

Dual Diagnosis: Substance Abuse and Mental Illness



and a review of the
major **PSYCHIATRIC
MEDICINES**

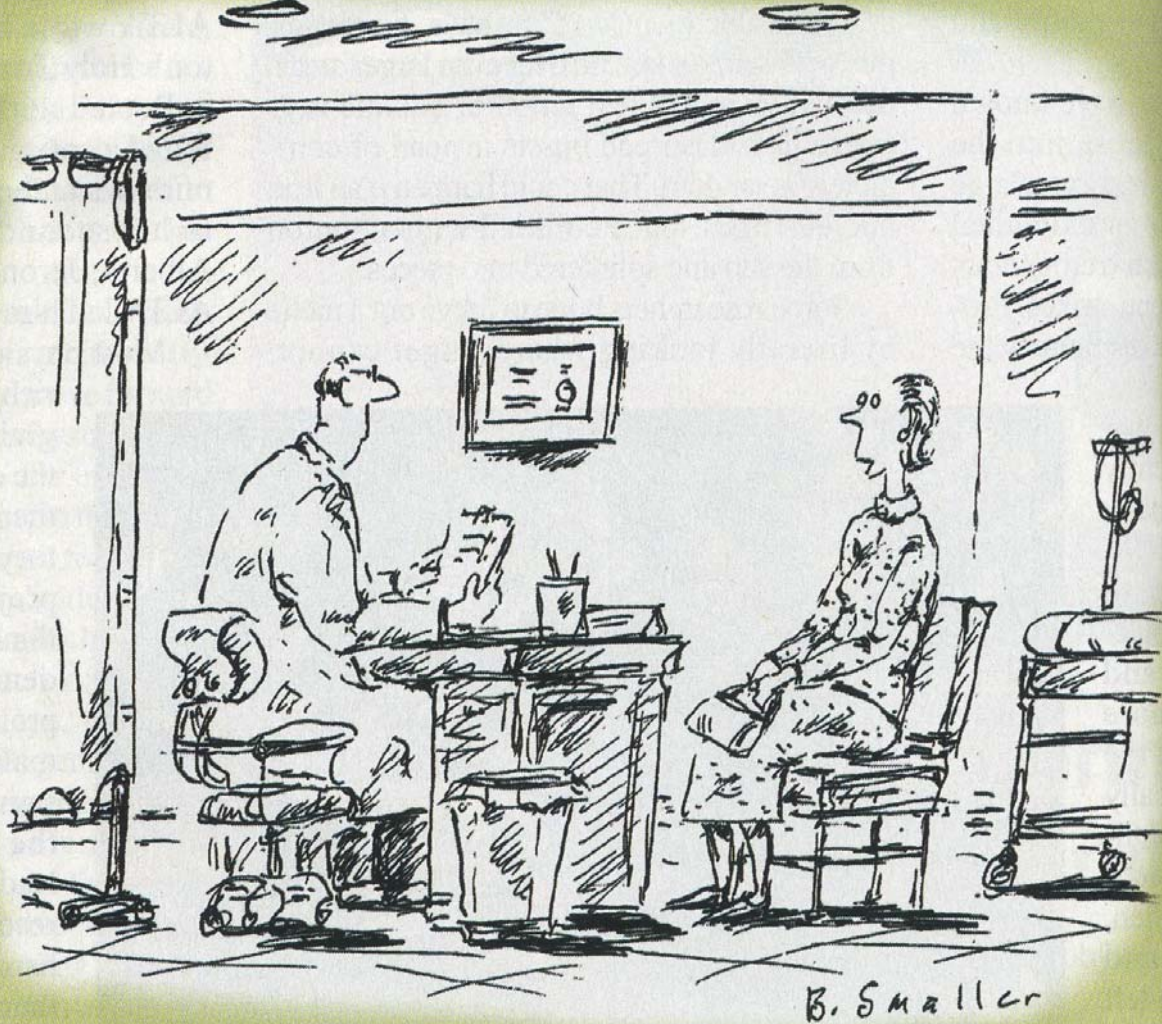
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Addiction Medicine Division

Special appreciation to Gary L. Viale, Pharm D., BCPP, FCSHP



“I think the dosage needs adjusting. I’m not nearly as happy as the people in the ads.”

Psychopathology

- Psychopathology refers to problematic patterns of thought, feeling, and behavior
 - Disrupted functioning at home, work, and in the person's social life
 - Patterns that cause distress in the person or in others
 - Psychopathology literally means sickness of the mind
- Psychopathology varies between and within cultures

Psychological Disorders Commonly Seen in Addictions Treatment

- Schizophrenia
- Mood disorders
 - Bipolar disorder (manic depression)
 - Depressive disorders
- Anxiety disorders

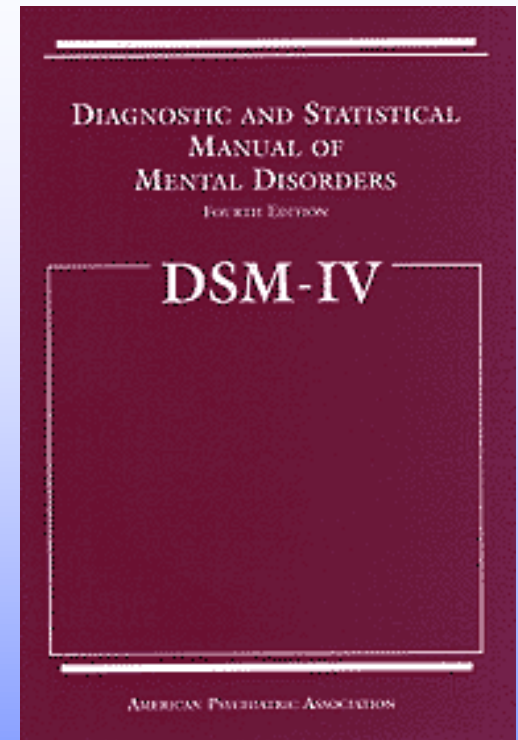
Descriptive Diagnosis

- Abnormality is reflected in discrete symptoms
- As in physical illness, symptoms fall into discrete clusters called syndromes
- Syndromes are assumed to have discrete causes and are to be treated using different therapies

DSM-IV

- The American Psychiatric Association published a diagnostic manual that attempts to classify signs and symptoms into syndromes
 - Signs are observable phenomena (temperature)
 - Symptoms are reports from patients (headache)

- The current edition is termed the DSM-IV
 - The DSM-IV uses a multi-axial system of diagnosis
 - The axes cover symptoms as well as medical conditions, stress, and current level of function



