

Scripps Research Alcohol Center Neuroscience Course Mood & Anxiety Disorders

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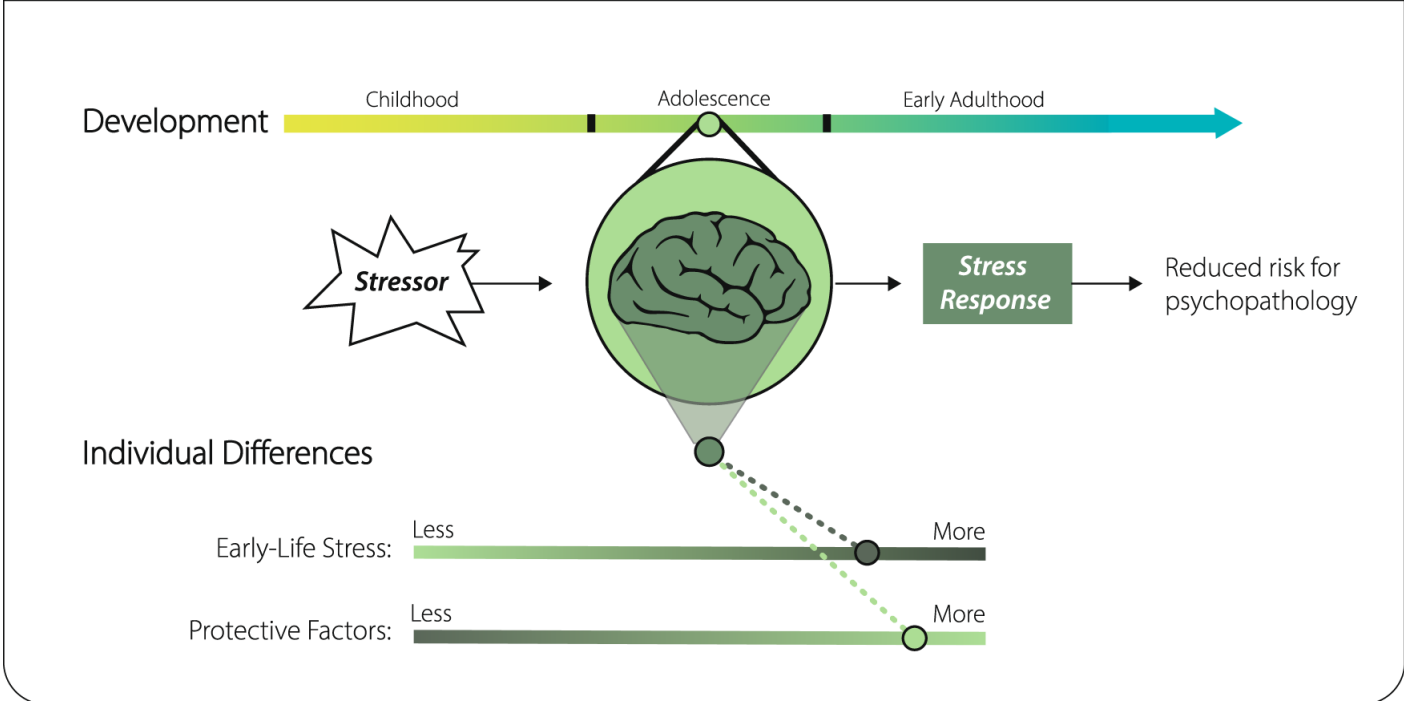
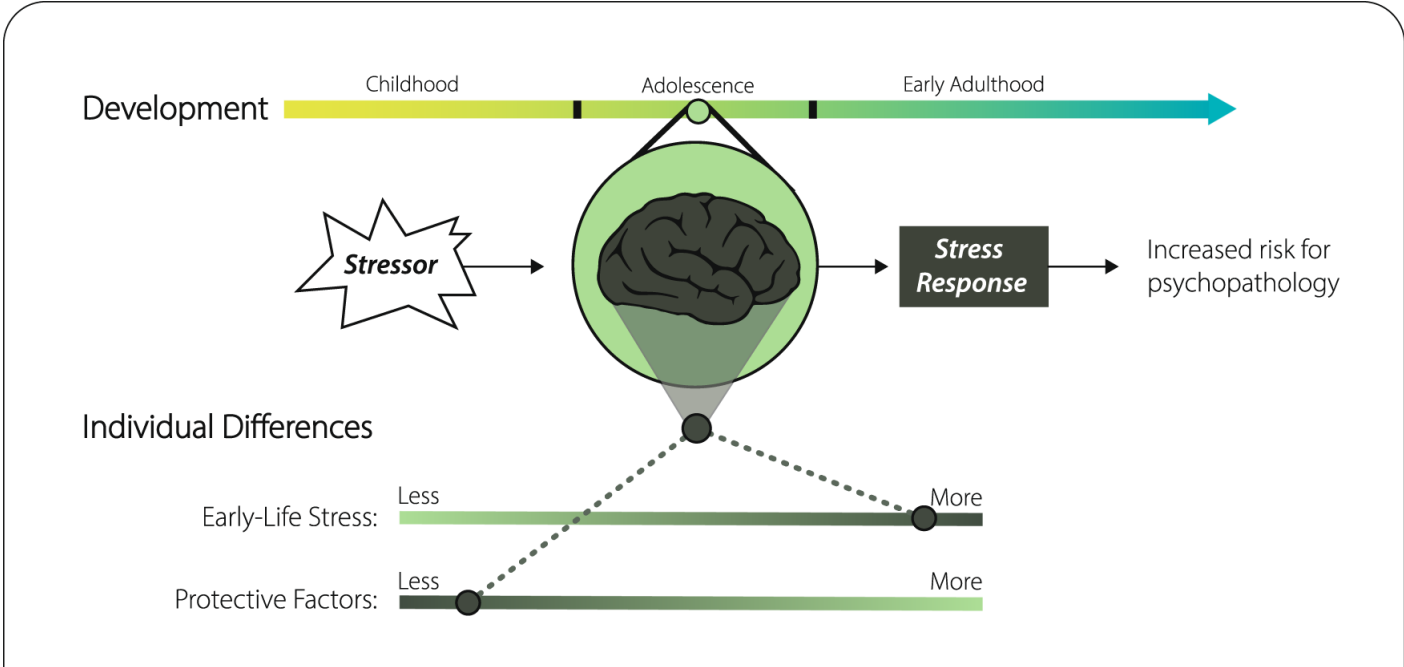
Interns

July 19, 2024

Adolescent Mental Health

- Globally, one in seven 10-19-year-olds experiences a mental disorder, accounting for 13% of the global burden of disease in this age group.
- Depression & anxiety are among the leading causes of illness and disability among adolescents.
- Suicide is the fourth leading cause of death among 15-29 year-olds.

