



A Modern Epidemic: Depression and Anxiety

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Objectives

- Review the definition and diagnostic signs and symptoms of GAD/MDD
- Review HAM-D scale for depression
- Review prevalence and comorbidities of GAD/MDD
- Review neurobiology of GAD/MDD
- Discuss effective medical, non-medical, and alternative management of GAD/MDD

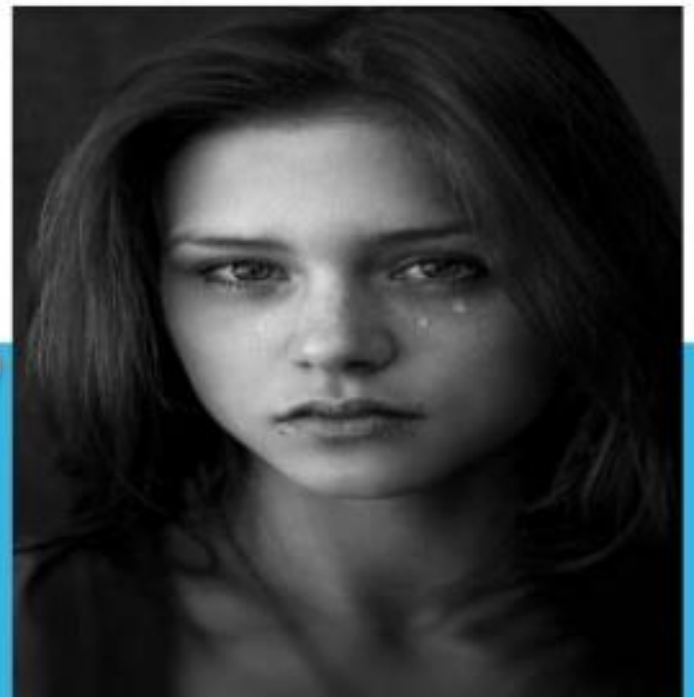
DEPRESSION

DEPRESSION VS. SADNESS

- Sadness- the feeling of sorrow or unhappiness
- Sadness and depression have similar reactions except for depression lasts longer than sadness
- Depression can affect someone's mood, cause them to feel drained, and cause someone to feel down for weeks/ months.
- Sadness doesn't last very long, it can be something that makes you sad that day and then you eventually get over it.



VS.



WHO IS AFFECTED BY DEPRESSION?

FACT ↓

An estimated one in ten Americans suffer from depression, an illness that affects both physical and mental well-being. Often chronic in nature, depression can be triggered by adverse life circumstances or occur simply "out of the blue." Frequently, a combination of genetic, psychological and environmental factors contribute to the onset of depression.



FACTS ABOUT DEPRESSION

- One of the most common illnesses found in human beings
- Serious and sometimes can be chronic
- Afflicts 20 percent of the population in the United States and worldwide
- Women are two to three times more likely to fall victim to the mood disorder than men
- Depression tends to run in families
- Approximately one in five adults in the United States suffer from depression one time in their lives
- Affects more than 17 million Americans each year
- Hundreds of thousands of medications are given out each year to treat depression

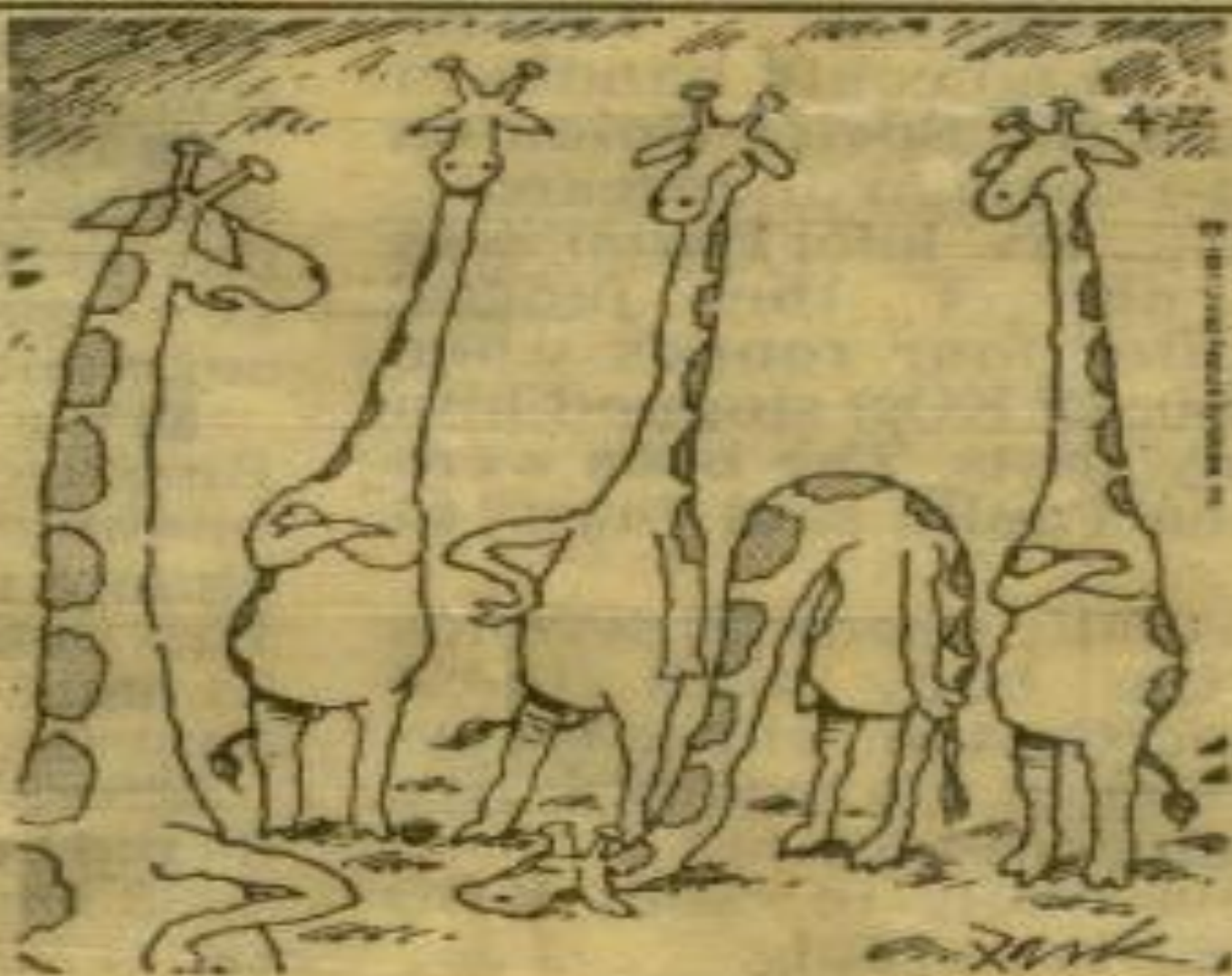


DSM-IV Definition of Depression ("SIG E CAPS")

- Sleep disturbance that includes insomnia or hypersomnia
- Interest diminished or lack of pleasure in almost all activities most of the day, nearly every day
- Guilt or feelings of worthlessness
- Energy is lacking nearly daily

DSM-IV Definition of Depression ("SIG E CAPS")

- Concentration lacking with a diminished ability to think, or indecisiveness
- Appetite change or unintentional weight loss or gain ($\geq 5\%$ of body weight in a month)
- Psychomotor agitation or retardation
- Suicidal ideation that can include recurrent thoughts of death



"I understand one of you is depressed."