The Axes of DSM-IV

Axis Description

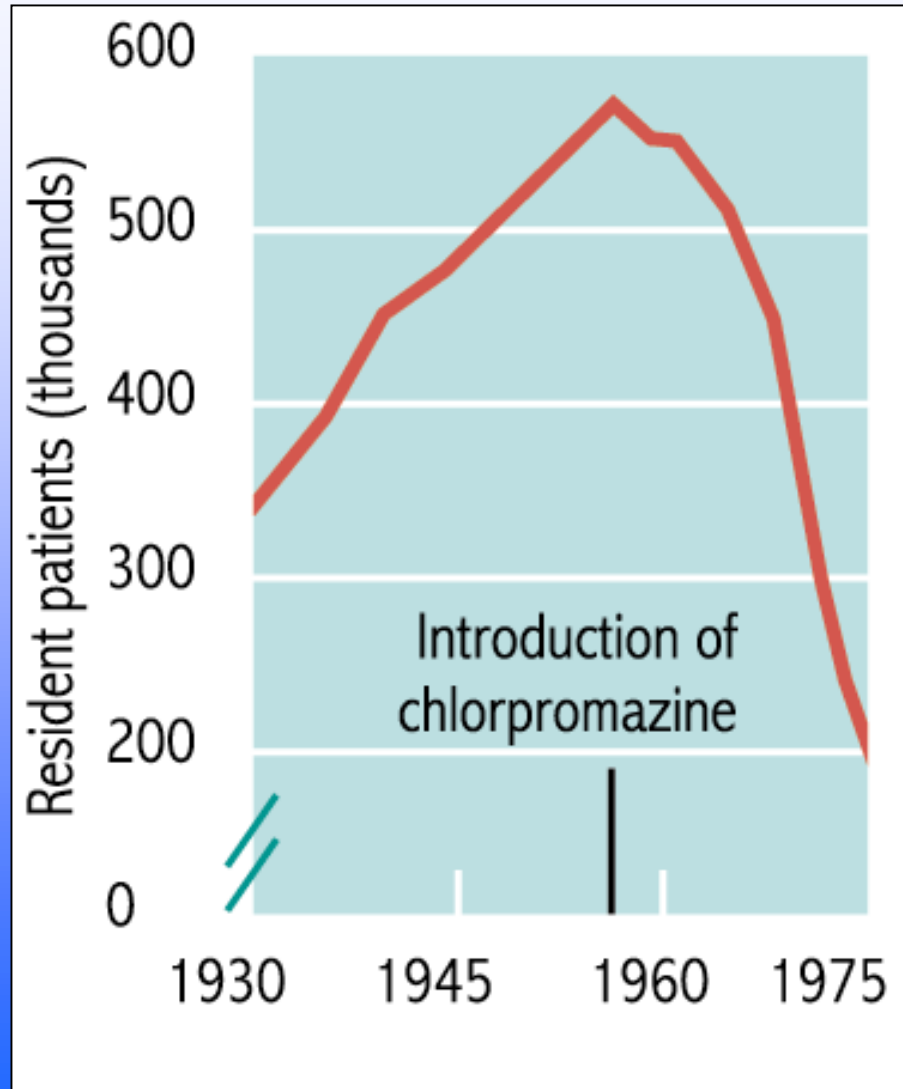
- I Presenting Symptoms causing distress
 - II How the person carries themselves throughout their life
 - III Medical conditions that may be relevant to understanding or treating a psychological disorder
 - IV Psychosocial and environmental problems
 - V Global assessment of functioning (GAF)
-

(Source: DSM-IV, American Psychiatric Association, 1994)

Pharmacotherapy

- Psychotropic medications are drugs that act on the brain to alter mental function
- Prior to 1956, schizophrenia was virtually untreatable with many patients confined for life in mental hospitals
 - Chlorpromazine (Thorazine) was found to reduce severity of psychotic thought, allowing people to live outside of mental institutions

Impact of Chlorpromazine on Institutionalization



Psychotropic Mechanisms of Action

- Psychotropic drugs can alter behavior via:
 - An interaction with neurotransmitters in brain
 - Some release specific transmitters
 - Some block the reuptake of transmitters
 - Some interact with postsynaptic receptors
 - Some may act within neuron cells
 - A placebo effect
 - Subjects believe in the efficacy of the drug and show an actual change in function (analgesia or relief from pain shows moderate placebo effects)