Critical role for stress & our response to stress in mental health



<https://www.nature.com/articles/s41467-022-33416-4>

HOW CHRONIC

STRESS

AFFECTS YOUR

BRAIN



• <https://www.youtube.com/watch?v=WuyPuH9ojCE>

Mood disorders

- **Major depression.** A teen with this type has a depressed or irritable mood, along with other signs, for at least 2 weeks. He or she may also lose interest or pleasure in normal activities.
- **Persistent depressive disorder (dysthymia).** A teen with this type has a long-lasting, low-grade, depressed or irritable mood for at least 1 year.
- **Bipolar disorder.** This type causes a mix of manic episodes and depressed periods, or times of flat or dulled emotional response.
- **Disruptive mood dysregulation disorder.** A teen with this type has ongoing grouchiness. He or she has a hard time controlling behavior.
- **Premenstrual dysmorphic disorder.** This type causes depressive symptoms, grouchiness, and tension before a menstrual period.
- **Mood disorder caused by a health problem.** Many conditions can trigger symptoms of depression. These include cancer, injuries, infections, and chronic illnesses.
- **Substance-induced mood disorder.** These are depression symptoms from the effects of medicine or other forms of treatment, drug abuse, or exposure to toxins.

Symptoms of teen depression

- appearing sad, irritable, or tearful
- changes in appetite or weight
- a decreased interest in activities once seen as pleasurable
- regular complaints of boredom
- a decrease in energy
- difficulty concentrating
- feelings of guilt, worthlessness, or helplessness
- alcohol or drug misuse
- major changes in sleeping habits
- talking about or thinking of suicide
- withdrawal from friends or after-school activities
- worsening school performance

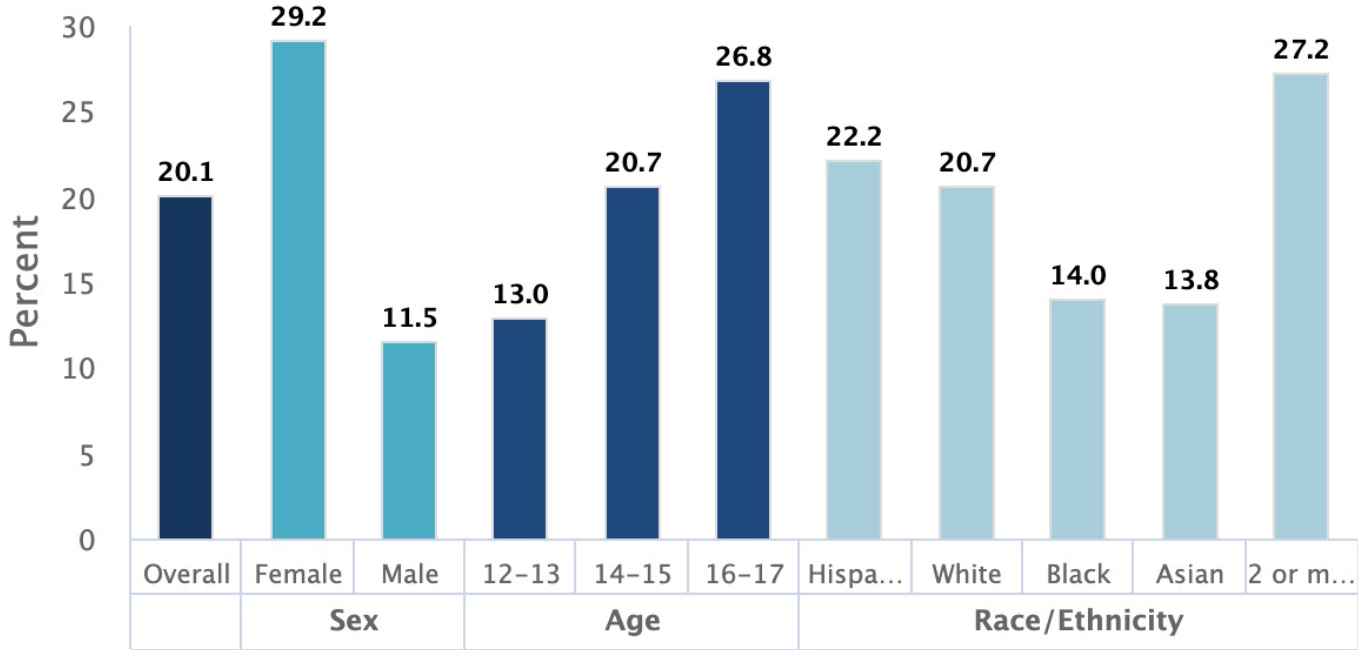
Symptoms that are present most of the day, nearly every day, for at least two weeks



Depression

Past Year Prevalence of Major Depressive Episode Among U.S. Adolescents (2021)

Data Courtesy of SAMHSA



Teen Depression: More than just moodiness



Being a teenager can be tough, but it shouldn't feel hopeless. If you have been feeling sad most of the time for a few weeks or longer and you're not able to concentrate or do the things you used to enjoy, talk to a trusted adult about depression.

Do I have depression?

- Do you often feel sad, anxious, worthless, or even "empty"?
- Have you lost interest in activities you used to enjoy?
- Do you get easily frustrated, irritable, or angry?
- Do you find yourself withdrawing from friends and family?
- Are your grades dropping?
- Have your eating or sleeping habits changed?
- Have you experienced any fatigue or memory loss?
- Have you thought about suicide or harming yourself?

Depression looks different for everyone. You might have many of the symptoms listed above or just a few.

How do I get help for depression?

- Talk to a trusted adult** (such as your parent or guardian, teacher, or school counselor) about how you've been feeling.
- Ask your doctor** about options for professional help. Depression can be treated with psychotherapy (also called "talk therapy"), medication, or a combination of medication and talk therapy.
- Try to spend time with friends or family**, even if you don't feel like you want to.
- Stay active and exercise**, even if it's just going for a walk. Physical activity releases chemicals, such as endorphins, in your brain that can help you feel better.
- Try to keep a regular sleep schedule.**
- Eat healthy foods.**

You're not alone, and help is available. You can feel better. To get help, call or text the 988 Suicide & Crisis Lifeline at 988 or chat at 988lifeline.org.

Bipolar Disorder in Teens and Young Adults: Know the Signs

Bipolar disorder is a mental illness that causes unusual and extreme shifts in mood, marked by episodes of mania and depression. During these episodes, symptoms last for days or weeks at a time.



Common signs & symptoms of mania

- Showing intense happiness or silliness
- Having a very short temper or seeming extremely irritable
- Talking very fast or having racing thoughts
- Having an inflated sense of ability, knowledge, and power
- Doing reckless things that show poor judgment



Common signs & symptoms of depression

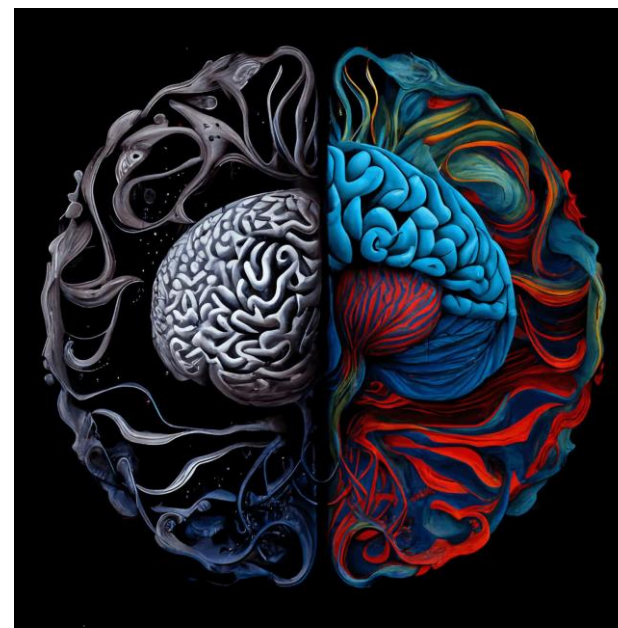
- Feeling very sad or hopeless
- Feeling lonely or isolating from others
- Eating too much or too little
- Having little energy and no interest in usual activities
- Sleeping too much

If you or someone you know is struggling or having thoughts of suicide, help is available.

