Bipolar Affective Disorder is an endogenous disease characterized by alternation of phases, maniac and depressive, with presence of a light interval between them (the bipolar course).

Bipolar Disorder

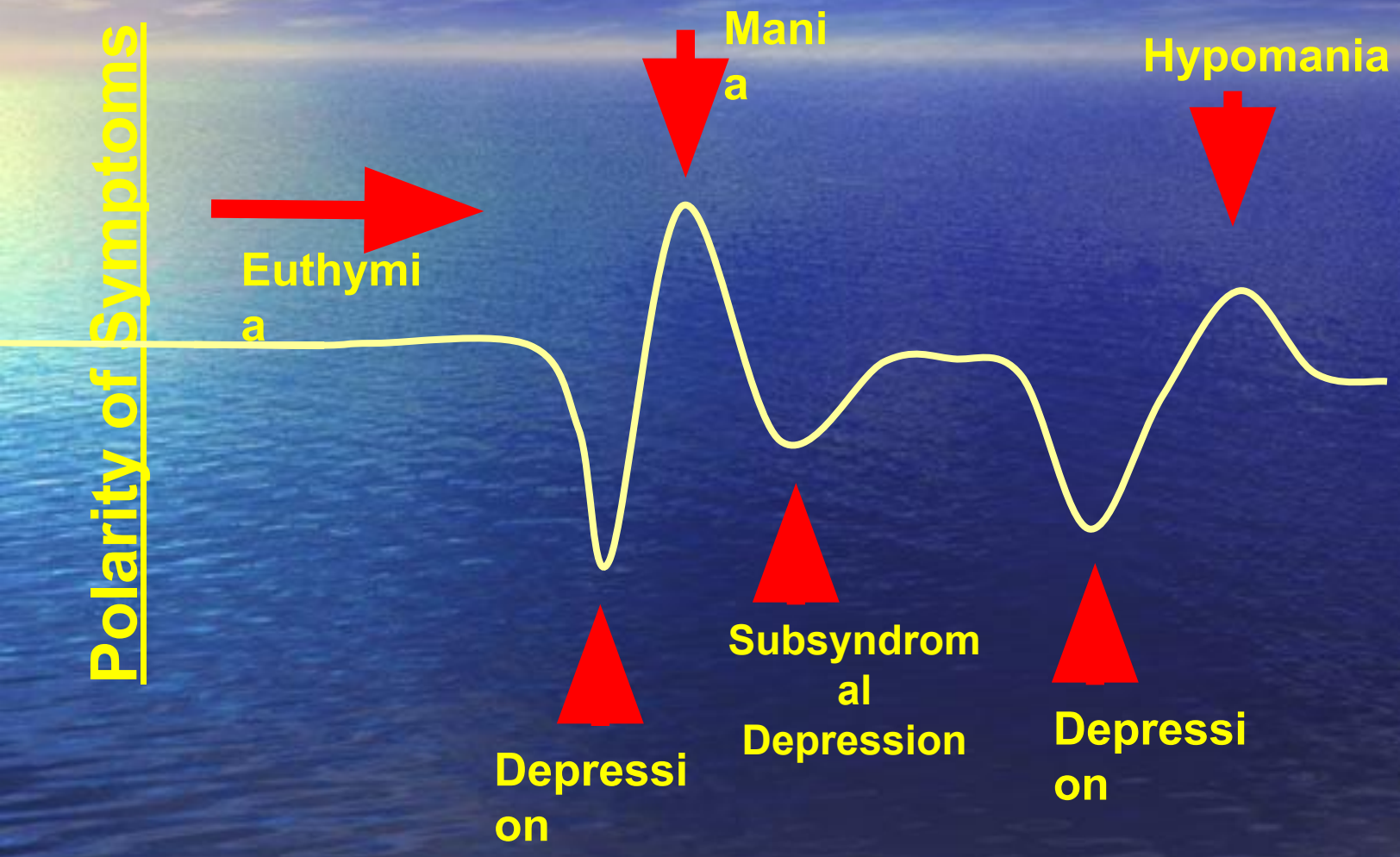
- It is a spectrum of affective episodes including:
  - Major depressive episode
  - Manic episode
  - Mixed episode
  - Hypomanic episode
  - Rapid cycling

- Bipolar I Disorder
- Bipolar II Disorder
- Bipolar III Disorder
- Cyclothymia

Bipolar Disorder

- may manifest itself only by its maniac or depressive phases (the monopolar course).
- In any type of the course there is no progression and destruction of the personality.

Longitudinal Assessment of the Course of Bipolar Disorders



Subtypes of Bipolar Disorder

Bipolar I: Depression with Classic Mania

Bipolar II: Depression with Hypomania

Bipolar III: Antidepressant Associated Hypomania

Bipolar I or II Disorder ? What is the difference?