Some Diagnoses Influenced By Serotonin Dysfunction

**Eating/Sexual
Disorders**

Appetitive/Dysfunctionitive

Panic Disorder

Anxiety

Obsessionality

OCD/PTSD

Serotonin

Mood

**Major
Depression**

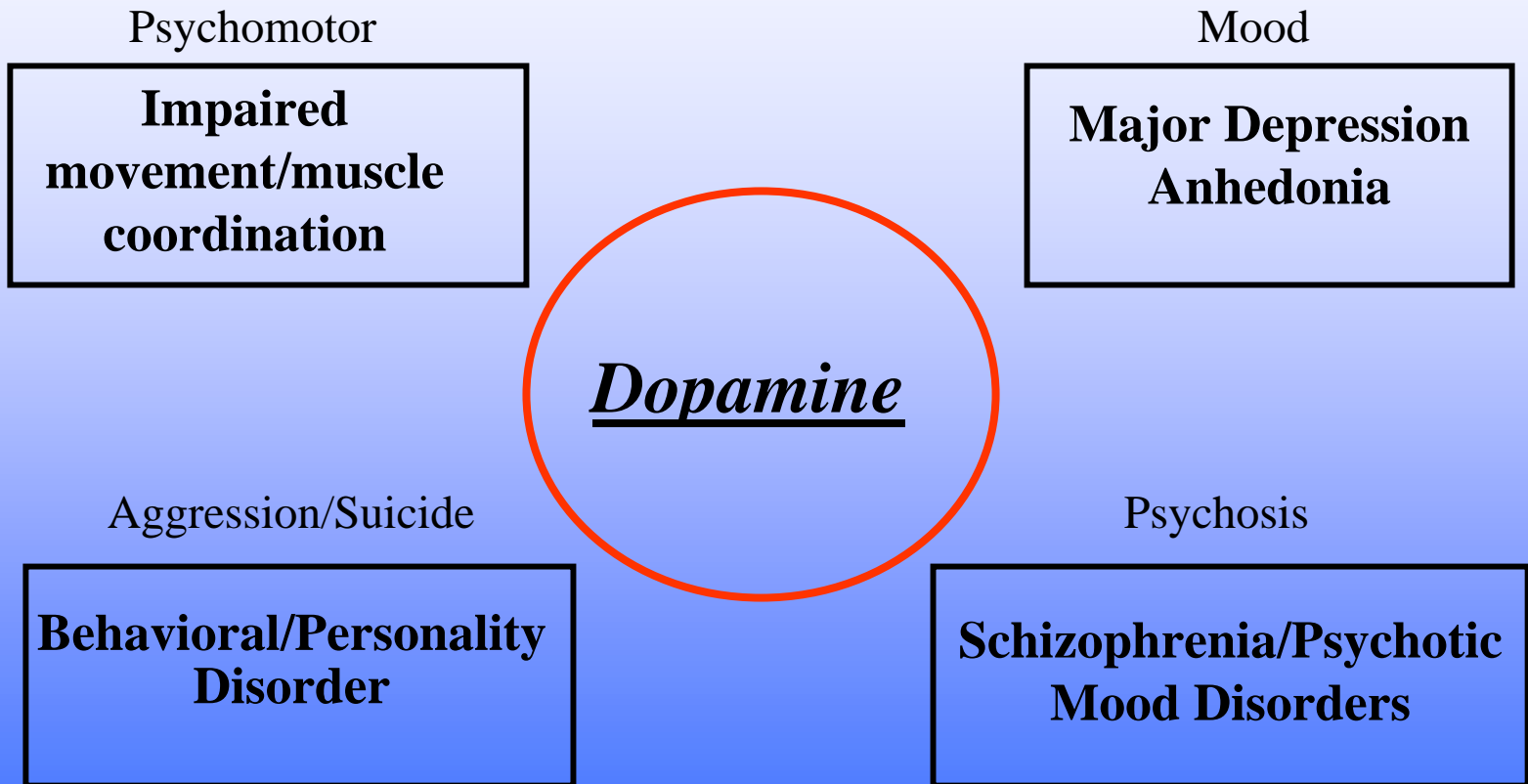
Aggression/Suicide

**Behavioral/Personality
Disorders**

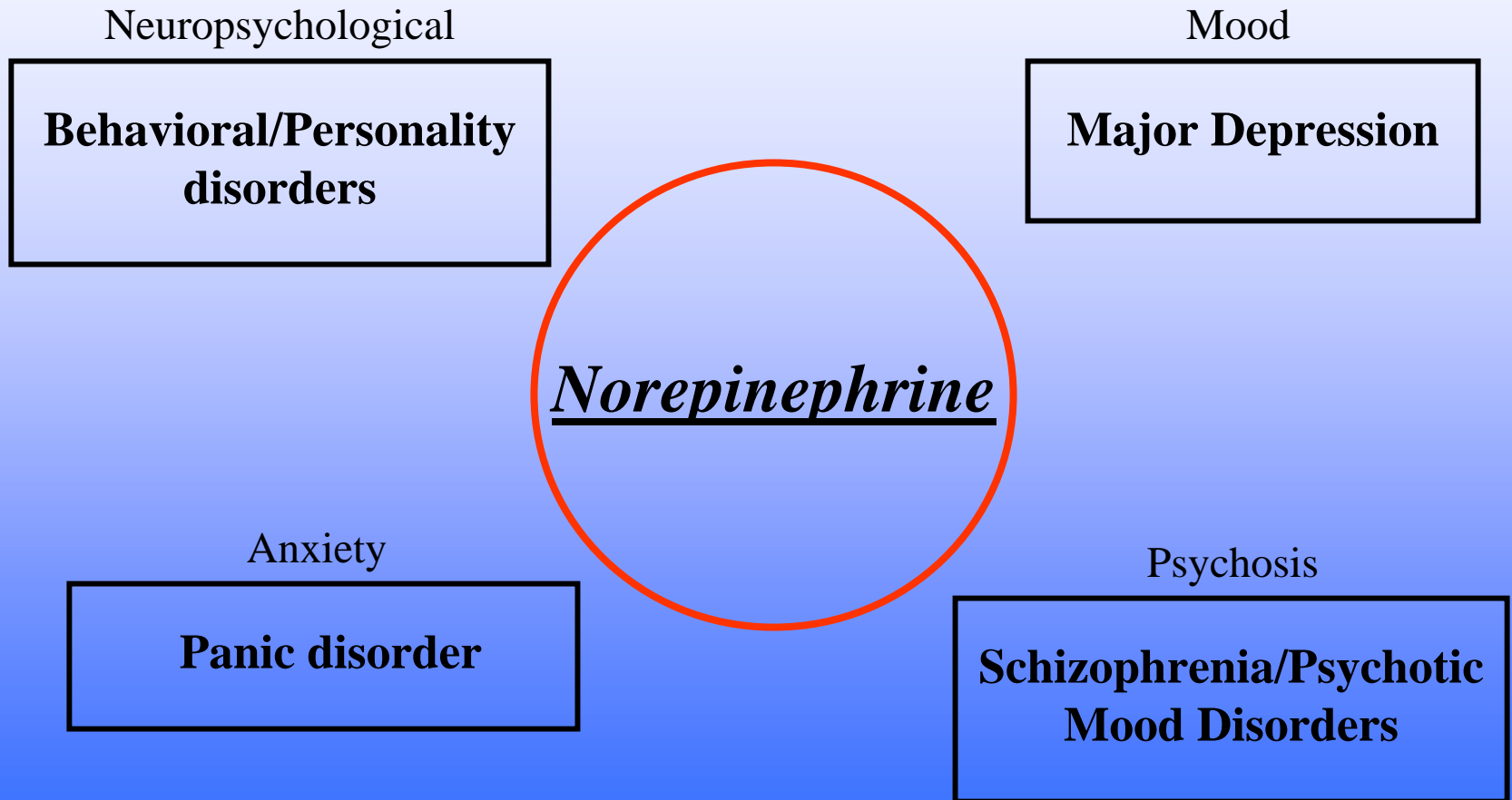
Psychosis

**Schizophrenia/Psychotic
Mood Disorders**

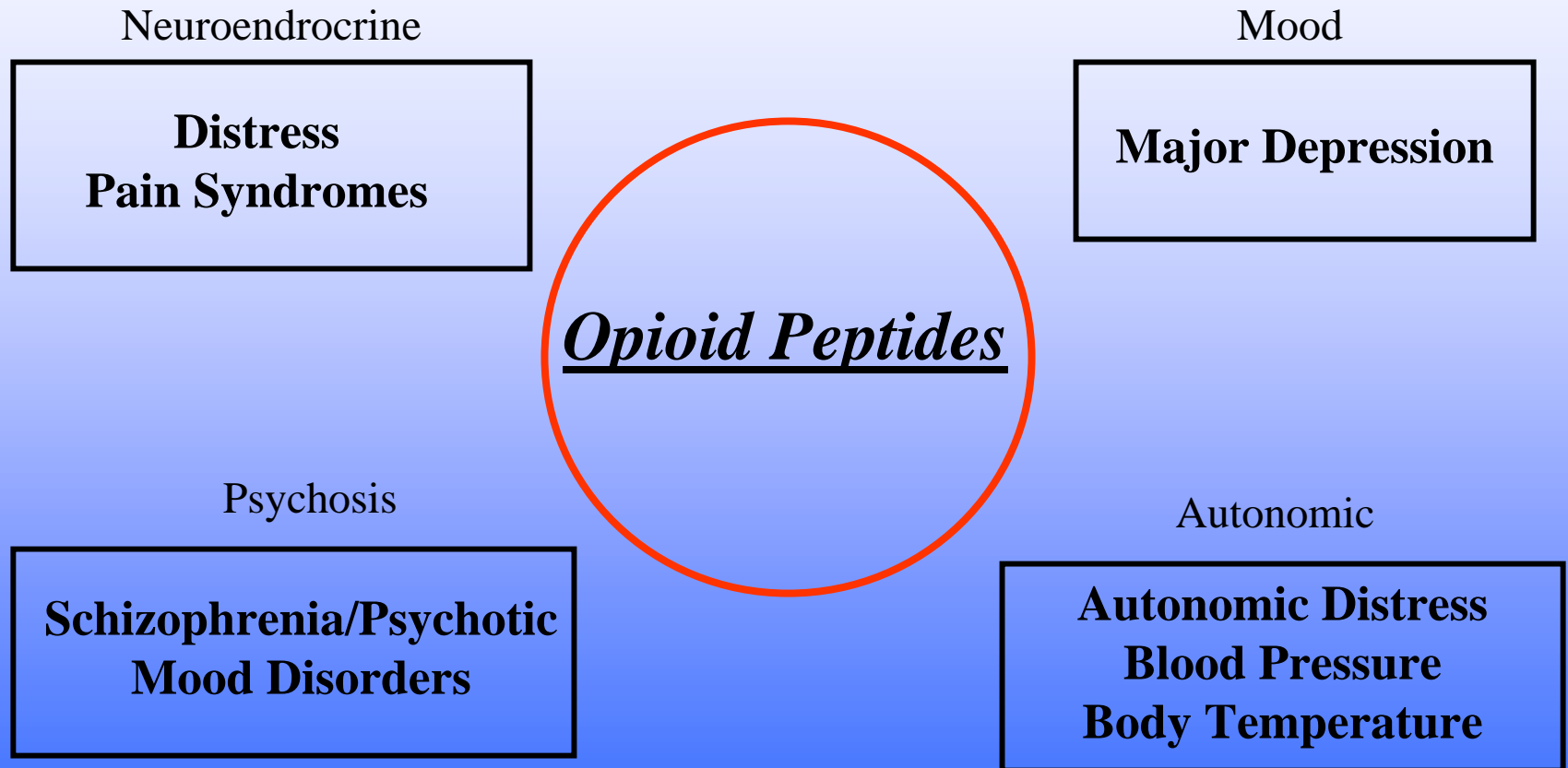
Some Diagnoses Influenced By Dopamine Dysfunction