For crisis counseling and support,
call or text **988**

(988 Suicide & Crisis Lifeline).

In life-threatening situations,
call **911**.



Bipolar Disorder

- According to the National Institute of Mental Health (NIMH), an estimated 2.9% of adolescents ages 13 to 18 years old will be diagnosed with bipolar disorder in their lifetime.
- It can be challenging to accurately diagnose bipolar disorder in teens.
- Symptoms can seem like typical teenage behavior, though more extreme in some cases.
- Symptoms may also overlap with other conditions such as attention deficit hyperactivity disorder (ADHD), anxiety, and depression.

How do we treat depression in teens?

- First-line of treatment in adolescents is Psychotherapy
- Only antidepressants approved, Fluoxetine (Prozac) and Escitalopram (Lexapro)
 - Although uncommon, children and teens may have an increase in suicidal thoughts and behavior
- A combination of both psychotherapy and antidepressants may be the most effective approach.
- In some teens, depression is so severe that a hospital stay is needed, especially if there is danger of harm to self and others.

Anxiety Disorders

- **Generalized anxiety disorder:** persistent and excessive worry about daily activities or events
- **Panic disorder:** panic attacks and fear of continued panic attacks
- **Social anxiety disorder:** high levels of fear and worry about social situations that might make the person feel humiliated, embarrassed or rejected
- **Agoraphobia:** excessive fear, worry and avoidance of situations that might cause a person to panic or feel trapped, helpless or embarrassed
- **Separation anxiety disorder:** excessive fear or worry about being separated from people with whom the person has a deep emotional bond
- **Specific phobias:** intense, irrational fears of specific objects or situations that lead to avoidance behavior and significant distress
- **Selective mutism:** consistent inability to speak in certain social situations, despite the ability to speak comfortably in other settings, primarily affecting children

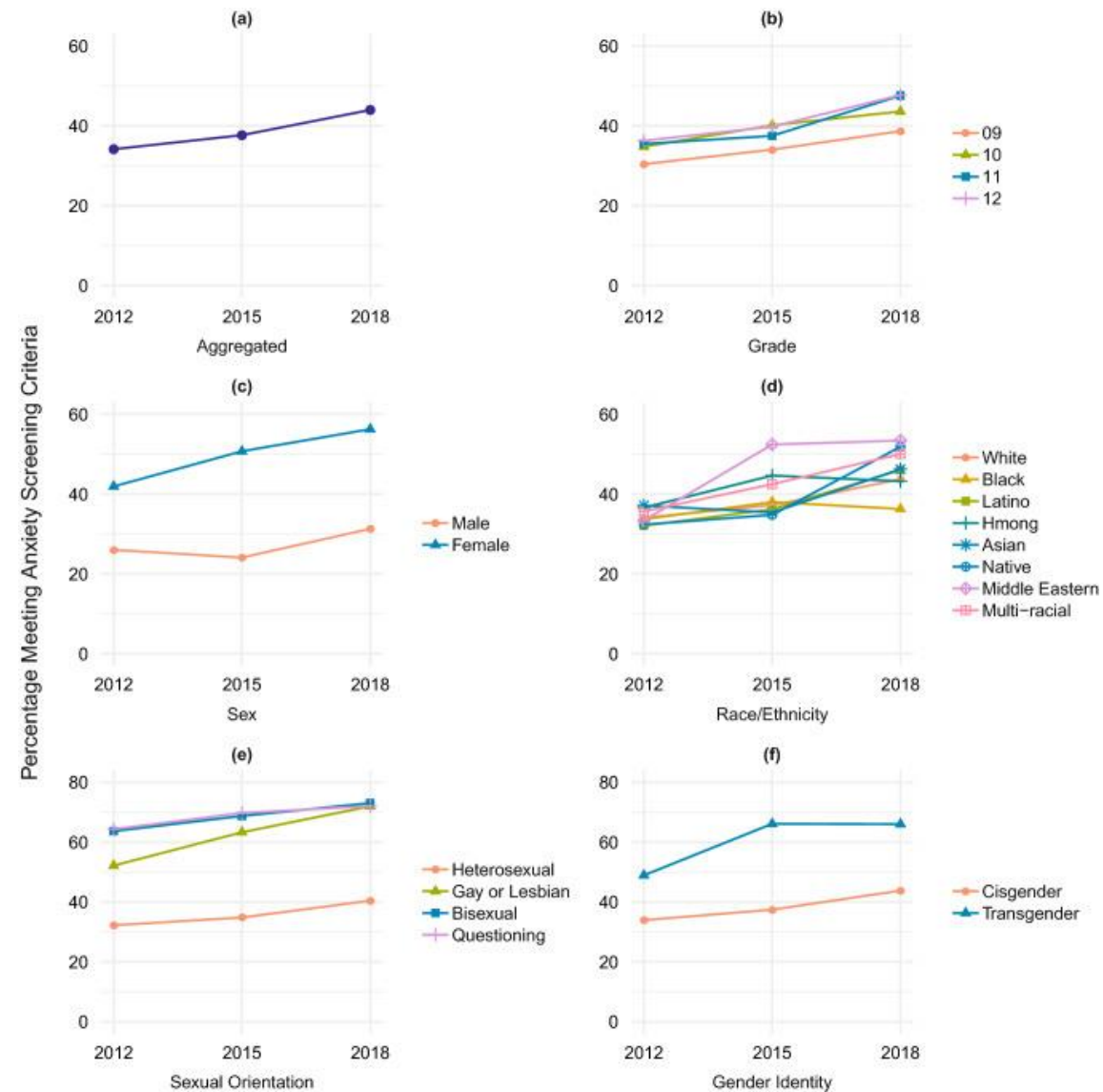
Generalized Anxiety (Symptoms)

- feeling constantly agitated, tense, or restless
- being sensitive to criticism or extremely self-conscious
- always worrying about things that aren't likely to happen
- avoiding difficult or new situations that make them anxious
- being withdrawn
- having trouble concentrating and starting or finishing schoolwork
- having trouble sleeping
- changed eating habits
- They may also have physical symptoms such as:
 - a racing heart
 - feeling dizzy
 - sweating
 - shaking
 - shortness of breath
 - feeling 'butterflies' in their stomach
 - headaches
 - having aches (especially in their neck, shoulders and back)

*Symptoms
occurring more
days than not in
past 6 months*



Anxiety Disorders



'M SO STRESSED OUT!

