Psychopharmacology for the non-prescriber: Depression Management

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Topics to be Covered Today

- Depression Differential Diagnosis
- Depression Biology
- Depression Medications: mechanism of action & pearls for prescribing

Goals

- To be able to accurately diagnose major depression, ruling out possible medical and medication problems that can mimic depression
- To feel confident in screening for bipolar for all of your patients with depression
- To understand proposed theories for mechanism of action of antidepressant medications
- To understand basic prescribing principles for depression
- To effectively help your patients with depression

Before considering medication…

- Do you have the correct diagnosis?
- Did you overlook a bigger psychiatric problem?
- Has the primary care doctor ruled out other causes of depression?
- Is medication warranted?
- Would another strategy be better?
- How will you measure success?

MDE Symptoms

5/9 symptoms

*1 of which must be Depressed mood or Anhedonia

***Anhedonia**

***Depressed Mood**

Recurrent Thoughts of Death or Suicide

Poor Concentration

Psychomotor Retardation or Agitation

Sleep Disturbance

App or Weight Changes

Feelings of Worthlessness or Excessive Guilt

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____

=Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
☐	☐	☐	☐

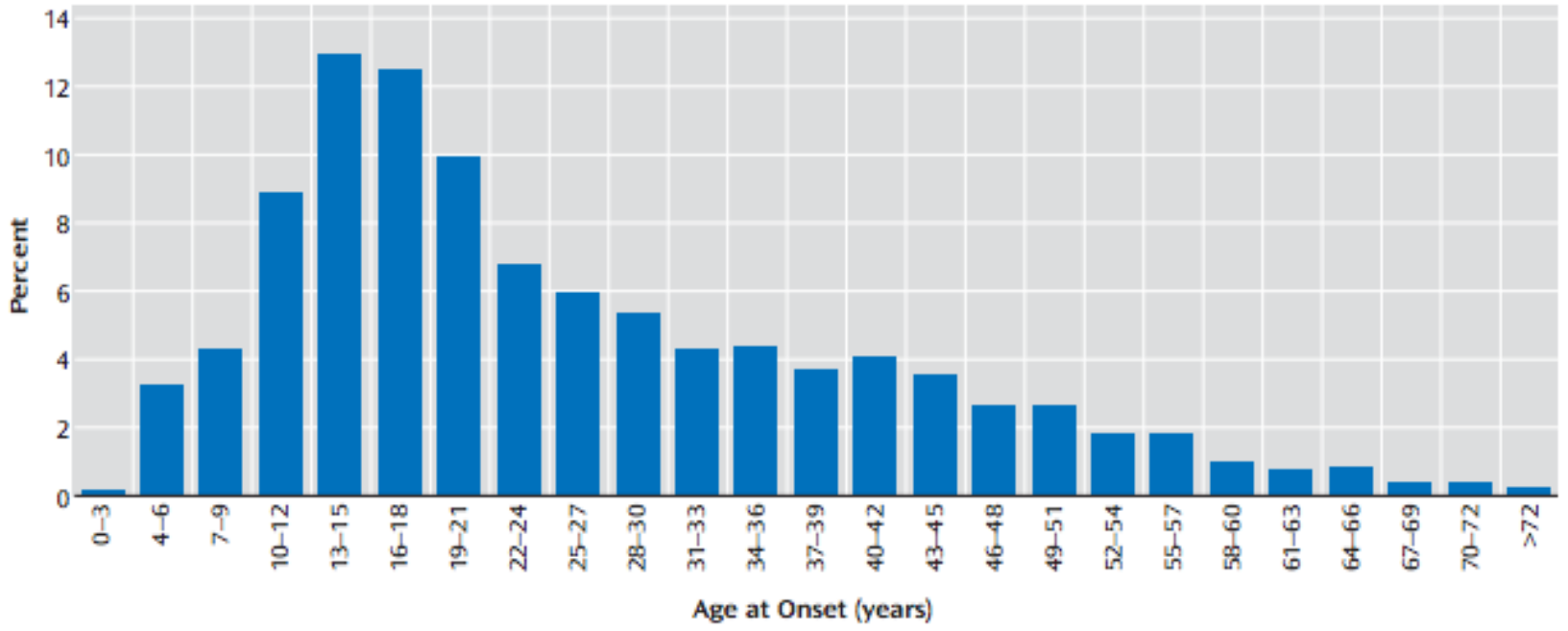
PHQ-9

PHQ-9 score	Severity of Major Depressive Episode
10-14 and at least 5 symptoms endorsed as present “more than half the days”	Mild
15-19 or at least 5-6 symptoms endorsed as present “more than half the days”	Moderate
>20 and at least 7-9 symptoms endorsed as present “more than half the days”	Severe

Depression Age at Onset

AGE AT ONSET AND DEPRESSION COURSE

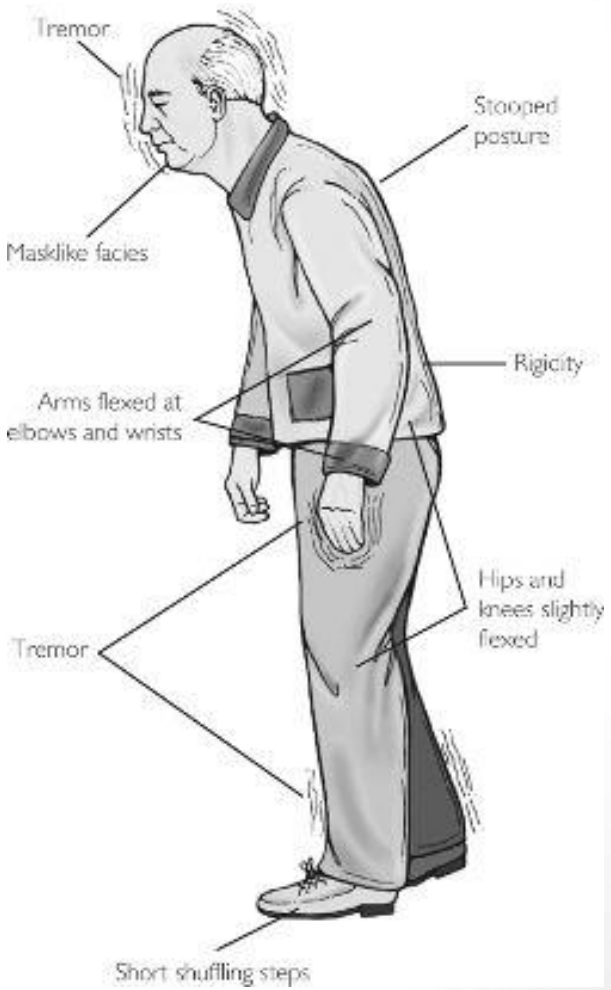
FIGURE 1. Distribution of Age at Onset of First Major Depressive Episode



Am J Psychiatry 164:10, October 2007

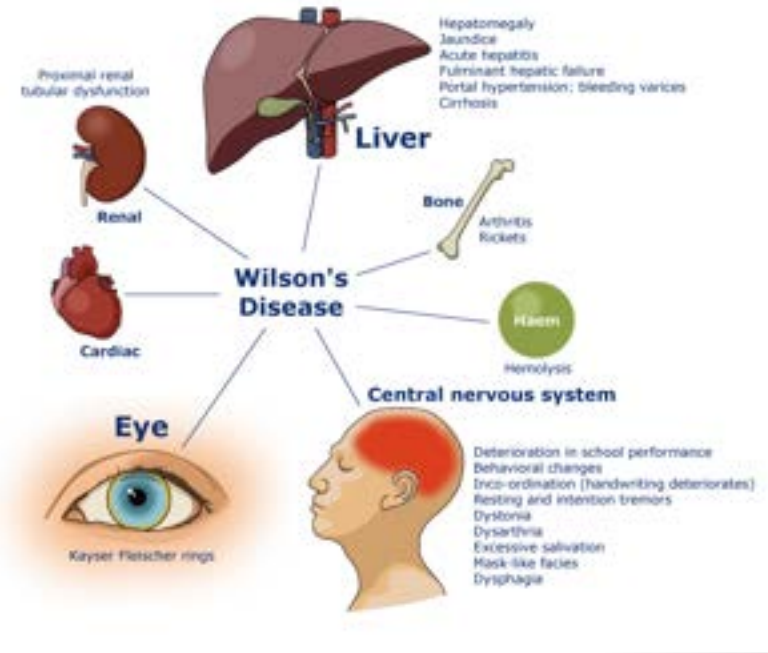
Medical Conditions Associated with Mood Symptoms

- Neurologic:
  - Parkinson's Disease
  - Huntington's Disease
  - Traumatic Brain Injury
  - Dementia
  - Multiple Sclerosis
  - Stroke