- Bipolar I
  - 1+ manic or mixed episodes
  - May have other mood episodes
- Bipolar II
  - 1 + major depressive episodes AND
  - 1 + hypomanic episodes
  - Never manic or mixed episode

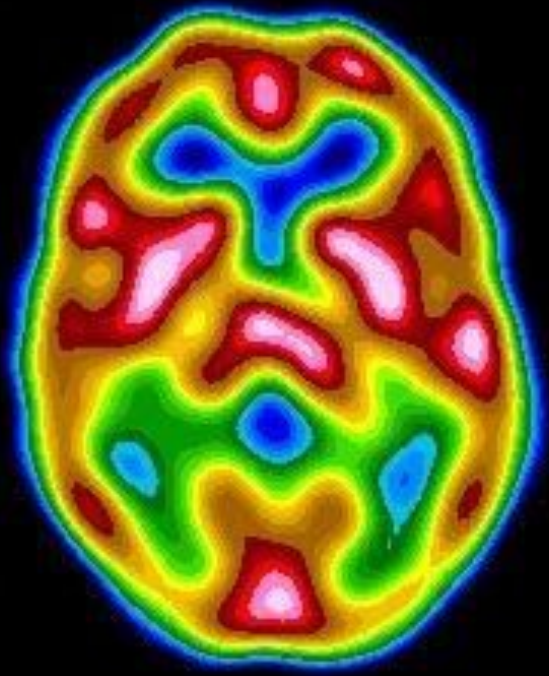
Prevalence Rates and Course

- Bipolar I
  - Lifetime: 0.4-0.8 %
  - = in men and women
  - Men>manic episodes
  - Women>depressive episodes
  - Women>rapid cycling
  - age of manifestation = 20
  - Recurrent course
  - 60-70% of manic episodes occur before or after a depressive episode

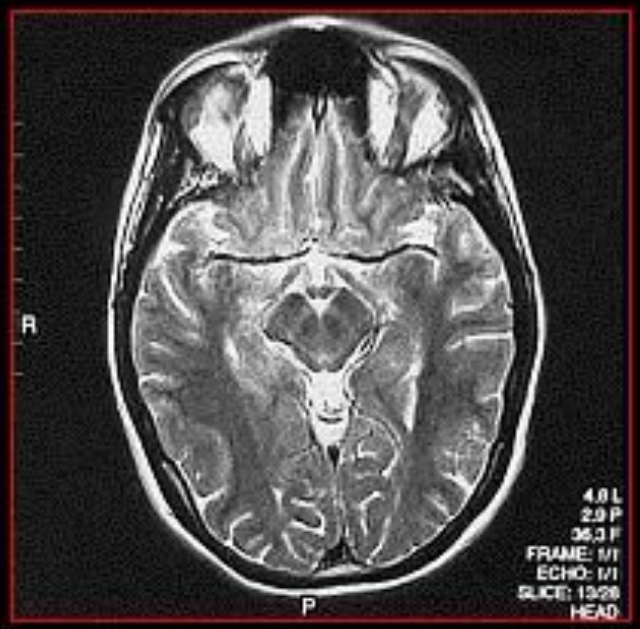
Prevalence Rates and Course

- Bipolar II
  - Lifetime: 0.5%
  - May be more common in women than men
  - Men>hypomanic than depressive episodes
  - Women>depressive than hypomanic episodes
  - Women>rapid cycling
  - 60-70% of hypomanic episodes occur before or after a depressive episode
  - Interval between episodes decrease with age
  - Less data overall

