spanning 15 generations

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