Psychiatric Disorders

Learning about the brain from diagnosis to treatment

Tedi Asher
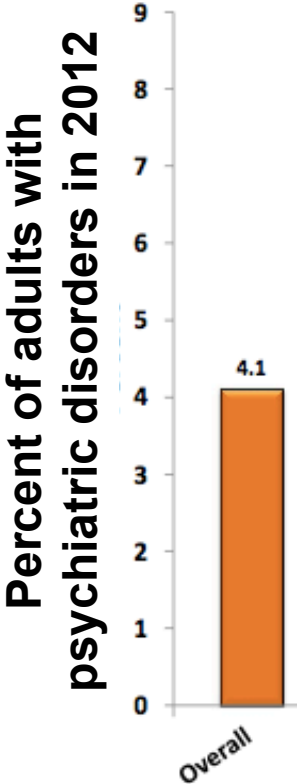Harvard Medical School

Talk overview

Part I: Defining psychiatric disorders

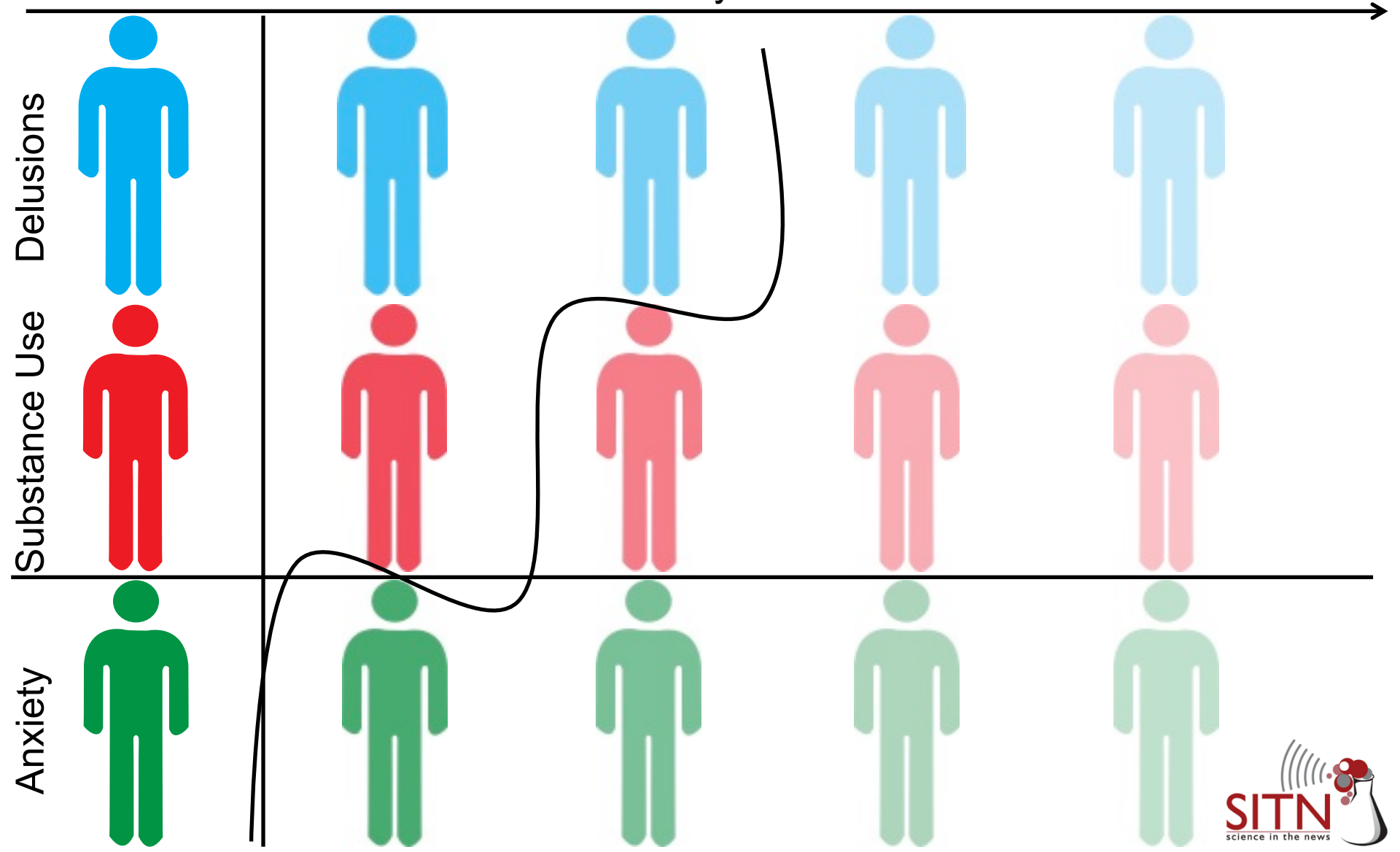Part II: Biological underpinnings of depression

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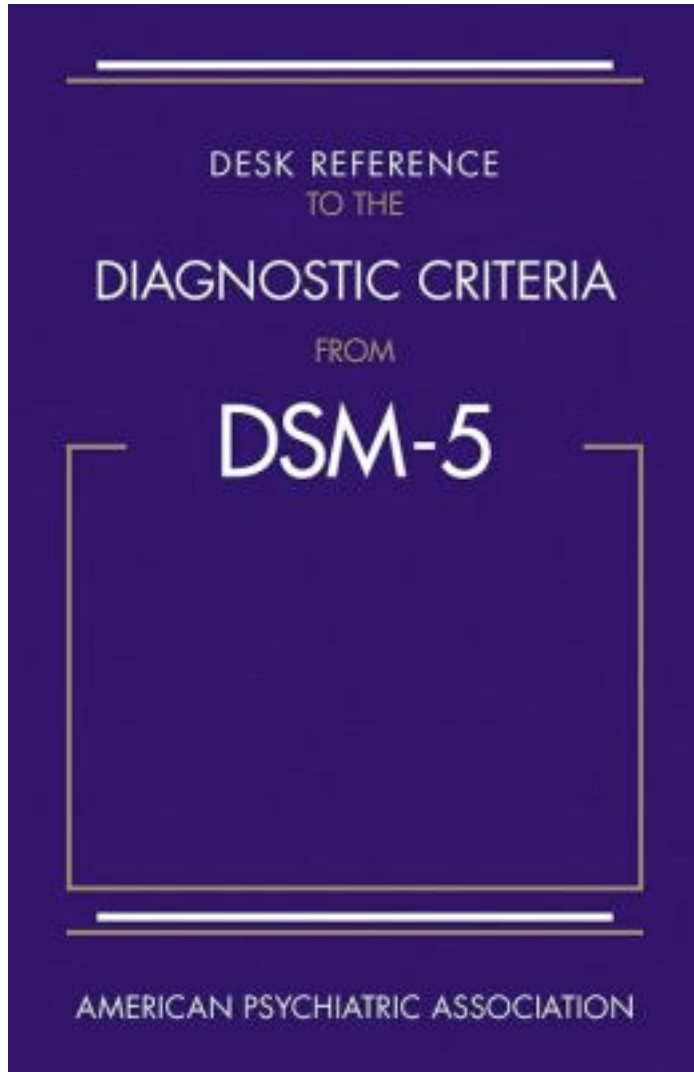
Psychiatric disorders affect everyone

Differentiating health from disorder… a tricky business

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

"… 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 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

