Mood disorders

Mood and affect

Mood:

- a pervasive and sustained emotion or feeling tone that influences a person's behaviour and colors his or her perception of being in the world

Affect:

- external expression of mood
- affect is variable over time, in response to changing emotional states
- it's display to others through: facial expression, hands gestures, tone of the voice

Affective/mood disorders

- Depressive episode
- Recurrent depressive disorder
- Manic/hypomanic episode
- Bipolar affective disorder
- Persistent mood disorders:
  - dysthymia
  - cyclothymia
- Other and unspecified mood disorders

Epidemiology of depression

- Lifetime prevalence: 17%
  - F: 9-26%
  - M: 5-12%
- Annual incidence: 1,59%
  - F: 1,89%
  - M: 1,1%

Epidemiology of depression

- Sex

  F > M (2:1)

– hormonal differences?

– effects of childbirth?

– different socials stressors?

– learned helplessness?

Epidemiology of depression

- Age

– mean age: 40 yrs (20-50)

- Marital status

– most often in person without close interpersonal relationship/ divorced/ separated

Epidemiology of depression

- Socioeconomic and cultural factors
  - no correlation with socioeconomic status
  - more often in rural than urban areas
- No differences between races

Comorbidity

Individuals with major depressive disorder are at increased risk of having one or more additional comorbid disorders. The most frequent disorders are:

- alcohol abuse/dependence
- panic disorder
- OCD
- social phobia
- eating disorders

Comorbidity

	Substance use disorder	Panic disorder	OCD
MDD	21%	10%	12%
BD	61%	21%	21%

Comorbid substance use disorders and anxiety disorders worsen the prognosis of the illness and markedly increase the risk of suicide among patients who are unipolar major depressive or bipolar.

Etiology of mood disorders

- Biological factors:
  - genetics
  - neurotransmitters
  - structural/ functional changes
  - psychoneuroendocrynological factors
  - photic changes (SAD)
- Psychosocial factors:
  - life events
  - personality

Genetics

- Lifetime risk for the development of mood disorders:
  - 1 parent: 10-25%,
  - both parents: 20-50%

- Twin studies:
  - monozygotic: 70-90%,
  - dizygotic: 16-35%.
- Molecular genetics:
  - causative genes: on chromosomes X, 11, 18q 22q, 1, 4, 5, 6, 7, 10, 16, 21,.

Neurotransmitters and mood

- Monoamine hypothesis:
  - Norepinephrine (NA),
  - Serotonin (5-HT),
  - Dopamine (D).

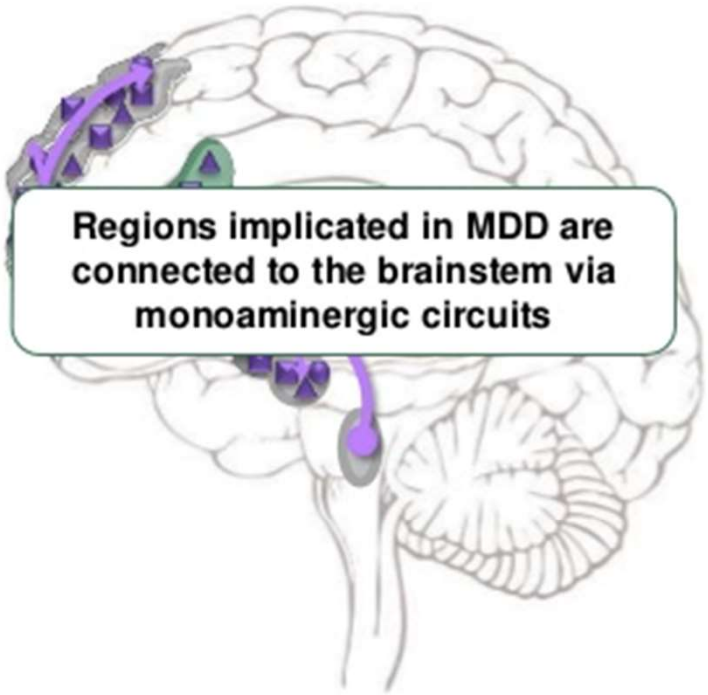
Monoamine Hypothesis

- Posits that depression is caused by reduced monoamine function in the brain
- Iproniazid and imipramine had antidepressant effect and later shown to enhance central 5-HT and NA transmission.
- Reserpine depletes monoamine stores and produces depressive symptoms.
- ADs increase monoamine transmission e.g. SSRIs inhibit reuptake, MAOIs inhibit degradation
- However, cause of depression is more complex than central reduced monoamine function
- MAOIs and SSRIs cause immediate increase in monoamines yet do not immediately alleviate symptoms