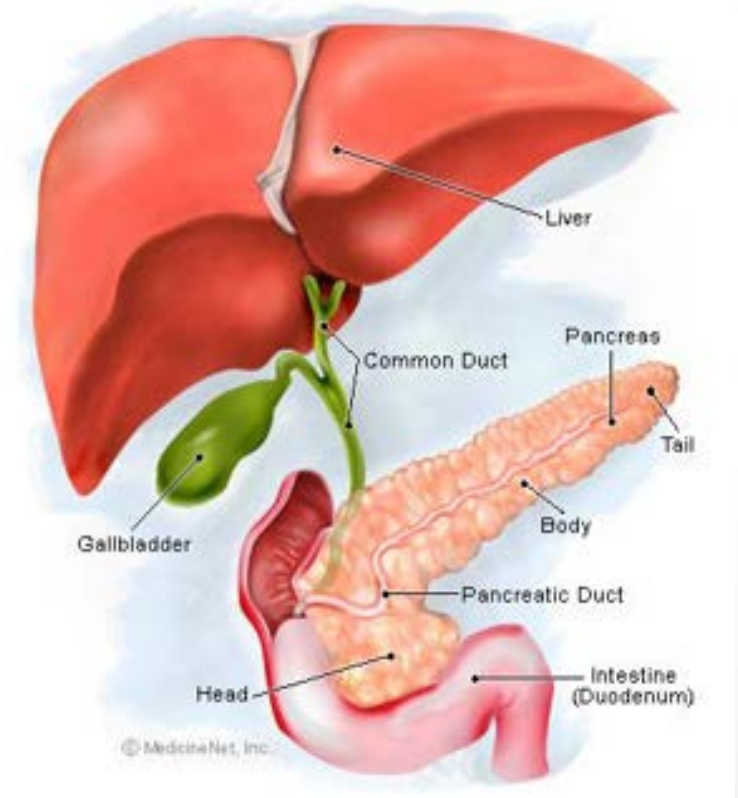
Medical Conditions Associated with Mood Symptoms

- <u>Metabolic</u>
  - Electrolyte disturbance
  - Renal failure
  - Vitamin deficiencies/excesses
  - Acute intermittent porphyria
  - Wilson's
  - Environmental toxins
  - Heavy metal exposure



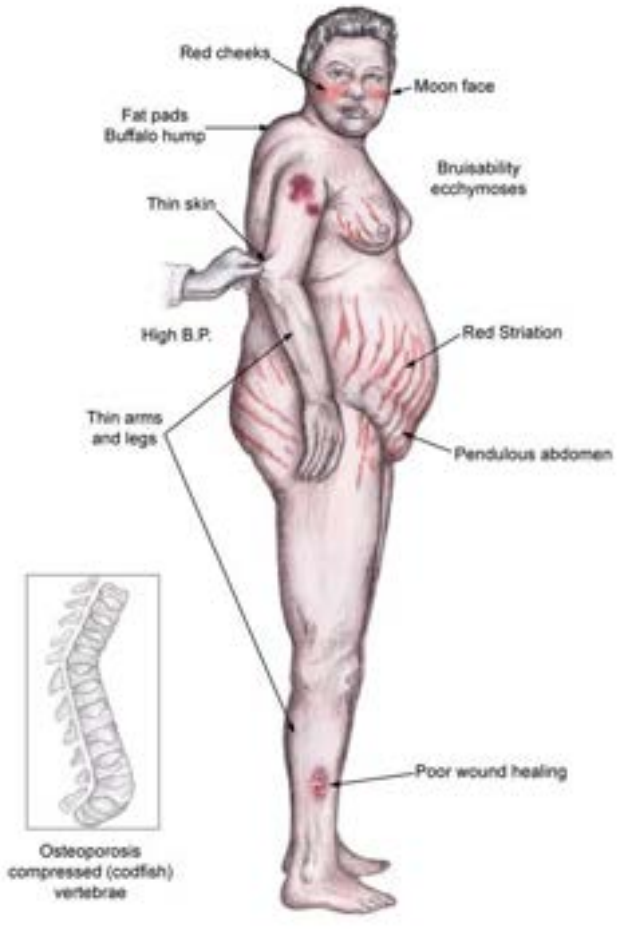
Medical Conditions Associated with Mood Symptoms

- <u>Gastrointestinal</u>
  - Irritable bowel
  - Chronic pancreatitis
  - Crohn's disease
  - Cirrhosis
  - Hepatic encephalopathy



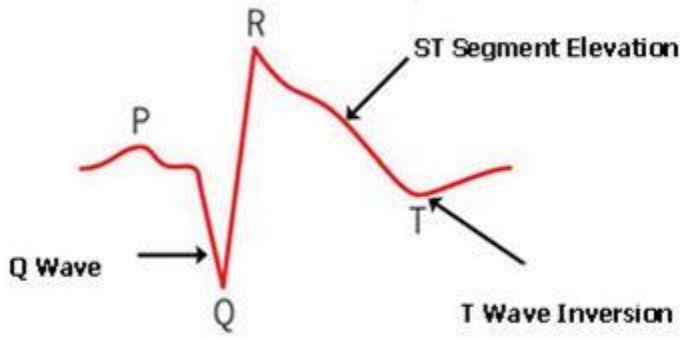
Medical Conditions Associated with Mood Symptoms

- Endocrine
  - Hypo/hyperthyroidism
  - Cushing's disease
  - Addison's disease
  - Diabetes mellitus
  - Parathyroid dysfunction



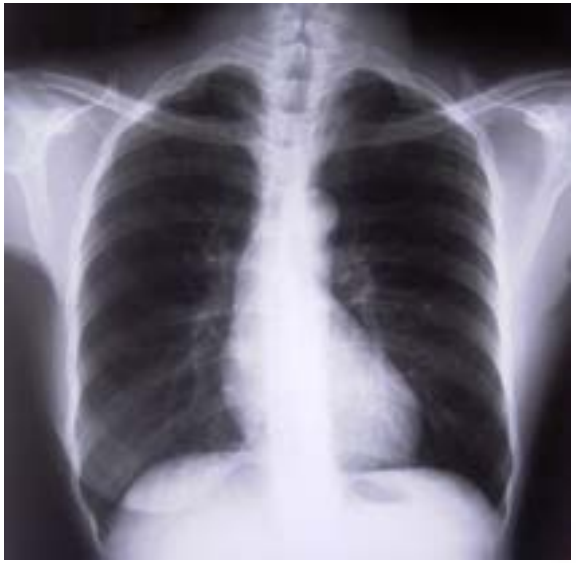
Medical Conditions Associated with Mood Symptoms

- Cardiovascular
  - Myocardial infarction
  - Angina
  - CABG
  - Cardiomyopathies



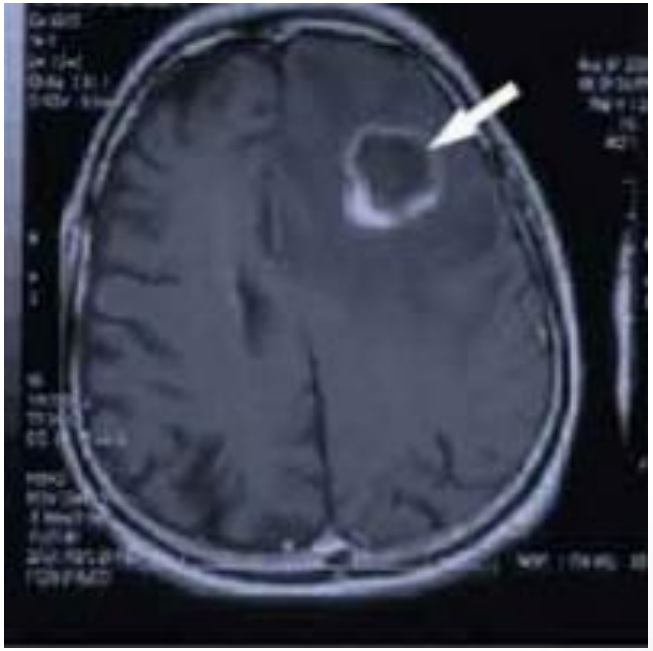
Medical Conditions Associated with Mood Symptoms

- Pulmonary
  - COPD
  - Sleep apnea
  - Restrictive airway disease



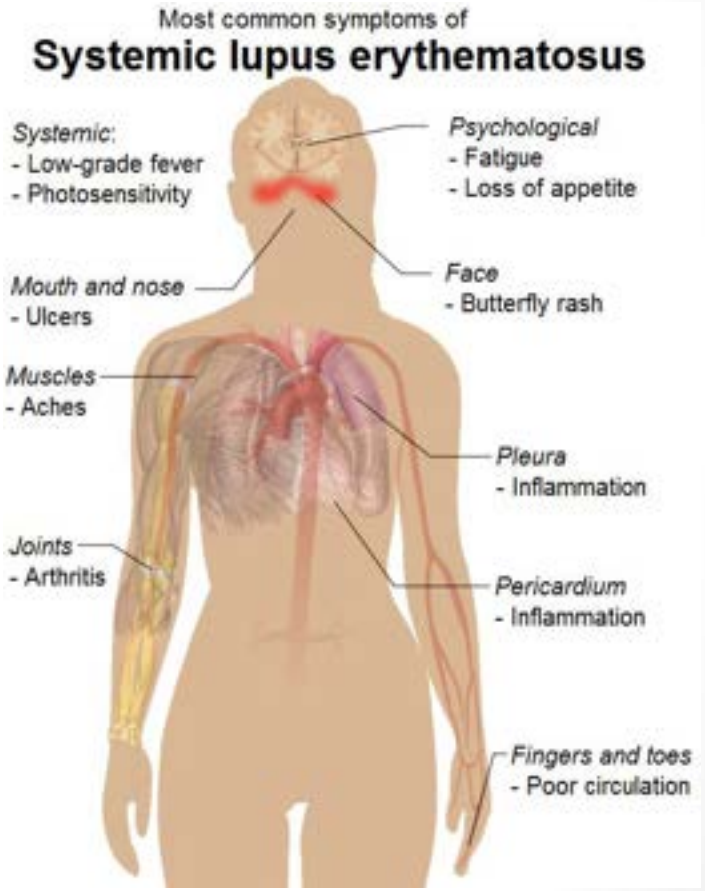
Medical Conditions Associated with Mood Symptoms

- Malignancies/Hematologic Diseases
  - Pancreatic carcinomas
  - Brain tumors
  - Toxoplasmosis
  - Anemia
  - Paraneoplastic effects of lung neoplasms