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How do we measure this?
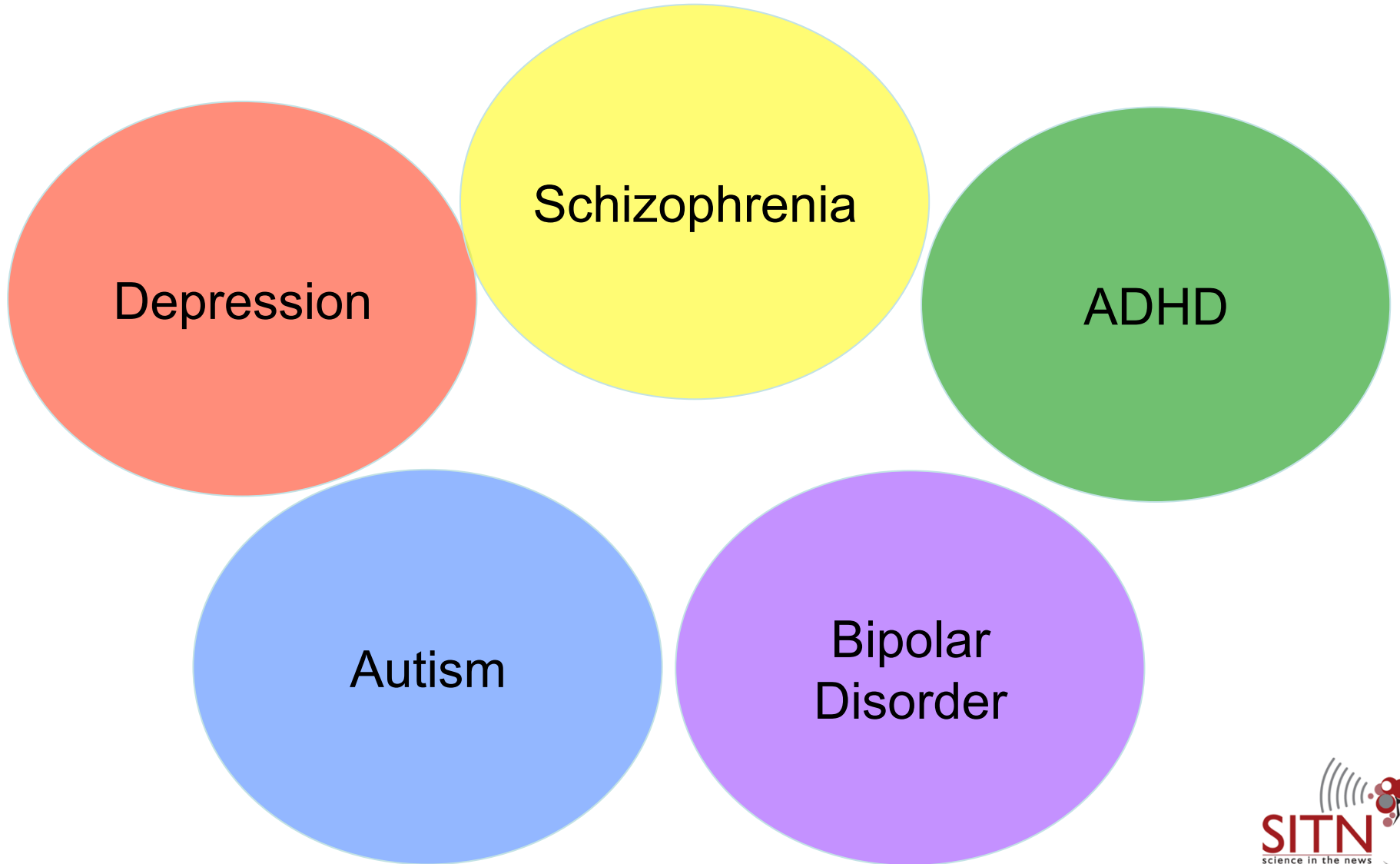
The result is… categorically defined disorders
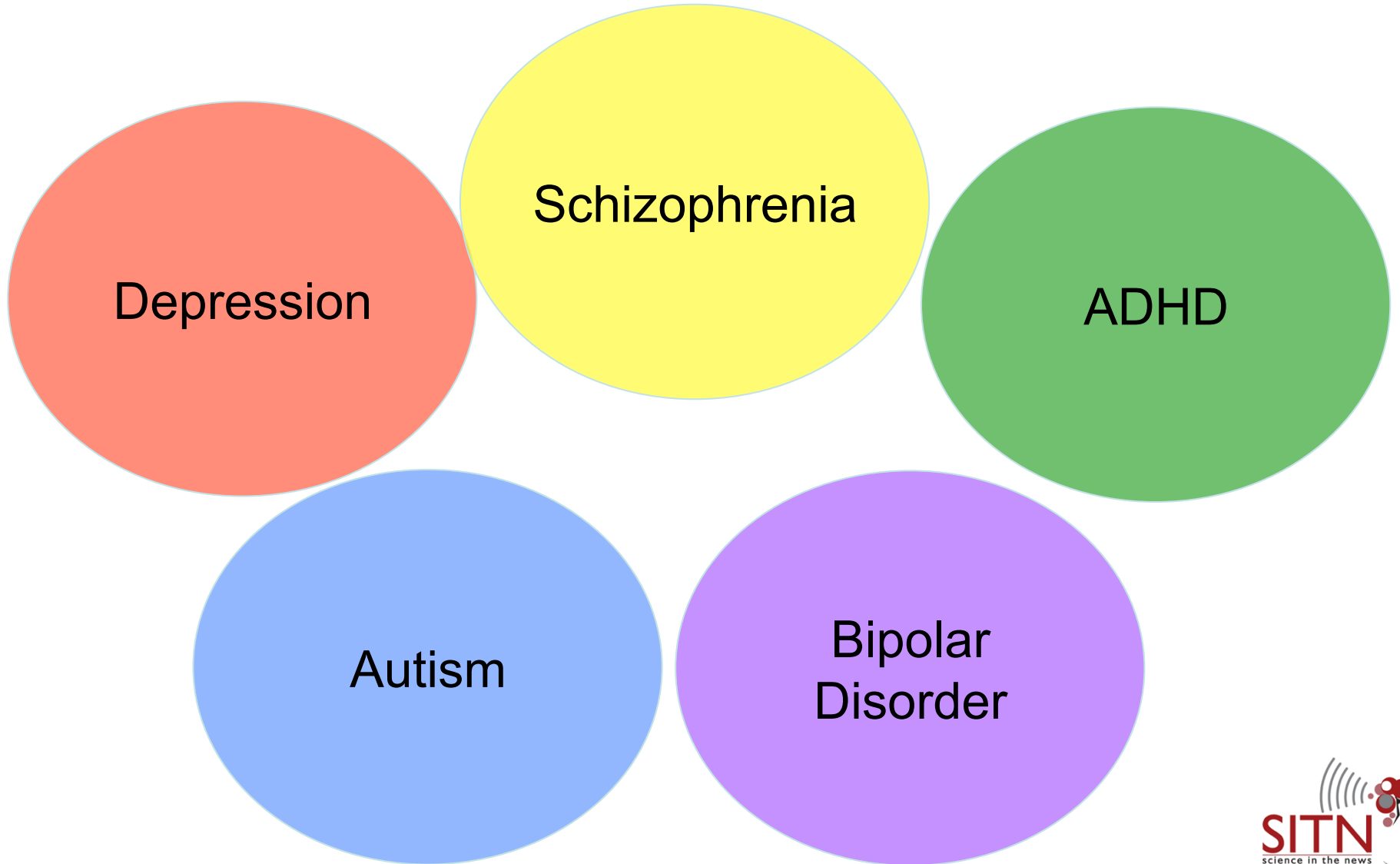
Defining depression (Major Depressive Disorder)

Depression

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

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The result is… categorically defined disorders

Depression
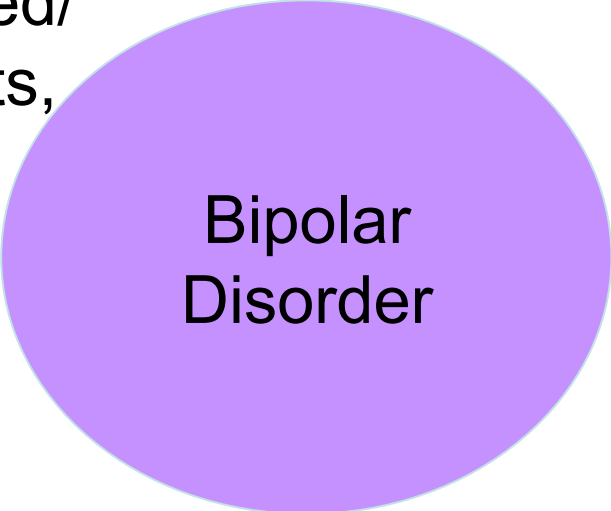
Schizophrenia

ADHD

Autism

Bipolar
Disorder

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

Schizophrenia

A disorder affecting young adults characterized by…

"Positive" symptoms: *e.g.* hallucinations, delusions, disorganized thinking

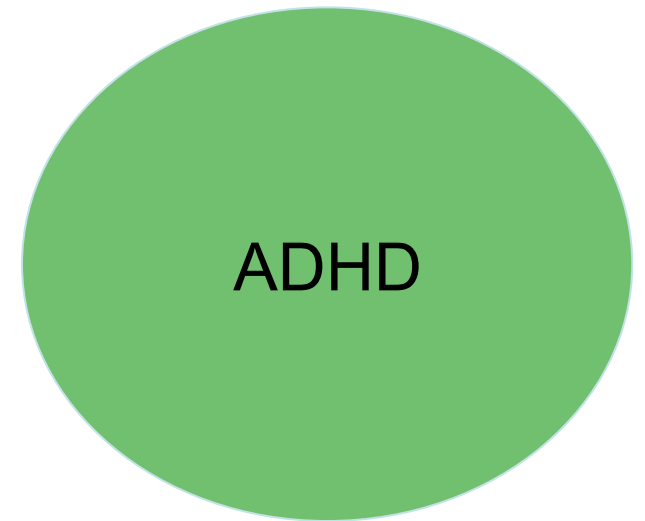**"Negative" symptoms**: *e.g.* avolition, diminished emotional expression

