Genes and Disorders

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Schizophrenia

A disorder that lasts for at least six months and includes at least one month of active-phase symptoms

- Symptoms can be conceptualized as falling into two broad categories of positive and negative
- Positive: reflect an excess or distortion in thought content, perception, language and thought process, and self-monitoring of behavior
- Negative: restrictions in range and intensity of emotional expression, in fluency and productivity of thought and speech, and in the initiation of goal-directed behavior

--as described in DSM-IV-TR
A. *Characteristic symptoms*: Two (or more) of the following, each present for a significant portion of time during a one-month period

- 1. delusions
- 2. hallucinations
- 3. disorganized speech
- 4. grossly disorganized or catatonic behavior
- 5. negative symptoms, i.e., affective flattening, alogia, or avolition
B. **Social/occupational dysfunction**: For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset.

C. **Duration**: Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms that meet Criterion A and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form.
D. *Schizoaffective and Mood Disorder exclusion*: Schizoaffective Disorder and Mood Disorder With Psychotic Features have been ruled out because either (1) no Major Depressive, Manic, or Mixed Episodes have occurred concurrently with the active-phase symptoms; or (2) if mood episodes have occurred during active-phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.
E. *Substance/general medical condition exclusion*: The disturbance is not due to the direct physiological effects of a substance or a general medical condition.

F. *Relationship to a Pervasive Developmental Disorder*: If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month.
Heritability for Schizophrenia

- The lifetime risk for schizophrenia in the general population is collectively reported at about 1%.
- Risk to siblings of affected person = 10%
- Risk to offspring of affected person = 13%
- Risk to parents of affected person = 6%
  - Non-Schizophrenic parents
- Risk to second-degree relatives = 5%
- Adoption studies have shown an increased risk in biological first-degree relatives, but not non-biological relatives
  - 7.9% versus 0.9%
Twin studies have shown that MZ twins have an increased risk of 41%-65% while DZ twins have a risk of 0%-28%.

Thus heritability has been concluded to be between 80%-85%.

However, it should be noted that inheritance is the predisposition or liability to develop the disorder, not the certainty of having the disease.
Heritability contd.

- Through studies, gene linkage is suspected in 2 gene areas:
  - 13q14.1-q32
  - 1q21-q22
- Schizophrenia is a complex, non-Mendelian disorder. Mode of transmission, if known, can reveal much.
  - Oligogenic: small number of genes of moderate effect
  - Polygenic: many genes of small effect
  - Combination of both.
Schizophrenia and You

- Studies have discovered Schizophrenia is a highly genetic disorder. No genetic component has been isolated, but evidence points to strong genotypic factors.
- If a “Schizophrenia gene” were discovered and your family had a history of the disease, would you take any measures to eliminate the disorder from your family?
Dissociative Identity Disorder (DID)

- The presence of two or more distinct identities or personality states that recurrently take control of behavior with an inability to recall important personal information.

- It reflects a failure to integrate various aspects of identity, memory, and consciousness.

--as described in DSM-IV-TR
West (1967) defined a dissociative reaction as a “state of experience or behavior wherein dissociation produces a discernable alteration in a person’s thoughts, feelings, or actions, so that for a period of time certain information is not associated or integrated with other information as it normally or logically would be.”
A. The presence of two or more distinct identities or personality states (each with its own relatively enduring pattern of perceiving, relating to, and thinking about the environment and self).

B. At least two of these identities of personality states recurrently take control of the person’s behavior.

C. Inability to recall important information that is too extensive to be explained by ordinary forgetfulness.

D. The disturbance is not due to the direct physiological effects of a substance or a general medical condition.
Other Phenotypic Symptoms

- Memory problems
- Depersonalization
- Derealization
- Trance
- Flashbacks
- Child voices
- Persecutory voices
- Voices commenting on one’s actions
- Voices arguing or conversing
- Finding evidence for behavior without memory of behavior
- “Made” feelings
- “Made” thoughts
- “Made” actions
- Influence playing on body
- Thought insertion
- Thought withdrawal
- Somatoform/conversion
- Identity confusion
- Disconcerting experiences of self-alteration
- Time loss
- Fugues
Heritability for DID