Is it stress or anxiety?

Ways to Cope

- Keep a journal.
- Download an app with relaxation exercises.
- Exercise and eat healthy.
- Get regular sleep.
- Avoid excess caffeine.
- Identify and challenge your negative thoughts.
- Reach out to your friends or family.

Find Help

If you are struggling to cope, or the symptoms of your stress or anxiety begin to interfere with your everyday life, it may be time to talk to a professional. Find more information about getting help on the National Institute of Mental Health website at www.nimh.nih.gov/findhelp.



nimh.nih.gov/stressand anxiety

NIMH Identifier No. OM 20-4319

How do we treat anxiety disorders in teens?

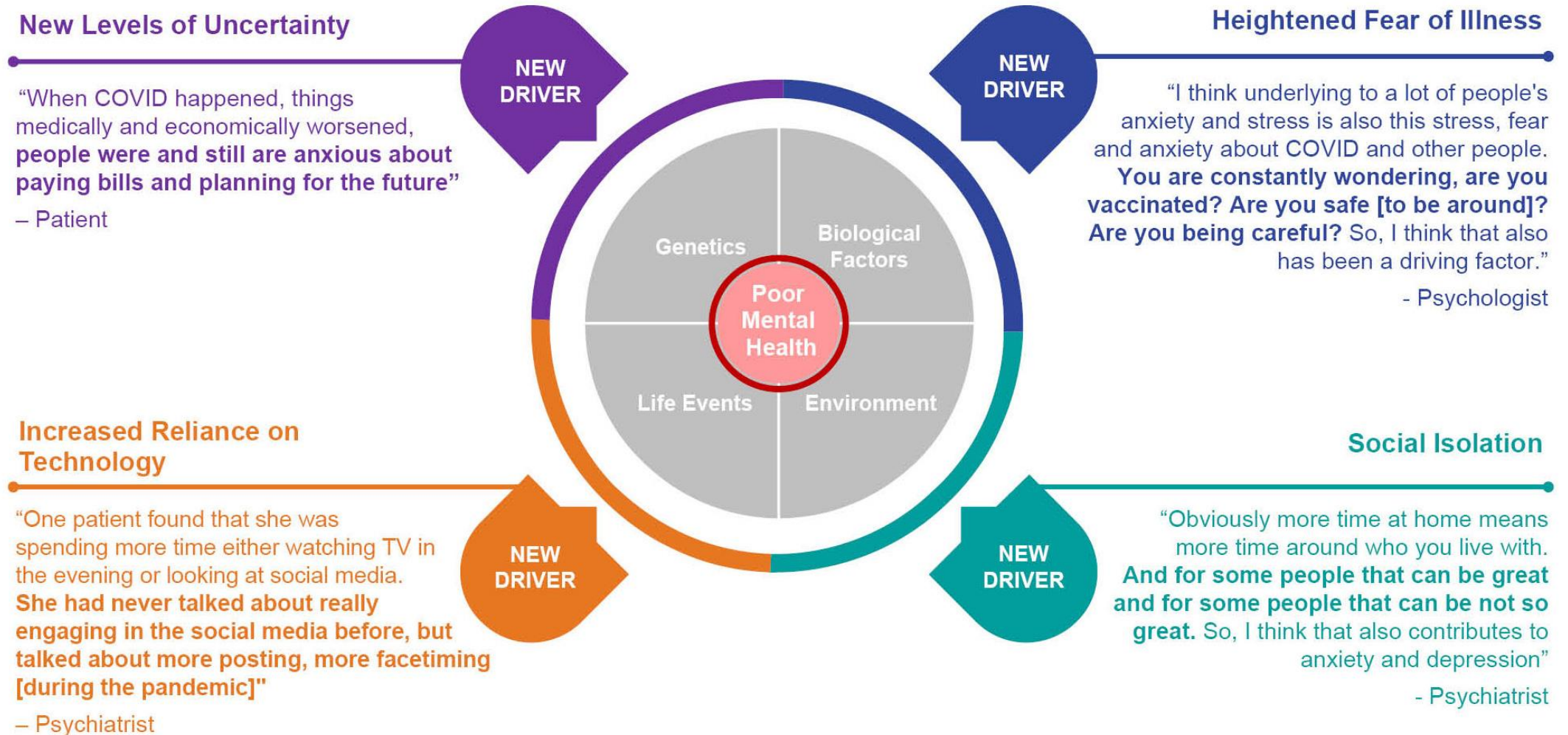
- Psychological therapy, such as: family therapy or cognitive behavioral therapy (CBT). These are specially adapted for teenagers. These can be face-to-face or online.
- Rarely, medicines may be recommended to help treat anxiety in teenagers. Special care is needed in teenagers starting medication. They will be closely monitored by an experienced mental health clinician if they need medicines.



Causes of mood & anxiety disorders

- **Genetics:** Teenagers with a family history of mood or anxiety disorders may be at higher risk of developing them.
- **Trauma:** Teenagers with a history of trauma — such as sexual abuse, violence, or involvement in an accident — may be more likely to experience anxiety and depression.
- **Environment:** A teenager's social, school, and home environments can have an impact on their mental health. Difficulties such as abuse and neglect, divorce in the family, being bullied, poverty, learning disabilities, and struggling to fit in may all contribute to depression and anxiety.
- **Differences in the brain:** Changes in teenagers' brain circuits that are involved in responses to danger and rewards can **increase stress levels**. Teenagers with depression and anxiety may also have different levels of neurotransmitters — such as dopamine, serotonin, and norepinephrine— in their brains. These affect the regulation of moods and behavior.
- **Substance misuse:** Drug and alcohol misuse may affect teenagers' moods and lead to depression & anxiety. They may turn to these substances to self-medicate their emotions.
- **Stresses of puberty:** Teenagers who are experiencing puberty may go through hormonal changes that affect their mood and deal with the stresses of a changing body, which can make them feel different than their peers.
- **Negative thought patterns:** Depression and anxiety in teenagers may be linked to negative thought patterns. If teenagers have regular exposure to negative thinking — often from their parents — they may also develop a negative worldview.

Pandemic as the tipping point?

