Psychiatric Disorders
Learning about the brain from diagnosis to treatment

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Talk overview

Part I: Defining psychiatric disorders

Part II: Biological underpinnings of depression

Part III: The future of psychiatric diagnosis and treatment
Psychiatric disorders affect everyone

Percent of adults with psychiatric disorders in 2012

 adapted from NIH
Differentiating health from disorder... a tricky business

Intensity

Delusions

Substance Use

Anxiety
What are psychiatric disorders?

Currently, psychiatric disorders are diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM), published by the American Psychiatric Association (APA).
What are psychiatric disorders? The DSM-5 definition

“… a syndrome characterized by clinically significant disturbance in an individual’s cognition, emotion regulation, or behavior that reflects a dysfunction in the psychological, biological, or developmental processes underlying mental function.”
Some difficulties with this definition…

A group of symptoms – no biological definition

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How do we measure this?
The result is... categorically defined disorders

- Depression
- Schizophrenia
- ADHD
- Autism
- Bipolar Disorder
Defining depression (Major Depressive Disorder)

According to the DSM, 5+ of the following symptoms must be present for 2 weeks:

1. Depressed mood every day
2. Diminished pleasure / interest in daily activities every day
3. Significant change in weight
4. Insomnia or hypersomnia every day
5. Psychomotor agitation or retardation every day
6. Fatigue every day
7. Feelings of worthlessness and excessive guilt
8. Decreased ability to concentrate
9. Recurrent thoughts of death
The result is... categorically defined disorders

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The result is... categorically defined disorders

A disorder affecting adults characterized by...

**Depressive episodes:** e.g. sadness, anxiety, guilt, hopelessness

**Manic episodes:** e.g. elevated/irritable mood, racing thoughts, easily distracted

Bipolar Disorder
The result is… categorically defined disorders

A disorder affecting young adults characterized by…

“Positive” symptoms: e.g. hallucinations, delusions, disorganized thinking

“Negative” symptoms: e.g. avolition, diminished emotional expression

Schizophrenia
The result is… categorically defined disorders

A behavioral disorder affecting children characterized by…

- Attention deficits
- Hyperactivity
- Impulsiveness
The result is… categorically defined disorders

A disorder affecting young children characterized by…

Impaired social interaction

Impaired verbal and non-verbal communication
What do we know about the underlying biology?
Defining depression (Major Depressive Disorder)

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Antidepressant drugs

- Tricyclic antidepressants (TCA’s), e.g. Imipramine: first treatment for depression
- Later replaced by selective serotonin reuptake inhibitors (SSRI’s), e.g. Prozac
Questions?
Antidepressant drugs: How do they work?

Depressed

Antidepressant

Less Depressed

How???
The brain is composed of cells called neurons.
Neural circuits are composed of neurons that communicate using chemical signals called neurotransmitters.
Antidepressants target the serotonin neurotransmitter system.
Normally, serotonin is taken back up by the cell that released it through the serotonin transporter.
Antidepressants block reuptake of serotonin into cells and allow serotonin to continue interacting with other neurons.
Antidepressant drugs increase serotonin levels outside the cell…

… and decrease depressive symptoms
The serotonin hypothesis of depression
Gene associations suggest a link between serotonin and depression.
Gene variants of serotonin transporter correlate with rates of depression in humans

The serotonin system is associated with depression
But… antidepressant efficacy is relatively low

Depressed → Less Depressed → Not Depressed

Serotonin can’t be the whole picture
Novel therapeutics target multiple neural systems

Even the newest therapies aren’t completely effective… are we treating the right thing?
Questioning the definition of psychiatric disease

Depression

Schizophrenia

ADHD

Autism

Bipolar Disorder

How accurately do psychiatric diagnoses reflect the underlying biology?
GWAS studies show that these psychiatric disorders share genetic components.

- Depression
- Schizophrenia
- ADHD
- Autism
- Bipolar Disorder
The reality... shared symptoms and genetics
Perhaps a symptom-based system is not the best diagnostic approach....

- Depression
- Schizophrenia
- ADHD
- Autism
- Bipolar Disorder
Toward a new biologically-based diagnostic approach: RDoC

Trait: Anxiety

Biological Complexity

http://www.nimh.nih.gov/research-priorities/rdoc/rdoc-constructs.shtml#potential_threat
Summary

- Psychiatric disorders are currently defined by symptoms

- Much of what we understand about the biology of psychiatric disorders comes from experience with pharmacotherapies

- The current aim is to develop a biologically-based system for diagnosing psychiatric disorders
Thank you!

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addgene
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Questions?