The result is… categorically defined disorders

A behavioral disorder affecting children
characterized by…

Attention deficits

Hyperactivity

Impulsiveness
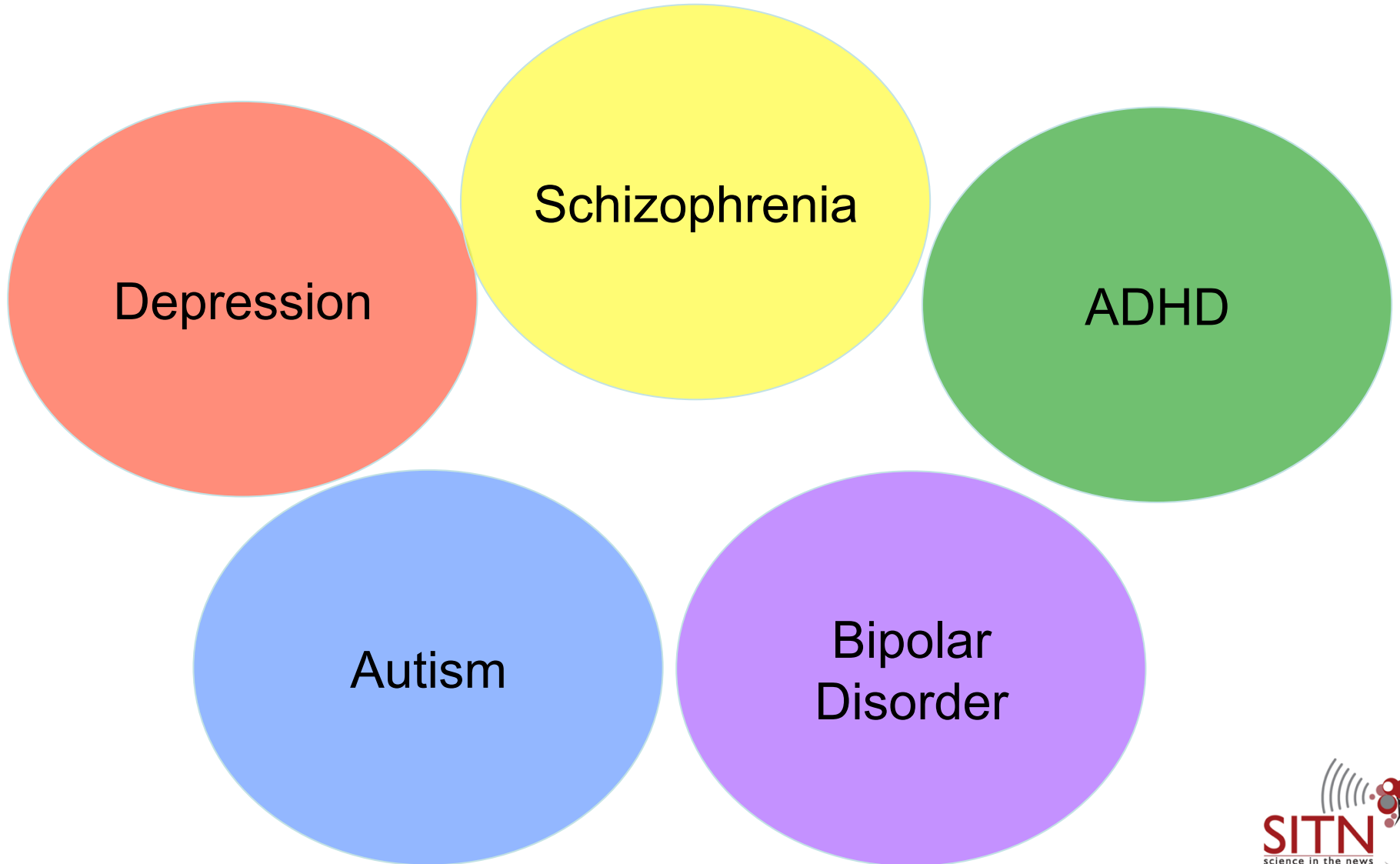
ADHD

The result is… categorically defined disorders

A disorder affecting young children characterized by…

Impaired social interaction

Impaired verbal and non-verbal communication

Autism

What do we know about the underlying biology?

# Defining depression (Major Depressive Disorder)

5+ of the following symptoms 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

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Depression
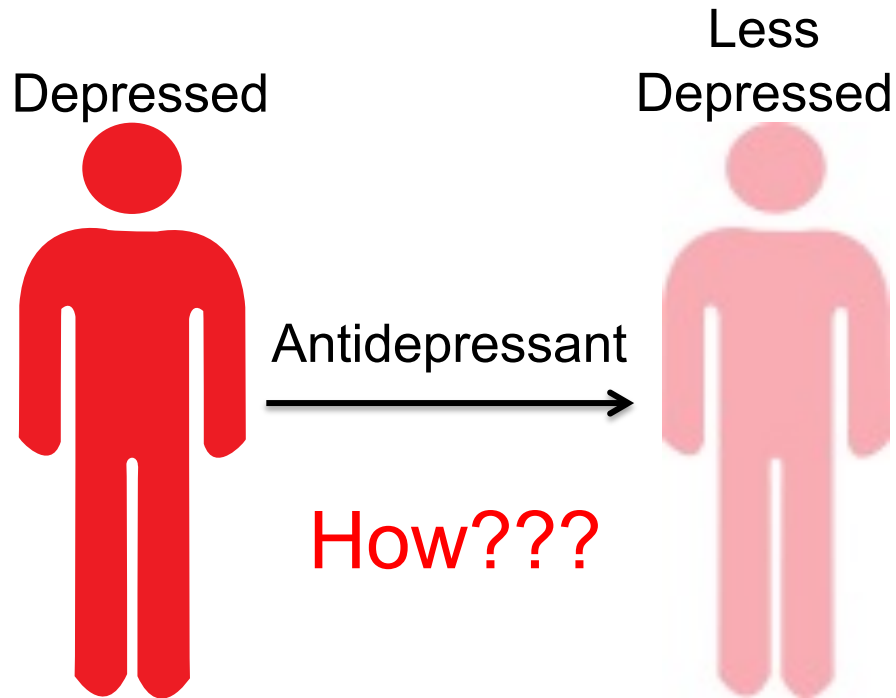
DSM-5

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Antidepressant drugs

- Tricyclic antidepressants (TCA's), *e.g.* Imipramine: first treatment for depression

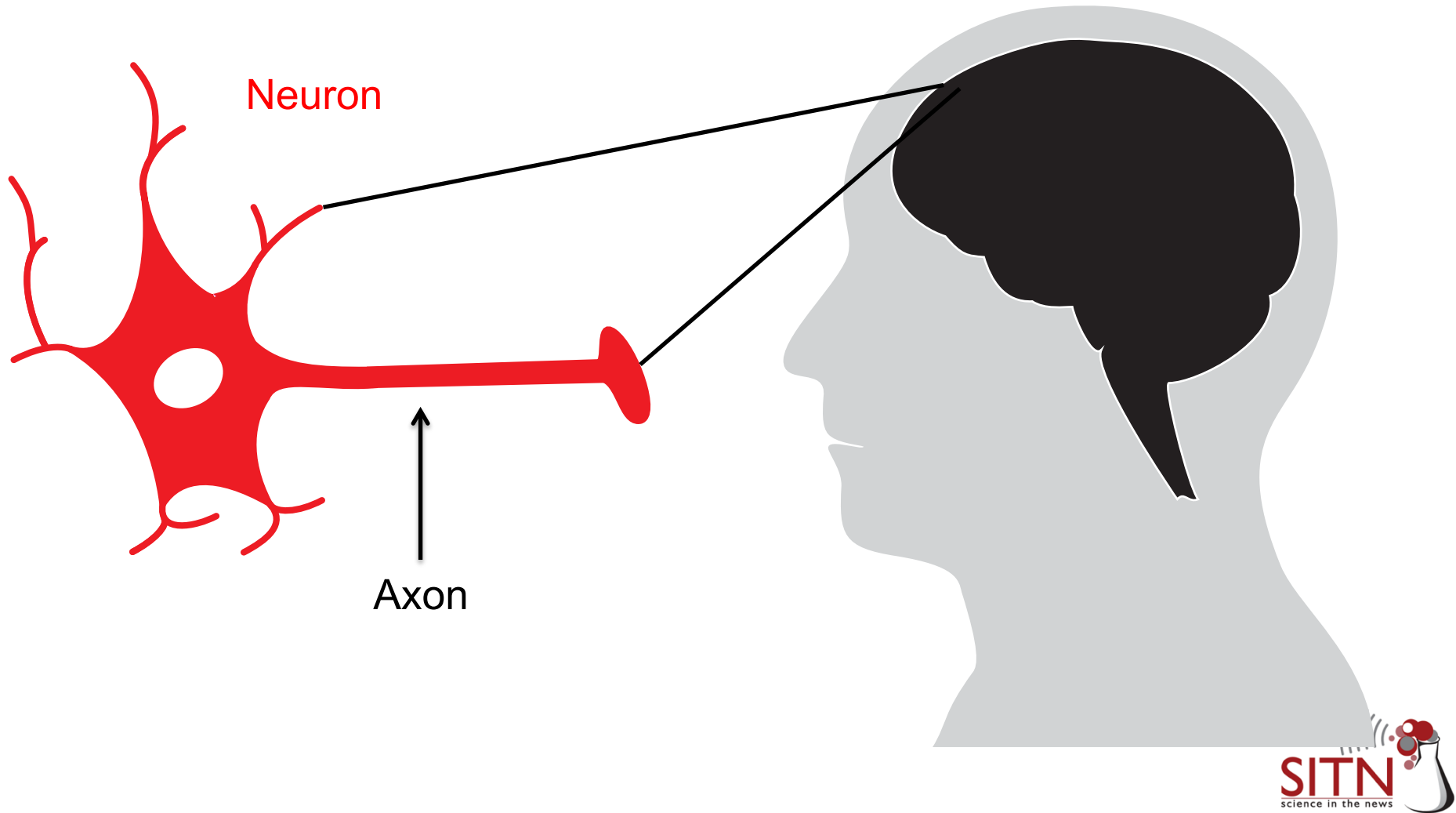- Later replaced by selective serotonin reuptake inhibitors (SSRI's), *e.g.* Prozac