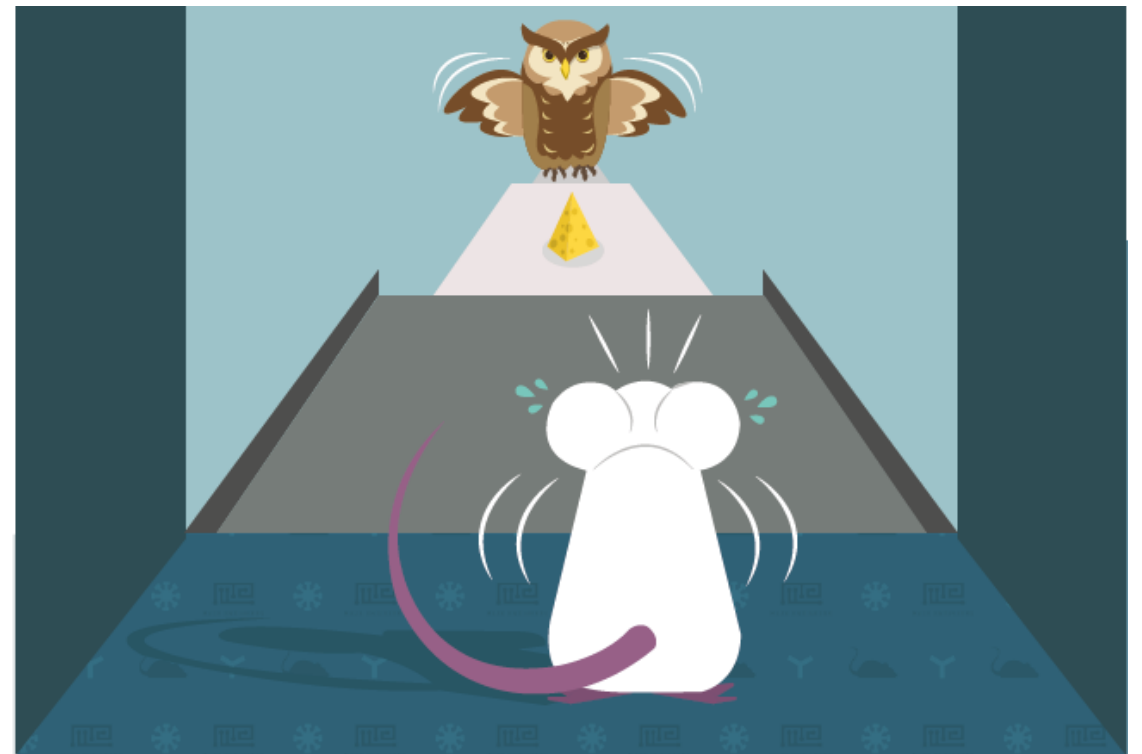




<https://www.youtube.com/watch?v=wr4N-SdekqY&t=3s>

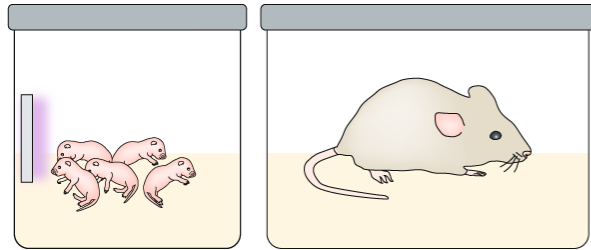
Using animal models to study mood & anxiety disorders

- Rodents are like humans in anatomy, physiology, and genetics
- Display behaviors that resemble those of humans with mood & anxiety disorders
 - Decreased sociability
 - Increased despair-like behavior
 - Sleep disturbances
 - Loss of interest in palatable foods
 - Increased anxiety-like behavior



Rodent models of depression (producing a depressive-like state)