Medical Conditions Associated with Mood Symptoms

- <u>Autoimmune Disease</u>
  - Systemic Lupus Erythematosus
  - Rheumatoid arthritis
  - Fibromyalgia



Medical Conditions Associated with Mood Symptoms

<u>Infectious</u>

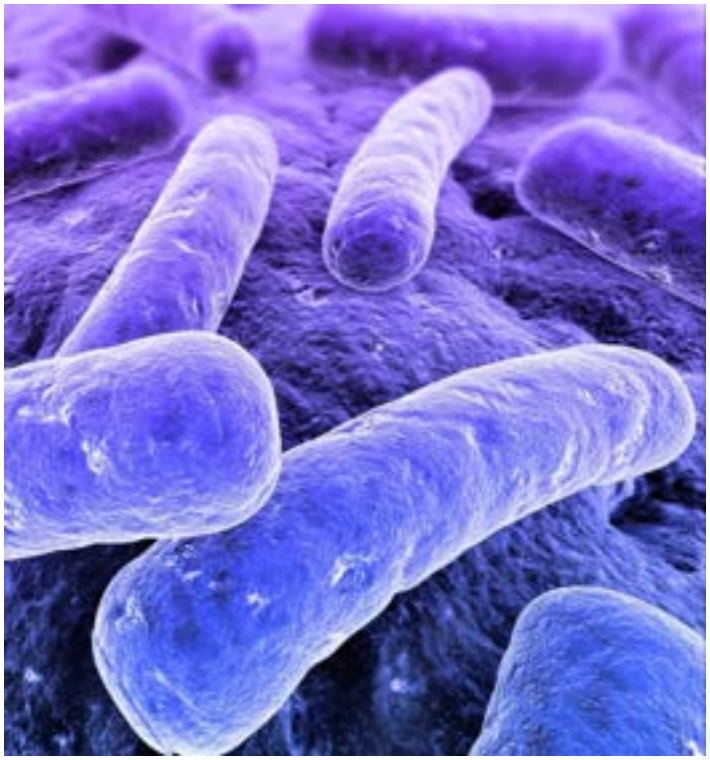
Toxoplasma Gondii

HIV

Lyme's Disease

Mononucleosis

…



Substance Abuse Mimicking a Mood Episode

- Acute Cocaine intoxication can look like mania or psychosis or an anxiety disorder
- After the high wears off, patients may appear depressed
- Bath Salt intoxication can look like mania, psychosis

Substance Abuse Mimicking a Mood Episode

- **Heroin** intoxication can look like depression or cognitive deficit
- **Heroin** withdrawal may look like an anxiety disorder or even hypomania
- **ETOH** withdrawal can look like an anxiety disorder, mania, hypomania or psychosis

Possible Depression Side Effect

- Steroids
- Chantix
- Seizure medications
- Antidepressants can destabilize mood in bipolar disorder
- Interferon
- B-blockers
- Accutane
- Calcium channel blockers
- Alcohol
- Barbiturates
- Statins
- Zovirax
- Some anticonvulsants
- Some anti-parkinson's drugs
- Benzodiazepines
- Hormone altering drugs
- Stimulants
- Proton pump inhibitors and h-2 blockers
- Anticholinergic drugs for GI

Medication Interactions

- Timing of new medication
- Timing of dose change
- Drug interactions

Major Depressive Episodes

can be a part of

- Major Depressive Disorder
- Bipolar Disorder (Types I & II)
- Schizoaffective D/O (BP & Dep type)

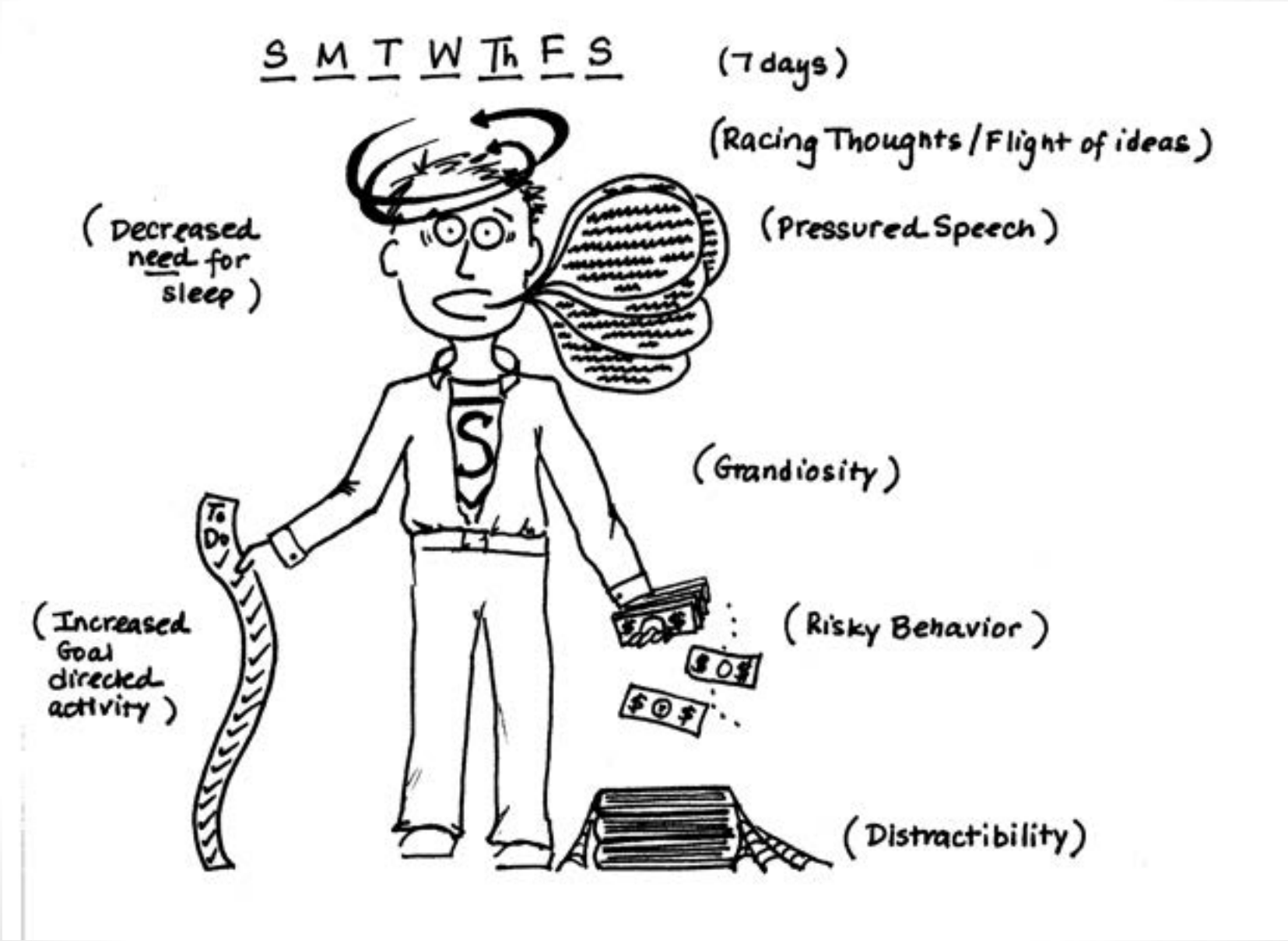
Red Flag: Bipolar Disorder

When you see a depressed patient, **Always** screen for past episodes of **Mania**

Manic Episode DSM-V Criteria

- At Least ***1 Week*** Duration
- ***Elevated*** *mood* (+3 other sx) or
- ***Irritable*** *mood* (+4 other sx)
- Additional Symptoms:
  - Decreased **NEED** for sleep
  - Grandiosity
  - Pressured speech
  - Increased goal directed activity
  - Flight of Ideas/Racing thoughts
  - Distractibility
  - Risky Behavior

Manic Episode Symptoms



Bipolar Depression V. Major Depressive Disorder (Unipolar Depression)

- Bipolar Depression is a **DIFFERENT** than Major Depressive Disorder
- Treatment for Bipolar Depression is NOT the same
- Bipolar Depression treatment: Quetiapine, Zyprexa/Prozac combination pill, Lurasidone (Latuda), Lithium, Lamotrigine, Depakote
- Do not give antidepressants for Bipolar Depression
- Antidepressants are harmful to patients with Bipolar Depression

Clinical Features	MDE in MDD	MDE in Bipolar D/O
Onset	later	earlier
Number of episodes	fewer	more
Gender ratio	F>M	F=M
family history	MDD & BP	MDD & BP
sleep	less	more
appetite	less	more
psychotic symptoms	less common	more common
suicide rates	15% (inpt hx), 7% (outpt hx)	10-19%
lithium response	less	better
antidepressant efficacy	better	worse