Some Diagnoses Influenced By Norepinephrine Dysfunction

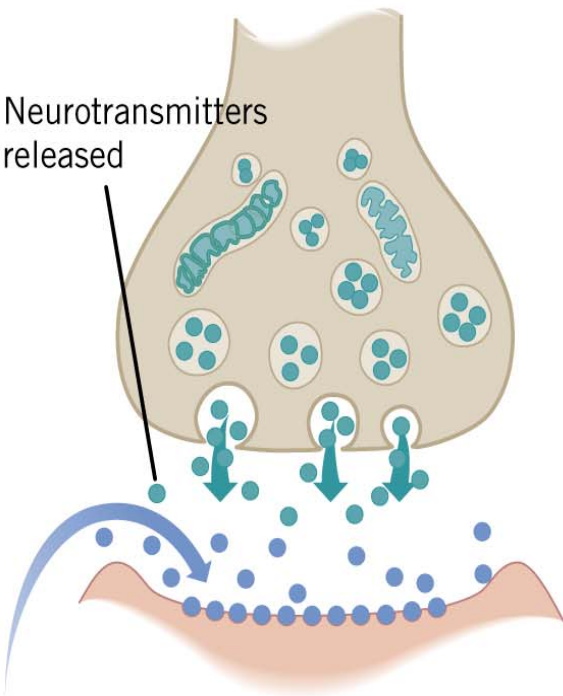


Some Diagnoses Influenced By Opioid Peptides Dysfunction



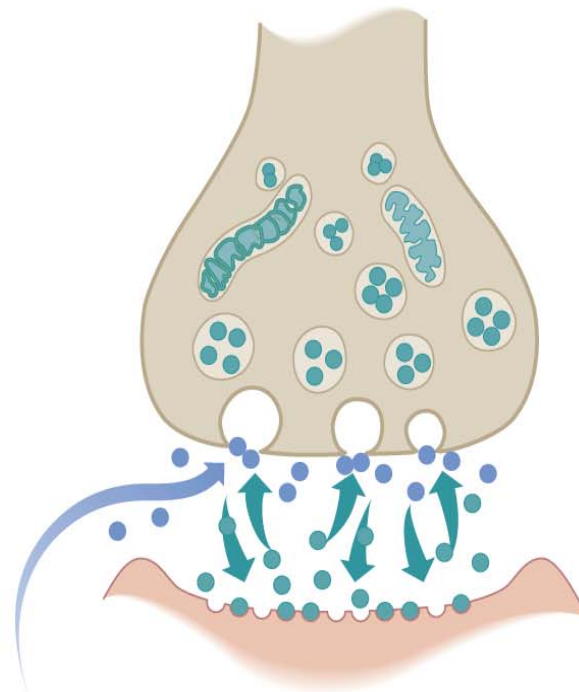
Mechanism of Actions

(a) Decreases neural transmission by "locking up" receptor sites



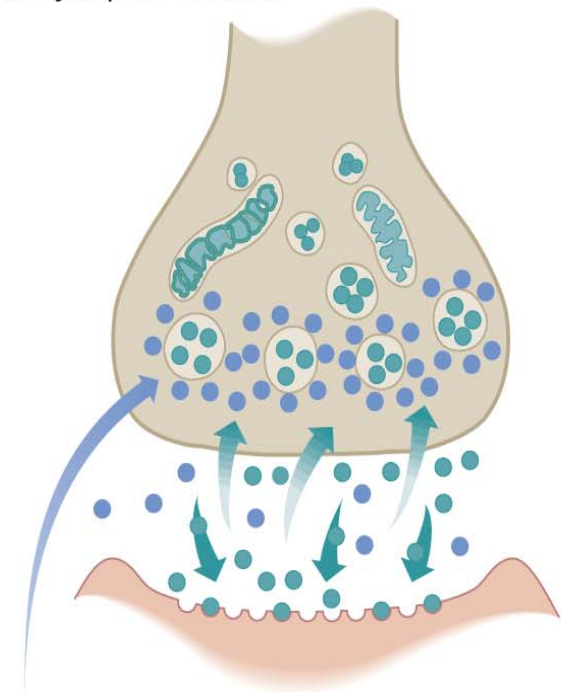
Drug binds with receptors to prevent them from being activated by the neurotransmitters in the synapse.

(b) Increases neural transmission by blocking reuptake



Drug blocks neurotransmitters from being taken back into the presynaptic membrane, leaving the neurotransmitters in the synapse longer.

(c) Increases neural transmission by blocking breakdown of neurotransmitters in synaptic vesicles



Drug prevents the neurotransmitter returning from the synapse from being broken down for storage, which keeps it available at the synapse.

Co-Occurring Disorders

Dual diagnosis is a term describing those persons who suffer from co-occurring mental illness and substance abuse disorders.

Prevalence

- 19.4 million (9.2%) adults with a substance abuse disorder
- 19.2 million (9%) adults with independent mood disorders including major depression, dysthymia, manic depression
- 23 million (11%) adults with independent anxiety disorders

Prevalence

- Roughly, 50% of individuals with severe mental illness are affected by substance abuse
- 37% of alcohol abusers and 53% of drug abusers have at least one serious mental illness
- Of all people diagnosed as mentally ill, 29% abuse alcohol and other drugs

Prevalence

- An estimated 50% of homeless adults with serious mental illnesses have a co-occurring substance abuse disorder.

Prevalence

- 47% of schizophrenics also have a substance abuse disorder (4x the general population)
- 61% of people with bipolar disorder also have a substance abuse disorder (more than 5x that of the general population)

Prevalence

- The drugs most commonly used is alcohol followed by marijuana, cocaine and methamphetamine.
- Prescription sedative and pain killer drugs are also abused in this population.

Prevalence

- Have a higher risk for hospitalization, violence, depression, suicide, homelessness, HIV infection and incarcerations.

Justice Services



- *16% of jail and prison inmates are estimated to have serious mental and substance abuse disorders.*
- *Among detainees with mental disorders, 72% also have a co-occurring substance abuse disorder.*

Suicide and AOD Use

- Psychoactive drugs are present at autopsy in 30–50% of suicides
- Intoxication predisposes to suicide in those at risk by:
 - disinhibiting usual constraints on the person
 - providing ‘courage’
 - clouding judgement and the ability to see alternatives
 - deepening mood or worsening psychosis
 - misadventure.

Why Such a High Rate?

- High-risk use of AODs can precipitate or exacerbate mental health problems:
 - psychosis in the mentally vulnerable (esp. from cannabis and stimulants)
 - depression (esp. from alcohol)
 - anxiety / social and phobia / panic attacks (esp. alcohol & benzodiazepines)
- Shared underlying causes / antecedents
 - genetics
 - environmental influences
- ‘Self-medication’ hypothesis

Problematic AOD use and mental health problems share many antecedents.

Co-Occurring Disorders: So What?

- Increased rates of violence (perpetrator and victims)
- Homelessness
- Poor treatment compliance
- Reduced or potentiated effect of medication
- Slower recovery from AOD-related problems
- Higher suicide rates.

Some Explanations for Co-occurring Disorders

1. Substance induced temporary disorders
2. Substances intensify prior psychiatric conditions
3. A few psychiatric disorders increase the risk for substance use disorders

- Drugs can cause psychiatric symptoms
- These last days to weeks
- They clear spontaneously

Time Frames for Symptom Abatement with Abstinence

- Depression and anxiety due to alcohol dependence: 4–6 weeks (maybe longer)
- Psychosis due to amphetamines and/or cannabis: 7–10 days
- Prolonged symptoms beyond these periods suggest an underlying mental health problem.