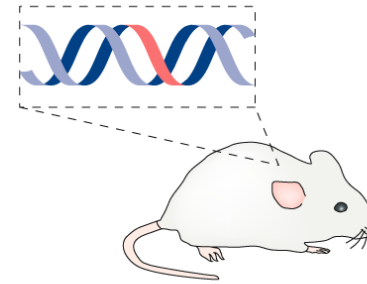
a Early life stressors



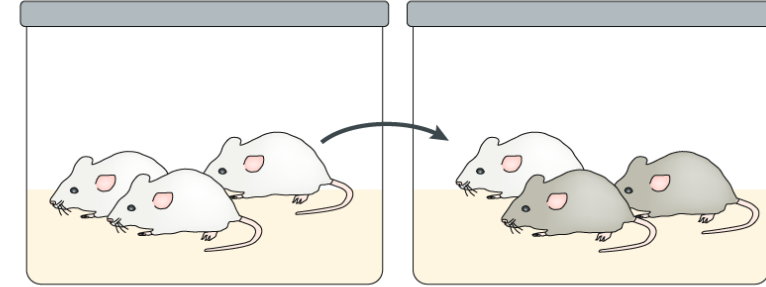
b Learned helplessness



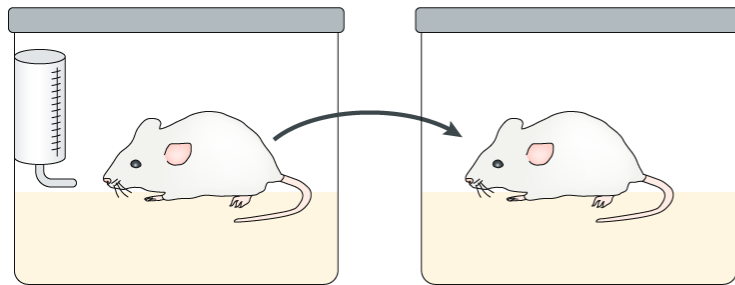
e Genetic modification



f Social instability



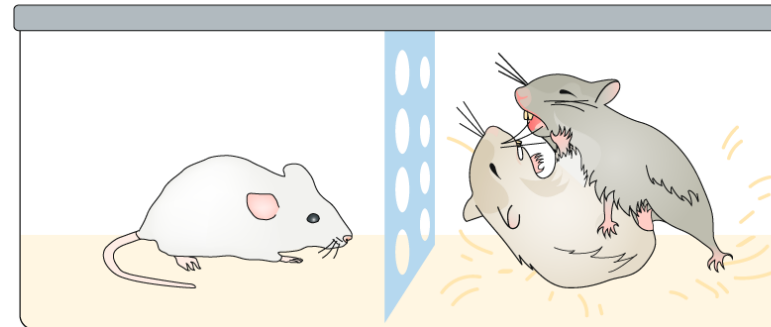
c Drug withdrawal



d Corticosterone manipulation or immune activation



g Social transmission of stress

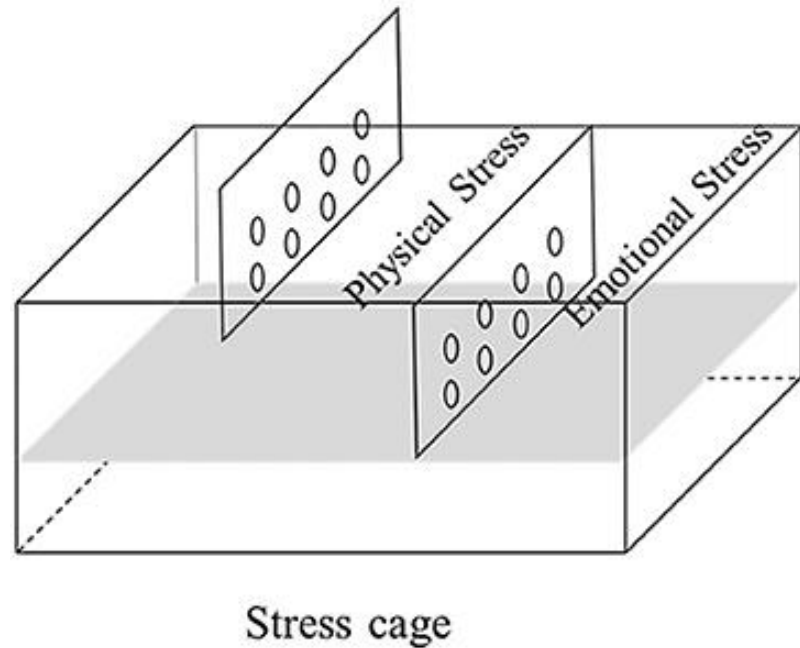


h Social defeat stress



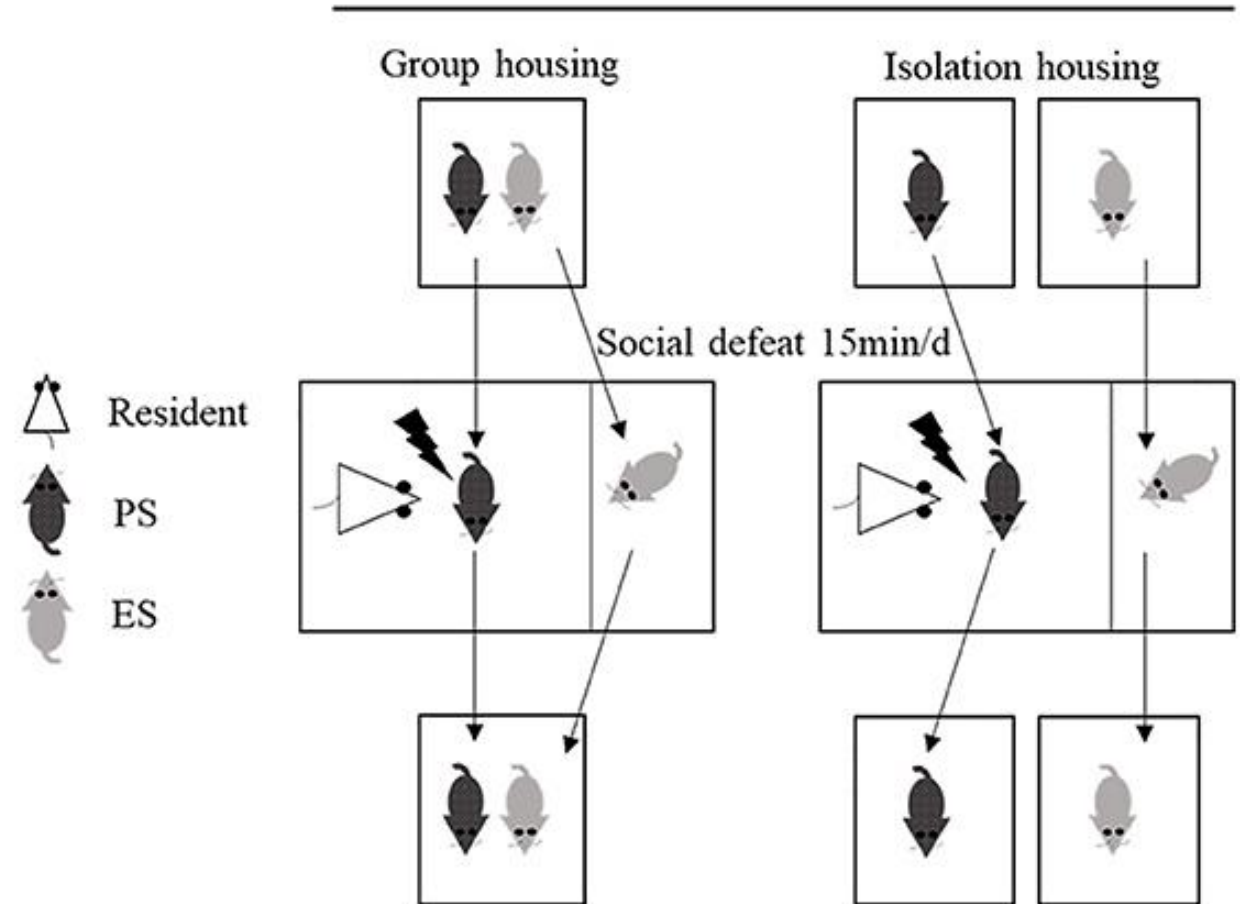
Example rodent model of anxiety disorders (producing an anxiety-like state)