Non-medication strategies

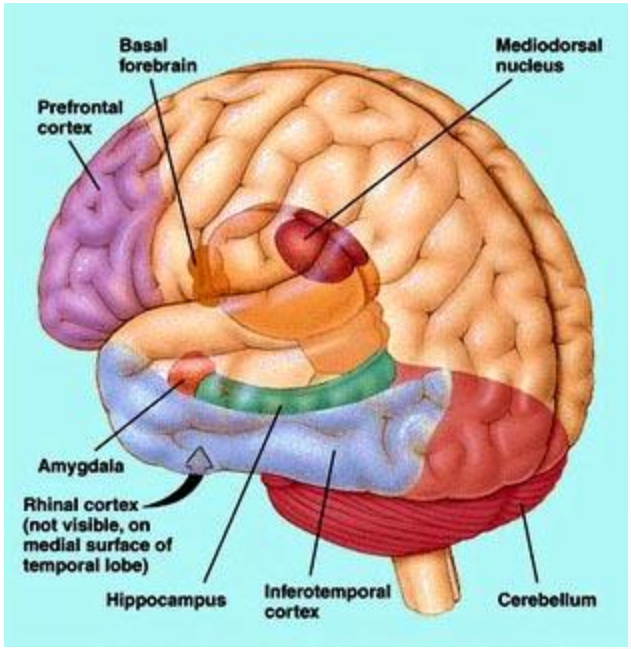
Psychotherapies

- Psychodynamic
- Cognitive
- Interpersonal
- Behavioral Activation
- EMDR
- Solution-focused
- Motivational
- Problem Solving Therapy

Biology of Depression

- Depression linked to decreased volume in prefrontal cortex and hippocampus

- Genomic Studies of Mood Disorders – The Brain a Muscle? Niculescu, Alexander Genome Biology 2005, 6:215.1-215.4



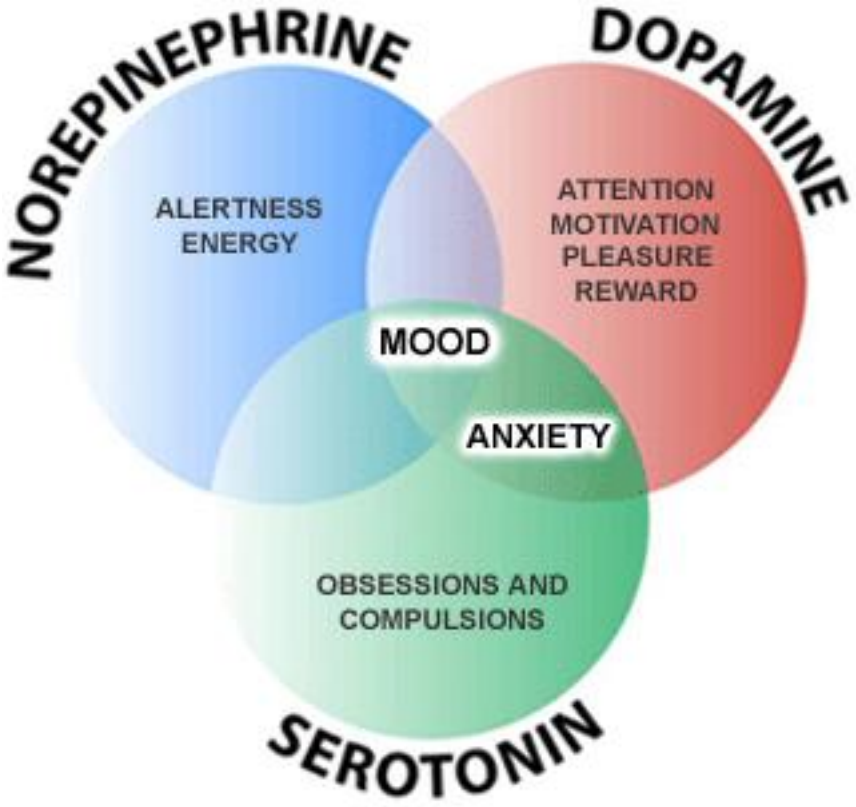
Biology of Depression

- Thyroid disorders are found in 5-10% of patients with depression
- Depressed patients may have a blunted Growth Hormone release in sleep
- Somatostatin may be decreased in the CSF of depressed patients and elevated in manic patients

Biology of Depression: Abnormal Sleep

- Most common symptoms of depression.
  - Longer to fall asleep
  - Awakenings
  - Changes in REM stage on EEG
  - Less restful sleep

Main Neurotransmitters Involved with MDD



- Acetylcholine
- Histamine
- Glutamate
- GABA
- NMDA
- Glycine

Medication Selection
&
Side Effects

Medication Management for MDD

- About 50% will show a reduction in symptoms
- This does not necessarily mean a remission of symptoms
- Rates of full remission are lower
- Effect of any antidepressant takes **4-6 weeks** minimum
- Problems do not go away, just feel less burdened
- More than one medication trial may be needed

Antidepressant Options

Selective Serotonin Reuptake Inhibitors (SSRIs)

Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs)

Mirtazapine

Dopamine/Norepinephrine Reuptake Inhibitors

Trazodone

Tricyclic Antidepressants (TCA)

Monoamine Oxidase Inhibitors (MAOIs)

Other (Vortioxetine, Vilazodone)