Diagnosing Depression

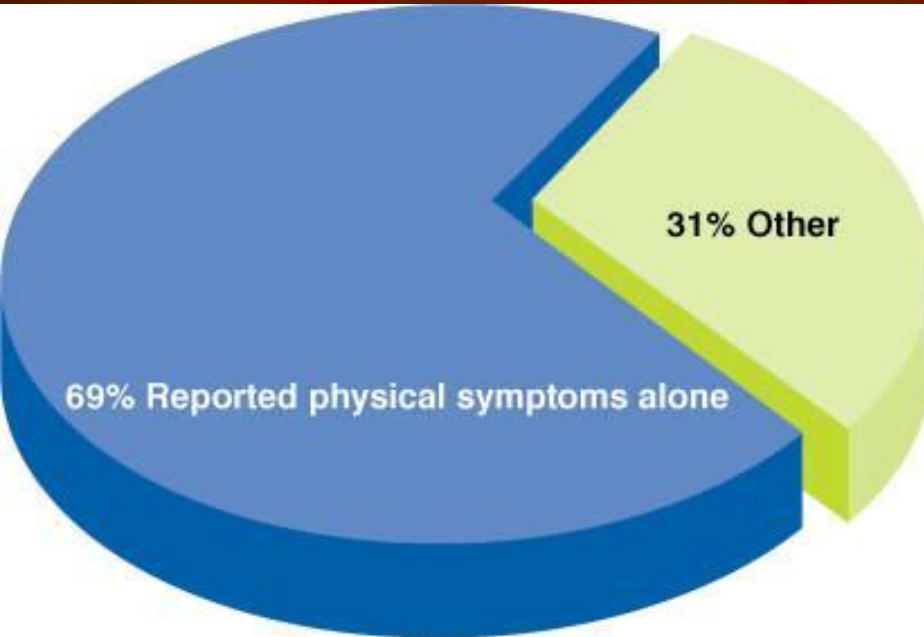
- Major Depression
(≥ 2 weeks)
 - Minor Depression
(≥ 2 weeks)
 - Dysthymia
(≥ 2 years)
- ≥ 5 depressive symptoms, including depressed mood or inability to experience pleasure, causing significant impairment in social, occupational, or other important areas of functioning
 - 2 to 4 depressive symptoms, including depressed mood or inability to experience pleasure, causing significant impairment in social, occupational, or other important areas of functioning
 - 3 or 4 dysthymic symptoms, including depressed mood, causing significant impairment in social, occupational, or other important areas of functioning

Depression – The Physical Presentation

- Somatic symptoms frequently accompany depression
- Depressed patients can present with ONLY somatic symptoms
- 90% depressed patients report comorbid anxiety symptoms

Depression – The Physical Presentation

In primary care, physical symptoms are often the chief complaint in depressed patients



In a *New England Journal of Medicine* study, 69% of diagnosed depressed patients reported unexplained physical symptoms as their chief complaint¹

N = 1146 Primary care patients with major depression

Reference:

1. Simon GE, et al. *N Engl J Med.* 1999;341(18):1329-1335.

Depression Assessment Tools

Patient Administered

- Beck Depression Inventory-II (BDI-II)
- Inventory of Depressive Symptomatology (IDS)
- Quick Inventory of Depressive Symptomatology (QIDS)
- Zung Self-Rating Depression Scale (SDS)

Physician Administered

- Hamilton Rating Scale for Depression (HAM-D)
- Montgomery-Asberg Depression Rating Scale (MADRS)
- Cornell Dysthymia Rating Scale (CDRS)
- Center for Epidemiologic Studies Depression Scale (CES-D)

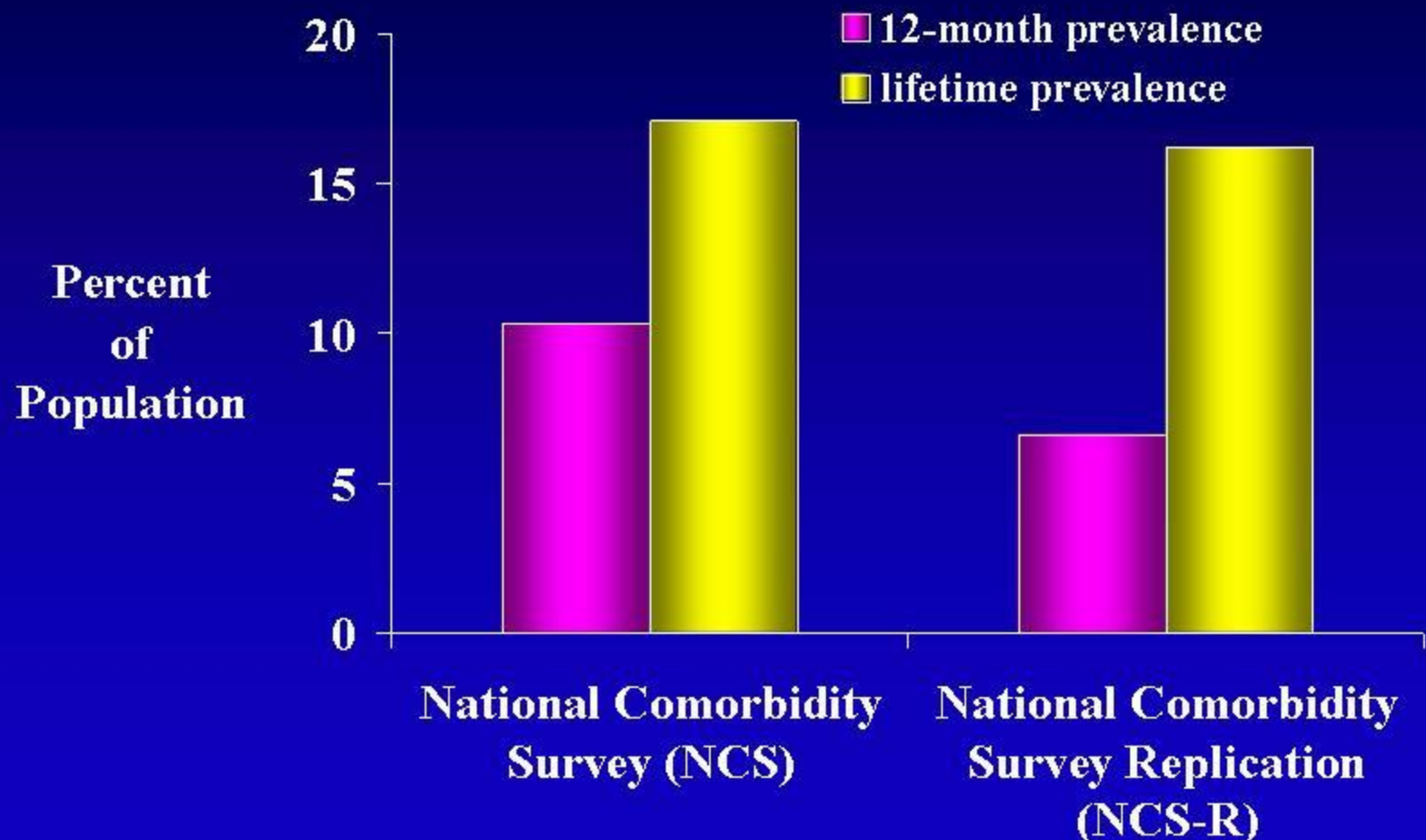
The Hamilton Rating Scale for Depression

- 17-item and 14-item versions of symptoms covering:
 - depressed mood, feelings of guilt, suicide,
 - early insomnia, middle insomnia, late insomnia, difficulty with work & activities
 - psychomotor retardation, agitation, psychological
 - anxiety, somatic anxiety, change in appetite,
 - somatic symptoms (backache, headache, muscle aches, heaviness in limbs)
 - loss of energy, genital symptoms
 - loss of weight, insight, diurnal variation

The Hamilton Rating Scale for Depression

- Scoring is on a 3-point to a 5-point scale; add all items for a total score
- The higher the score, the worse the depression:
 - 10 to 13 = mild
 - 14 to 17 = mild to moderate
 - >17 = moderate to severe