- Little evidence has been found to support genetic predispositions to Dissociative Identity Disorder.
- Dissociation lies on a continuum ranging from daily, minor dissociations, like daydreaming, to major pathological forms, like DID (MPD).
- Severe dissociation can occur when a child is physically and/or sexually abused.
DID and You

- DID is frequently questioned as to whether or not it is a legitimate disorder.
  - Study in Northern Ireland

- What are your opinions/experiences with DID and what would you do if you were confronted with a person of this disorder?
Bipolar I Disorder

- A clinical course that is characterized by the occurrence of one or more Manic Episodes or Mixed Episodes.
- Often individuals have also had one or more Major Depressive Episodes.

-- as described in DSM-IV-TR
Bipolar II Disorder

- A clinical course that is characterized by the occurrence of one or more Major Depressive Episodes accompanied by at least one Hypomanic Episode.

-- as described in DSM-IV-TR
Criteria for Manic Episode
--as prescribed by DSM-IV-TR

- A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week.

- B. During the period of mood disturbance, three (or more) of the following symptoms have persisted and have been present to a significant degree:
  1. inflated self-esteem
  2. decreased need for sleep
  3. more talkative than usual or pressure to keep talking
  4. flight of ideas or subjective experience that thoughts are racing
  5. distractibility
  6. increase in goal-directed activity or psychomotor agitation
  7. excessive involvement in pleasurable activities that have a high potential for painful consequences
Criteria for Manic Episode contd.

--as prescribed by DSM-IV-TR

- C. The symptoms do not meet criteria for a Mixed Episode.
- D. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.
- E. The symptoms are not due to the direct physiological effects of a substance or a general medical condition.
Criteria for Major Depressive Episode
-- as prescribed by DSM-IV-TR

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

1. depressed mood most of the day, nearly every day, as indicated by either subjective report or observation made by others
2. markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
3. significant weight loss when not dieting or weight gain, or decrease or increase in appetite nearly every day
4. insomnia or hypersomnia nearly every day
5. psychomotor agitation or retardation nearly every day
6. fatigue or loss of energy nearly every day
7. feelings of worthlessness or excessive or inappropriate guilt nearly every day
8. diminished ability to think or concentrate, or indecisiveness, nearly every day
9. recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempts or a specific plan for committing suicide
Criteria for a Mixed Episode
-- as prescribed by DSM-IV-TR

- A. The criteria are met both for a Manic Episode and for a Major Depressive Episode nearly every day during at least a 1-week period.
- B. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.
- C. The symptoms are not due to the direct physiological effects of a substance or a general medical condition.
Criteria for Hypomanic Episode
-- as prescribed by DSM-IV-TR

A. A distinct period of persistently elevated, expansive, or irritable mood, lasting throughout at least 4 days, that is clearly different from the usual nondepressed mood.

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted and have been present to a significant degree:
   1. inflated self-esteem or grandiosity
   2. decreased need for sleep
   3. more talkative than usual or pressure to keep talking
   4. flight of ideas or subjective experience that thoughts are racing
   5. distractibility
   6. increase in goal-directed activity or psychomotor agitation
   7. excessive involvement in pleasurable activities that have a high potential for painful consequences
C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic.

D. The disturbance in mood and the change in functioning are observable by others.

E. The episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features.

F. The symptoms are not due to the direct physiological effects of a substance or a general medical condition.
Heritability of Bipolar Disorder

- Concordance of MZ twins with Bipolar found to be 60%.
  - DZ twins found to be 10% as well as traditional siblings.
- Adoption studies have shown genes more influential than environment: 18% v. 7%
- In population studies it has been found that first-degree relatives have a 10% risk factor.
  - Second-degree relatives have a 4% risk.
- Studies have focused on chromosomes 13q, 18q, and 22q as possessing risk genes.
Bipolar Disorder and You

- What preconceived notions of Bipolar Disorder did you have before coming to class? How have they changed?
OCD
Obsessive-Compulsive Disorder

**Definition**
A disorder in which a person has recurrent and unwanted thoughts and/or a need to perform repetitive and rigid actions or mental acts.