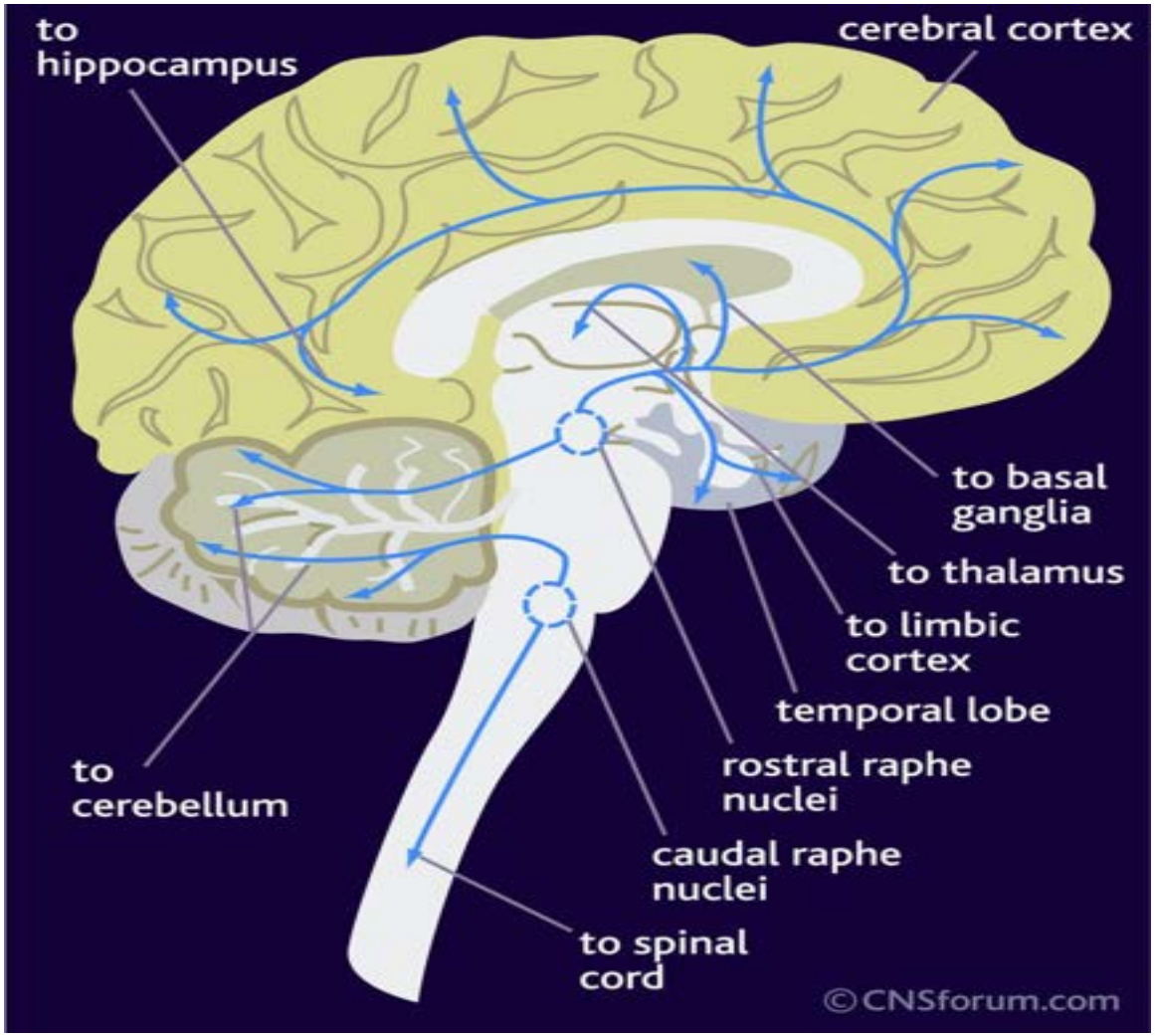
Antidepressant chart

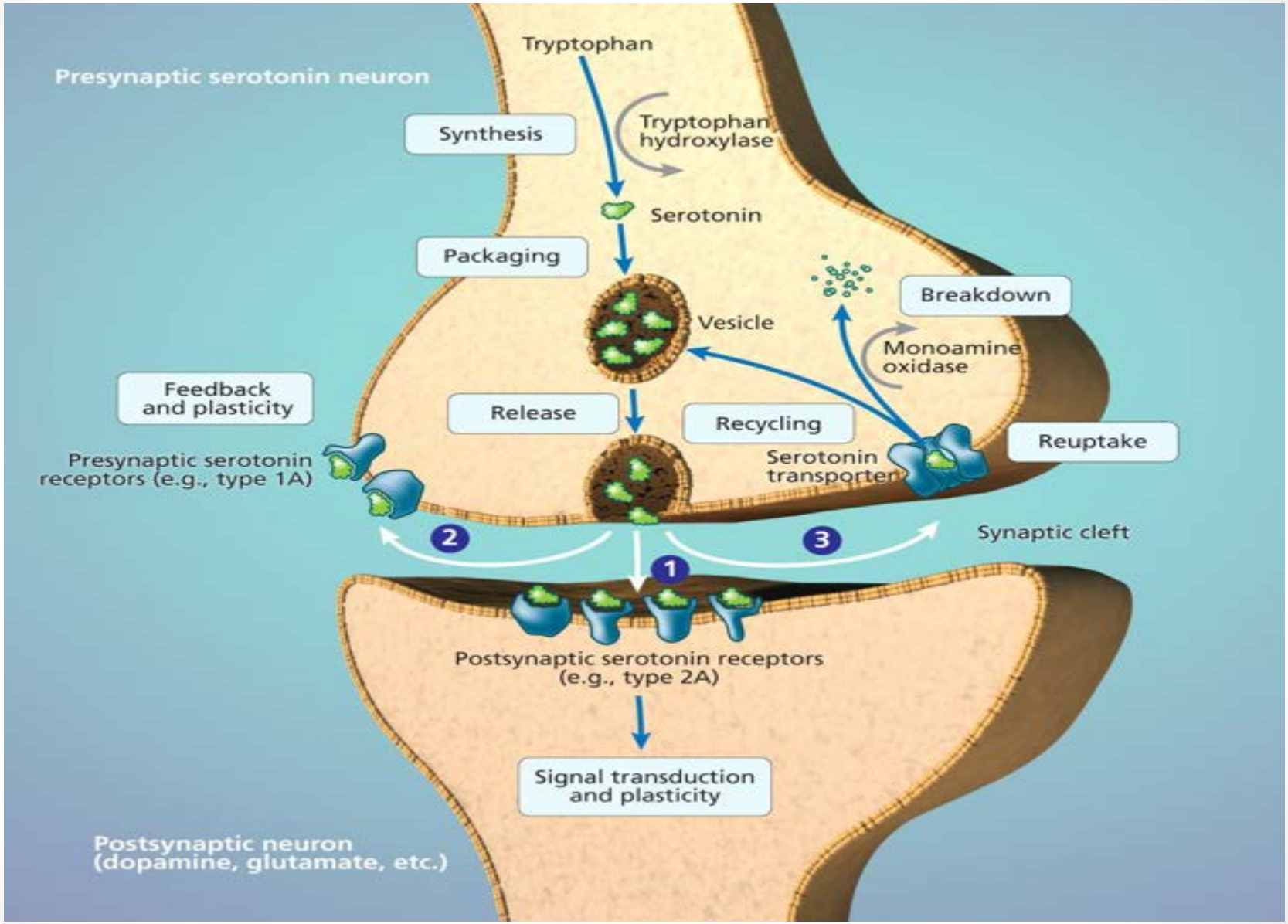
Neurotransmitter (Nt) or receptor (R)	MAOI	TCA	SSRI	bupropion	venlafaxine	duloxetine	trazodone	mirtazapine
Serotonin Nt	+	+	+		+	+	+	+
5HT-1 receptor	+	+	+		+	+	+	+
5HT-2 receptor	+	+	+		+	+	X	**X**
5HT-3 receptor	+	+	+		+	+	+	**X**
alpha-2 R								**X**
alpha-1 R	**X**	**X**					**X**	
Dopamine Nt	+			+				
Norepinephrine Nt	+	+		+	+	+		+
Histamine-1 R	**X**	**X**					**X**	**X**
Muscarinic (M-1) R	**X**	**X**						

Serotonin

- Natural neurotransmitter found in our bodies
- Plays major role in communication between neurons
- Thought to be decreased in patients with depression and anxiety
- Medications that boost the body's ability to make normal levels of serotonin can positively impact depression and anxiety
- May lead to various effects depending upon which serotonin receptor is stimulated

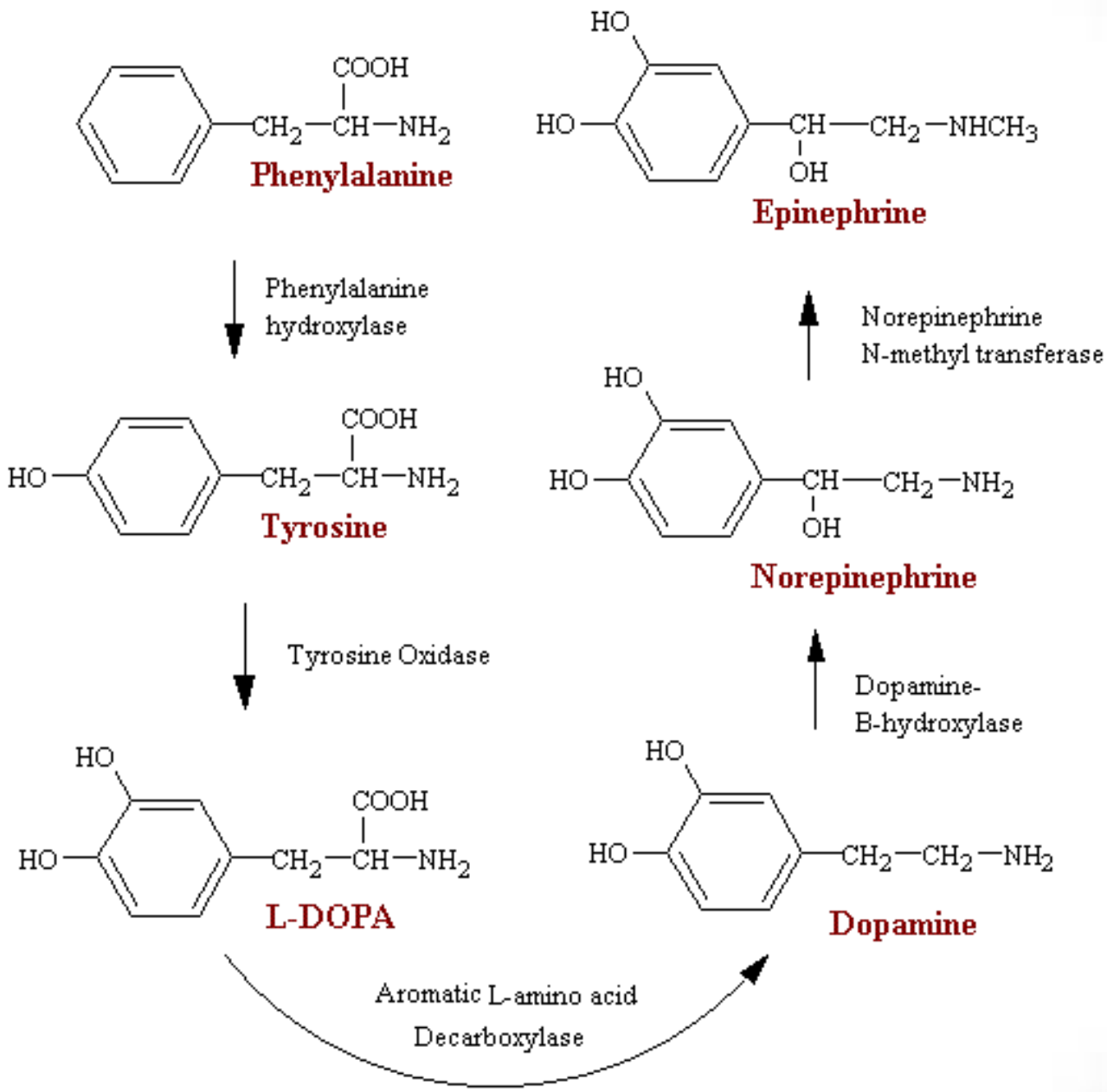
Serotonin


to hippocampus
cerebral cortex
to basal ganglia
to thalamus
to limbic cortex
temporal lobe
rostral raphe nuclei
caudal raphe nuclei
to spinal cord
to cerebellum
©CNSforum.com