Prevalence of Depression



Kessler et al., *Arch Gen Psychiatry*, 1994; Kessler et al., *JAMA*, 2003

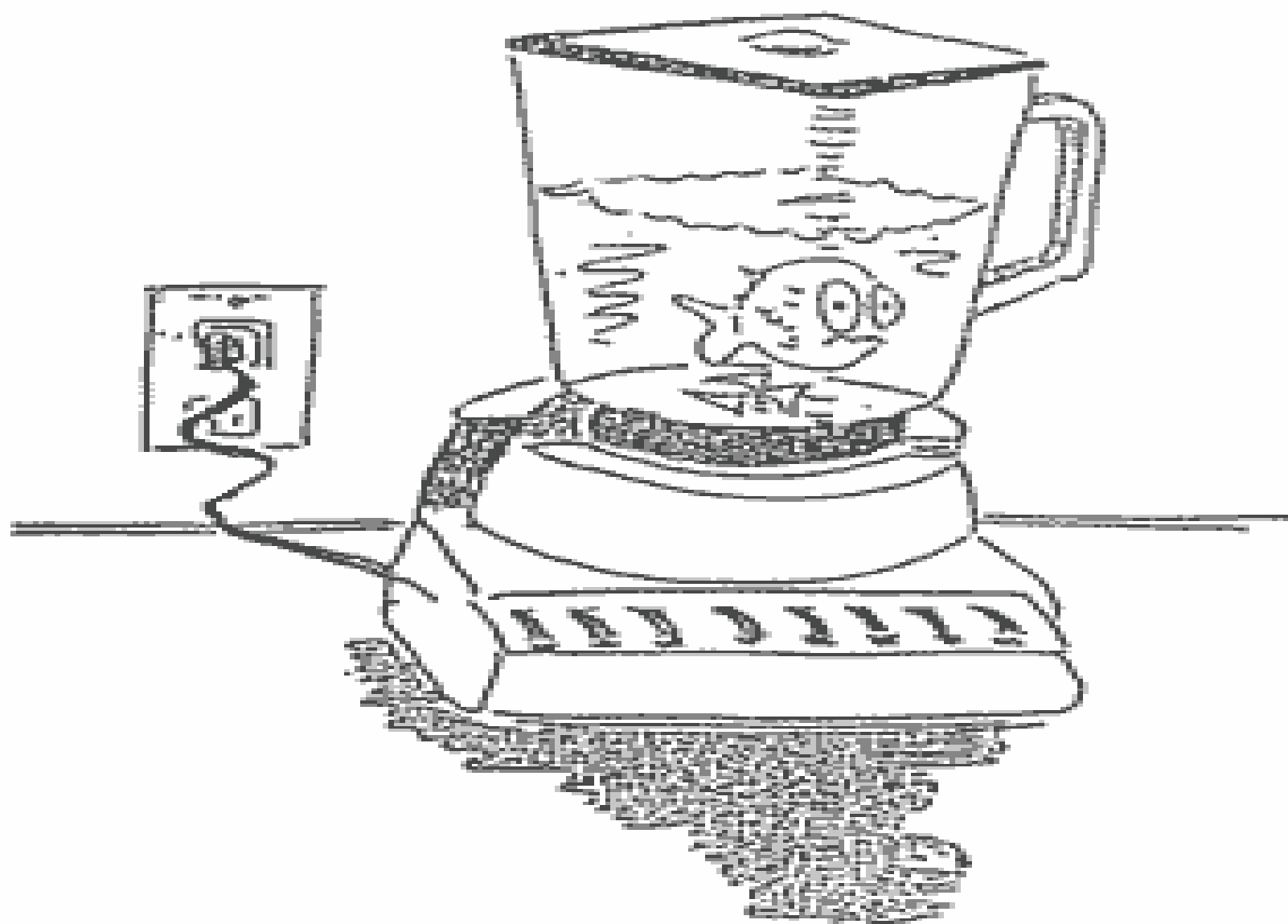
ANXIETY

DSM-IV Definition of Anxiety

- Persistent worry that is excessive and that the patient finds hard to control
 - work responsibilities, money, health, safety, car repairs, and household chores
- 3 of 6 symptoms usually present
 1. High levels of muscle tension
 2. Irritability
 3. Difficulty concentrating
 4. Sleep disturbances
 5. Restlessness
 6. Easily fatigued

DSM-IV Definition of Anxiety

- Interference with work, family life, social activities, or other areas of functioning
- Worry is out of proportion in its duration or intensity to the actual likelihood or impact of the feared situation or event
- Frequently develop stress related physical illnesses such as:
 1. IBS
 2. TMJ
 3. Bruxism (grinding teeth during sleep)
 4. HTN



Onset of Anxiety

- Insidious onset that can begin relatively early in life, although it can be precipitated by a sudden crisis at any age above 6-7 years of age
- Many will say that they cannot remember a time in their lives when they were not worried about something
- Not unusual for people to develop GAD in their early adult years or even later in reaction to chronic stress or anxiety-producing situations

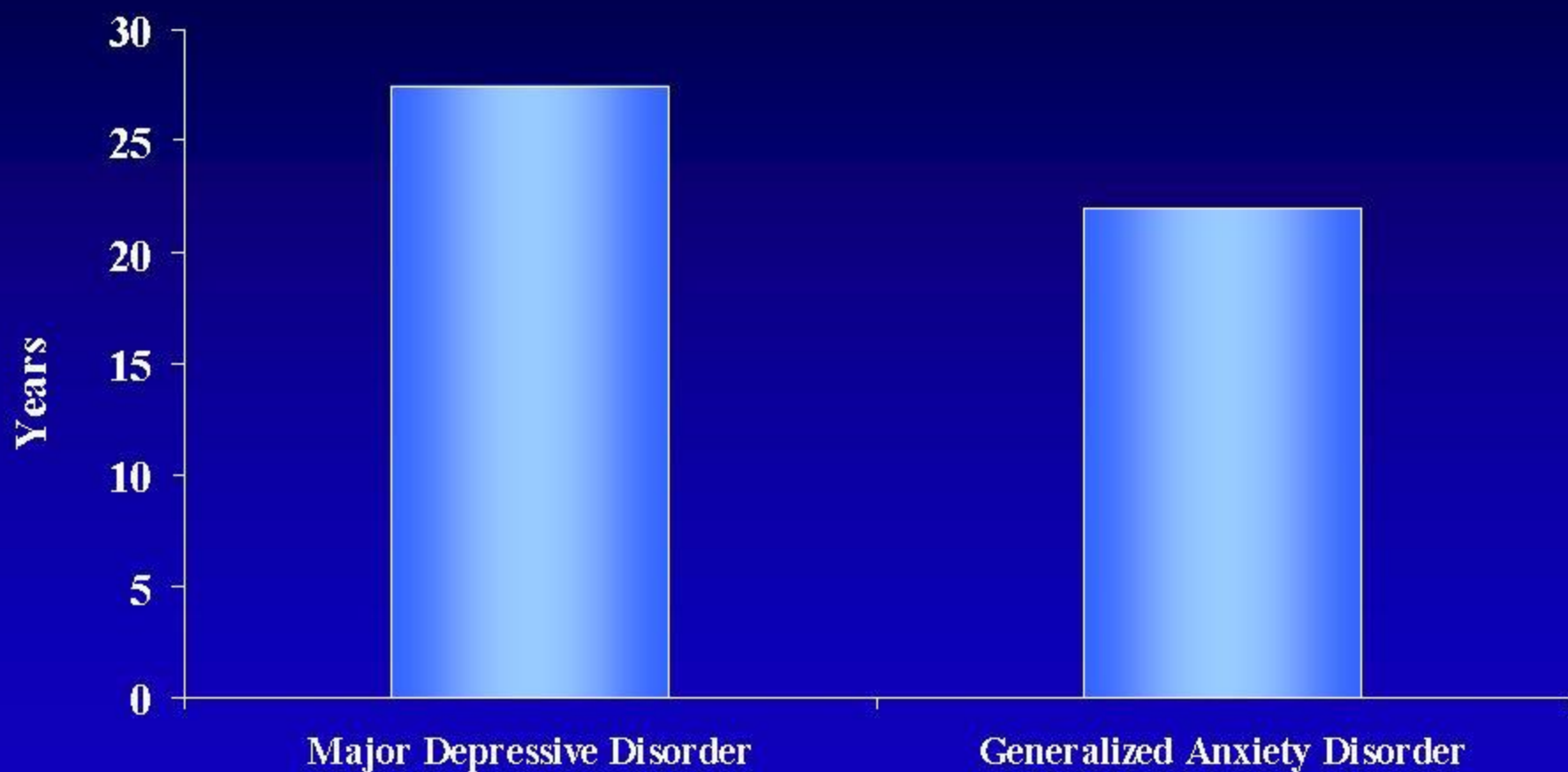
Onset of Anxiety

- Disorders typically develop in childhood or adolescence
- By the age of 16 years, approximately 10% of young people will have an anxiety disorder of some type, with most occurring in females
- Those who already have comorbid social anxiety disorder and MDD are nearly 9x more likely to have a recurrence of MDD and are 6x more likely than the general population to attempt suicide