Causes

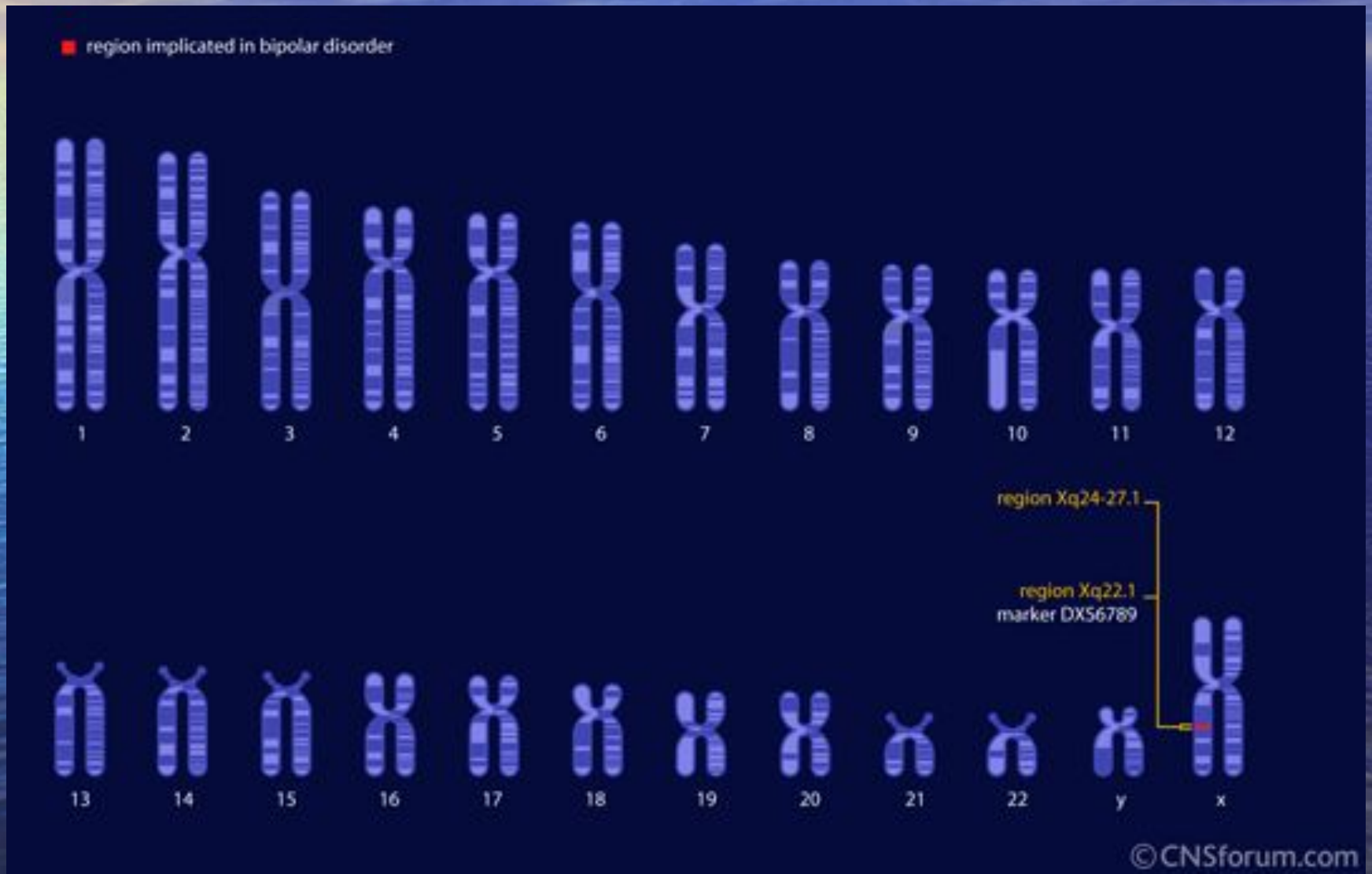


SPECT



MRI

Genetics


region implicated in bipolar disorder
1
2
3
4
5
6
7
8
9
10
11
12
region Xq24-27.1
region Xq22.1
marker DXS6789
13
14
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y
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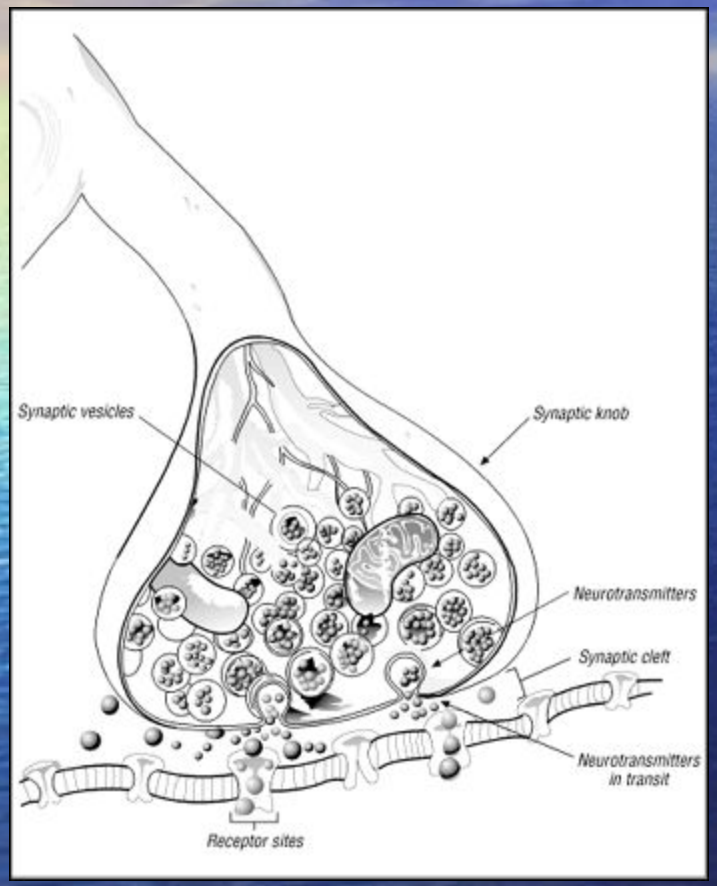
Hereditary Factors

- 1st degree relatives have significantly higher rates
- Twin and adoption studies indicate genetic predisposition
- May reflect external factors

Biochemical Hypothesis

- low level of norepinephrine
- Dopamine implicated in the study of mania and psychotic symptoms
- Serotonin

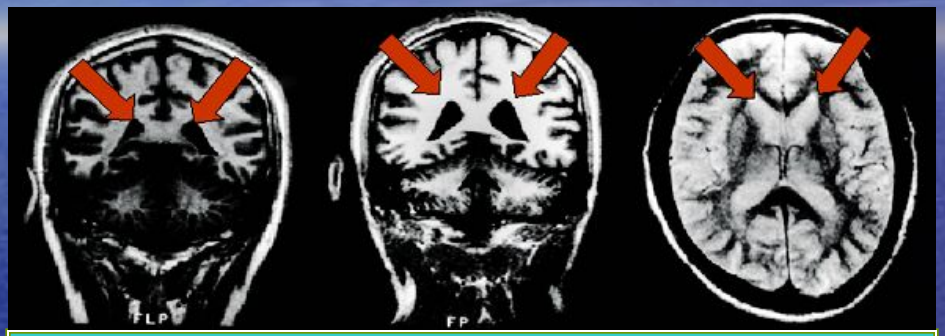
Alterations in Brain Function: Neurotransmission (NT) Model