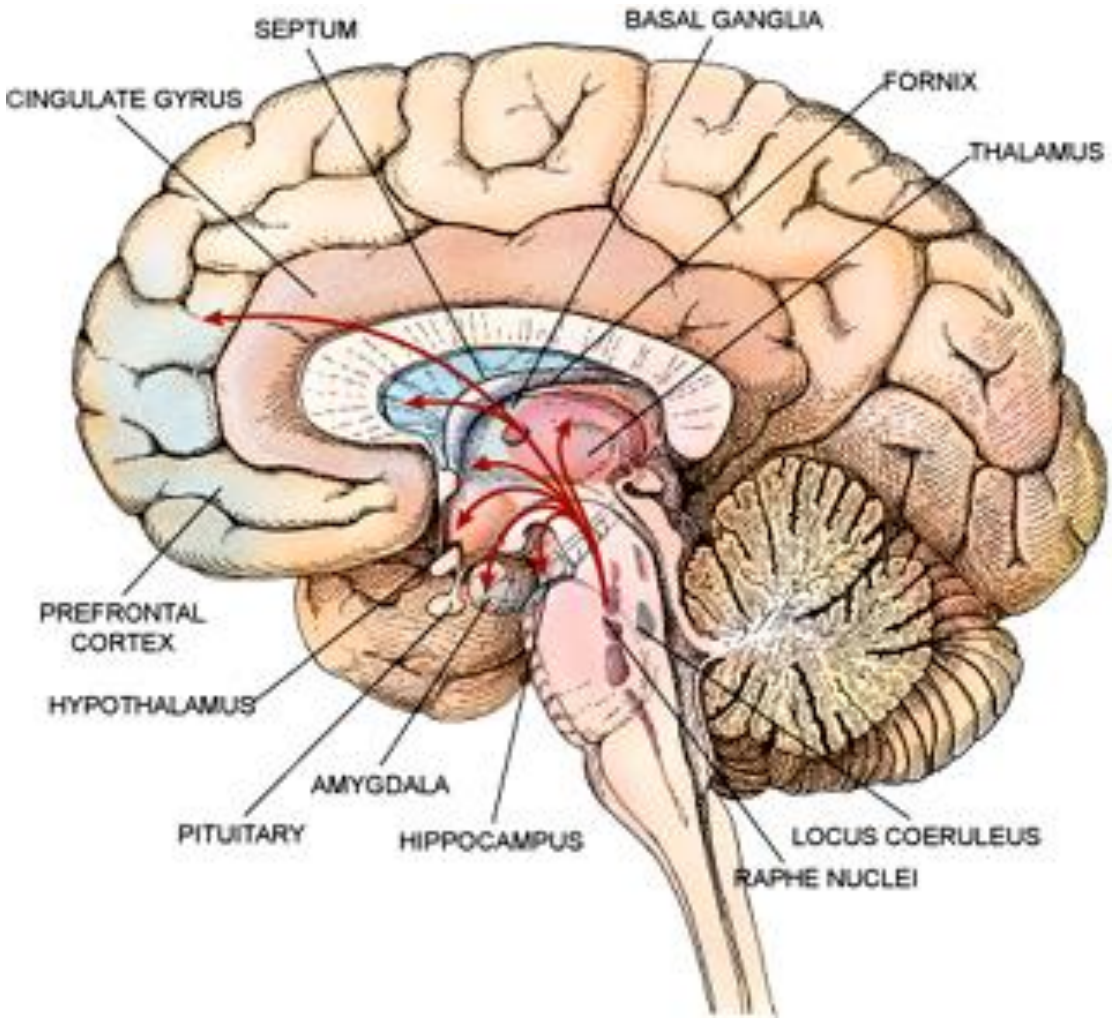

Presynaptic serotonin neuron
Tryptophan
Synthesis
Tryptophan hydroxylase
Serotonin
Packaging
Vesicle
Breakdown
Monoamine oxidase
Feedback and plasticity
Release
Recycling
Reuptake
Presynaptic serotonin receptors (e.g., type 1A)
Serotonin transporter
Synaptic cleft
1
2
3
Postsynaptic serotonin receptors (e.g., type 2A)
Signal transduction and plasticity
Postsynaptic neuron (dopamine, glutamate, etc.)

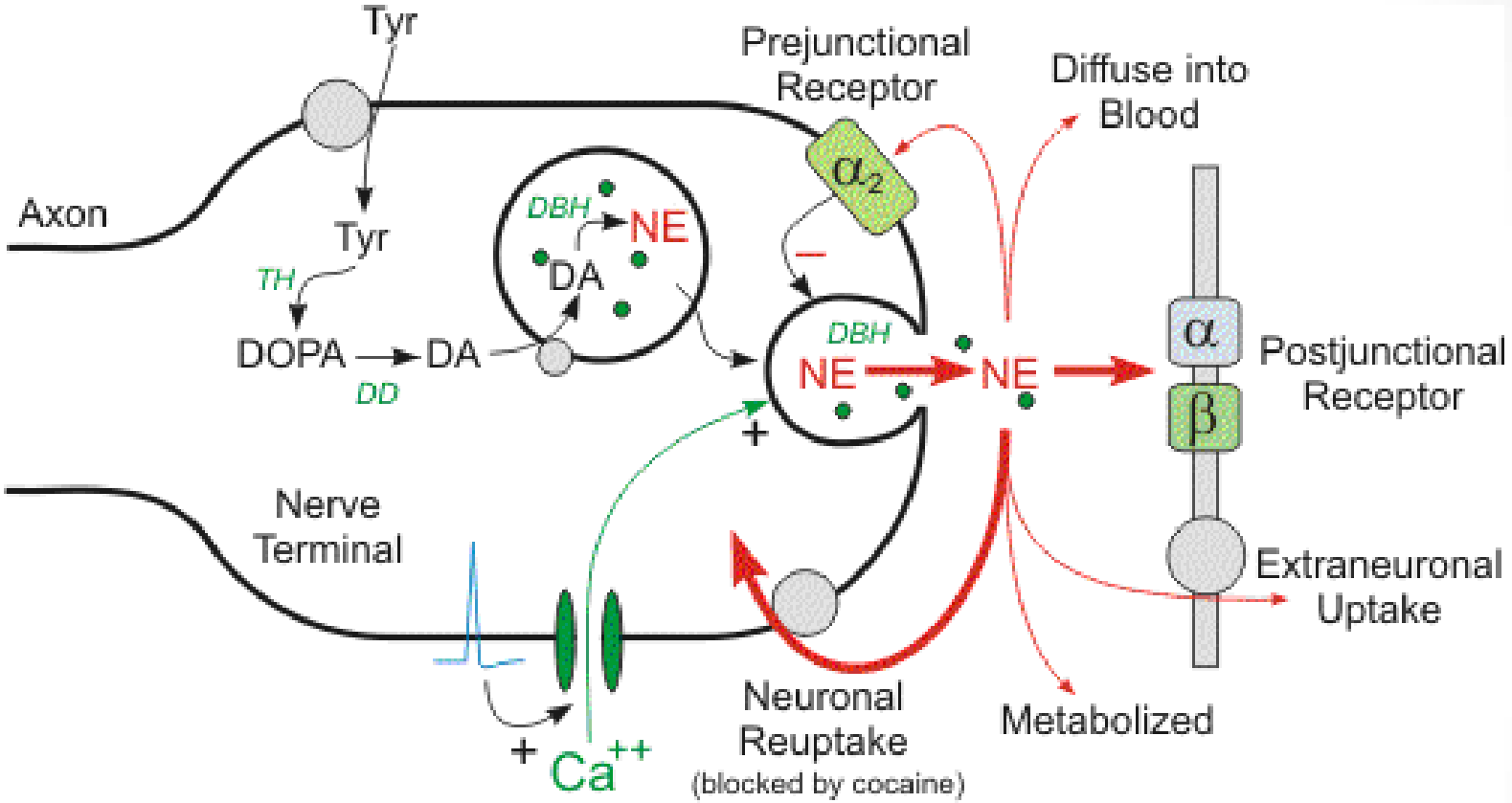
Norepinephrine

- Neurotransmitter found naturally in our bodies
- Thought to play a role in brain functioning, cardiovascular system & other roles
- Low levels may be present in depression and anxiety
- Too much NE may lead to high blood pressure, fast pulse, activation, anxiety


COOH
CH2—CH—NH2
Phenylalanine
HO
HO
CH—CH2—NHCH3
OH
Epinephrine
Phenylalanine
hydroxylase
Norepinephrine
N-methyl transferase
HO
COOH
HO
CH2—CH—NH2
Tyrosine
HO
HO
CH—CH2—NH2
OH
Norepinephrine
Tyrosine Oxidase
Dopamine-
B-hydroxylase
HO
COOH
HO
CH2—CH—NH2
L-DOPA
HO
HO
CH2—CH2—NH2
Dopamine
Aromatic L-amino acid
Decarboxylase

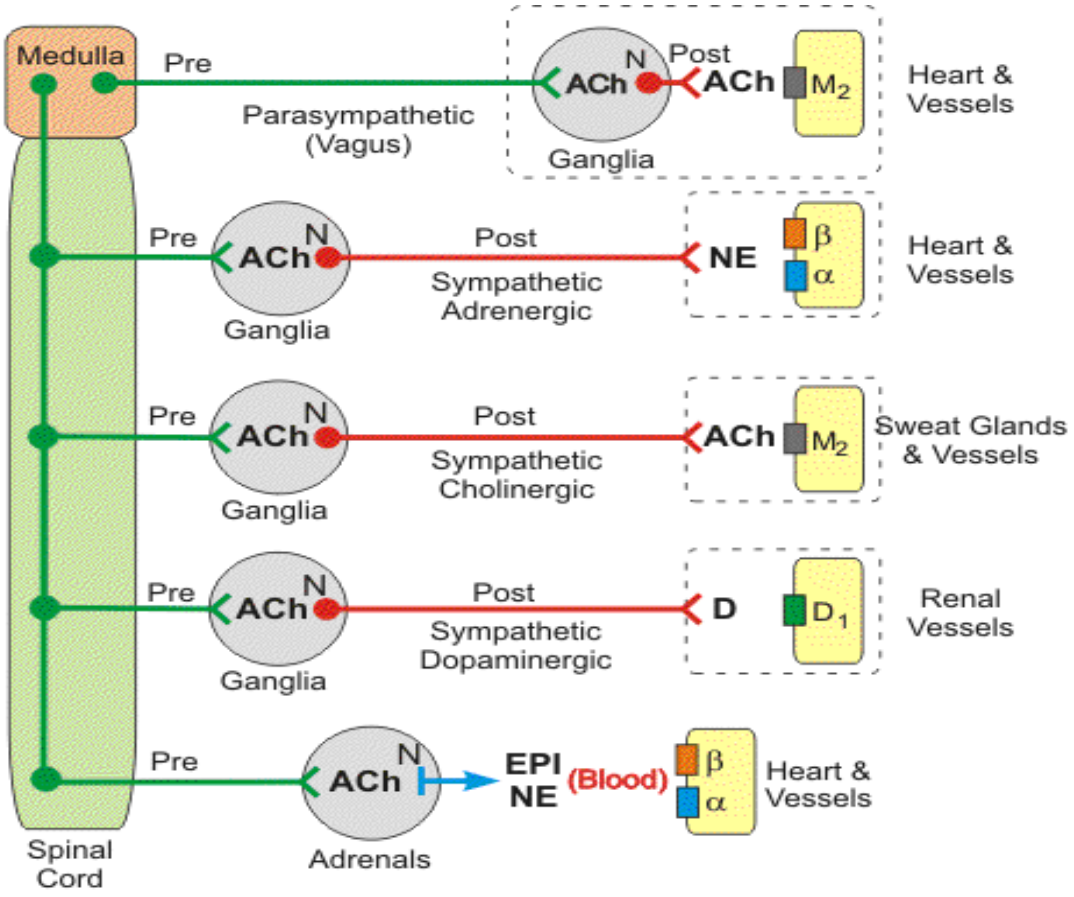
Norepinephrine Producing Cells





Tyr = tyrosine; TH = tyrosine hydroxylase; DD = DOPA decarboxylase;
DA = dopamine; DBH = dopamine β-hydroxylase; NE = norepinephrine