Schizophrenia

- Schizophrenia refers to a profound disturbance in human function including:
 - Thought: Illogical thought systems (delusions) and loosening of associations
 - Perception: Presence of hallucinations
 - Language: Word salad, disconnected ideas
 - Affect: Emotion (often flat or absent)
- Symptoms can be viewed as:
 - Positive: Delusions are an added function
 - Negative: Signal the absence of a function (flat affect)

Epidemiology of Schizophrenia

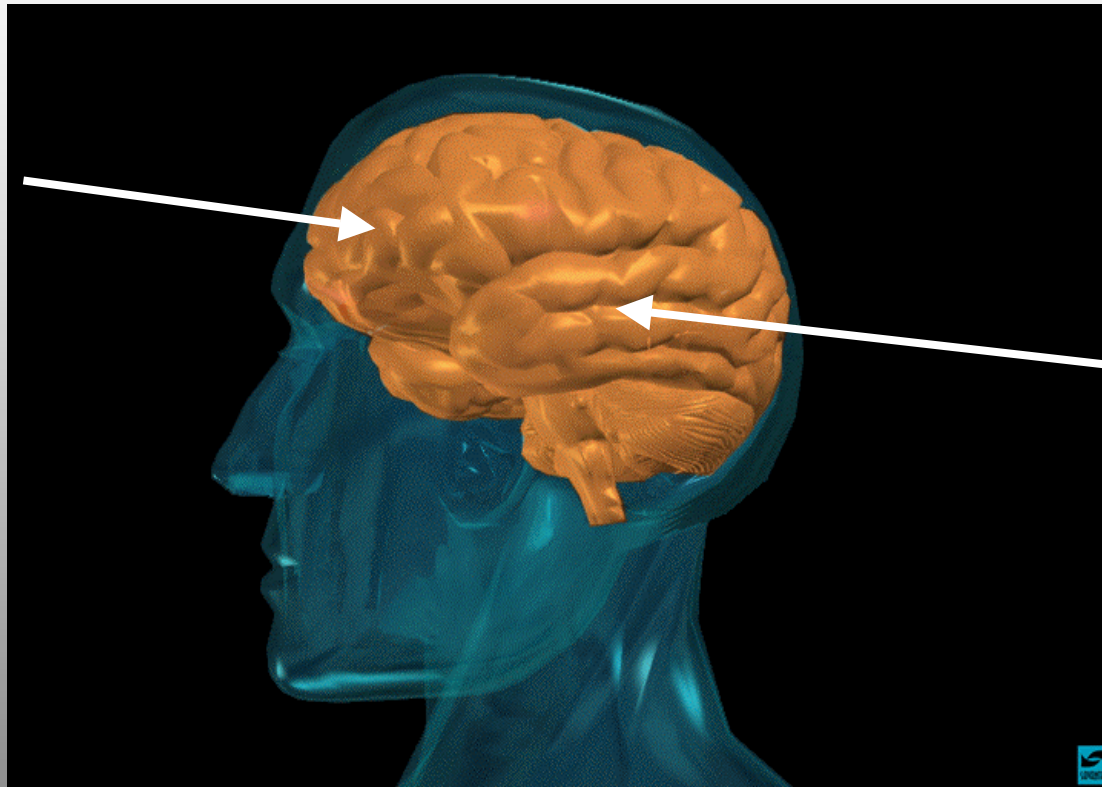
- 1% of lifetime prevalence (over 2,000,000 Americans)
- 200,000 new cases per year in USA
- 300,000 acute schizophrenic episodes annually
- 0.025 – 0.5% of total population treated for schizophrenia in any one year
- 2/3 of these require hospitalization
- More prevalent than Alzheimer's disease, multiple sclerosis, insulin-dependent diabetes

Dopamine and Schizophrenia

- The positive symptoms of schizophrenia reflect too much brain dopamine activity
 - Antipsychotic drugs are effective antagonists of dopamine receptors (block the action of dopamine)
 - Drugs such as amphetamine release dopamine from terminals; too much amphetamine exposure can induce a psychotic state in humans
- Negative schizophrenic symptoms may reflect brain damage.

Schizophrenia: How antipsychotic meds work

Decreased
activity
prefrontal
cortex
(negative
symptoms)



Increased
activity
mesolimbic
structures
(positive
symptoms)



Schizophrenia: Core Symptoms/Spectrum Disorder

Positive Symptoms

Delusions

Hallucinations (hearing)

Disorganized speech

Negative Symptoms

No emotions

Unmotivated

Nothing pleasurable

Substance Use Disorders Among Schizophrenics

Lifetime Risks: General Population

- Schizophrenia 1%
- Nicotine dependence 28% men & women
- Alcohol dependence 12% men, 5% women
- Marijuana dependence 5%
- Cocaine dependence 2%

Lifetime Risks: Schizophrenic Population

- Nicotine dependence 70%
- Alcohol dependence 37%
- Marijuana dependence 23%
- Cocaine dependence 13%

Consequences

- General population
- Special issues in schizophrenics

Consequences of Alcohol in General Population

- Intoxication: Poor judgment, anger, violence, impaired coordination
- Medical complications: Cardiomyopathy, anemia, cirrhosis
- Hallucinations
- Delirium tremens

Consequences of Alcohol in Schizophrenics: Special Issues

- Small amounts have greater effect
- Alcohol can increase cognitive deficits and enhance depression

Consequences of Methamphetamine in the General Population

- Myocardial infarction
- Arrhythmias
- Cerebrovascular accident
- Chestpains (when smoked), dyspnea, hyperthermia, chest X ray normal
- Paranoia
- Mood swings
- Depression (severe)

Consequences of Methamphetamine in Schizophrenics: Special Issues

- Destabilization and symptoms reemergence
- Frequent rehospitalizations
- Increased odds of violent behavior
- Increased risk of HIV infections
- Poor overall treatment compliance

Combined Methamphetamine and Alcohol Use

- Direct toxic effect on myocardium
- Increased risk of panic states
- Increases duration of elevated blood pressure (hypertension crisis)

To produce an effect:

1. A drug must bind to and interact with receptors (located on cell membranes)
2. Receptors are usually located on the surface of neurons
3. Drug-receptor binding leads to a change in the functional properties of the neuron

Receptors for Drug Action

Receptor: a large molecule (usually a protein) present on the surface of or within a cell.

Neurotransmitters : biologically active, naturally occurring endogenous compounds produce their effects by binding to receptors.

EXAMPLE

- Serotonin (5-HT) is a neurotransmitter that binds to more than 25 different serotonin receptor proteins
- Each receptor has a small difference in amino acid composition. They have been named as 5-HT₁, 5-HT₂, 5-HT_{2a}, etc.
- A given drug can bind to one or multiple receptors.

Understanding receptor subtypes allows for the development of new medications that are more selective in where they target their action causing fewer side effects

Resulting in improved patient
medication compliance!