- Catecholamine hypothesis:
  - Same hypothesis for schizophrenia & major depression
  - Depressive symptoms: NT activity deficits
  - Mania and psychosis: hyper NT activity
- NTs: Serotonin, GABA, norepinephrine, dopamine
- Alternative hypothesis
  - NT dysregulation leads to loss of mood stabilization

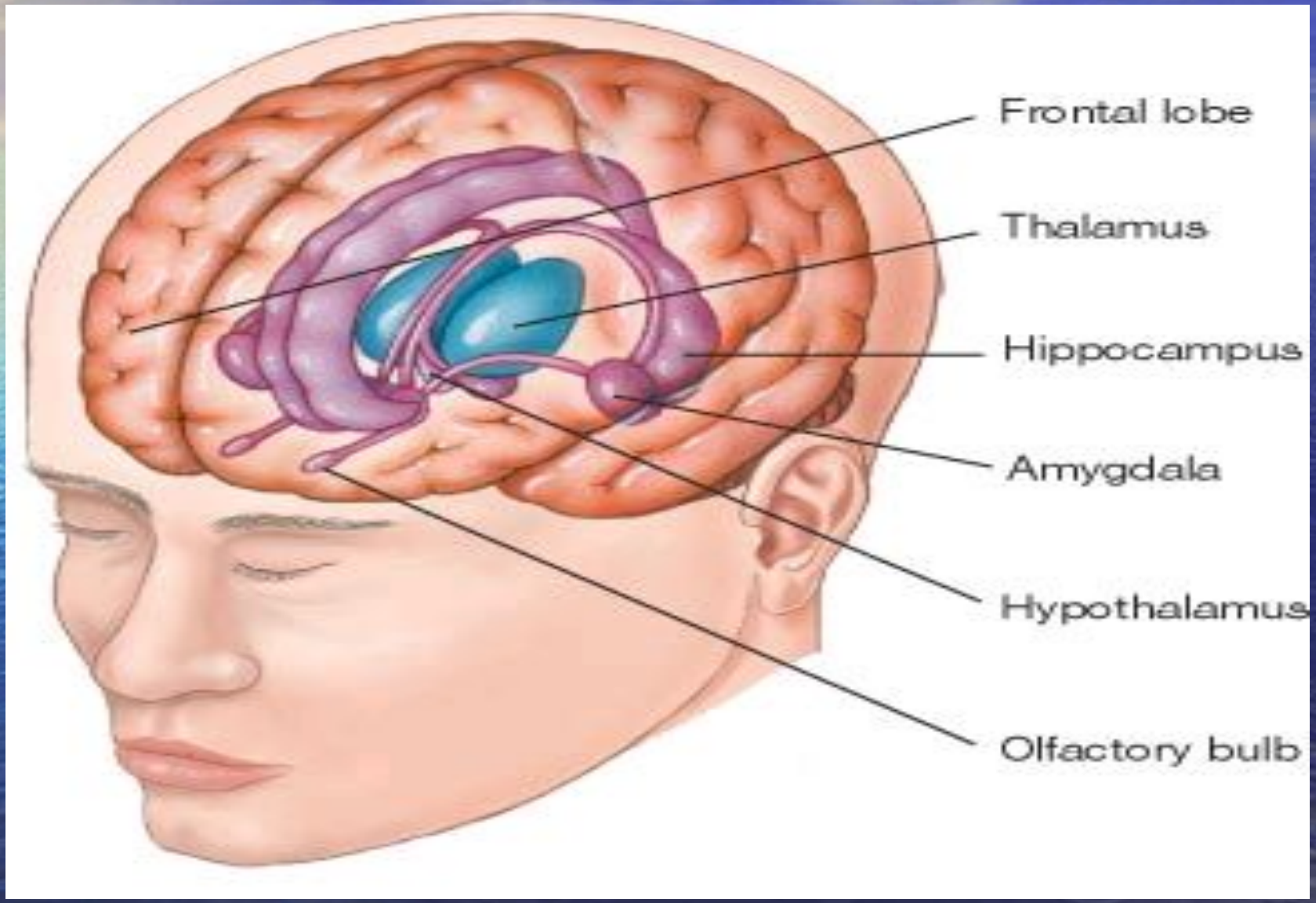
Bipolar Brain: Differences in Size

- Frontal cortex shrinks
- Enlarged ventricles
  - Possible association with tissue loss
- Enlarged amygdala
  - Part of limbic system: memory, emotions, motivation, fear