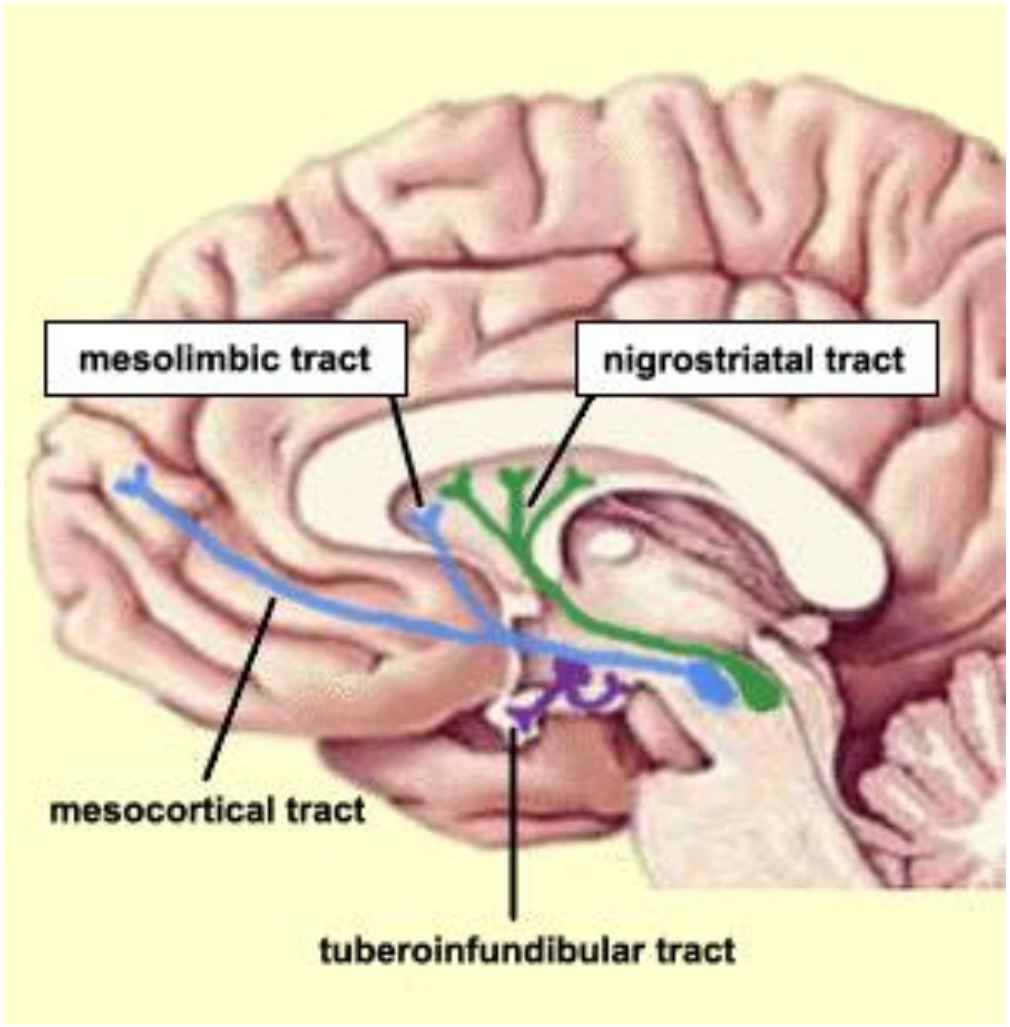
Norepinephrine's Role in the Body



CNS = central nervous system; Pre = preganglionic; Post = postganglionic;
ACh = acetylcholine; N = nicotinic receptor; NE = norepinephrine; EPI = epinephrine;
D = dopamine; M_2 = muscarinic receptor; β = β-adrenoceptor; α = α-adrenoceptor;
D_1 = dopaminergic receptor

Dopamine

- Natural neurotransmitter found in our bodies
- Involved with brain systems responsible for mood, psychosis, movement disorders, balance of prolactin, etc.
- Too much dopamine may lead to agitation & psychosis


mesolimbic tract
nigrostriatal tract
mesocortical tract
tuberoinfundibular tract

5HT (Serotonin) receptors

- + 5HT-1 Receptors: reduce symptoms of depression and anxiety
- +5HT-2 Receptors: agitation, akathisia, anxiety, insomnia, myoclonic jerks, sexual dysfunction
- +5HT-3 Receptors: Nausea, Gi Distress, headaches

Alpha 1 Receptors

- If you BLOCK Alpha-1 adrenergic receptors: orthostatic hypotension, reflex tachycardia, dizziness

Alpha 2 receptors

- Normally, alpha-2 receptors inhibit the release of NE and Serotonin
- **Block** the Alpha-2 Receptors: increase NE and Serotonin

Histamine Receptors

- **Block** histaminic (H1) receptors: sedation and weight gain

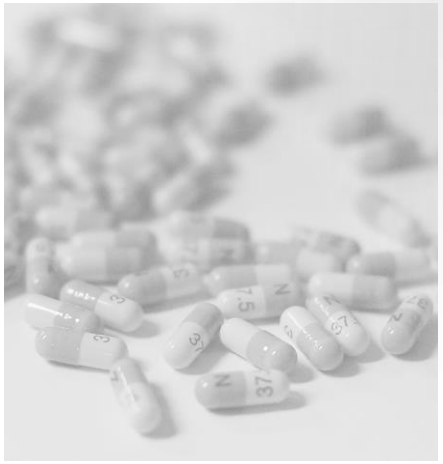
M1 receptors

- **Block** the Muscarinic (M1) receptors: (=anticholinergic/antimuscarinic effects)
  - blurred vision
    - dry mouth
    - Fast heart rate
    - Constipation
    - Trouble getting urine out
    - Confusion/memory impairment
- Geriatric patients are more sensitive to anticholinergic side effects

Antidepressant chart

Neurotransmitter (Nt) or receptor (R)	MAOI	TCA	SSRI	bupropion	venlafaxine	duloxetine	trazodone	mirtazapine
Serotonin Nt	+	+	+		+	+	+	+
5HT-1 receptor	+	+	+		+	+	+	+
5HT-2 receptor	+	+	+		+	+	X	**X**
5HT-3 receptor	+	+	+		+	+	+	**X**
alpha-2 R								**X**
alpha-1 R	**X**	**X**					**X**	
Dopamine Nt	+			+				
Norepinephrine Nt	+	+		+	+	+		+
Histamine-1 R	**X**	**X**					**X**	**X**
Muscarinic (M-1) R	**X**	**X**						

MAOI



- Consider as 4th line option
- Many side effects
- Must adhere to strict food restrictions to prevent hypertensive crisis
- Many drug-drug interactions
- Can be very effective for some patients
- Newer versions in patch form
- Can be lethal in overdose
- Now a transdermal version available

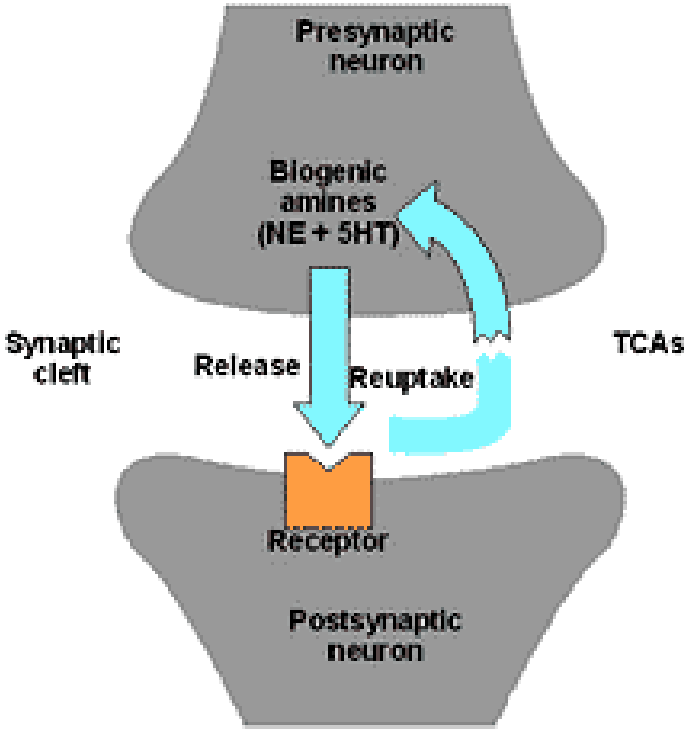
Antidepressant chart

Neurotransmitter (Nt) or receptor (R)	MAOI	TCA	SSRI	bupropion	venlafaxine	duloxetine	trazodone	mirtazapine
Serotonin Nt	+	+	+		+	+	+	+
5HT-1 receptor	+	+	+		+	+	+	+
5HT-2 receptor	+	+	+		+	+	X	**X**
5HT-3 receptor	+	+	+		+	+	+	**X**
alpha-2 R								**X**
alpha-1 R	**X**	**X**					**X**	
Dopamine Nt	+			+				
Norepinephrine Nt	+	+		+	+	+		+
Histamine-1 R	**X**	**X**					**X**	**X**
Muscarinic (M-1) R	**X**	**X**						