*Obsession* = a persistent thought, idea, impulse, or image that is experienced repeatedly, feels intrusive, and causes anxiety.

*Compulsion* = a repetitive and rigid behavior or mental act which that persons feel the must perform in order to prevent or reduce anxiety.

**Symptoms/Phenotype**
- Recurrent obsessions or compulsions
- Past or present recognition that the obsessions or compulsions are excessive or unreasonable
- Significant distress or impairment, or disruption by symptoms for more than one hour a day
Symptoms/Phenotype Continued...

- Obsessions often take the form of obsessive wishes, impulses, images, ideas, or doubts
- Common obsessions = dirt or contamination, violence and aggression, orderliness, religion, and sexuality
- May develop a compulsive act into a detailed and elaborate ritual

- Common compulsions = cleaning compulsions, checking compulsions, and constant striving for symmetry, order, and balance in one’s actions and surroundings, touching, verbal, and counting compulsions
Heritability Info

- As many as 2% of the population suffer from OCD
- Equally common in men and women
- Does not seem to vary among races or cultural/ethnic groups.
- Diathesis-stress perspective = individuals with the disorder typically have a biological vulnerability toward experiencing anxiety that is brought to fruition by psychological and sociocultural forces.
- Certain genes may combine to determine whether a person reacts to life stressors calmly or in an uptight, anxious way
- During the earliest stages of life, some infants consistently become very aroused when stimulated while other infants remain quiet
- Easily aroused infants may have inherited defects in GABA functioning or other biological limitations that predispose them to anxiety disorders
OCD Video!
In what ways is anxiety evolutionary? Environmental? Beneficial? Harmful? Do you buy into the diathesis-stress idea that individuals with OCD typically have a biological vulnerability toward experiencing anxiety that is brought to fruition by psychological and sociocultural forces?
Substance Dependence

- A cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues use of the substance despite significant substance-related problems.
- A pattern of repeated self-administration that can result in tolerance, withdrawal, and compulsive drug-taking behavior.
Criteria for Substance Dependence
--as prescribed by DSM-IV-TR

- A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:
  - 1. tolerance, as defined by either of the following:
    - A. a need for markedly increased amounts of the substance to achieve intoxication or desired effect
    - B. markedly diminished effect with continued use of the same amount of the substance
Criteria for Substance Dependence contd.
--as prescribed by DSM-IV-TR

2. Withdrawal, as manifested by either of the following:
   A. the characteristic withdrawal syndrome for the substance
   B. the same substance is taken to relieve or avoid withdrawal symptoms

3. The substance is often taken in larger amounts or over a longer period than was intended

4. There is a persistent desire or unsuccessful efforts to cut down or control substance use

5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects

6. Important social, occupational, or recreational activities are given up or reduced because of substance use

7. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
Heritability of Alcoholism

- Genes have been identified to influence metabolism of alcohol and have effects on alcohol-dependence risk.
  - ALDH2 and ADH2
  - CYP2A6 has an influence on nicotine
- Adoption studies have shown an increased risk for adopted children with alcoholic biological parents over those with nonalcoholic adoptive parents.
- Twin studies have shown correlations in MZ twins.
ALDH2 effect on Metabolism

- Ethanol converted by enzyme dehydrogenase to toxic metabolite acetaldehyde which is converted by enzyme acetaldehyde dehydrogenase to acetic acid.
- Single point mutation in gene ALDH2 on chromosome 12 leads to an inactive enzyme
  - Those with mutation have substantially elevated blood acetaldehyde concentrations after ingestion and experience “flushing” response.
  - Impaired metabolism of alcohol associated with ALDH2 lead to unpleasant reactions after ingestion which may result in lower consumption and lower risk of dependence.
Substance Dependence and You

College is the time to party. If you do have a family history of alcoholism, or if you did, how does/would that govern your actions as a 20-something year old living in the prime age of the party scene?
Anorexia Nervosa

Definition

- A disorder marked by the pursuit of extreme thinness and by and extreme loss of weight
- *Restricting-type anorexia nervosa* = reduce weight by restricting their food/caloric intake

Symptoms/Phenotype

- Refusal to maintain body weight above a minimally normal weight for age and height.
- Intense fears of gaining weight, even though underweight
- Disturbed body perception, undue influence of weight or shape on self-evaluation, or denial of the seriousness of the current low weight
- In postmenarcheal females, amenorrhea
Some less talked about symptoms...

