

# What should a psychiatrist know about genetics?

ISPG Residency Education  
Taskforce

# Introduction

---

- What does genetics have to do with psychiatry?
  - psychiatric illnesses run in families
  - the major psychiatric disorders have a high heritability
  - specific genes may be associated with vulnerability
  - genetic biomarkers may help predict risk
  - gene variants are associated with response to treatment

# What disorders are we including

---

- ◉ Bipolar disorder
- ◉ Schizophrenia
- ◉ Anxiety Disorders
- ◉ Substance use disorders
- ◉ Alzheimer's
- ◉ ID
- ◉ Autism
- ◉ ADHD
- ◉ OCD
- ◉ Eating Disorders

# Introduction (2)

---

- What genetic issues may arise for a clinician?
  - a patient may ask about genetic vulnerability
  - a patient may ask about reproductive choices
  - patients may inquire about genetic testing
  - you may be referred a patient with a genetic syndrome
  - you may wish to get pharmacogenetic testing

# Introduction (3)

---

- What genetic issues may be relevant to the career development of a psychiatrist?
- As a result of this educational intervention, the resident will
  - demonstrate the ability to read the current literature on genetic findings
  - accurately interpret media reports relevant to the genetics of disease
  - stay current with the tools of practice including genetic tests, biomarkers, and pharmacogenetic testing

# **What should a psychiatrist know about genetics**

---

- ① **1) Basic principles of genetics**
- ② **2) Family studies and heritability of psychiatric disorders**
- ③ **3) Common variants in psychiatry**
- ④ **4) Rare variants in psychiatry**
- ⑤ **5) Epigenetics**
- ⑥ **6) Pharmacogenetics**
- ⑦ **7) Ethical and social issues related to genetics**
- ⑧ **8) Principles of genetic counseling**

# Basic principles of medical genetics

---

- ◉ DNA – RNA – protein
- ◉ DNA organization on chromosomes and localization in the nucleus
- ◉ Meiosis and recombination
- ◉ Haplotypes and linkage disequilibrium
- ◉ Genetic variation in populations (pathogenic and normal)
- ◉ Genetic linkage and its detection
- ◉ Testing for genetic association
- ◉ Definitions



# Family studies and heritability

---

- Concepts of heritability, relative risk
- Use of twin, family, and adoption studies
- Heritability of bipolar disorder, schizophrenia, autism, major depression, alcohol use disorders, and other major psychiatric disorders.
- Liability threshold model of complex genetic disorders
- Calculation of recurrence risk based on family history



# Common variants in psychiatry

---

- What can we learn from a GWAS study?
- What have we learned from GWAS/common variant studies in psychiatry?
  - importance of the MHC in schizophrenia
  - importance of ApoE in Alzheimer's
  - importance of calcium channel genes in BP
  - genetic overlap between BP and SZ

How to interpret a Manhattan plot

Relationship between variant frequency and effect size

# Rare variants in psychiatry

---

- What is a CNV? What illnesses are they important in? (ASD, ID, SZ, BP)
- What are the psychiatric symptoms of common medical genetic syndromes?
- What can we learn from sequencing studies?
  - role of *de novo* variants in autism
  - sequence variants in other conditions
  - SNVs

# Epigenetics

---

- What is gene expression? What influences it?
- How do environmental changes impact gene expression ?
- GxG and GxE
- How can we study changes in gene expression?
  - role of peripheral cell studies
  - brain collections and their use
  - induced pluripotent stem cells

Methylation, acetylation, histone changes  
Transgenerational epigenetic changes

# Pharmacogenetics and pharmacogenomics

---

- Drug metabolizing genes: cytochrome p450 system
- Therapeutic response and side effects
  - tests for antipsychotic-induced weight gain
- Pharmacogenetics of antidepressants
- Antipsychotics
- Mood stabilizers
- Anxiolytics
- Addictions
- Clinical tests and how to use them

# Ethical and social issues

---

- History of eugenics
- What is the public perception of genetic testing? Psychiatric genetics?
- What are the advantages/disadvantages of population genetic screening programs? Guidelines for screening. GINA
- Who owns genetic information? Myriad genetics case
- Genetic testing and special populations/minorities. Discrimination and underrepresentation.

# Principles of genetic counseling

---

- How to talk with families about etiology, genetics and environment
- How to talk about risk
- Psychological issues related to the presentation of genetic information
- When to refer to a medical geneticist or genetic counselor



# Conclusions and further reading

---

- Every psychiatrist should know *the basic principles of genetics, the role of genes in psychiatric disorders and their treatment, the ways in which environment affects gene expression, ethical issues in the use of genetic information, and how to talk to families about genetics.*
- Reference: <http://g-2-c-2.org//>  
**Genetics/genomics competency center**