TCAs

- Usually not first line option secondary to side effect profile
- Many possible drug-drug interactions
- Can be lethal in overdose
- Used in lower doses for pain management

Mechanism of action of tricyclic antidepressants



TCAs

- Cochrane review by Guaiana, Barbui, Hotopf 2007
- Included 194 Randomized controlled studies
- Amitriptyline for depression compared with other TCAs and newer antidepressants
- Amitriptyline was at least as effective, perhaps slightly more effective

Antidepressant chart

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Serotonin Nt	+	+	+		+	+	+	+
5HT-1 receptor	+	+	+		+	+	+	+
5HT-2 receptor	+	+	+		+	+	X	**X**
5HT-3 receptor	+	+	+		+	+	+	**X**
alpha-2 R								**X**
alpha-1 R	**X**	**X**					**X**	
Dopamine Nt	+			+				
Norepinephrine Nt	+	+		+	+	+		+
Histamine-1 R	**X**	**X**					**X**	**X**
Muscarinic (M-1) R	**X**	**X**						

SSRIs

- First line for treatment of depression and anxiety
- Generally greater tolerability overall
- 50% of patients will have symptom improvement with SSRI
- Ok to try another if one doesn't work
- Monitor for sexual side effects, initial increase (x 2 weeks) in anxiety, GI sx, headaches, akathisia

SSRIs

- Fluoxetine (Prozac) – longest half life
- Fluvoxamine (Luvox)
- Sertraline (Zoloft)
- Paroxetine (Paxil) – shortest half life, more sedating, some weight gain
- Citalopram (Celexa) – risk of QTc prolongation
- Escitalopram (Lexapro)

Antidepressant chart

Neurotransmitter (Nt) or receptor (R)	MAOI	TCA	SSRI	bupropion	venlafaxine	duloxetine	trazodone	mirtazapine
Serotonin Nt	+	+	+		+	+	+	+
5HT-1 receptor	+	+	+		+	+	+	+
5HT-2 receptor	+	+	+		+	+	X	**X**
5HT-3 receptor	+	+	+		+	+	+	**X**
alpha-2 R								**X**
alpha-1 R	**X**	**X**					**X**	
Dopamine Nt	+			+				
Norepinephrine Nt	+	+		+	+	+		+
Histamine-1 R	**X**	**X**					**X**	**X**
Muscarinic (M-1) R	**X**	**X**						

Bupropion (Wellbutrin)

- Tends to be more activating
- May be a good option for patients with low energy, increased appetite
- Can cause weight loss, increased anxiety, rare seizure risk
- Also shown to be helpful for smoking cessation
- Contraindicated in people with bulimia and seizure disorders
- Dose range 100-450mg (increased seizure risk above 400mg)
- Start at 100mg daily x 4 days then increase to 200mg daily
- Choose extended release for less side effects

Antidepressant chart

Neurotransmitter (Nt) or receptor (R)	MAOI	TCA	SSRI	bupropion	venlafaxine	duloxetine	trazodone	mirtazapine
Serotonin Nt	+	+	+		+	+	+	+
5HT-1 receptor	+	+	+		+	+	+	+
5HT-2 receptor	+	+	+		+	+	X	**X**
5HT-3 receptor	+	+	+		+	+	+	**X**
alpha-2 R								**X**
alpha-1 R	**X**	**X**					**X**	
Dopamine Nt	+			+				
Norepinephrine Nt	+	+		+	+	+		+
Histamine-1 R	**X**	**X**					**X**	**X**
Muscarinic (M-1) R	**X**	**X**						

Venlafaxine (Effexor)

- Considered a “clean TCA”
- Same mechanism of action as TCA without all of the additional side effects
- Can cause a slight increase in blood pressure
- Helpful for depression and anxiety

Venlafaxine (Effexor)

- Initial starting dose 37.5mg or 75mg, usual effective dose 150-375mg
- Watch for sedation and withdrawal
- Extended release less side effects
- Some people are very sensitive to this medication, so I tend to start low
- Acts as an SSRI at lower doses

Duloxetine (Cymbalta)

- Same mechanism of action as venlafaxine
- May help with pain as well as depression
- Doesn’t have the same warnings about high blood pressure as venlafaxine
- Initial dose 20mg twice daily, max dose 90mg daily
- Can have severe withdrawal symptoms

Antidepressant chart

Neurotransmitter (Nt) or receptor (R)	MAOI	TCA	SSRI	bupropion	venlafaxine	duloxetine	trazodone	mirtazapine
Serotonin Nt	+	+	+		+	+	+	+
5HT-1 receptor	+	+	+		+	+	+	+
5HT-2 receptor	+	+	+		+	+	X	**X**
5HT-3 receptor	+	+	+		+	+	+	**X**
alpha-2 R								**X**
alpha-1 R	**X**	**X**					**X**	
Dopamine Nt	+			+				
Norepinephrine Nt	+	+		+	+	+		+
Histamine-1 R	**X**	**X**					**X**	**X**
Muscarinic (M-1) R	**X**	**X**						

Trazodone

- Usually too sedating at regular doses for depression
- Can use lower doses to help with insomnia
- Rare risk of priapism (1/6000)
- DOCUMENT RISK of PRIAPISM
- Starting dose 25-50mg (usual dose range 25-200mg, max dose for depression is 500mg)
- Watch for feeling “hung over” the next morning

Antidepressant chart

Neurotransmitter (Nt) or receptor (R)	MAOI	TCA	SSRI	bupropion	venlafaxine	duloxetine	trazodone	mirtazapine
Serotonin Nt	+	+	+		+	+	+	+
5HT-1 receptor	+	+	+		+	+	+	+
5HT-2 receptor	+	+	+		+	+	X	**X**
5HT-3 receptor	+	+	+		+	+	+	**X**
alpha-2 R								**X**
alpha-1 R	**X**	**X**					**X**	
Dopamine Nt	+			+				
Norepinephrine Nt	+	+		+	+	+		+
Histamine-1 R	**X**	**X**					**X**	**X**
Muscarinic (M-1) R	**X**	**X**						

Mirtazapine

- May be a good option for patients with low appetite, weight loss and insomnia
- Monitor for weight gain & sedation
- Give at bedtime
- More sedating at lower doses
- Less GI sx, headaches, anxiety or sexual dysfunction
- Starting dose: 7.5mg or 15mg (max dose 60mg)

Antidepressant chart

Neurotransmitter (Nt) or receptor (R)	MAOI	TCA	SSRI	bupropion	venlafaxine	duloxetine	trazodone	mirtazapine
Serotonin Nt	+	+	+		+	+	+	+
5HT-1 receptor	+	+	+		+	+	+	+
5HT-2 receptor	+	+	+		+	+	X	**X**
5HT-3 receptor	+	+	+		+	+	+	**X**
alpha-2 R								**X**
alpha-1 R	**X**	**X**					**X**	
Dopamine Nt	+			+				
Norepinephrine Nt	+	+		+	+	+		+
Histamine-1 R	**X**	**X**					**X**	**X**
Muscarinic (M-1) R	**X**	**X**						

Vilazodone (Viibryd)

- 5HT (serotonin) reuptake inhibition
- 5HT1A receptor – partly stimulates this
- Newer antidepressant
- Less sexual side effects
- Watch for withdrawal, taper off of it
- Expensive
- Dose range 10-40mg daily; start at 10mg daily x 7 days then increase to 20mg daily

Vortioxetine (Brintellix)

- Serotonin reuptake inhibitor
- **5HT1a R** stimulation (may boost serotonin and dopamine downstream)
- **5HT1B R –** partly stimulates (may lead to increased Ach and histamine – possible procognitive actions)
- **5HT1D R** - blocks
- **5HT7 R** blocks (may prevent insomnia sometimes associated with SSRIs, via GABA in various parts of brain)
- **5HT3** blocks (more tolerable, less nausea, less GI)

Vortioxetine (Brintellix)

- Start at 5mg or 10mg
- Max dose is 20mg daily

Antidepressant Withdrawal Syndrome

- Feels like the Flu, mood lability, more anxiety, strange neuro symptoms (zap down the arm, “floaty” feeling in the head
- Usually resolves by several days, but can last up to 2 weeks
- Meds with shorter half life have greater risk of causing withdrawal if abruptly discontinued
- Fluoxetine least risk for withdrawal syndrome
- Paxil, Venlafaxine, duloxetine, Desvenlafaxine
  - high risk of withdrawal

Depression Treatment

- APA guidelines for adults after **complete remission** in the acute phase...continue with the same meds at the same dose for 4-9 months along with clinical visits every 1-3 months

- Pediatric guidelines are similar to these adult guidelines

- Though ped guidelines recommend continuing treatment for 1 yr and monitoring monthly for 6 months after full remission

(Wagner)

Depression Treatment not working?

- Considerations
  - Adherence to medication?
  - Side effects not tolerable?
  - Duration of trial with medication
  - Adequate dosing?
  - Other medical problems complicating clinical picture?
  - Engaged in therapy?
  - New stressors impacting mood?
  - Is it time to switch to a new medication?
  - 2 SSRI trials then move on to alternative mechanism for antidepressant

"Of course you feel great. These things are loaded with antidepressants."


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ANDERSON
"I think we should cut back on my antidepressant.
I watched 'Old Yeller' and it was hysterical."

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