Anxiety

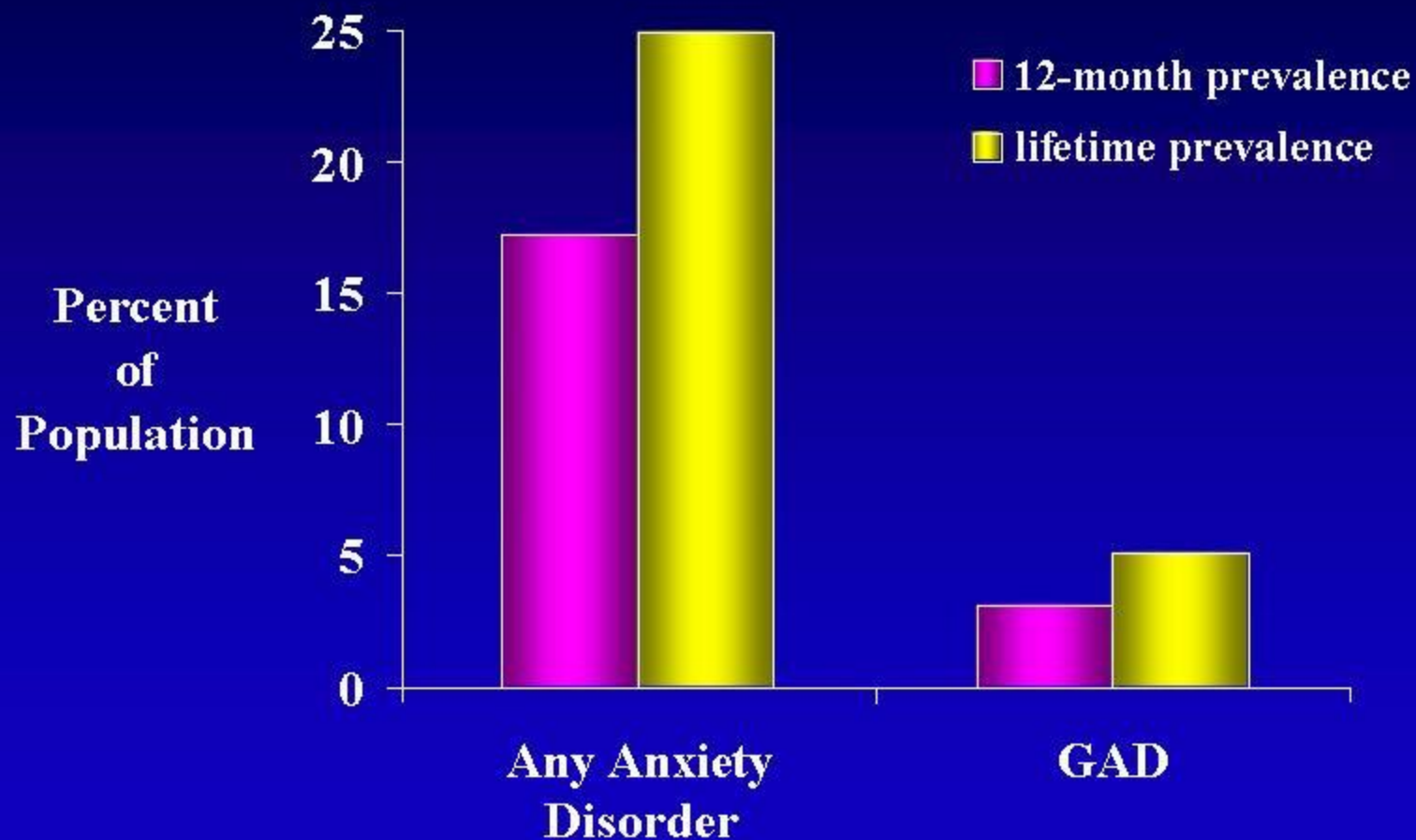
- Incidence rising in the U.S.
 - Worse over past several years due to economy
- One of the most common mental health problems
- Significant public health implications
 - Frequency with which they occur
 - Persistence of some associated conditions
 - Disability associated with them

Mean Age of Onset of Mood Disorders



American Psychiatric Association, 2000; Wittchen et al., *Arch Gen Psychiatry*, 1994; Schneier et al., *Arch Gen Psychiatry*, 1992.

Prevalence of Anxiety Disorders



Kessler et al., *Arch Gen Psychiatry*, 1994; Wittchen et al., *Arch Gen Psychiatry*, 1994

Comorbidity and Its Relevance

- Depression comorbid with Anxiety
 - Mask GAD symptoms
 - Hamper GAD diagnosis and treatment
 - Exacerbate GAD symptoms

Comorbidity of GAD/MDD

- Psychiatric comorbidity is a concern because it is associated with greater functional impairment and more extensive utilization of health services
- People with comorbid anxiety and depression are slower to respond to both psychotherapy and pharmacologic intervention