Treatment of Psychiatric Disorders

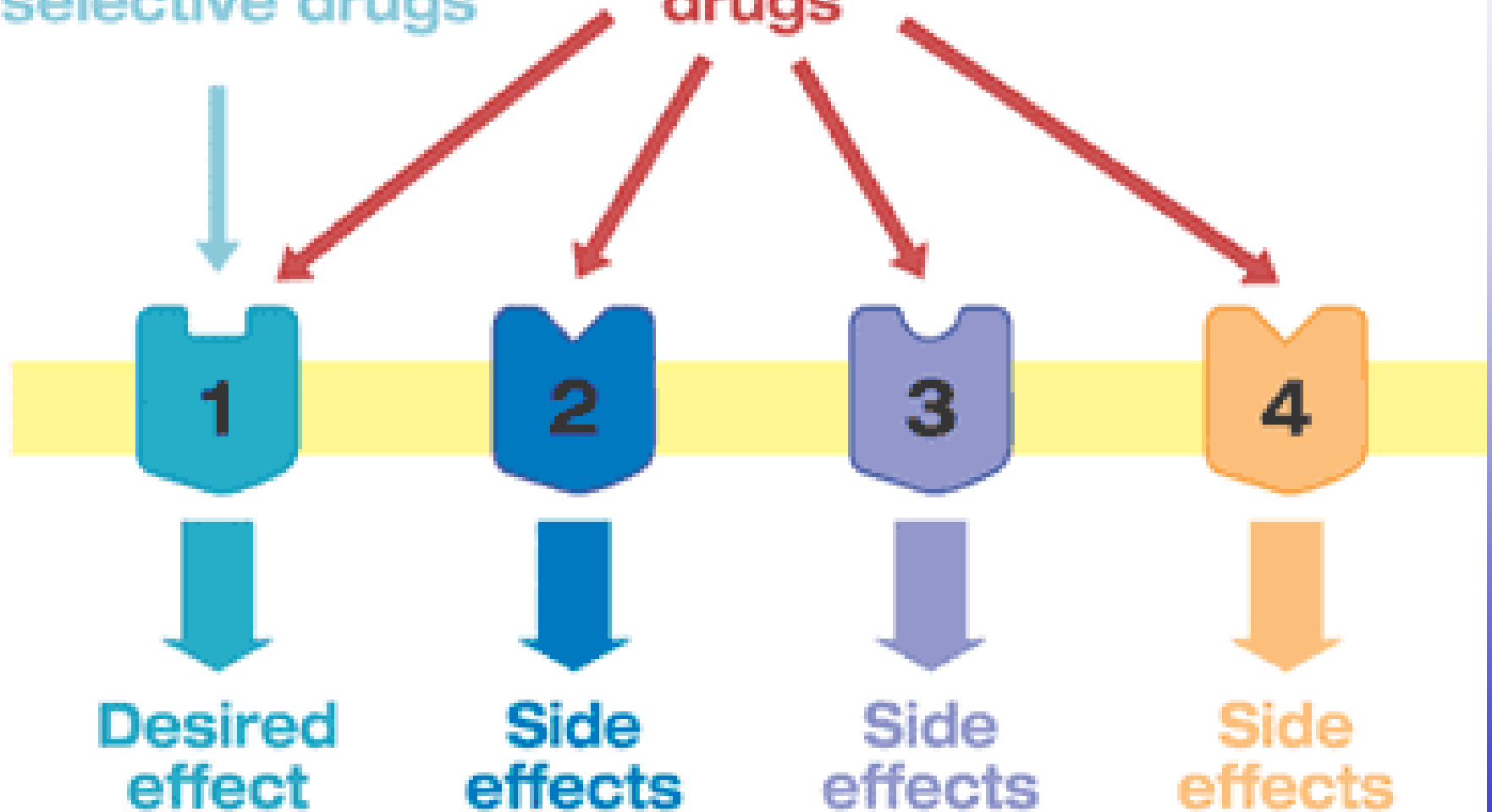
Compliance Improvements Can Mean:



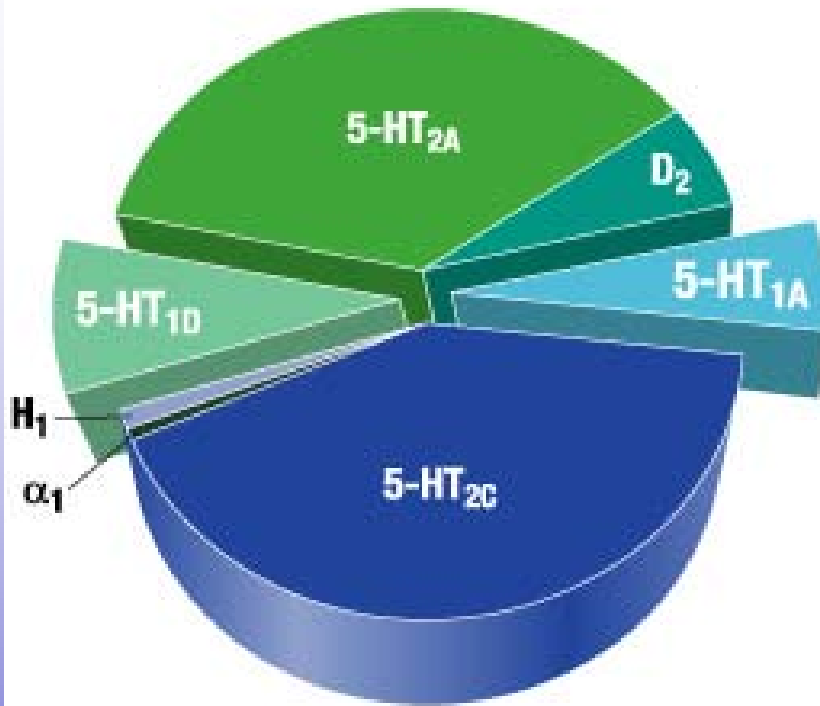
Receptor Subtypes

Subtype-selective drugs

Non-selective drugs



Ziprazidone (Geodon)



POSITIVE SYMPTOMS

D₂ - Antagonism

Efficacy in positive symptoms

High 5-HT_{2A}/D₂ - Affinity ratio

antipsychotic efficacy, reduced EPS
(compared to D₂ antagonism alone)

NEGATIVE SYMPTOMS

5-HT_{2A} - Antagonism

Efficacy in negative symptoms

OVERALL SYMPTOMS

5-HT_{2C} - Antagonism

Antipsychotic activity

COGNITIVE AND DEPRESSIVE SYMPTOMS AND SYMPTOMS OF SOCIAL IMPAIRMENT

5-HT_{1A} - Agonism

Antidepressant and anxiolytic activity and improved cognition

5-HT_{1D} - Antagonism

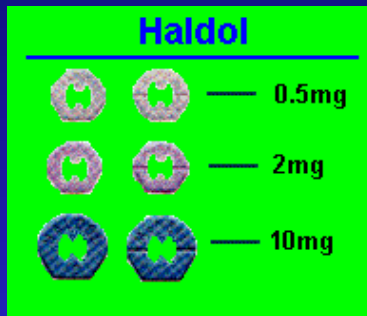
Efficacy in depressive symptoms

Anti-psychotic Medications

- Clozaril (clozapine)
- Risperdal (risperidone)
- Zyprexa (olanzapine)
- Seroquel (quetiapine)
- Geodon (ziprasidone)
- Abilify (aripiprazole)
- Invega (paliperidone)

Antipsychotic Medications

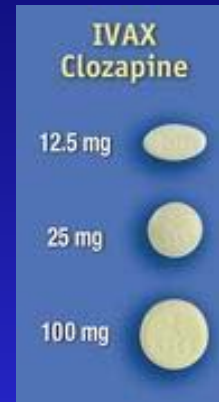
Haldol®
(haloperidol)



Geodon®
(ziprasidone)



Clozaril®
(clozapine)



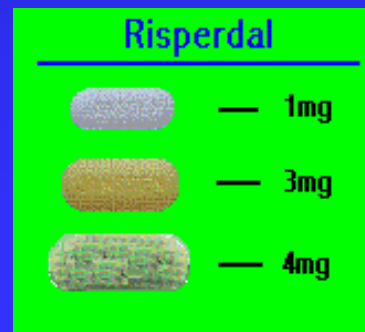
Seroquel®
(quetiapine)



Zyprexa®
(olanzapine)



Risperdal®
(risperidone)



Abilify®
(aripiprazole)





Depression and Antidepressant Medications

Epidemiology of Depressive Disorders

- High rate of occurrence
- 5% lifetime prevalence
- 10 –14 million people in U.S. depressed in a given year
- Episodes of long duration
- > 50% rate of occurrence
- Morbidity comparable to angina and advanced coronary artery disease
- High mortality from suicide