Major Depressive Disorder

Circuits and Neurotransmitters

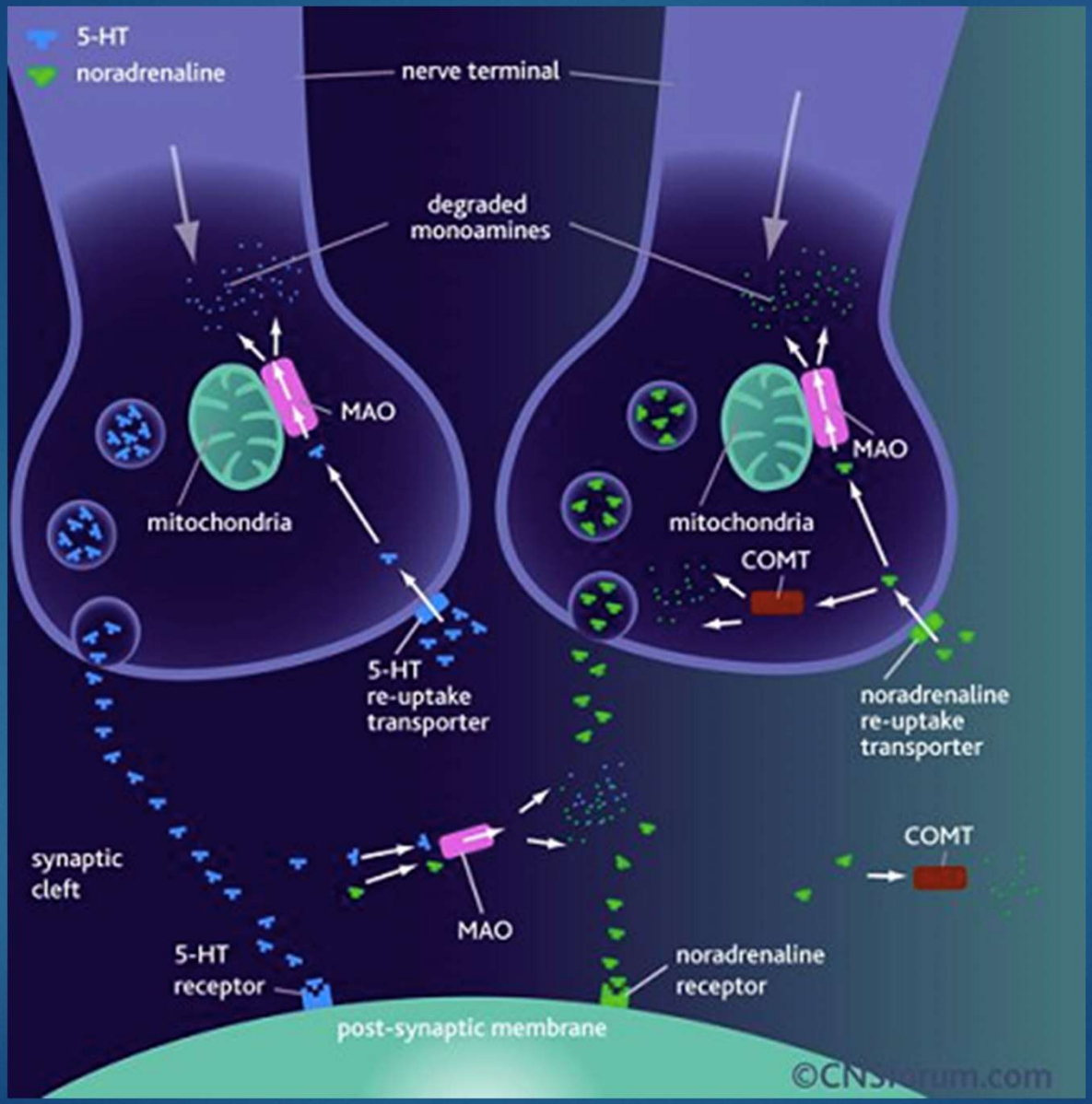
monoamine neurotransmitter projections



Regions implicated in MDD are connected to the brainstem via monoaminergic circuits

When there is an appropriate amount of monoamine neurotransmitter activity, neuronal activity throughout the brain functions normally.