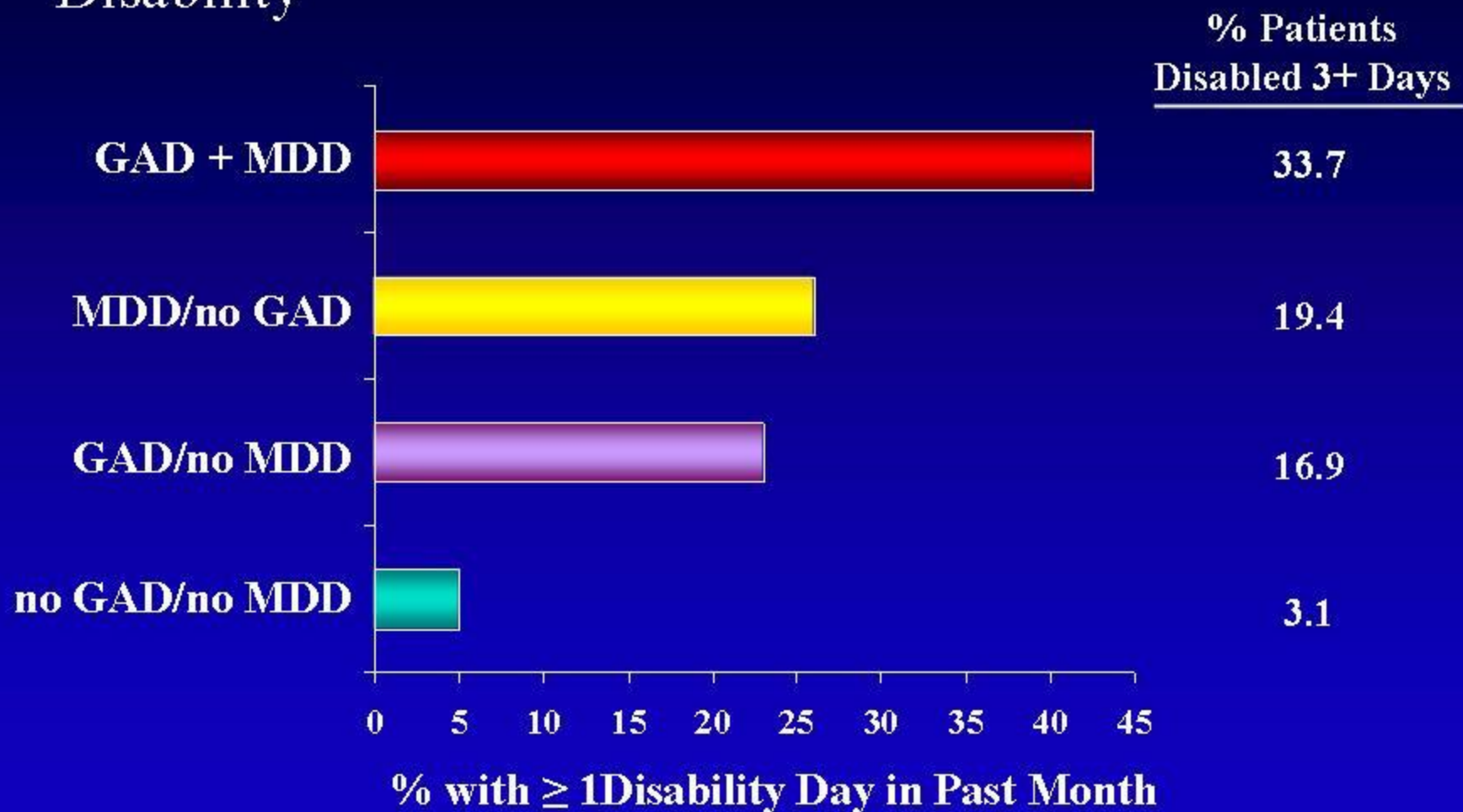
Comorbidity of Depression and Anxiety

Course of Illness

- When anxiety and depression coexist, anxiety disorders are more likely to occur first
 - Most cases of lifetime MDD occur in patients with a previously diagnosed (primary) psychiatric disorder
 - Anxiety disorders are most common primary disorders (59.2%) in patients with MDD
- Comorbidity associated with increased severity, persistence, and functional impairment

Comorbidity of Depression and Anxiety

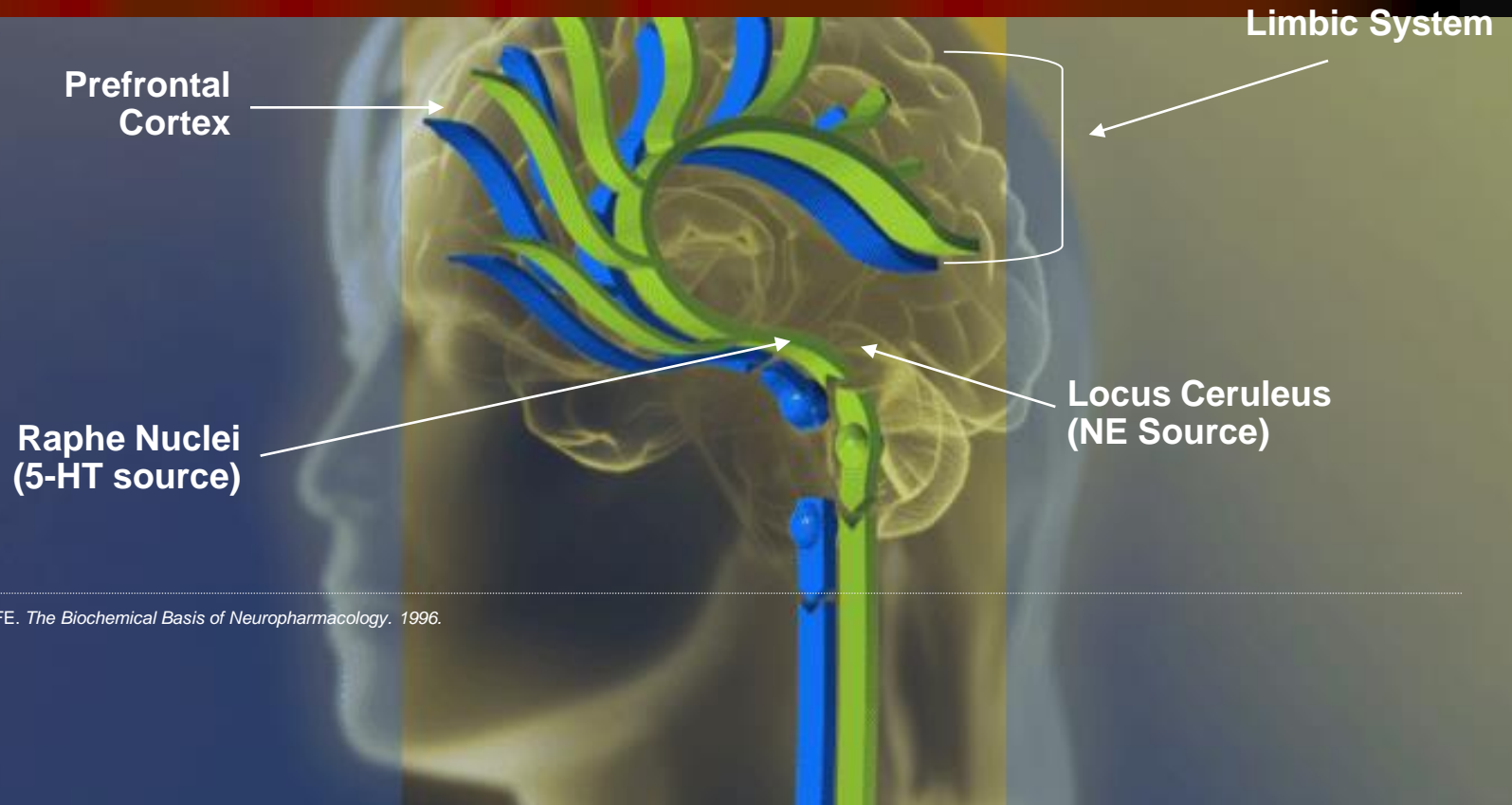
Disability



Neurobiology of Depression and Anxiety



Serotonin^{5HT} and Norepinephrine^{NE} in the brain



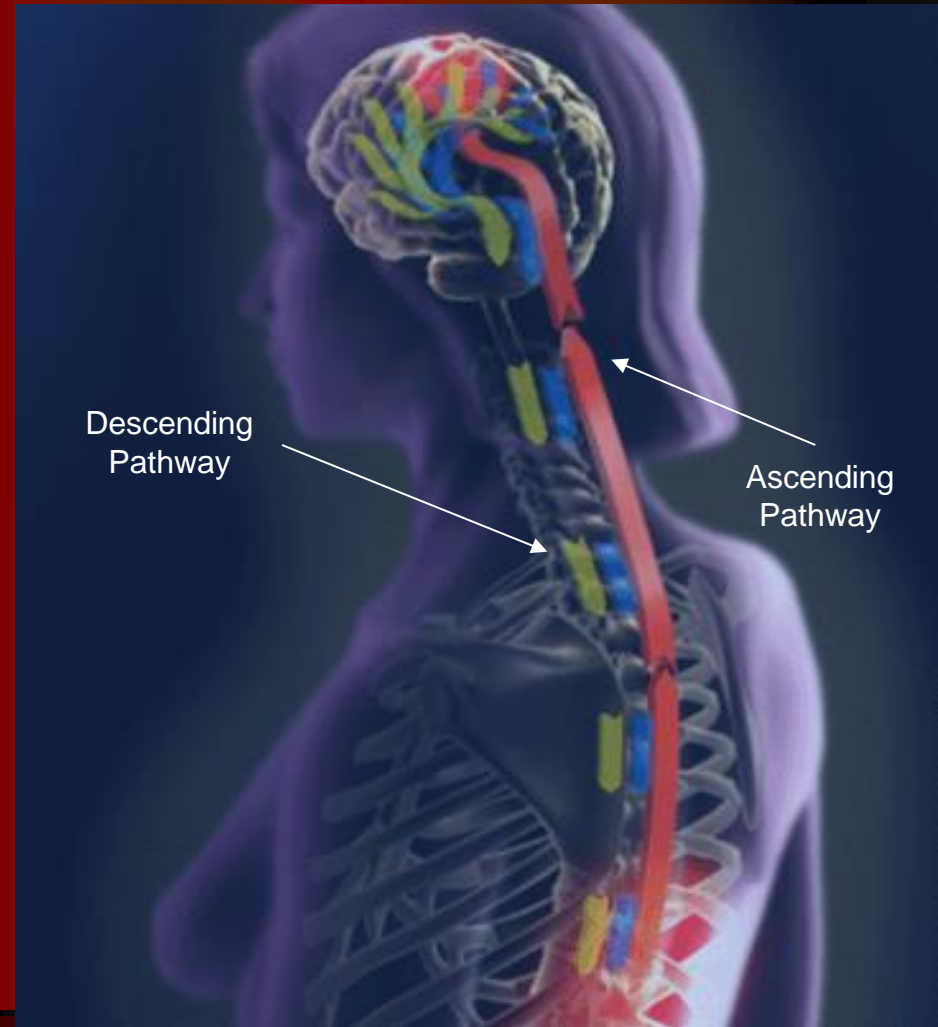
The neurotransmitter pathway

It's not all in your head

- **Dysregulation of Serotonin (5HT) and Norepinephrine (NE) in the brain are strongly associated with depression**
- **Dysregulation of 5HT and NE in the spinal cord may explain an increased pain perception among depressed patients¹⁻³**
- **Imbalances of 5HT and NE may explain the presence of both emotional and physical symptoms of depression.**