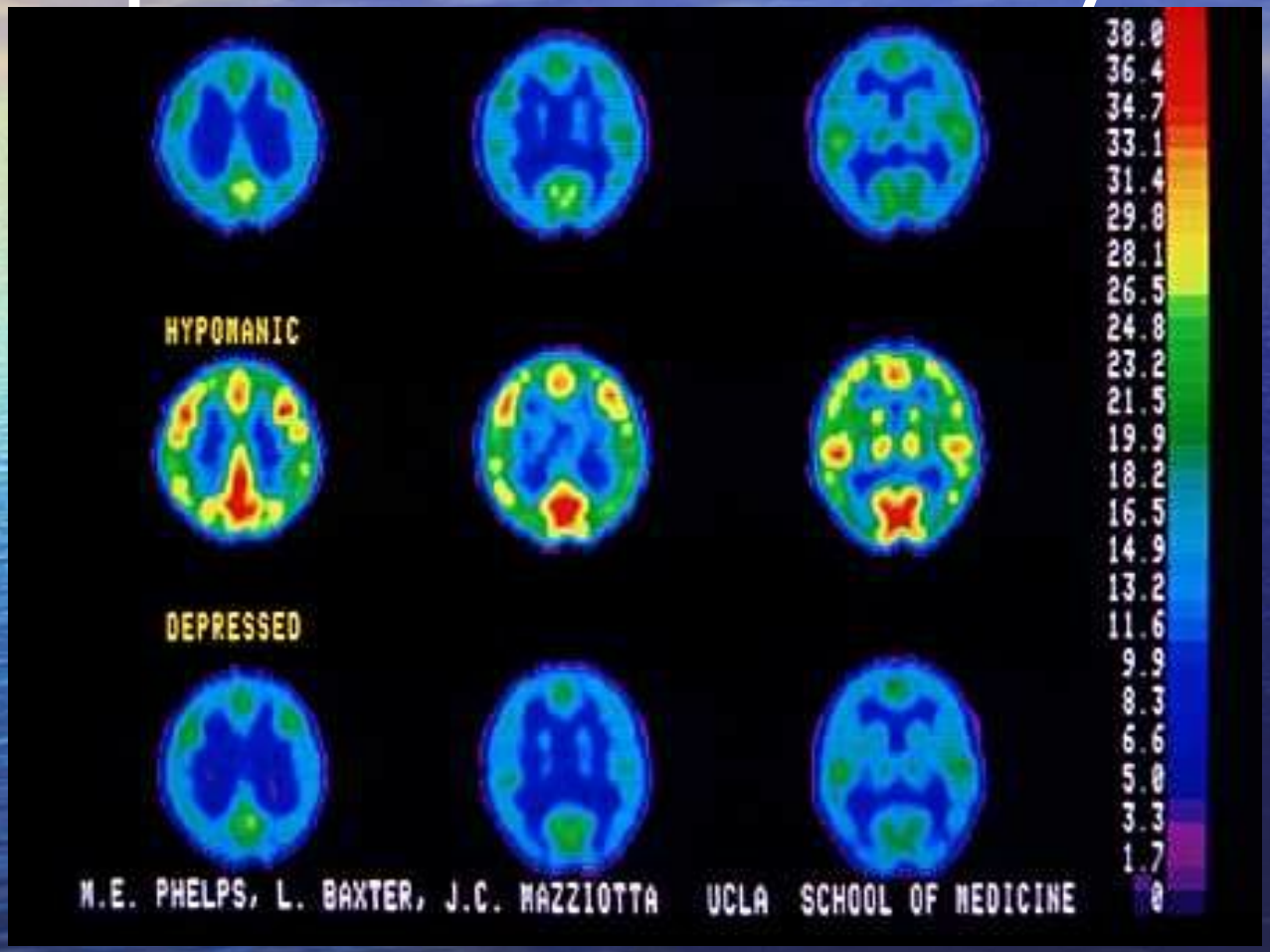


From left: view of a normal brain; patient with bipolar disorder has enlarged ventricles; bright white spots of hyperintensity associated with bipolar illness.

The Limbic System



Bipolar Brain: Activity



- PET scans: the individual shifts from depression to mania and back to depression over a 10 day period
- Blue and green: low levels of brain activity
- Red, orange, and yellow: high levels of brain activity

Signs & Symptoms

Mania (7 categories)	Depressive (6 categories)
Increased energy: Decreased sleep, increase in activities, restlessness **Speech disruptions:** rapid, pressured speech, clang associations **Impaired judgment:** Inappropriate behaviors and humor, risky behaviors, drug abuse, impulsiveness, grandiosity **Increased sexuality** **Changes in thought patterns:** flight of ideas, racing thoughts Inflated self-esteem, delusions **Changes in mood:** Irritability, excitability, exhilaration, euphoria **Changes in perceptions**	**Decrease in activity/energy:** Fatigue, lethargy, insomnia, social withdrawal, loss of interest in pleasurable activities **Physical changes:** Unexplained aches & pains, weight loss/gain, decreased/increased appetite, psychomotor agitation **Emotional changes:** Prolonged sadness, hopelessness, helplessness, loss of self-esteem, **Difficult moods:** Irritability, anger, anxiety, pessimism, indifference **Changes in thought patterns:** decreasing temp of thinking, ideas of guilt Inability to concentrate, memory problems, disorganized **Preoccupation with death:** Thoughts of death, suicidal ideation, feeling dead