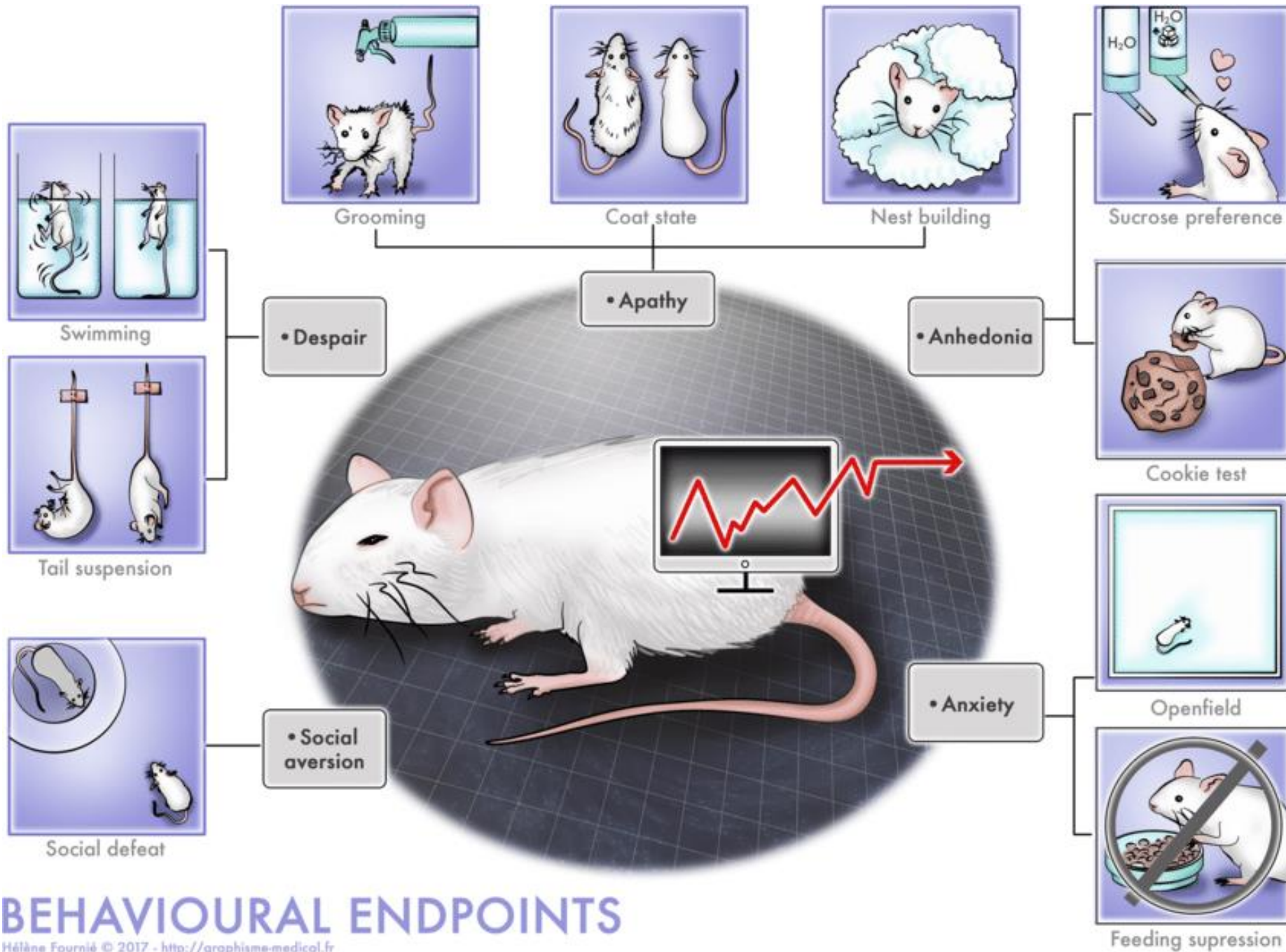
A



B

Physical and Emotional Stress





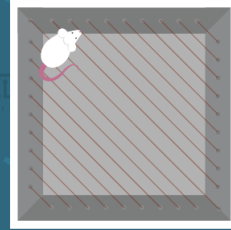
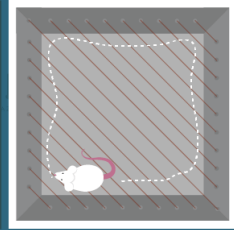
Measuring depressive-like behaviors

Planchez, Barbara & Surget, Alexandre & Belzung, Catherine. (2019). Animal models of major depression: drawbacks and challenges. *Journal of Neural Transmission*. 126. 10.1007/s00702-019-02084-y.

Measuring anxiety-like behaviors

Open Field

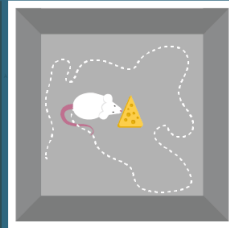
The arena is divided into two zones: the center and the perimeter. A more anxious mouse spends more time in the periphery.



Mice do not typically like to spend time in open spaces. They naturally exhibit a behavior known as thigmotaxis, which means they like touching something (i.e. the walls of the box) as they move.

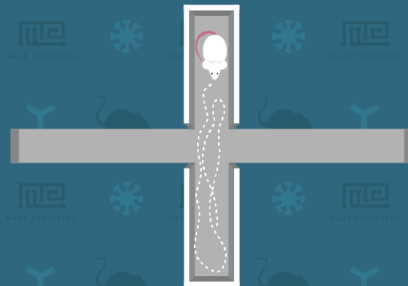
Novelty Suppressed Feeding

More anxious mice will take longer to approach and eat the food reward.

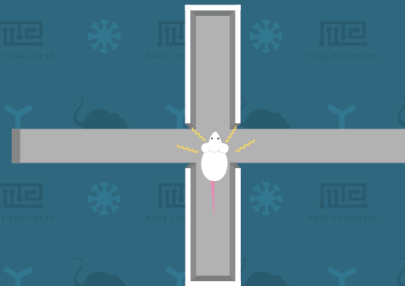


Mice prefer to explore areas or objects that they are familiar with. They are generally hesitant to venture into novel territory.

Elevated Plus Maze



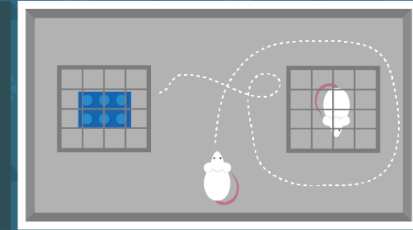
Anxiety is measured in this assay by comparing the amount of time spent in the closed arms to the amount of time spent in the open arms. More anxious mice will spend a greater proportion of time in the closed arms.



Not only do mice prefer to feel like they are in a small, enclosed space when they explore, but they also find the elevated open arms aversive.

Social Approach

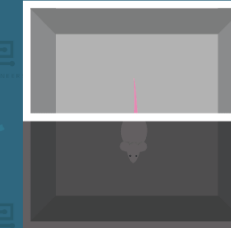
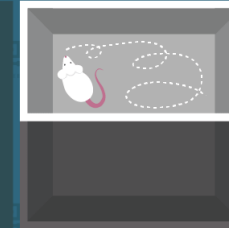
The proportion of time spent exploring the object is compared to the proportion of time spent investigating the stranger mouse. More socially anxious mice will spend more time with the object.



Mice should generally be inclined to spend more time with the mouse than the object. If that exploration ratio shifts towards the object, the mouse may find other mice aversive for some reason.

Light-Dark Box

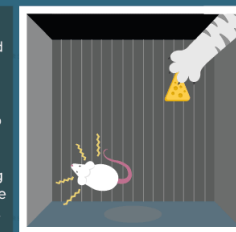
Less anxious mice will spend a greater proportion of time exploring the light area.



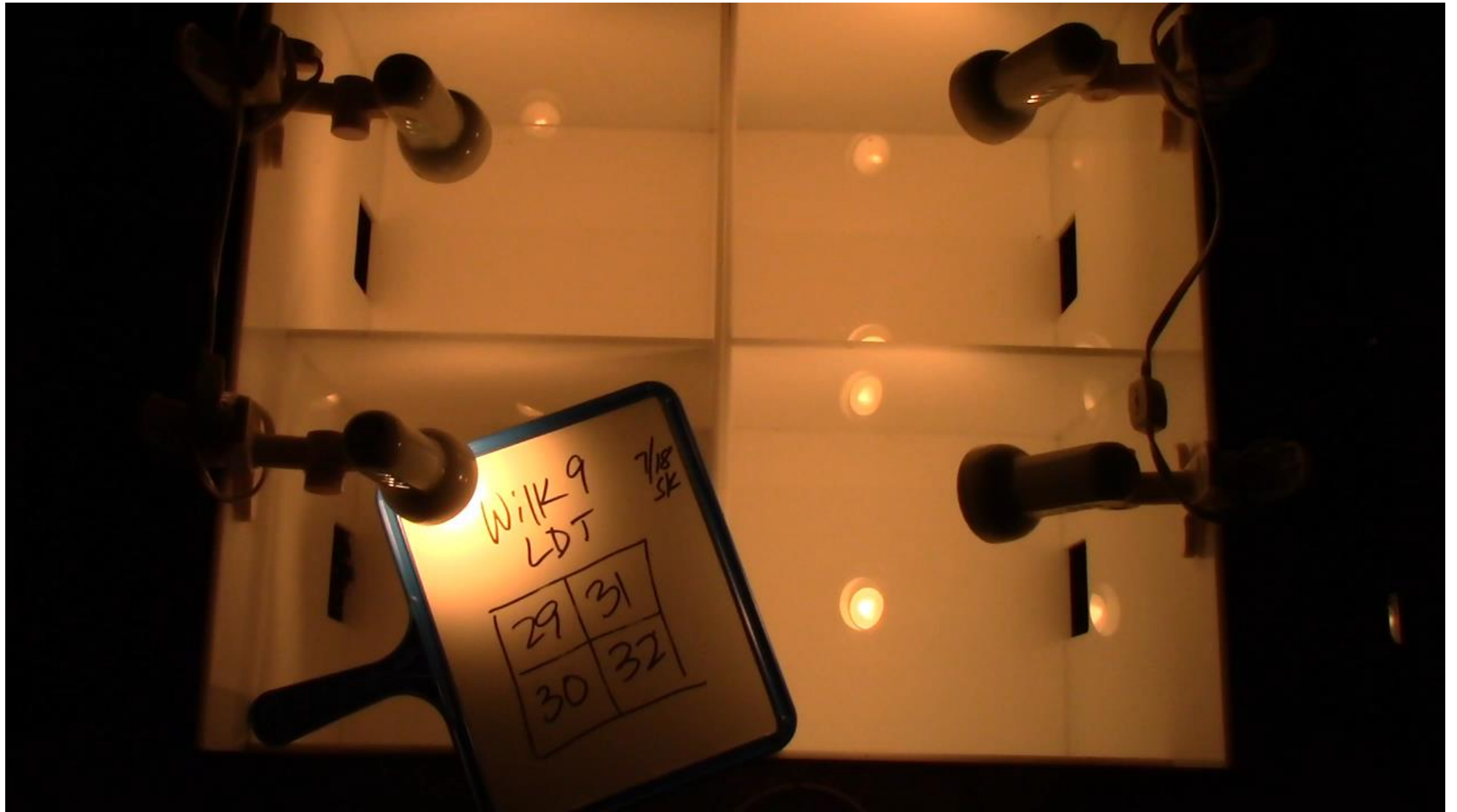
Mice find brightly lit, open areas aversive and dark, enclosed spaces more comfortable.