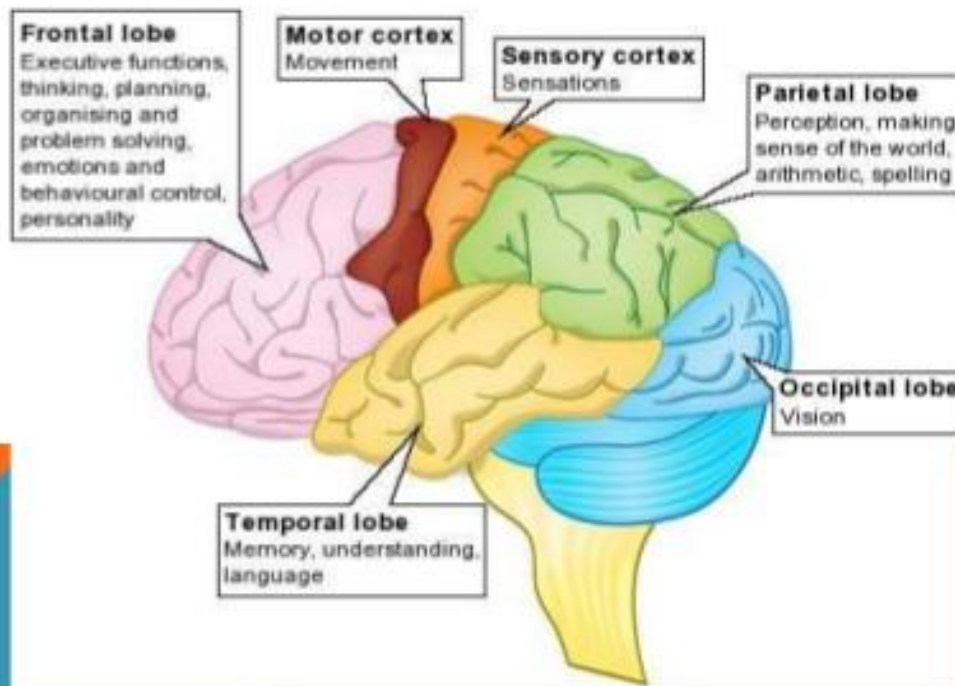
Adapted from References:

1. Stahl SM. *J. Clin Psych.* 2002;63:203-220.
2. Verma S, et al. *Int Rev Psychiatry.* 2000;12:103-114.
3. Blier P, et al. *J Psychiatry Neurosci.* 2001;26(1):37-43.



WHAT HAPPENS IN THE BRAIN

- Depression may be caused by episodic misfiring of areas of the left frontal lobe and the left temporal lobe as a result of genetic, environmental, social, or physiological factors.
- That conclusion coincides with clinical observations that stroke patients are at greater risk for depression if the stroke is on the left side of the brain, especially in the left frontal lobe.

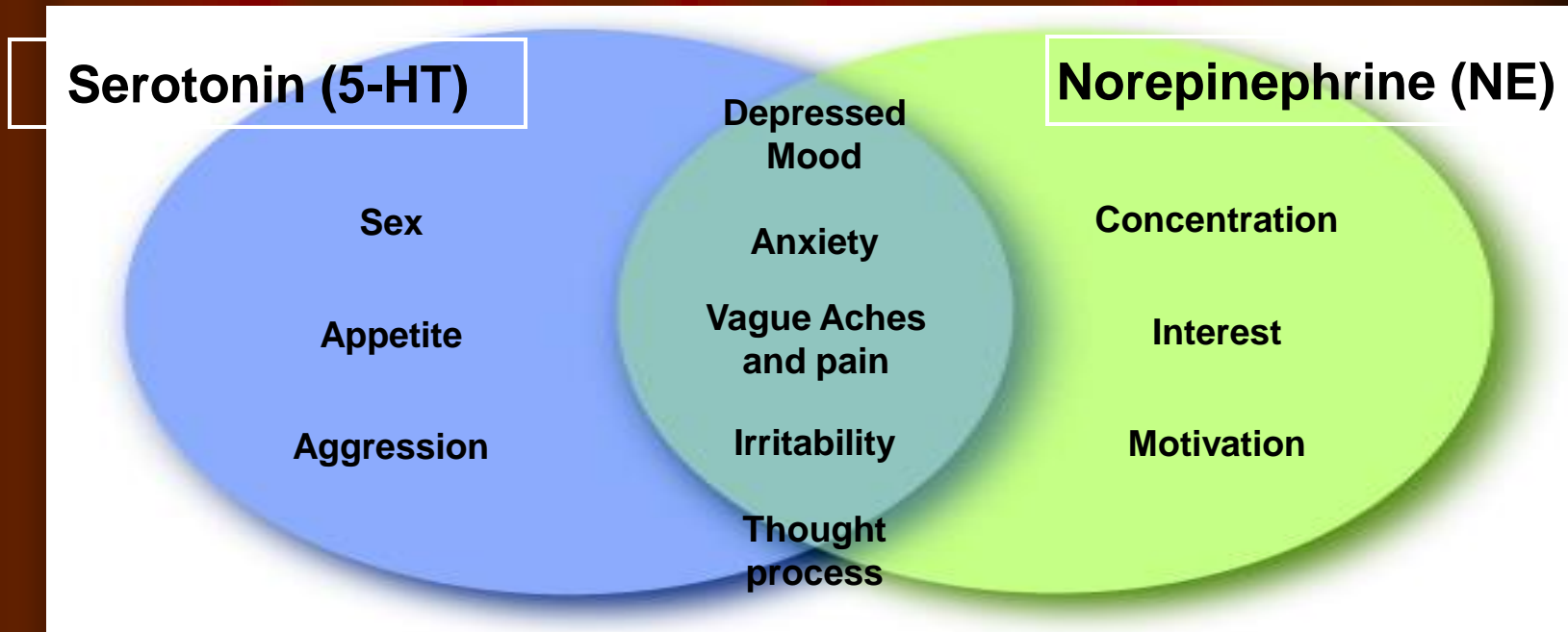


Neurobiology

- One hopeful aspect of the treatment of anxiety disorders is that some antidepressant treatments, which may be used in patients with comorbid anxiety and depression, promote neurogenesis
- Primates have reduced levels of neurogenesis throughout life, so the neurogenic potential of certain therapies has implications for the treatment of anxiety

There are at least two sides to the neurotransmitter story

Functional domains of Serotonin and Norepinephrine¹⁻⁴



- **Both serotonin and norepinephrine mediate a broad spectrum of depressive symptoms**

References:

1. Adapted from: Stahl SM. In: *Essential Psychopharmacology: Neuroscientific Basis and Practical Applications*: 2nd ed. Cambridge University Press 2000.

2. Blier P, et al. *J Psychiatry Neurosci*. 2001;26(1):37-43.
3. Doraiswamy PM. *J Clin Psychiatry*. 2001;62(suppl 12):30-35.
4. Verma S, et al. *Int Rev Psychiatry*. 2000;12:103-114.