Monoamine Neurotransmitters ● Serotonin (5-HT) ■ Dopamine (DA) ▲ Norepinephrine (NE)


5-HT
noradrenaline
nerve terminal
degraded monoamines
MAO
mitochondria
5-HT re-uptake transporter
MAO
mitochondria
COMT
noradrenaline re-uptake transporter
synaptic cleft
MAO
COMT
5-HT receptor
noradrenaline receptor
post-synaptic membrane
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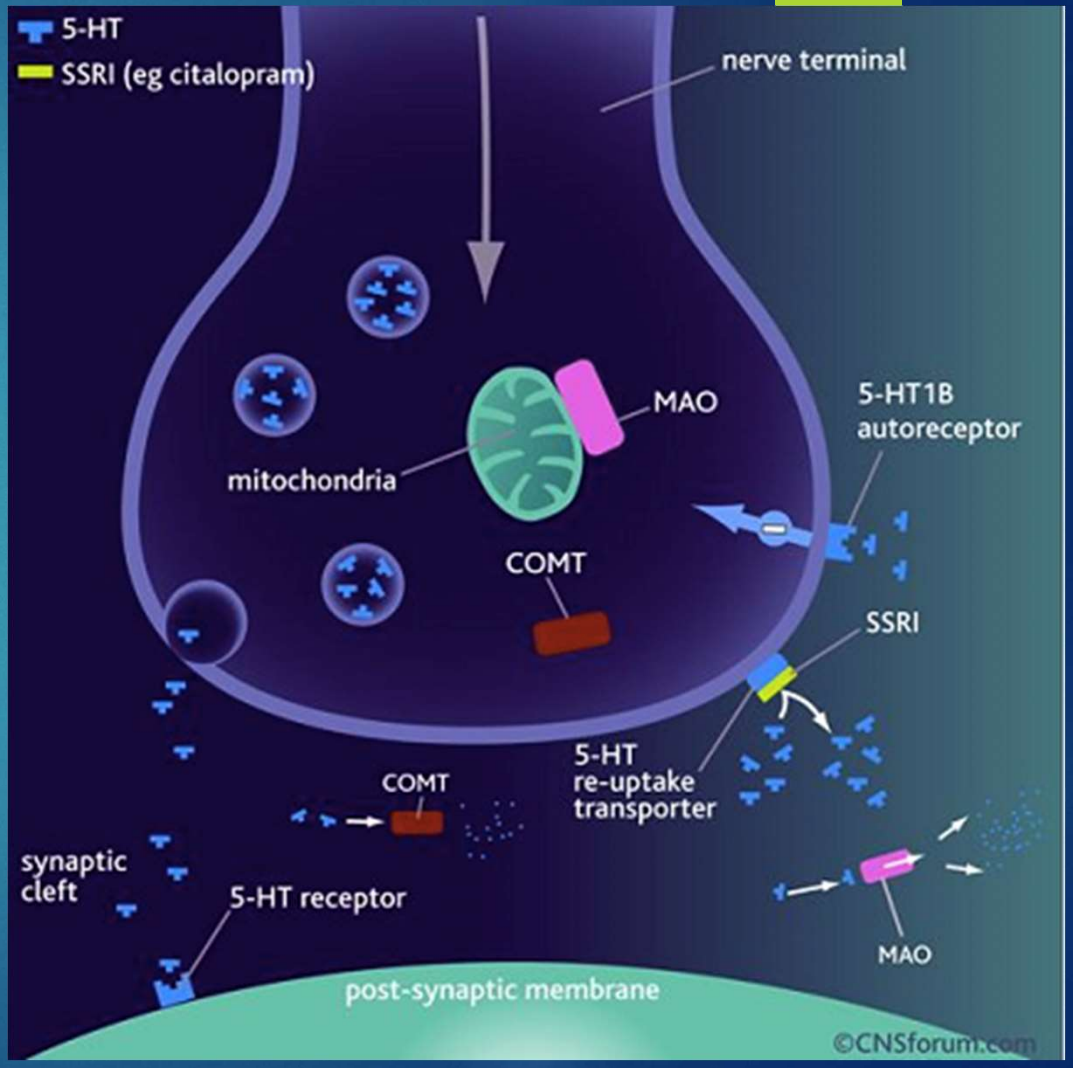
Reduced levels of 5HT in depression/ SSRI effects

The selective 5-HT re-uptake inhibitors (SSRIs) are thought to restore the levels of 5-HT in the synaptic cleft by binding at the 5-HT re-uptake transporter preventing the re-uptake and subsequentdegradation of 5-HT.

This re-uptake blockade leads to the accumulation of 5-HT in the synaptic cleft and the concentration of 5-HT returns to within the normal range.

This action of SSRIs is though to contribute to the alleviation of the symptoms of depression.