Depressed

Less Depressed

Antidepressant

How???
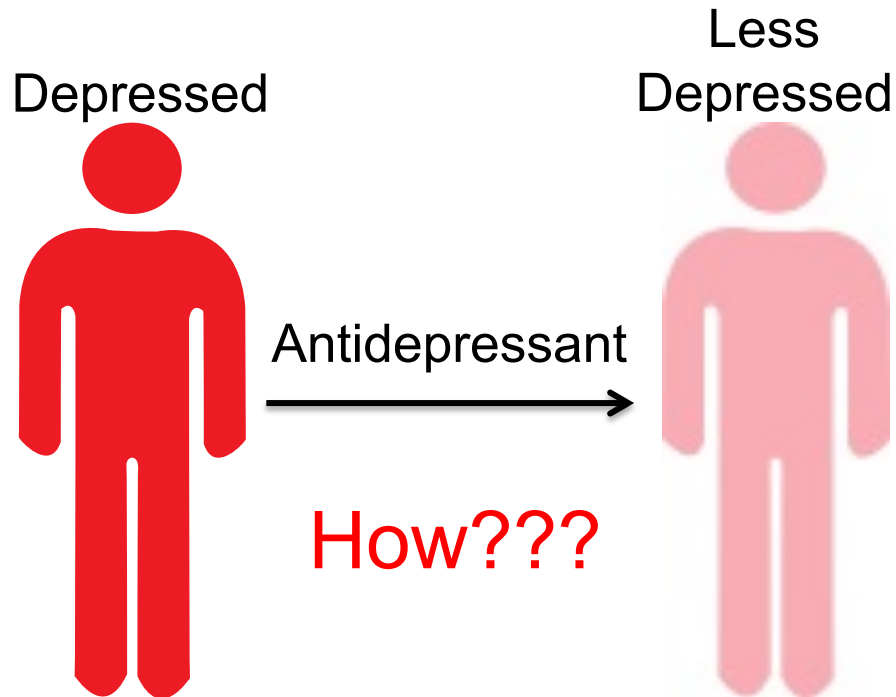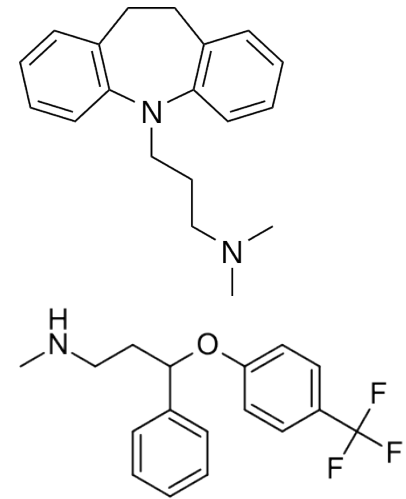
Questions?

Antidepressant drugs: How do they work?

The brain is composed of cells called neurons

Neuron

Axon

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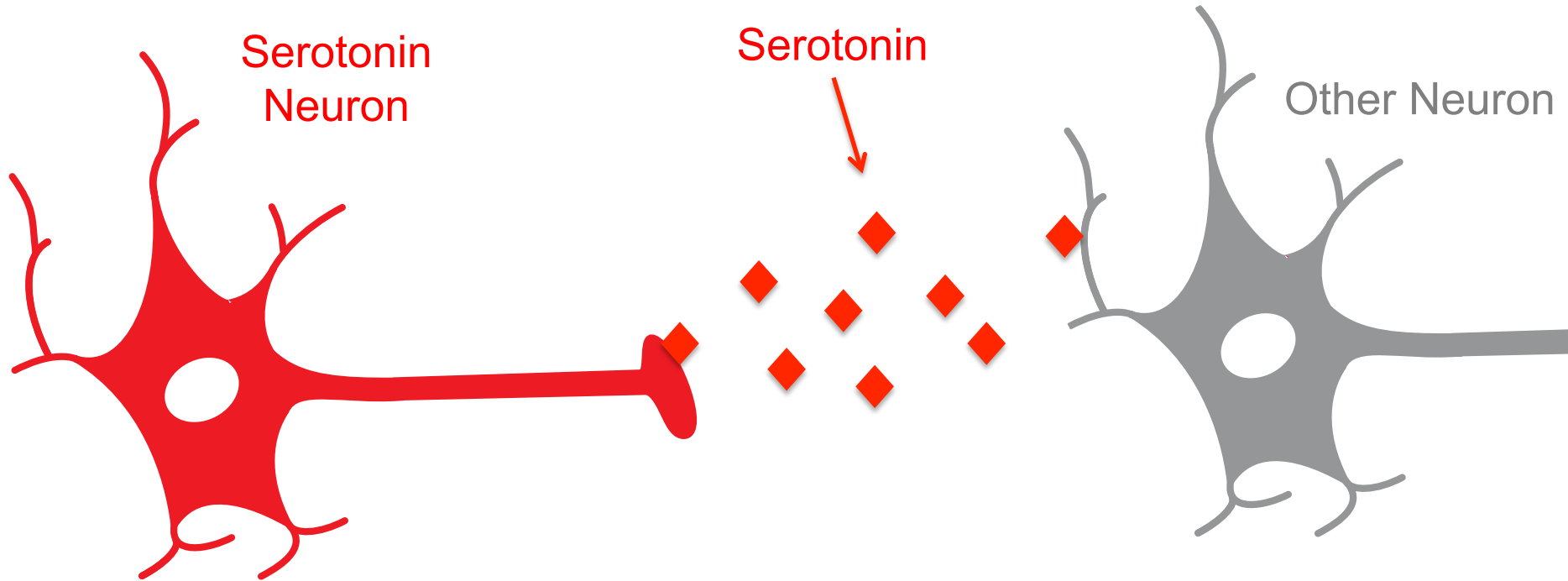science in the news

Neural circuits are composed of neurons that communicate using chemical signals called neurotransmitters

Neuron

**Neurotransmitter**

Other Neuron

Axon

Synapse

Circuit
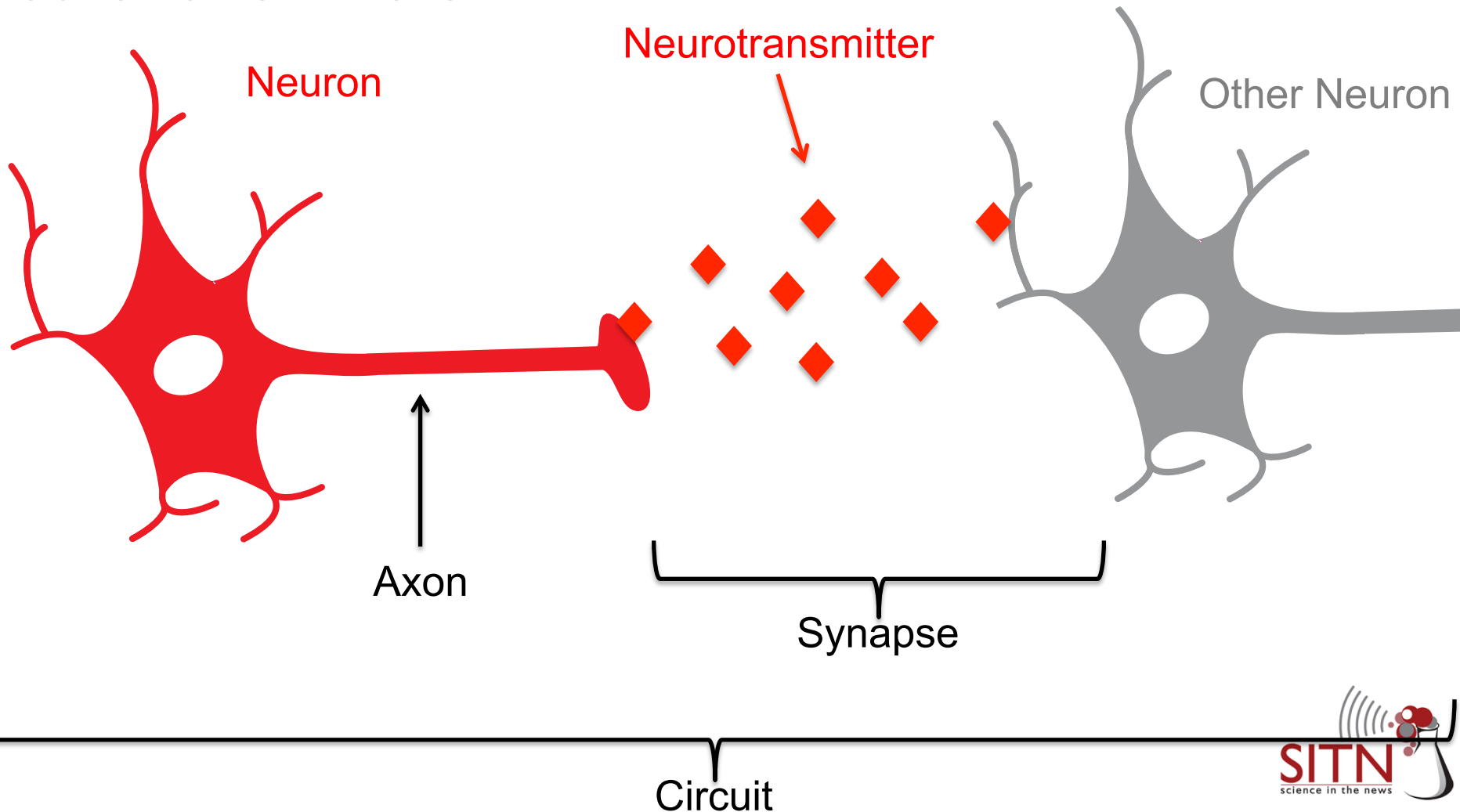
Antidepressants target the serotonin neurotransmitter system