Criteria for Major Depressive Syndrome

- Depressed mood and/or loss of interest or pleasure (pervasive for 2 weeks)
- 4 of the following symptoms (3 with both depressed mood and loss of interest or pleasure)

Physical

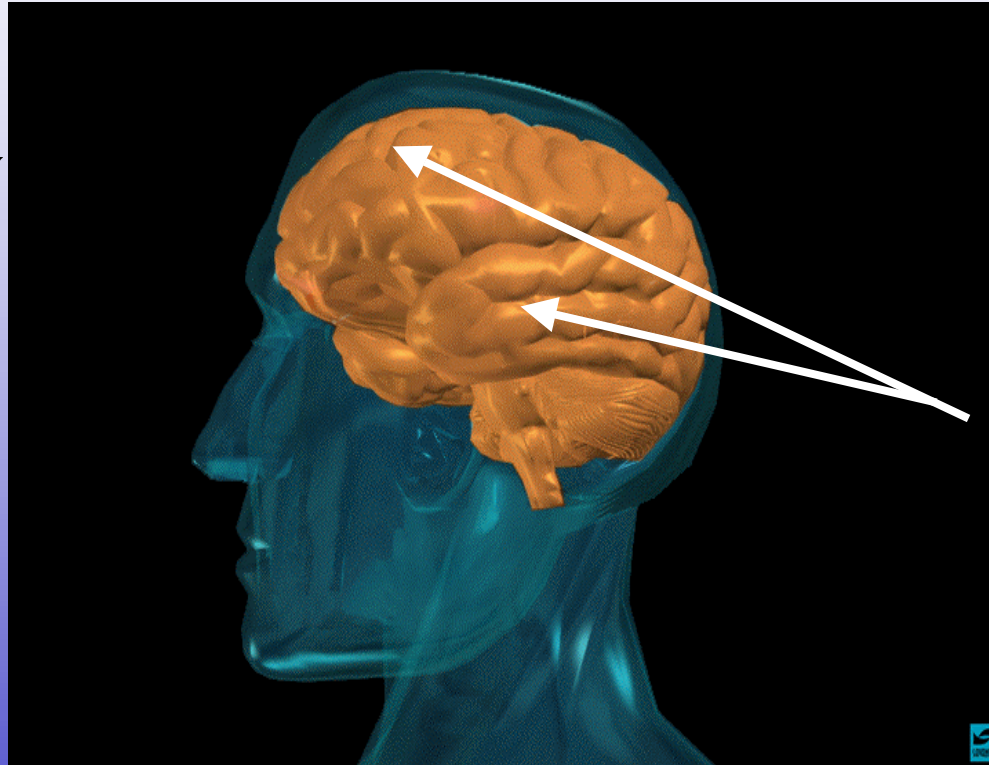
- Sleep disorder
- Appetite change
- Fatigue
- Psychomotor agitation/
retardation

Psychologic

- Low self esteem/guilt
- Poor concentration
indecisiveness
- Thoughts of death/
suicidal ideation

Depressive Disorders: How antidepressant meds work

Predominantly
lower levels
of dopamine
and serotonin
in the brain



Decreased
activity
throughout the
brain but focus
on mesolimbic
structures

Antidepressant Medication Side Effect Concerns

CNS

Activation

- insomnia
- anxiety
- nervousness
- agitation
- tremor

Sedation

- somnolence
- fatigue

GI

- nausea
- constipation
- *weight gain*
- dyspepsia

Sexual Function

- *decreased libido*
- *impotence*
- *ejaculation disorder*
- *anorgasmia*

Other (anticholinergic)

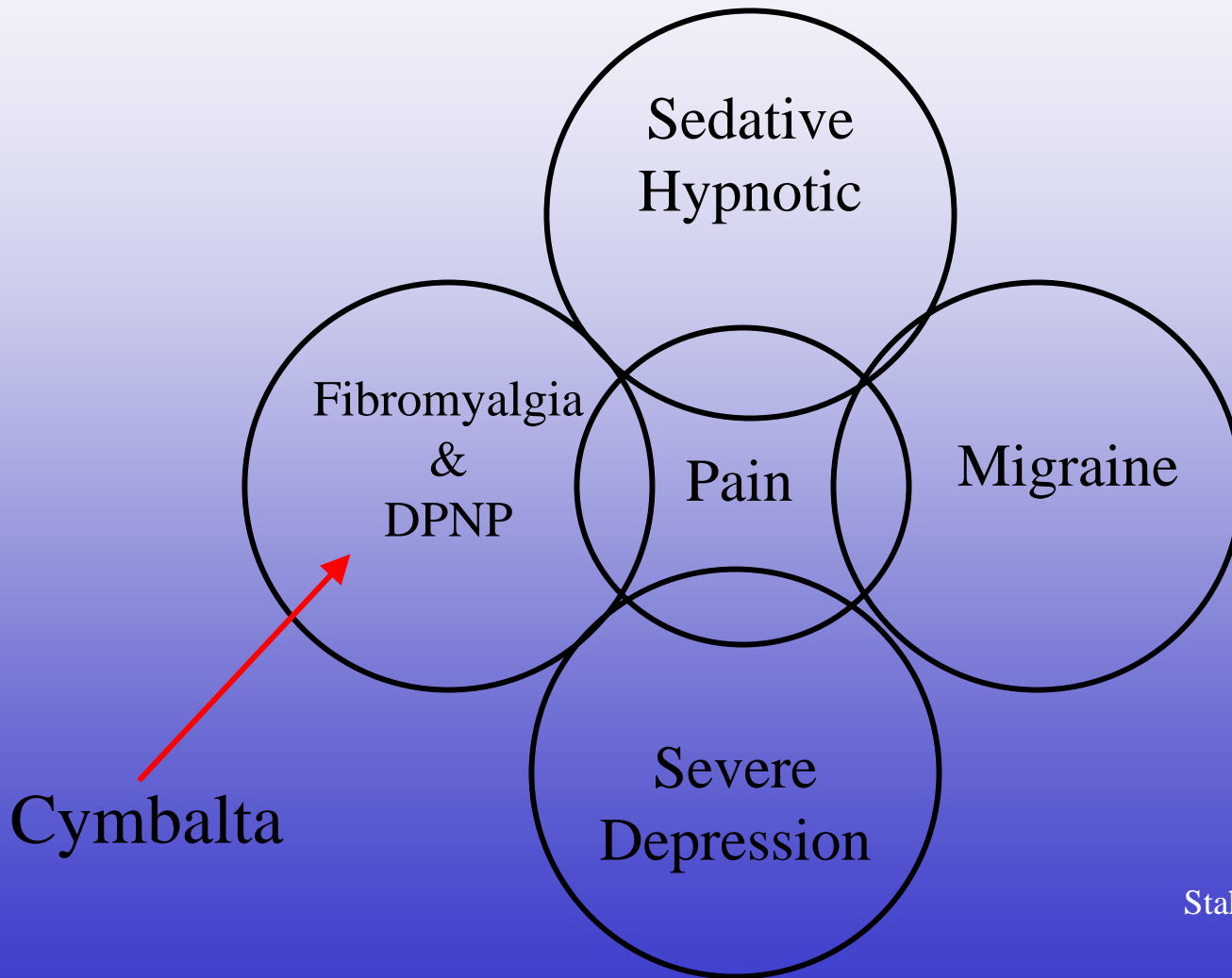
- dry mouth
- increased sweating
- urinary retention