Fear Conditioning

More anxious mice may exhibit increased freezing behavior in response to the conditioned stimulus or may take longer to perform a trained action or retrieve a food reward following the presentation of the conditioned stimulus.



This assay is derived from classical conditioning.



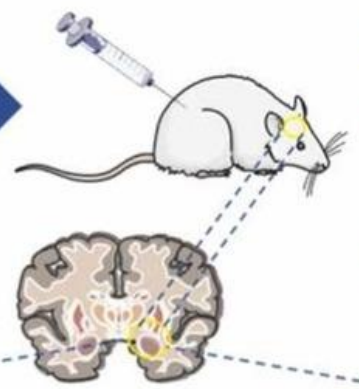
Adolescent depression
2-8%

Incidence
2/3

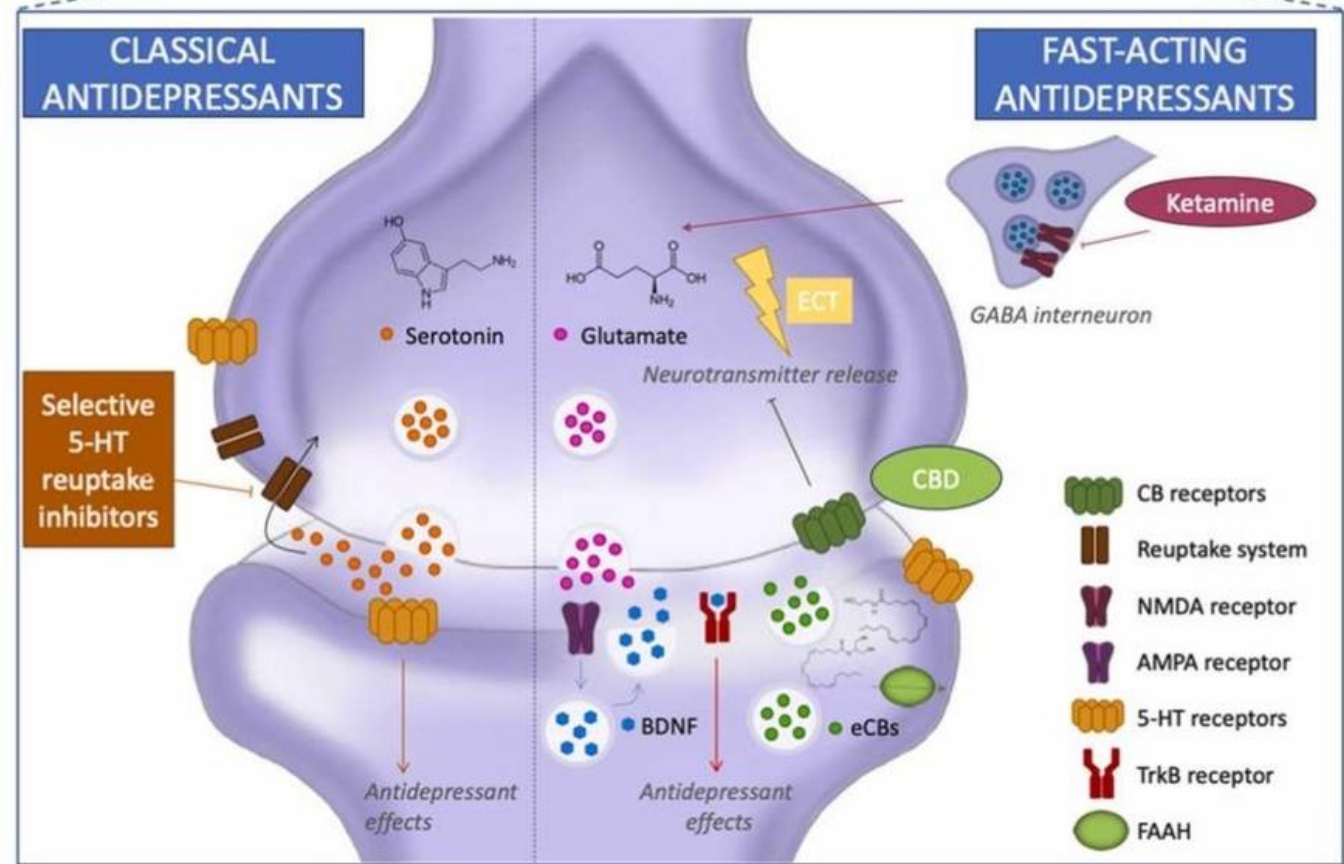
Treatment resistance
30-40%

Suicidal ideation

Novel rapid treatment options



1. Neuromodulators ECT
2. Consciousness-altering drugs Ketamine
3. Cannabinoids CBD



Sandra Ledesma-Corvi, Jordi Jornet-Plaza, Laura Gálvez-Melero, M. Julia García-Fuster, Novel rapid treatment options for adolescent depression, Pharmacological Research, Volume 201, 2024

Take home messages

- Mental health conditions can affect any of us.
- Stress management may be key.
- Take steps to control stress
- Healthy coping mechanisms (exercise), structure time, simplify life, have realistic expectations
- Reach out to family and friends
- Make and keep healthy friendships
- Seek treatment at the earliest sign of problem
- Ask for help (prevents depression from worsening)