Serotonin Neuron

Serotonin

Other Neuron

Normally, serotonin is taken back up by the cell that released it through the serotonin transporter

Serotonin
Transporter
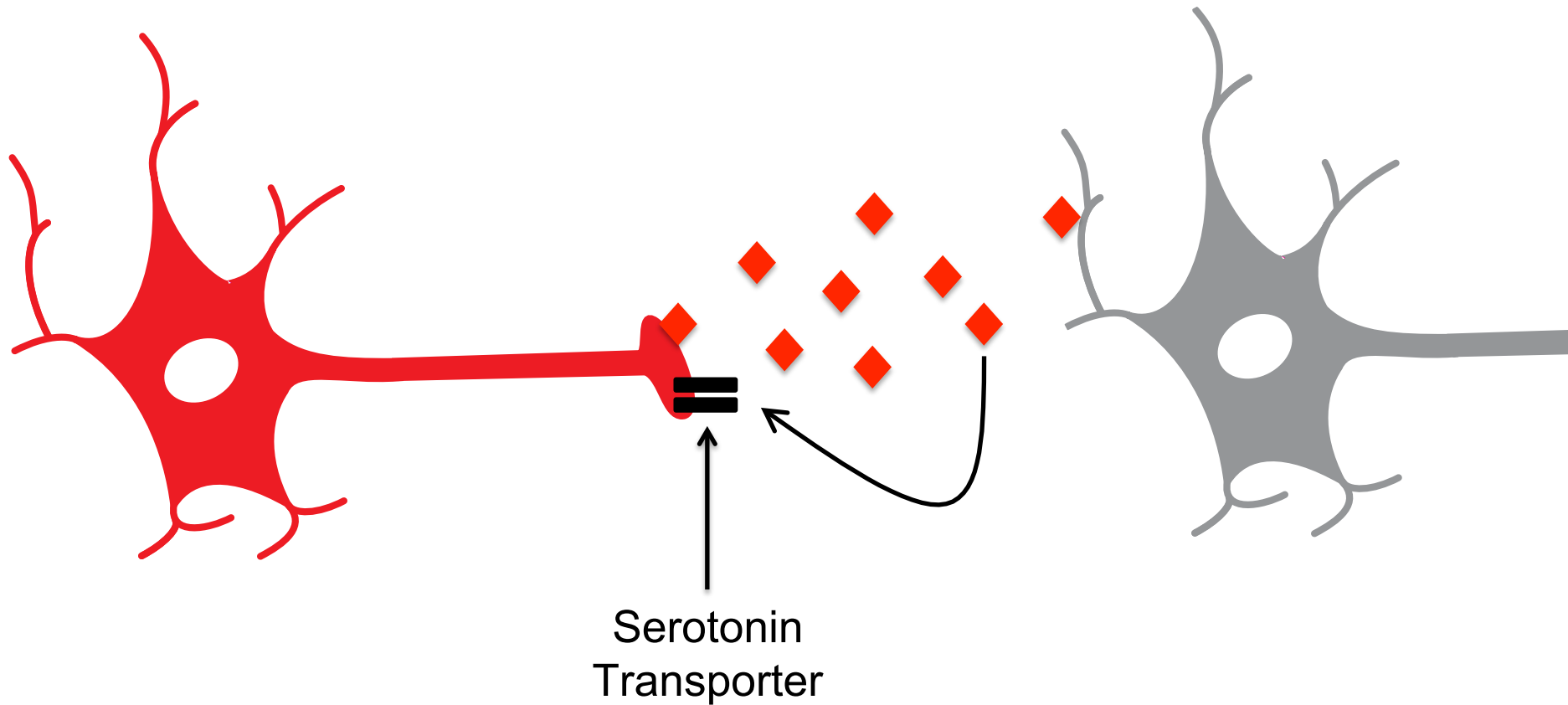
Antidepressants block reuptake of serotonin into cells and allow serotonin to continue interacting with other neurons