Depression Is A Highly Treatable Disorder

*Antidepressants are successful in
65% - 80% of all cases!*

*Best when combined with
counseling therapy*

Preferred Uses of Antidepressant Medications



Several Commonly Used Antidepressant Medications

- *Tricyclics*

Elavil, Tofranil, Anafranil, Pamelor, Norpramin, Sinequan

- *MAOIs*

Nardil, Parnate, Marplan, Emsam







- *SSRIs*

Prozac, Paxil, Zoloft, Luvox, Lexapro, Celexa

- *Miscellaneous Antidepressants*

Effexor, Wellbutrin, Remeron, Desyrel (trazodone), Serzone, **Cymbalta**







Antidepressant Medications (SSRIs)

Brand Name	Prozac®	Paxil®	Zoloft®	Luvox®	Lexapro®	Celexa®
Picture						
Generic Name	fluoxetine	paroxetine	sertraline	fluvoxamine	escitalopram	citalopram





Antidepressant Medications

Brand Name	Effexor®	Serzone®	Remeron®	Wellbutrin®
Picture	 A tan, octagonal tablet with the letters 'VW' and the number '50' embossed on it.	 A white, hexagonal tablet with 'BNS' and '100' embossed on it.	 An orange, oval tablet with the word 'Organon' embossed on it.	 A red, circular tablet with 'WELLBUTRIN' and '150' embossed on it.
Generic Name	venlafaxine	nefazodone	mirtazapine	bupropion




Antidepressant Medications (TCAs)

Brand Name	Tofranil®	Norpramin®	Elavil®	Aventyl®; Pamelor®	Sinequan®; Zonalon®	Anafranil®
Picture						
Generic Name	imipramine	desipramine	amitriptyline	nortriptyline	doxepin	Clomipramine (5-HT)

Antidepressant Medications

Brand Name	Surmontil®	Vivactil®	Ludiomil®	Asendin®
Picture				
Generic Name	trimipramine	protriptyline	maprotiline	amoxapine

Antidepressant Medications (MAOIs)

Brand Name	Parnate®	Nardil®	Marplan®
Picture			
Generic Name	tranylcypromine	phenelzine	isocarboxazid

Bipolar Disorder and Mood Stabilizers

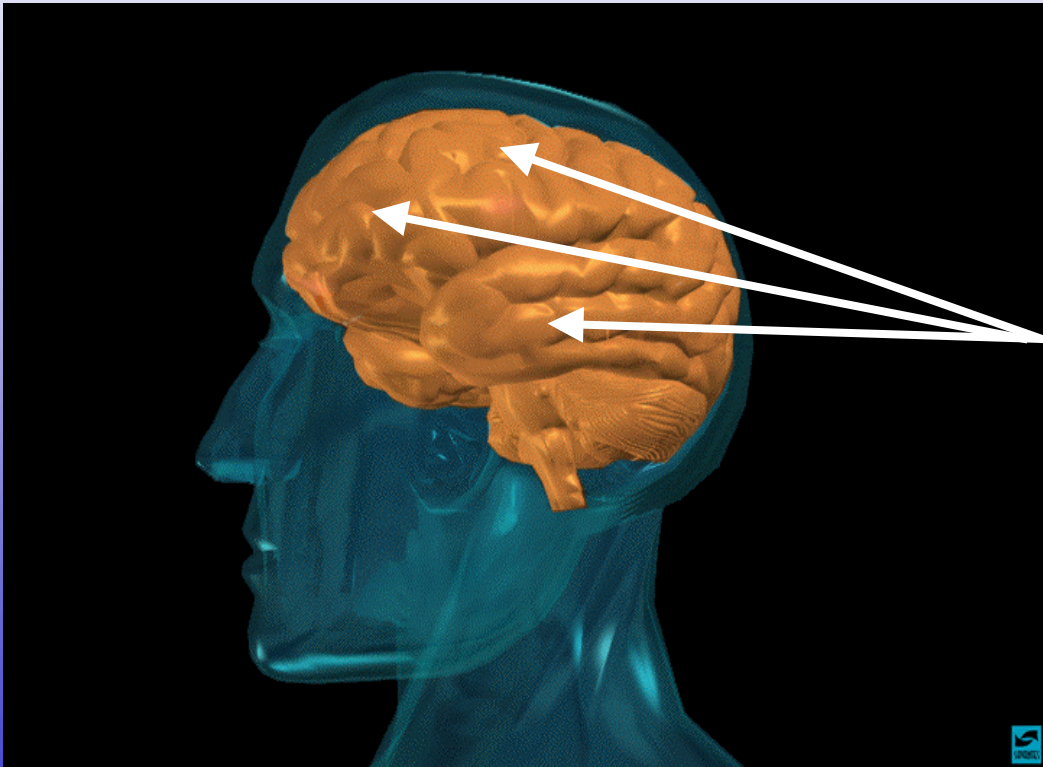
Epidemiology of Bipolar Disorder

- Prevalence: 1% of U.S. population (2.7 million people)
- Cause: Genetics plus developmental, social, cultural and environmental event.
- Peak Age of Onset: 15 – 19 years
- Mean Age of First Tx: 22 years
- Mean Age of First Hospitalization: 26 years
- Course of Illness:
 - High morbidity and mortality
 - Recurrent in most cases

Criteria for Mania

- A. Mood abnormally elevated, expansive or irritable
- B. At least 3 of the following symptoms:
 1. Grandiosity
 2. Decreased need for sleep
 3. Pressured speech
 4. Flight of ideas
 5. Distractibility
 6. Increase in activity'
 7. Activities – resulting in painful consequences
- C. Marked impairment in occupational functioning
- D. No delusions or hallucinations for as long as 2 weeks in the absence of prominent mood symptoms

Bipolar I Disorder: How anti-mania (mood stabilizer) meds work



Increased activity
throughout
various brain
areas

Treatment for Bipolar Disorder

Mood Stabilizers:

Lithium (Eskalith and others)

Tegretol (carbamazepine)

Depakote (divalproex, valproic acid)

Topamax (topiramate)

Lamictal (lamotrigine)

Trileptal (oxcarbazepine)

Mood Stabilizers

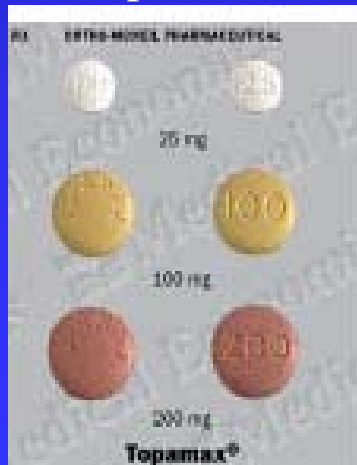
Depakene®/Depakote®
(divalproex sodium)



Eskalith® (lithium carbonate)



Topamax®
(topiramate)



Tegretol®
(carbamazepine)



Lamictal®
(lamotrigine)



Side Effect Profile:

- *Lithium toxicity looks like drunkenness but no smell of alcohol.*
- Lithium (Lithium carbonate) requires close monitoring of blood levels.
- Antipsychotic medications are sometimes used as anti-mania drugs in combination with mood stabilizers (I.e. Zyprexa, Seroquel).

Long Term Prognosis of Bipolar Disorder

- Untreated, high morbidity/mortality rates
 - 20 –25% attempt or commit suicide
 - Overall functional impairment great
- Lifetime rate of substance abuse is 50 –60%
 - Requires identification and therapy for both disorders
- Treatable disorder for high percentage of patients
 - Balance between side effects and control possible
 - On-going relationship with provider important



**Co-occurring Disorders Can
Be Treated Effectively**

**Integrated Treatment for Dual
Diagnosis:**

**Treat both conditions
concurrently**

Recovery refers to...

- The process by which people are able to live, work, learn, and participate fully in their communities
- The ability to live a fulfilling and productive life despite a disability
- A reduction or complete remission of symptoms
- The ability to help make important decisions affecting one's own life.