- Fear provides motivation for weight-loss
- Preoccupation with food as a result of food deprivation
- Think in distorted ways i.e. overestimate body size
- Maladaptive attitudes and misperceptions i.e. “I will become a better person if I deprive myself”
- Psychological problems such as depression, anxiety, low self-esteem, insomnia. These may be a result of starvation.
- Substance abuse
- Display obsessive-compulsive patterns, especially with food.
- Perfectionistic; typically precedes onset of disorder
Physical Problems/Symptoms

- Amenorrhea = cease to menstruate
- Lowered body temperature
- Low blood pressure
- Body swelling
- Reduced bone mineral density
- Slow heart rate
- Metabolic and electrolyte imbalances
- Dry, rough, and cracked skin
- Brittle nails
- Cold or blue hands and feet
- Hair loss
- Lanugo = fine hair that covers body
Recent research has suggested various genes that may leave certain persons susceptible to anorexia nervosa.

Relatives of people with eating disorders are up to 6 times as likely than others to develop an eating disorder.

Twin studies show that an identical twin whose twin has bulimia nervosa also develops the disorder in 23% of cases. The rate for fraternal twins is 9%.

Heritable biological traits such as low or very high serotonin activity may contribute to the development of eating disorders.

Brain: some researchers believe that the LH (lateral hypothalamus) and VMH (ventromedial hypothalamus) and chemicals such as GLP-1 work together to keep an individual at a weight set point. Dieting may cause hypothalamic activity that causes a preoccupation with food.
**THE ARTICLE**

**Thesis**
- Long-term weight-restored patients with AN have lower norepinephrine levels than controls
- NET (norepinephrine transporter) gene was involved in the genetic component of AN

**Conclusion**
- Testing with 87 Australian trios (parents + patient) showed that this specific genetic variant doubles the risk of developing AN-R
Nicole’s Experience

Three years with anorexia nervosa, restricting type
Discussion Time 😊

Any questions for me? Really, ask ANYTHING!!! What were your preconceptions about anorexia? Have any of your thoughts changed?
Huntington’s Disease

**Definition**
- An inherited disease, characterized by progressive problems in cognition, emotion, and movement, which results in dementia.

**Symptoms/Phenotype**
- Movement problems such as severe twitching and spasms
- Memory problems that worsen over time
- Personality changes and mood difficulties

**Heritability Info**
- Children of people with the disease have a 50% chance of developing it
Huntington’s Video!!!

Studying Families
DISCUSSION QUESTION 😊

In the video clip, the researcher voiced concerns about the test for Huntington’s being too readily available to the public. What do you think are responsible/ethical preconditions to having a Huntington’s test? Do you agree that is it equally moral to be tested as it is NOT to be tested for a person at risk?
Reading Disabilities

**Definition**
- The inclusion of learning problems in the DSM is controversial. While some say these are strictly educational and social problems, others reason that the additional problems created by these disorders and links to other psychological problems justify their clinical classifications.

**Symptoms/Phenotype**
- Reading is the primary academic problem in 80% of children diagnosed with a learning disability.

**Heritability**
- Learning disabilities have a 5% prevalence rate among all children.
- Males are more likely to have a learning disability.
- There is an elevated family history of learning disabilities for children who have one.
**Findings**
- Recent analyses suggest only about 20% of the families of children with reading disabilities manifest apparent linkage to Chromosome 15. Thus, most cases of heritable reading disability must be attributed to other genes such as Chromosome 6.
- Twin and sibling studies show that they have concordant DNA markers; detected linkages to both Chromosome 6 and 15.