Antidepressant
Drug
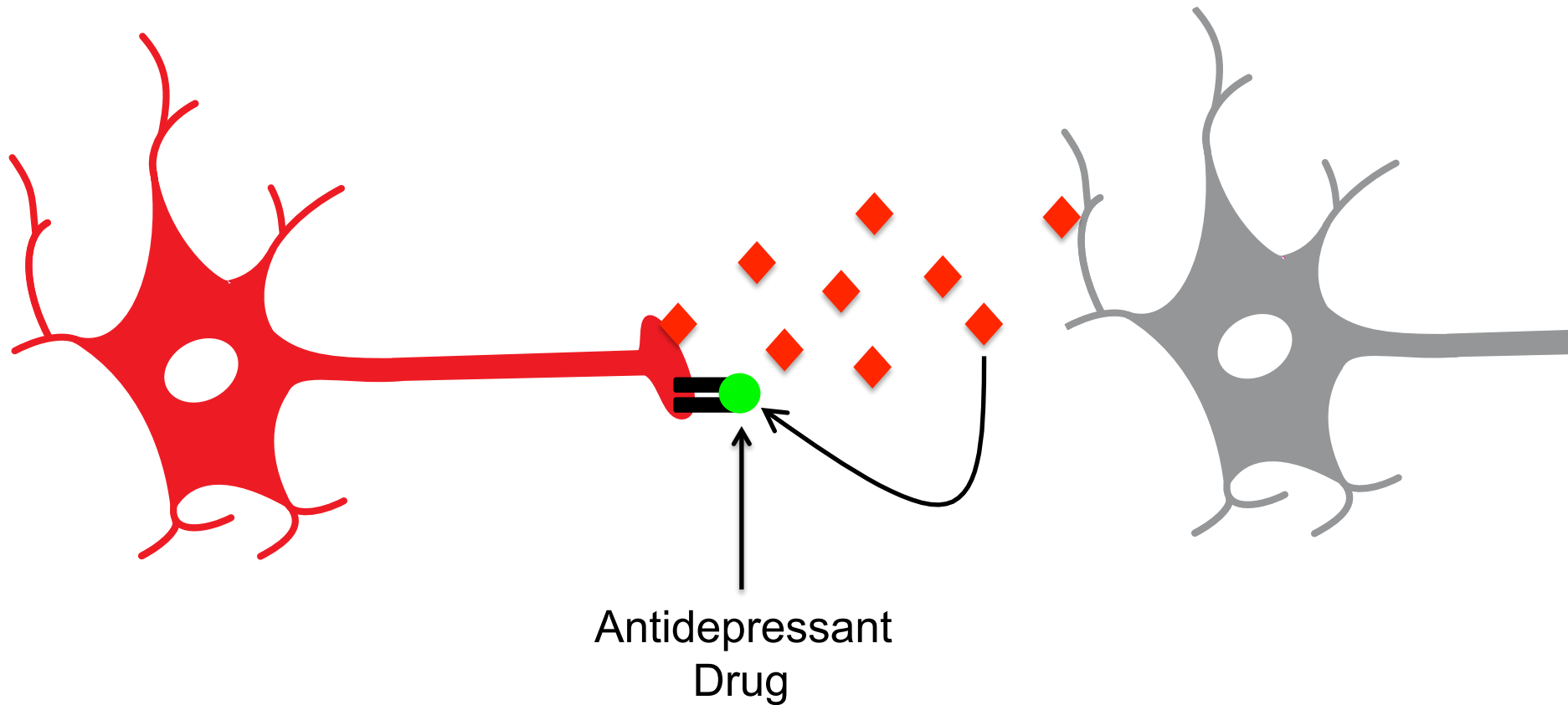
Antidepressant drugs increase serotonin levels outside the cell…
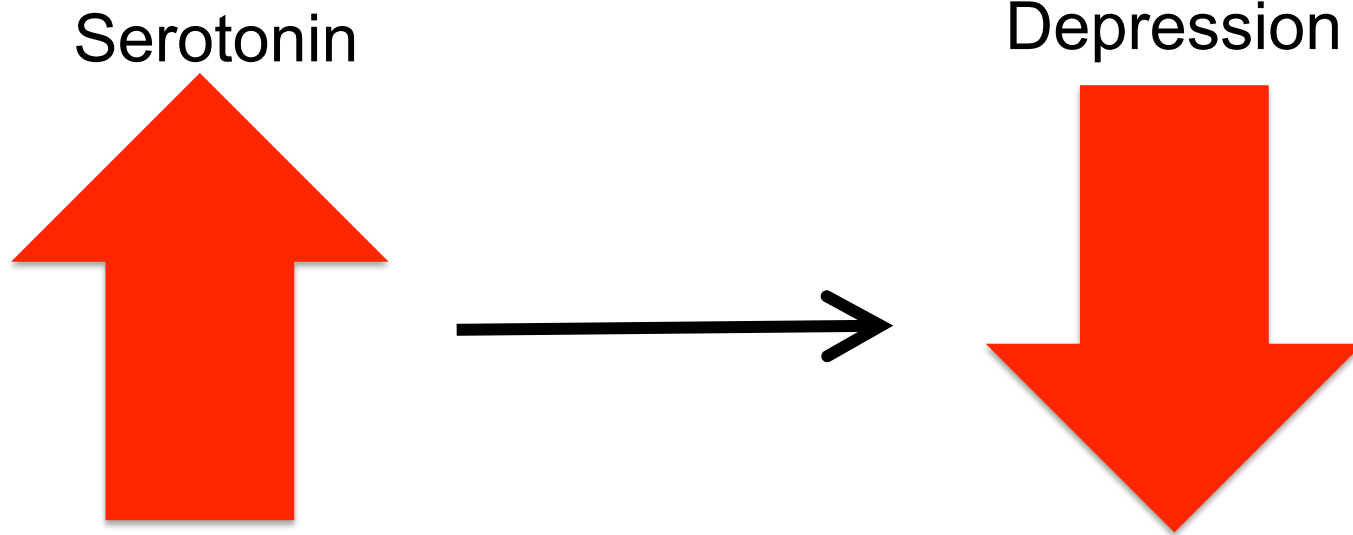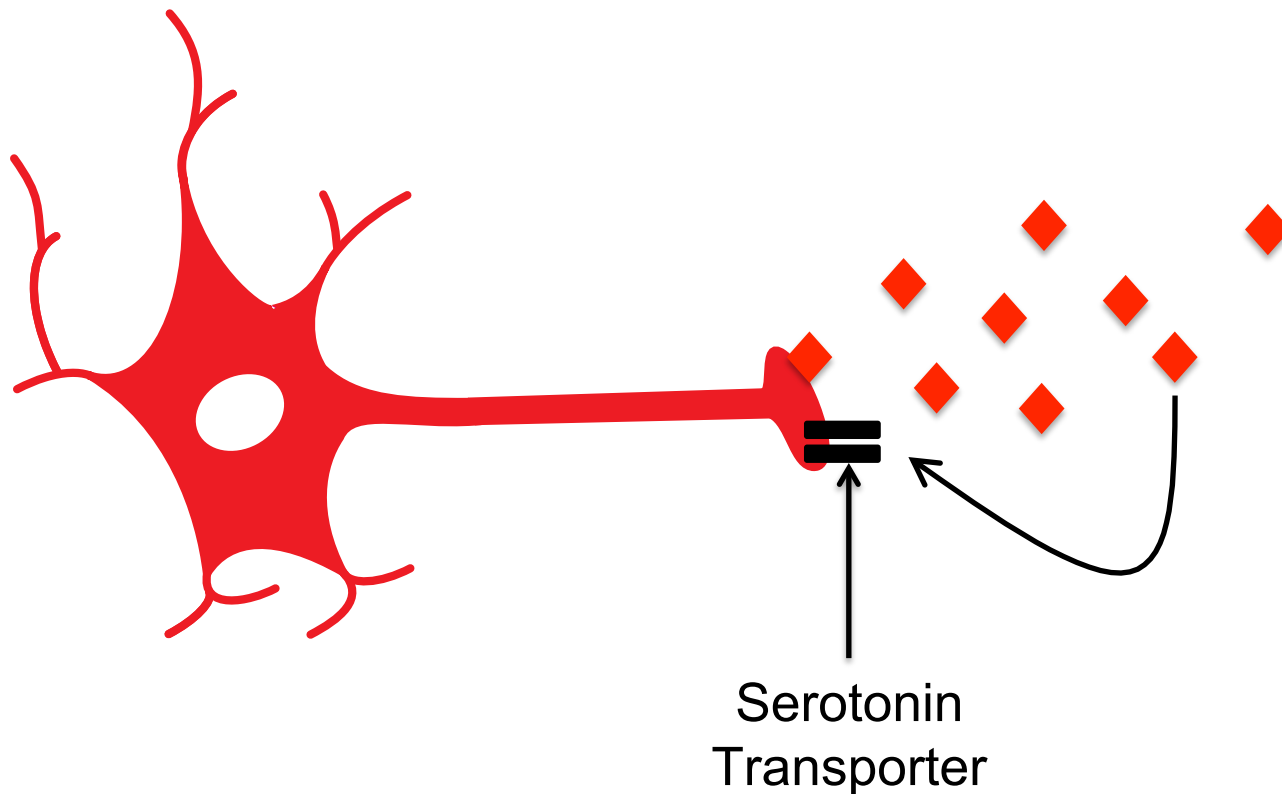
Depressed

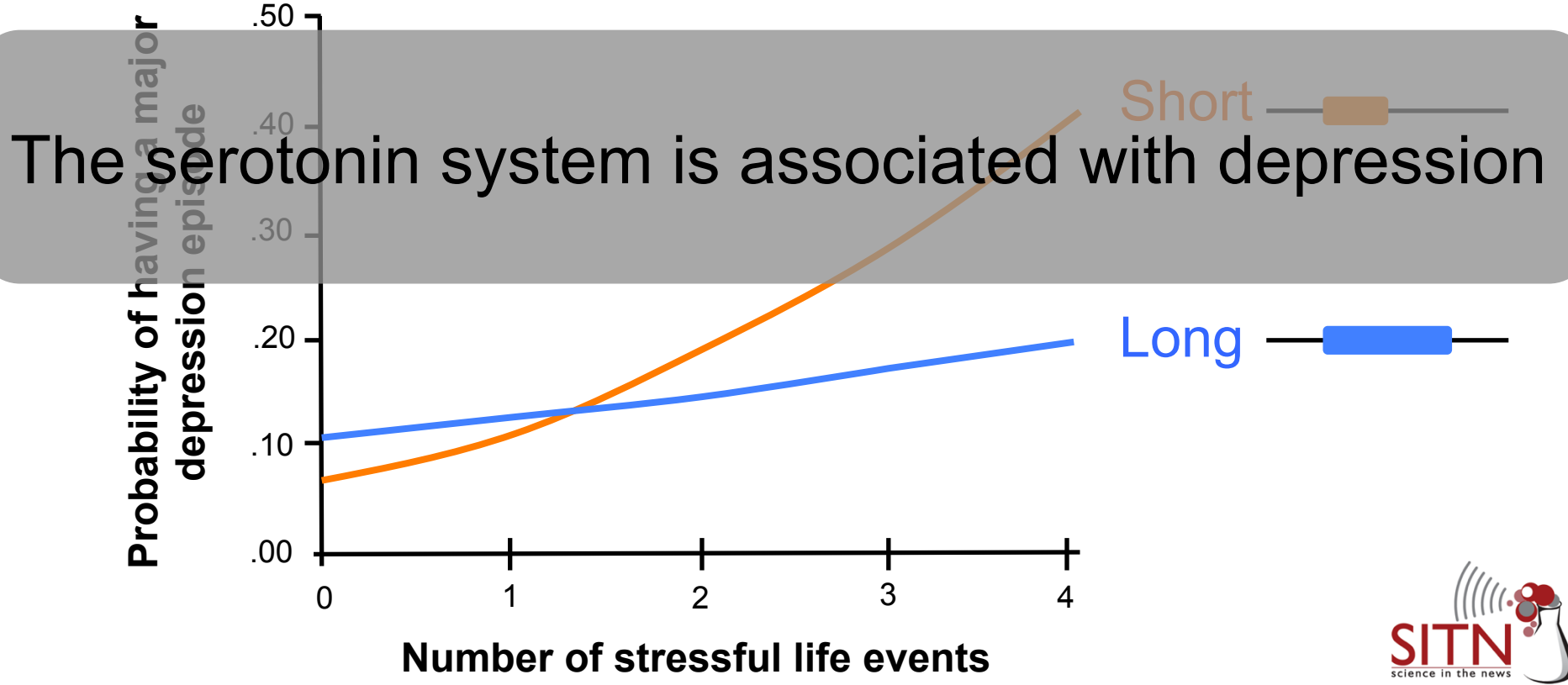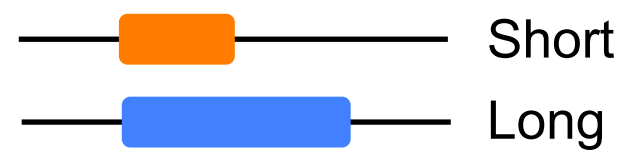Less Depressed