Depressive phase - Depressive syndrome

- sad and melancholic mood
- a delayed thinking
- a motor inhibition

The Unmistakable Triad of Depressive Episode

Hypothymia
Decreasing speed of Speech
Hypoactivity

3 Signs in 3 Days

Major Depressive Episode —Diagnostic Criteria

<u>Five or more</u> of the following symptoms are present most of the day, nearly every day, during a period of <u>at least 2 weeks</u>

1. Depressed mood

2. Loss of interest or pleasure in all, or almost all usual activities

Major Depressive Disorder —Diagnostic Criteria

<u>Five or more</u> of the following symptoms are present most of the day, nearly every day, during a period of <u>at least 2 consecutive weeks</u>

3. Significant weight loss or weight gain
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy
7. Feelings of worthlessness or excessive or inappropriate guilt
8. Diminished ability to think
9. Recurrent thoughts of death or suicide

SUICIDE RISK
Must Be Continually Monitored

- Suicide completion rates in patients with B.D. 10-15%
  - Presence of suicidal or homicidal ideation, intent, plans
  - Access to means
  - Psychotic features, severe anxiety
  - Substance abuse
  - History of previous attempts
  - Family history of suicide

Diagnostic Criteria Hypomanic Episode:

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least **4 days.**

B. During the period of the mood disturbance, three or more of the following symptoms (four if the mood is only irritable):

Diagnostic Criteria Hypomanic Episode:

- 1) inflated self-esteem or grandiosity
- 2) decreased need for sleep (feels rested after only 3 hours of sleep)
- 3) more talkative than usual or pressure to keep talking

Diagnostic Criteria Hypomanic Episode: (continued)

- 4) flight of ideas or subjective experience that thoughts are racing
- 5) distractibility (attention too easily drawn to unimportant external stimuli)
- 6) increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation

Diagnostic Criteria Hypomanic Episode: (continued)

- 7) excessive involvement in pleasurable activities that have a high potential for painful consequences (hyper sexuality, foolish business)

APA Diagnostic and Statistical Manual. 1994

Manic Episode - **Manic syndrome**

- inadequately high spirits
- acceleration of associative processes
- a motor excitement

The Unmistakable Triad of Manic Episode

Euphoria
Pressured Speech
Hyperactivity

3 Signs in 3 Days

Diagnostic Criteria Manic Episode:

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting **at least 1 week** (or any duration if hospitalization is necessary).

B. Same as for hypomanic episode

Diagnostic Criteria
Manic Episode: (continued)

C. The symptoms do not meet criteria for a Mixed Episode.

D. The mood disturbance is severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic symptoms.

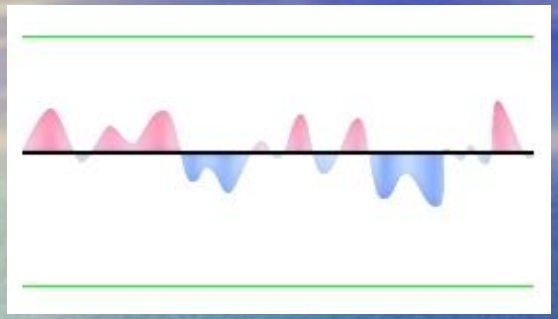
Diagnostic Criteria
Manic Episode: (continued)

E. The symptoms are not connected with the direct physiological effects of a substance (a drug of abuse, a medication, or other treatment) or a general medical condition (hyperthyroidism).

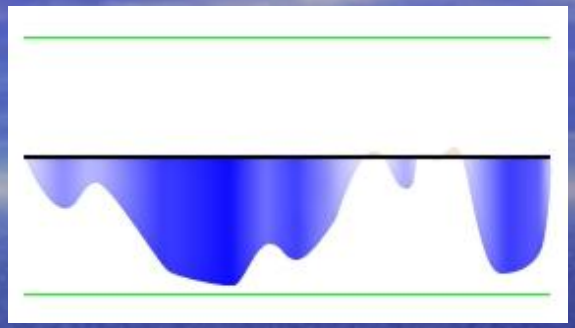
Mixed Episode

- Rapidly alternating moods (sadness, irritability, euphoria) accompanied by criteria for both a Manic Episode and a Major Depressive Episode.
- Duration of 1 week.
- includes agitation, insomnia, appetite deregulation, psychotic features, and suicidal thinking.