Neurobiology of Anxiety and Depression

Summary:

- Anxiety disorders commonly lead to MDD and MDD is frequently comorbid with GAD
- Functional anatomy of anxiety and depression involves (among others) the interaction between multiple areas of the brain which are complex for which studies continue
- Neurochemistry of GAD/MDD involves brainstem 5-HT and NE systems

Optimal Treatment of Depression and Anxiety

- Medications
- Psychotherapy

Treatment of Depression

Goals of Treatment

- Reduce/eliminate symptoms
- Restore function
- Prevent relapse and recurrence



Obstacles to Adequate Treatment of Depression

- Underdiagnosis and undertreatment
 - Only ~ 50% of depressed patients seek and receive adequate treatment
- Limitations of available therapies
 - Response/remission rates
 - Delayed onset of action
 - Safety/tolerability
 - Drug/food interactions
 - Toxicity in overdose
 - Complex dosing schedules/need for titration

Importance of Long-Term Treatment of Mood Disorders

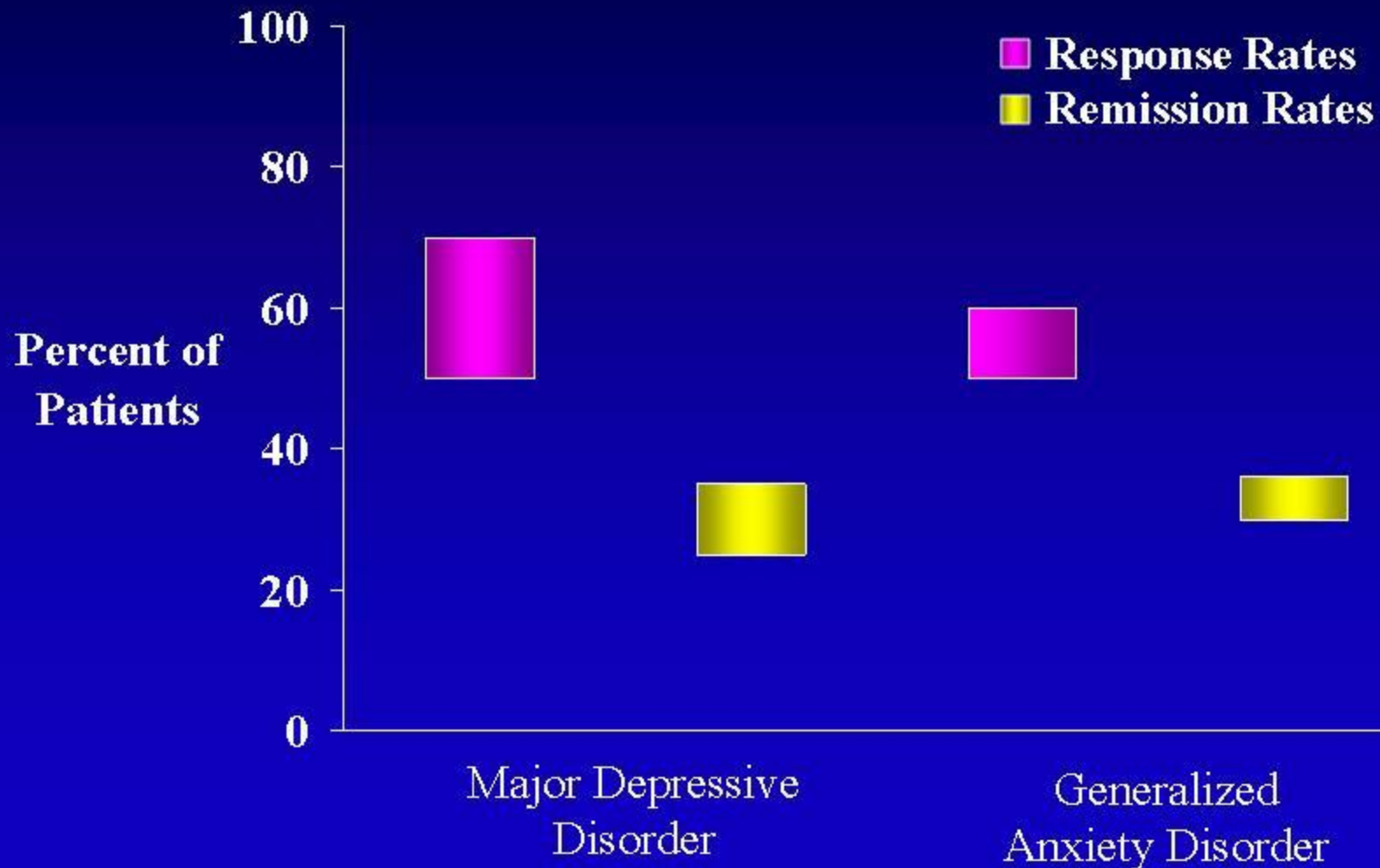
■ Depression

- Relapsing condition
- Requires minimum of 4 to 6 months treatment beyond initial symptom resolution

■ Generalized Anxiety Disorder

- Chronic medical condition
- Often requires treatment for at least 6 - 12 months