Antidepressant

… and decrease depressive symptoms

The serotonin hypothesis of depression

Serotonin

Depression

Gene associations suggest a link between serotonin and depression

Short

Long

Serotonin Transporter

Gene variants of serotonin transporter correlate with rates of depression in humans

Short

Long

The serotonin system is associated with depression

Probability of having a major depression episode

.50

.40

Short

.30

.20

Long

.10

.00

0   1   2   3   4
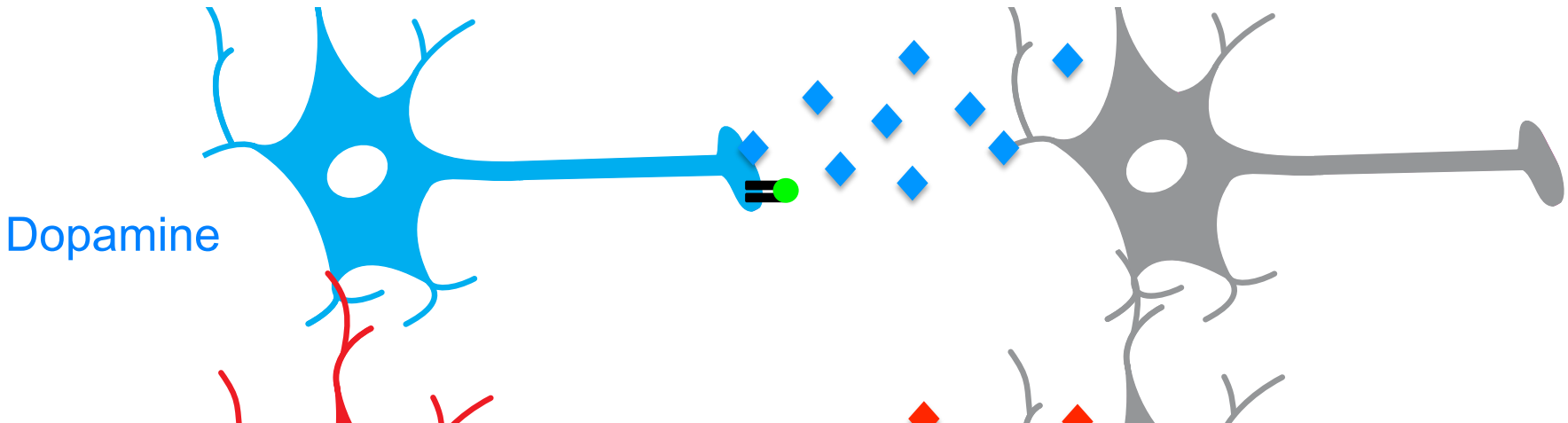
Number of stressful life events

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But… antidepressant efficacy is relatively low
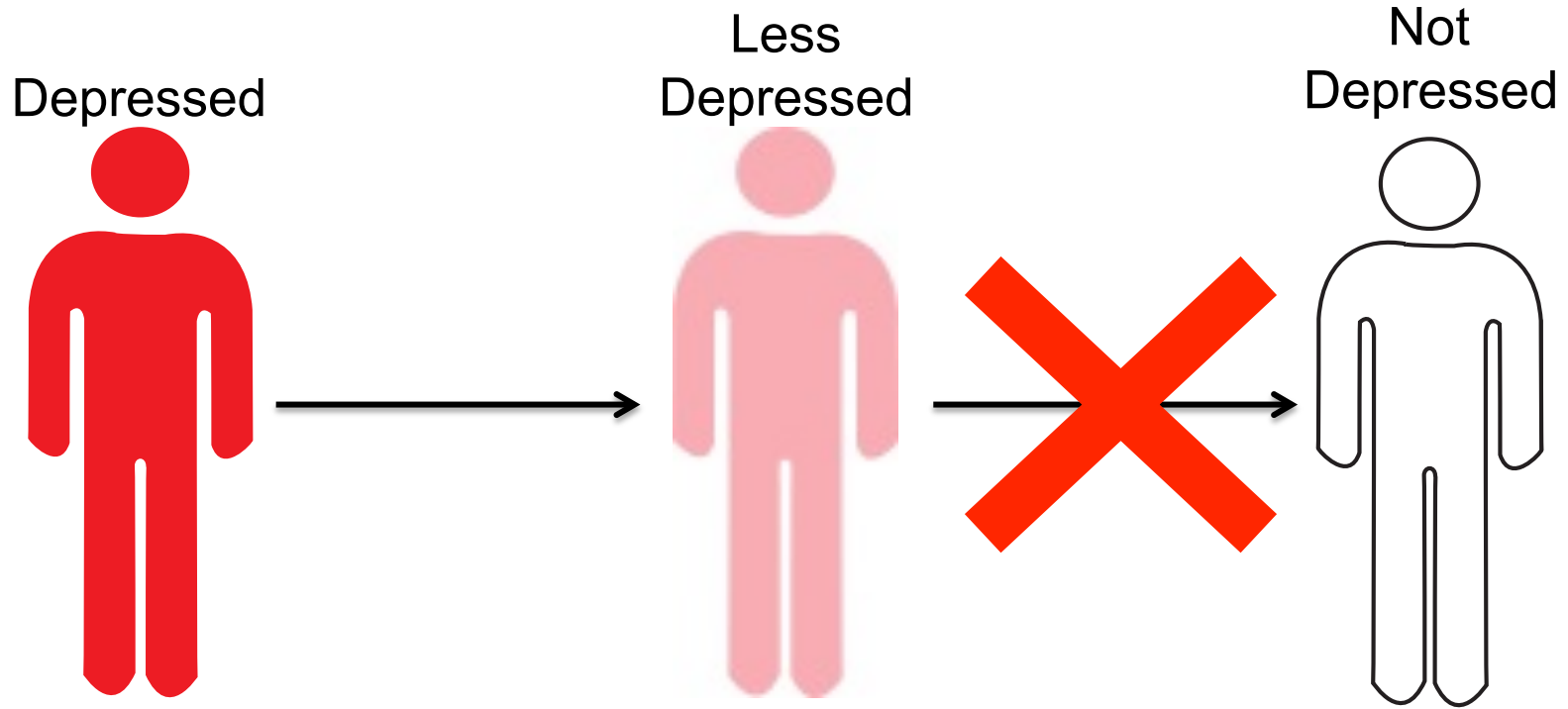
Serotonin can't be the whole picture