**Conclusion**
- Single-gene and quantitative genetics analyses are complementary and should both be exploited to understand completely the genetic causes of individual differences in behavior.
What type of genetic testing do you find most convincing, single-gene studies or quantitative studies with siblings or twins? Can you think of any ethical problems with either one?
**DYSLEXIA**

**Definition**
- A reading disorder in which a person shows a marked impairment in the ability to recognize words and comprehend what they read.

**Symptoms/Phenotype**
- Typically read slowly and haltingly and may omit, distort, or substitute words as they go.

**Heritability Info**
- Studies have linked various developmental disorders to genetic defects, but the research is limited and the precise causes of these disorders remains unclear.
Thesis

- Researchers at the University of Helsinki tested 20 Finnish families with cases of dyslexia. DYXC1 gene was disrupted in a number of those families.

Conclusion

- Dyslexia is a genetically complex condition, but DYXC1 should be regarded as a candidate gene for developmental dyslexia.
- Long-term: this may enable scientists to start working on drugs to treat the condition.
As the article suggests, should doctors test children for this particular genetic fault? Why or why not?
Autism

- Presence of markedly abnormal or impaired development in social interaction and communication and a markedly restricted repertoire of activity and interests.
- Manifestations of the disorder vary greatly depending on the developmental level and chronological age of the individual.
  - as described in DSM-IV-TR
Diagnostic Criteria for Autistic Disorder
--as prescribed by DSM-IV-TR

- A. A total of six (or more) items from (1), (2), and (3), with at least two from (1), and one each from (2) and (3):
  - (1) qualitative impairment in social interaction, as manifested by at least two of the following:
    - A. Marked impairment in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction
    - B. Failure to develop peer relationships appropriate to developmental level
    - C. A lack of spontaneous seeking to share enjoyment, interests, or achievements with other people
    - D. Lack of social or emotional reciprocity
Criteria for Autistic Disorder contd.
--as prescribed by DSM-IV-TR

(2) qualitative impairments in communication as manifested by at least one of the following:

- A. Delay in, or total lack of, the development of spoken language
- B. In individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others
- C. Stereotyped and repetitive use of language or idiosyncratic language
- D. Lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level
Criteria for Autistic Disorder contd.

--as prescribed by DSM-IV-TR

- (3) restricted repetitive and stereotyped patterns of behavior, interests, and activities, as manifested by at least one of the following:
  - A. Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus
  - B. Apparently inflexible adherence to specific, nonfunctional routines or rituals
  - C. Stereotyped and repetitive motor mannerisms
  - D. Persistent preoccupation with parts of objects
B. Delays or abnormal functioning in at least one of the following areas, with onset prior to age 3 years: (1) social interaction, (2) language as used in social communication, or (3) symbolic or imaginative play.

C. The disturbance is not better accounted for by Rett’s Disorder of Childhood Disintegrative Disorder.
Heritability estimates range from over 90%-100%.

There are currently no confirmed biological markers that aid in diagnosis.

- Evidence for linkage from 2-stage screen of 95 families to be on chromosome 2q with heterogeneity log of odds score of 1.96
- 2q, 7q, 15q11-q13, 19q, Xq

Classified as a complex genetic disease:

- No clear pattern of inheritance, moderate to high evidence it is inherited, multiple genes and environment may interact to cause disease; common in general population; and a susceptibility gene is found but only confers increased risk of disease and is not alone sufficient for the disease.
Autism and You

- Females better than males at empathizing while males are better than females at systemizing.
- Baron-Cohen says autism is an exaggerated version of male systemizing.
- Males account for more than 80% of the million plus Americans with Autistic Disorder.
- As we have read in this article and previously talked about gender differences the past couple of weeks, what are your takes on the preponderance of Autistic males?
Commentary Question

- Have you had experience first or second hand with any of these disorders? How did it affect you?
- If a disorder is in your family, how has it affected our decisions and behavior?