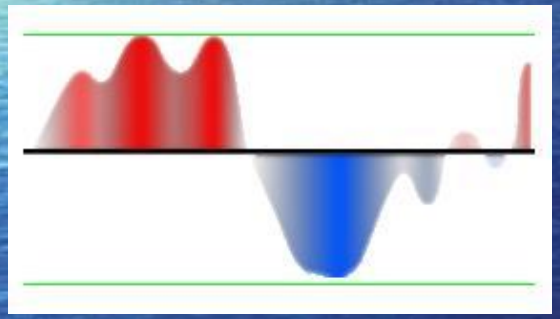
Cyclothymic Disorder



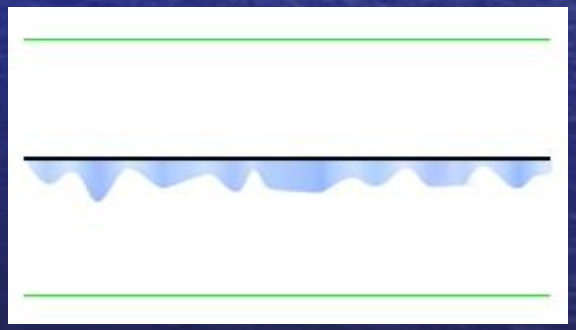
Major Depressive Disorder



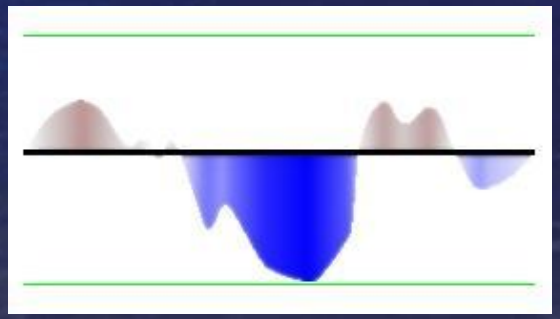
Bipolar I Disorder



Dysthymic Disorder



Bipolar II Disorder



Treatment options for bipolar depression

- Normothymics
- Psychotherapy
- Electroconvulsive Therapy (ECT)
- Antidepressants
- Antipsychotics

Medications for Bipolar Disorder

Mood Stabilizers

Divalproex DR	**Depakote**
Divalproex ER	**Depakote ER**
Carbamazepine ER	**Equetro**
Lamotrigine - M	**Lamictal**
Lithium - M	**Eskalith, Lithobid**

Lithium

- Much often recommended treatment for Bipolar Disorder
- 60-80% success in reducing acute manic and hypomanic states
- issue of non-compliance medication, side effects, and relapse rate with its use are being examined.
- Same drugs are used with Bipolar I and II- studies have been inclusive as to which drug might be better for BP II

Side Effects and Toxicity of Lithium

- Lithium demonstrates a narrow therapeutic window- close to toxic dose
- Are related to plasma concentration levels, so constant blood monitoring is key- that is why some doctors prefer Depakote
- Higher concentrations Of Lithium (1.0 mEq/L and up produce side effects, higher than 2 mEq/L can be serious or fatal)
- Symptoms can be neurological, gastrointestinal, weight gain, memory difficulty, cardiovascular violations
- Not advised to take during pregnancy, affects fetal heart development.

Lithium Doesn't Work?

- 40% of patients with Bipolar disorder are resistant to lithium or side effects hinder its effectiveness

- Therefore, we must consider alternative agents for treatment

Valproic Acid (Depakote)

- An anti-epileptic, it is probably the more often used anti-manic drug
- Best for rapid cycling and acute mania especially mixed episodes
- Side effects include sedation, lethargy,tremor, metabolic liver changes
- Can also be used for mood, and personality disorders

Carbamazepine (Tegretol)

- Superior to lithium for rapid-cycling, regarded as a second-line treatment for mania
- Side effects may include GI upset, sedation, ataxia, blurred vision and cognitive effects.
- GI upset can be decreased by taking with food.
- First-line for mixed episodes

Blood Monitoring

- Blood level monitoring required for Tegretol and Depakote.
- Weekly and then every 3 months.
- Toxicity- elevated serum level (overdose) can lead to death
- Toxic Effects
- Tegretol- neurologic and cardiac malfunctions
- Depakote- somnolence and coma

Atypical Antipsychotics: Don't be afraid of the word "antipsychotic"

Medications for Bipolar Disorder

Second Generation Antipsychotics

Aripiprazole - M	**Abilify**
Olanzapine - M	**Zyprexa**
Quetiapine - Depr	**Seroquel**
Risperidone	**Risperidal**
Ziprasidone	**Geodon**

Atypical Antipsychotics (AAPs)

Olanzapine (Zyprexa) 2.5mg-20mg/day
Quetiapine (Seroquel) 12.5-600mg/day
Risperidone (Risperdal) 0.25mg-6mg/d
Ziprasidone (Geodon) 20-160mg a day
Aripiprazole (Abilify) 5-30mg a day

listed in order of rate of weight gain/sedation

Atypical Anti-psychotics

- No support for use as primary first-line agents
- 4 types that more often used for BP- Clozapine, Risperidone, Qvetiapin and Olanzapine
- Clozapine is effective, yet not readily used due to potential serious side effects
- Olanzapine is approved for short-term use in acute mania

ECT

- 1] Mania very severe and not responding to medications.
- 2] Patient prefers ECT
- 3] Pregnant
- 4] Psychotic signs prominent.
- high suicidal risk