Novel therapeutics target multiple neural systems

Dopamine

Serotonin

Norepinephrine

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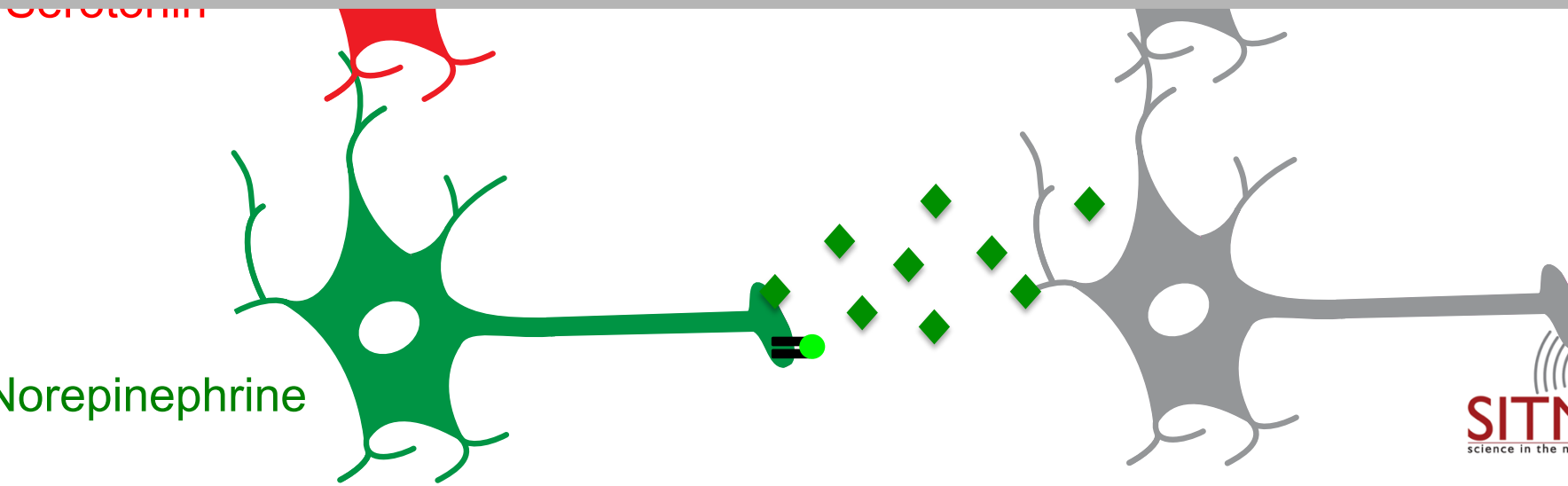
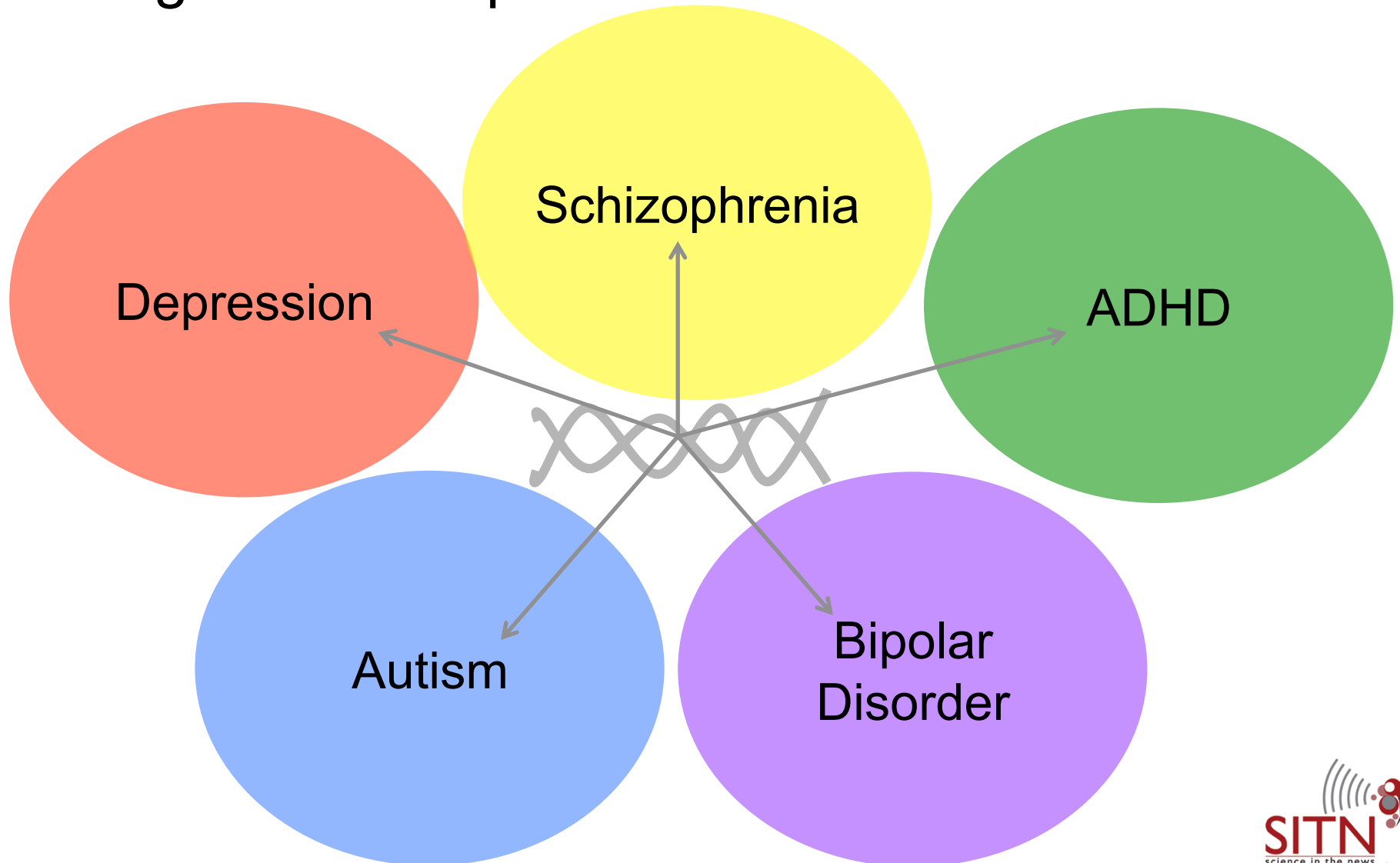# Questioning the definition of psychiatric disease

Depression

Schizophrenia

ADHD

Autism

Bipolar Disorder

How accurately do psychiatric diagnoses reflect the underlying biology?

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GWAS studies show that these psychiatric disorders share genetic components

The reality… shared symptoms and genetics

Perhaps a symptom-based system is not the best diagnostic approach….

Schizophrenia

Depression
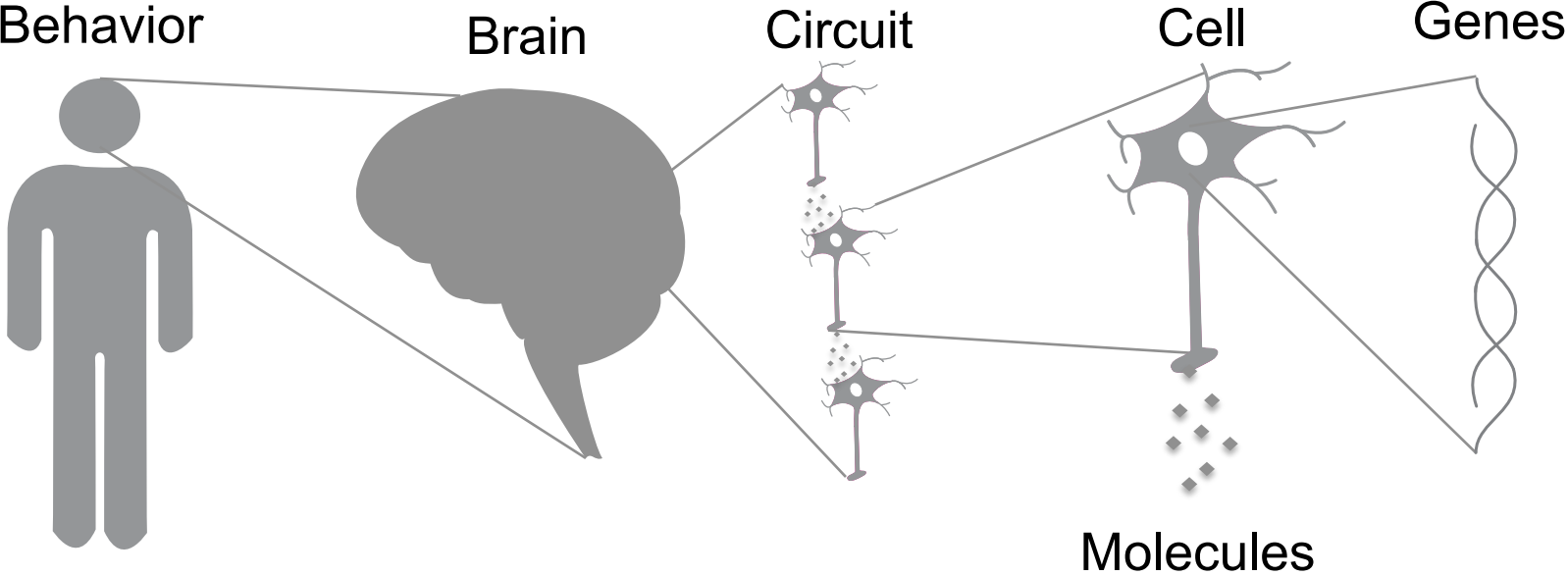
ADHD

Autism

Bipolar Disorder

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Toward a new biologically-based diagnostic approach: RDoC

Trait: Anxiety

Behavior   Brain   Circuit   Cell   Genes
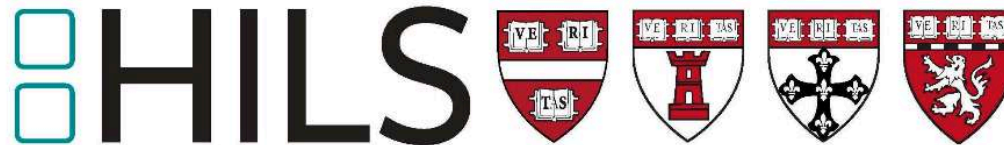
Molecules

Biological Complexity

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!

SITN would like to acknowledge the following organizations for their generous support of this event.

Questions?