Response and Remission Rates in Mood Disorders



Common Remission Criteria

MDD

$$\text{HAM}_{17} \leq 7$$

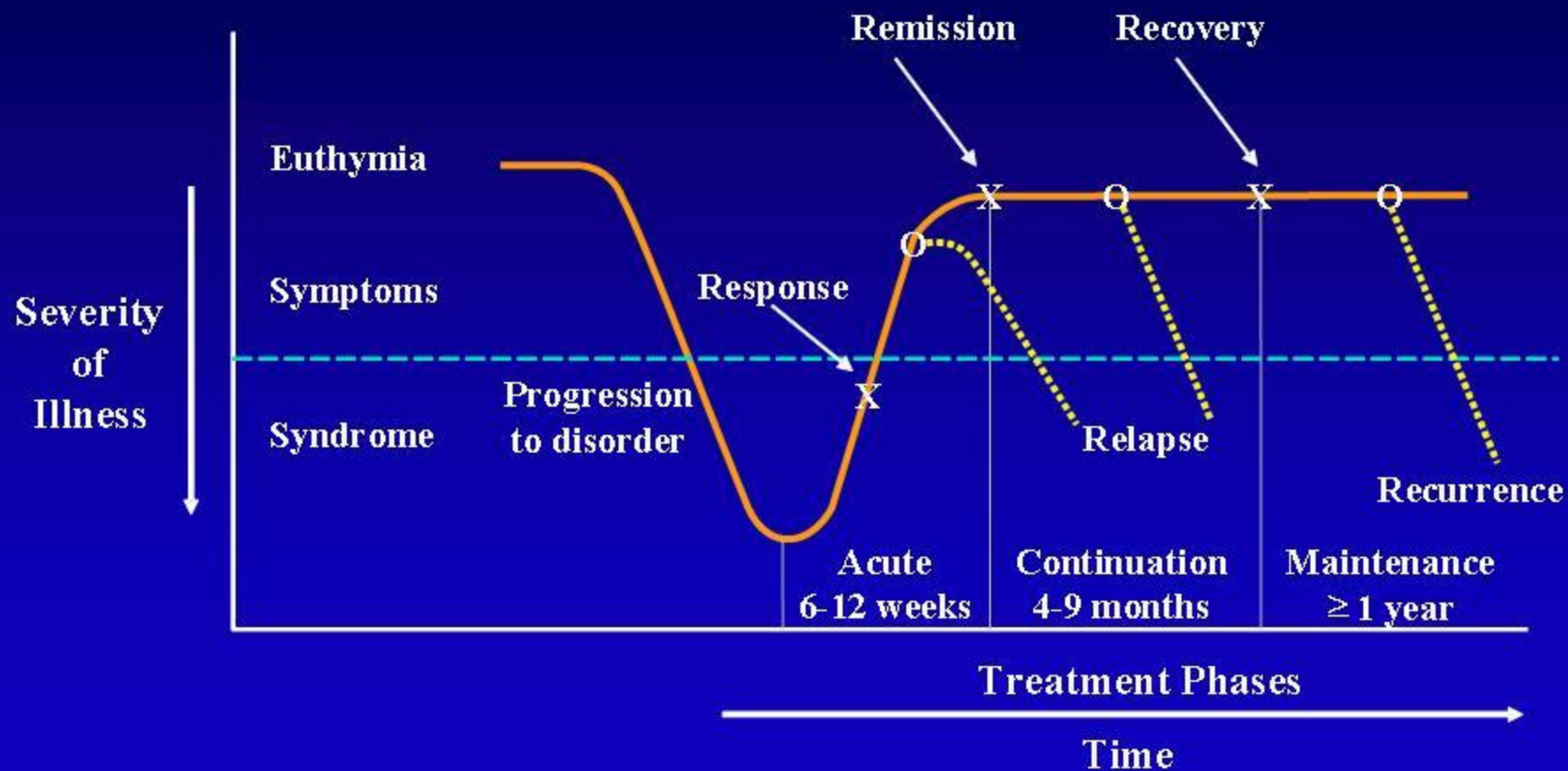
$$\text{MADRS} \leq 10$$

GAD

$$\text{HAMA} \leq 7$$

Treatment of Depression

Course of Illness and Phases of Treatment



Importance of Long Term Treatment

- 33% of patients discontinue therapy within the first month
 - 44% of patients discontinue therapy within the first 3 months
- Masand, Clin Ther. 2003; Hamilton, Br J Clin Pharmacol

SSRI Treatment for MDD and GAD

● Depression

- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Venlafexine (Effexor)
- Duloxetine (Cymbalta)
- Paroxetine (Paxil)
- Fluoxetine (Prozac)
- Sertraline (Zoloft)
- Vilazodone (Viibryd)
- Fluvoxamine (Luvox)

● Anxiety

- Escitalopram (Lexapro)
- Venlafexine (Effexor)
- Paroxetine (Paxil)
- Fluoxetine (Prozac)
- Sertraline (Zoloft)

Antidepressant Efficacy in Recurrence

SSRI/SNRI	MDD
Citalopram	++
Duloxetine	++
Escitalopram	++
Fluvoxamine	++
Fluoxetine	++
Paroxetine	++
Sertraline	++
Venlafaxine	++

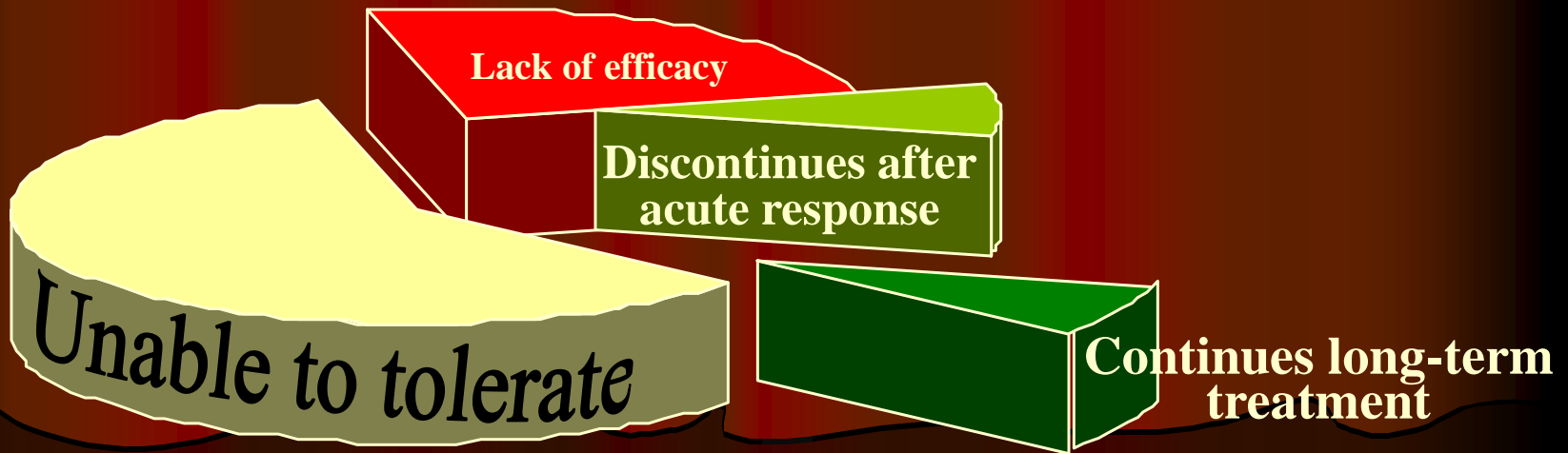
++ = Positive Placebo-Controlled Data

+ = Positive Open Trial(s) Only

Is there a need to protect patients from treatments only proven to have short-term efficacy?

- Effective medications are frequently discontinued over relatively short time periods
- Most patients using medications long-term are those who responded acutely and either perceive continued benefit or have suffered recurrence when attempting to taper

Few get long-term treatment in the real world



Risk Factors for Depressive Recurrence

- Residual symptoms
- More than three prior depressive episodes
- Chronic depression (episode > 2 years)
- Family history of mood disorders
- Comorbidities (e.g., anxiety disorder, substance abuse)

Alternative and complementary therapies of MDD/GAD

1. Hypnotherapy/music therapy
2. Osteopathic manipulative therapy
 - 2001 JAOA study in postpartum women, 8 weeks of OMT revealed 100% improvement with follow up evaluation
3. Ayurvedic medicine
 - Holistic system of healing which evolved in ancient India some 3000-5000 years ago focusing on life energies and balance
4. Yoga
5. Religious practice
6. Guided imagery meditation

Alternative and complementary therapies of MDD/GAD

- In the United States, over 40% of consumers used a complementary therapy over the course of the last year
- Biofeedback and relaxation techniques to lower physiologic arousal
- Massage therapy, hydrotherapy, shiatsu, and acupuncture have been reported to relieve muscle spasms or soreness
- An herbal remedy that has been used in clinical trials for treating GAD is **passionflower** (*Passiflora incarnata*)

Alternative and complementary therapies of MDD/GAD

● **St. Johns Wort**

- May be effective in helping to support depressed mood and mood fluctuations by maintaining the balance of Serotonin, Norepinephrine, Dopamine and GABA

● **Zinc**

- An essential mineral found in almost every cell
- Depression may be connected with low blood-zinc levels
- Studies involving zinc supplementation in depressed patients suggest that zinc has a strong anti-depressant activity

Alternative and complementary therapies of MDD/GAD

- **Electroconvulsive Therapy (ECT)**

- Procedure in which electric currents are passed through the brain, intentionally triggering a brief seizure
- Cause changes in brain chemistry that can quickly reverse symptoms of certain mental illnesses

- **Valerian Root**

- Direct sedative effect on the Central Nervous System
- Used as a calming agent to reduce headaches, nervousness and insomnia

Summary

- “SIG E CAPS” *mnemonic* to help interview those patients you suspect may have depression
- 90% of patients with MDD will have underlying GAD
- 5HT and NE are thought to be integral in pathway that leads to symptoms related to GAD/MDD
- Many medical and non medical therapies available that should include psychotherapy
- Ensure compliance with routine follow up visits as this can hamper efficacy of therapy

REFERENCES

BIBLIOGRAPHY

- *Ainsworth, P. (2000). *Understanding Depression*. Jackson: University Press of Mississippi.
There are theories to depression since a main cause has not been verified. The brain triggers off different moods and sends them to our body to make us react to things in different ways. Our brains all work differently and heredity may be a cause to our brain reactions.
- Mondimore, F. M. (2006). *Depression, The Mood Disease*. Baltimore: Johns Hopkins University Press.
Depression is serious and can be treated as a disease. Depression can cause a person to act a totally different way then they were before.
- Reinberg, S. (2012). Depression Hippocampal Volume Loss. *HealthDay Reporter*, 2.
Depression can become a disorder in the brain. Depression disorders are most likely in teens from the age of 13-18. The Hippocampus plays a role in the body which it responds to stress.
- *Wayne Katon, E. L. (2008). *The Depression Helpbook*. Boulder: Bull Publishing Company.
There are plenty of explanations and facts on how depression may come about in the brain. Medications are given out to help people who are depressed.