Classic & New Antidepressants

- Tricyclics, Tetracyclics (TCA)
- 5-HT Reuptake Inhibitors (SSRI)
  - Fluoxetine (& R-FLX), Paroxetine, Sertraline, Fluvoxamine, Citalopram
- NE/5-HT Reuptake Inh. (SNRI)
  - Venlafaxine, Milnacipran, Duloxetine
- DA/NE Reuptake Inh.: Bupropion
- 5-HT Rec. Modulators: Trazodone, Nefazadone
- Pre, Post-Synaptic agonist/antag: Mirtazapine
- MAO inhibitors: (reversible & not)

SSRIs Dosage

- Fluoxetine [Prozac] 10-80 mg/d
- Paroxetine [Paxil] 10-50 mg/d
- Sertraline [Zoloft] 25-200 mg/d
- Fluvoxamine [Luvox] 50-300 mg/d
- Citalopram [Celexa] 20-50 mg/d

- Initial response 2-4 wks, if not better after 3-4 wks □dose

Evidence-based, psychosocial treatments for bipolar disorder

- Cognitive-behavioral therapy (CBT)
- Interpersonal and Social rhythm psychotherapy (IPSRT)
- Family-focused therapy (FFT)
- Psychoeducation

Psychoeducation

21 groups sessions of 90 minutes each

Topics include:

- Awareness of the disorder (6 sessions)
  - Symptoms, etiology, triggers, course
- Drug Adherence (7 sessions)
  - Review of medications, blood tests, alternative therapies
- Avoiding substance abuse (1 session)
- Early Detection of New Episodes (3 sessions)
- Regular habits and stress management (4 sessions)
  - Includes problem-solving strategies

Schizoaffective Disorder

Schizoaffective disorder

- Endogenic psychosis
- Mixed symptoms of schizophrenia and mood disorder (manic or depression)
- Intense periods of symptoms and then remission (episodic course)

Schizoaffective Disorder

- Difficulty in conceptualization
- Risk for suicide (attempts in 23 to 42%)
- Less common than schizophrenia
- Rare in children
- More common in women, but developed later

schizoaffective disorder

- patients meets diagnostic criteria for both schizophrenia and an affective (mood) disorder— depression or bipolar disorder. In schizoaffective disorder, the experiencing of mood and psychotic symptoms occurs predominantly at the same time and the mood disturbance is long lasting.

Etiology

- Possible causes of schizoaffective disorder are similar to those of schizophrenia

(lust lecture)

Biologic Theories of Causation

- Genetic predisposition
- Neuropathologic changes
- Overactivity of dopamine system
  - **Positive symptoms of schizoaffective disorder attributed to hyperdophaminergic function (more receptors or increased sensitivity)**
  - **Many medications are dopamine antagonists**
  - **Dopamine agonists such as amphetamine mimic psychosis**

Classification

- Schizoaffective disorder. Depressions type
- Schizoaffective disorder. Manic type
- Schizoaffective disorder. Mixed type

Diagnostic Criteria for Schizoaffective Disorder

- At least two symptoms of psychosis from among the following, present for at least one month: Delusions; hallucinations; disorganized speech (strange, peculiar, difficult to comprehend); disorganized behavior (bizarre or child-like) ; catatonic behavior; minimal speech (approaching mutism); lack of drive; a wooden quality to one's emotions, or near-absent emotionality.

Diagnostic Criteria for Schizoaffective Disorder

- Delusions or hallucinations have occurred for at least two weeks in the absence of prominent mood symptoms.
- During the period of active illness, the individual meets criteria for one of the following mood disturbances: Major depressive episode, manic episode , mixed episode.
- The symptoms are not caused by a biologically active substances such as drugs, alcohol, adverse reaction to a medication or somatic illness.

Signs and symptoms of schizoaffective disorder may include

- Strange or unusual thoughts or perceptions
- Paranoid thoughts and ideas
- Delusions ideas
- Hallucinations, such as verbal
- Unclear or confused thoughts (disorganized thinking)
- Manic mood or a sudden increase in energy and behavioral displays that are out of character
- Irritability and poor temper control
- Thoughts of suicide or homicide
- Problems with attention and memory
- Lack of concern about hygiene
- Changes in energy and appetite
- Sleep disturbances,

such as difficulty falling asleep or staying asleep

Treatment

Normothymics are a mainstay of treatment for bipolar disorders and would be expected to be important in the treatment of patients with schizoaffective disorder.

-lithium,

-valproate (Depakote)

-carbamazepine (Tegretol)

Treatment

Antipsychotics (neuroleptics)

to treat psychotic symptoms, such as delusions and hallucinations.

paliperidone (Invega)

clozapine (Clozaril, FazaClo)

risperidone (Risperdal)

olanzapine (Zyprexa).

Treatment

Antidepressants.

When depression is the main mood disorder, antidepressants

Fluoxetine [Prozac] 10-80 mg/d

- **Paroxetine [Paxil] 10-50 mg/d**
- **Sertraline [Zoloft] 25-200 mg/d**
- **Fluvoxamine [Luvox] 50-300 mg/d**
- **Citalopram [Celexa] 20-50 mg/d**

Evidence-based, psychosocial treatments for Schizoaffective Disorder

- Cognitive-behavioral therapy (CBT)
- Interpersonal and Social rhythm psychotherapy (IPSRT)
- Family-focused therapy (FFT)
- Psychoeducation