In the presence of the SSRI, small amounts of 5-HT continue to be degraded in the synaptic cleft.



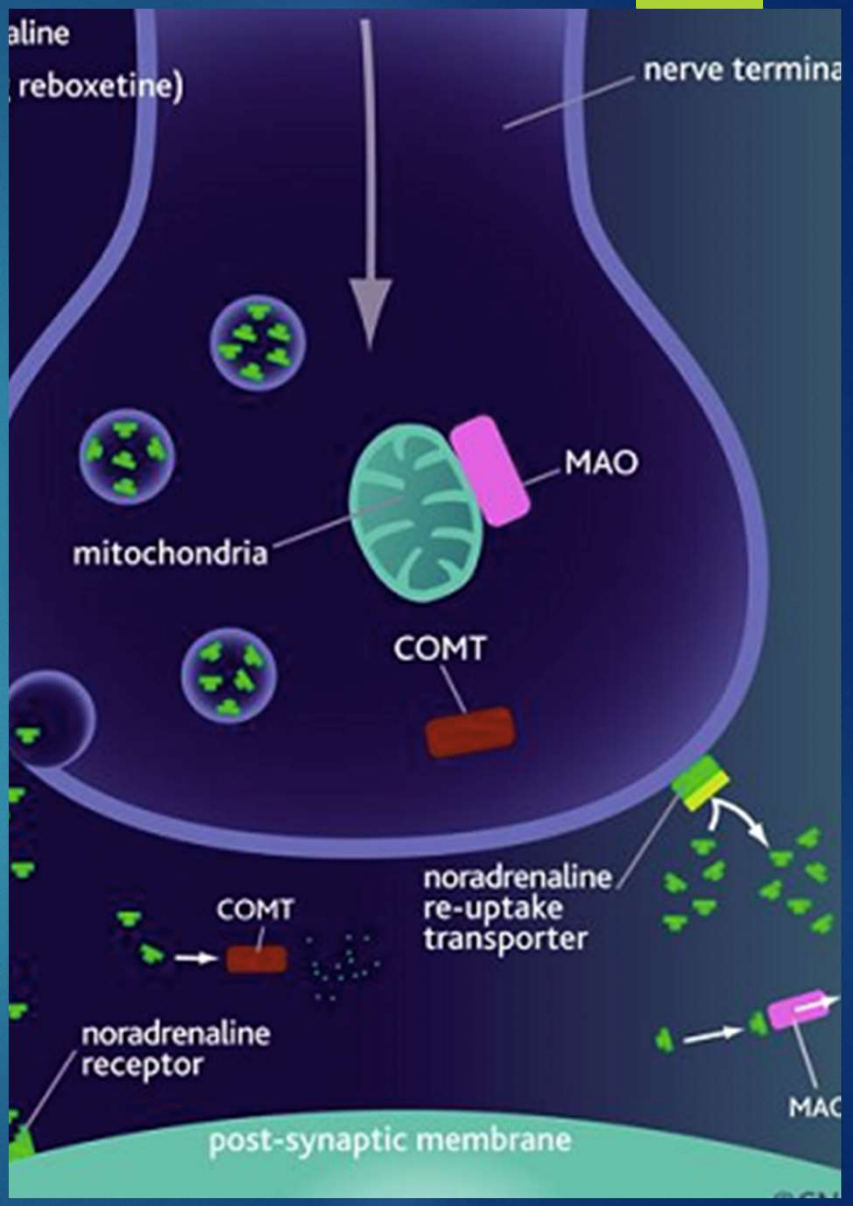
Reduced levels of NO in depression/ NARI effects

The selective noradrenaline re-uptake inhibitors (NARIs) are thought to restore the levels of noradrenaline in the synaptic cleft by binding at the noradrenaline re-uptake transporter preventing the re-uptake and subsequent degradation of noradrenaline.

This re-uptake blockade leads to the accumulation of noradrenaline in the synaptic cleft and the concentration of noradrenaline returns to within the normal range.

This action of NARIs is though to contribute to the alleviation of the symptoms of depression.

In the presence of the NARI, small amounts of noradrenaline continue to be degraded in the synapticcleft.



Norepinephrine

- The correlation suggested by basic science studies between downregulation or decreased sensitivity of β-adrenergic receptors and clinical antidepressant responses is probably the single most compelling piece of data indicating a direct role for the noradrenergic system in depression.
- The clinical effectiveness of antidepressant drugs with noradrenergic effects (venlafaxine, duloxetine) further supports a role for norepinephrine in the patophysiology of at least some of the symptoms of depression.

Serotonin

- With the huge effect that selective serotonin reuptake inhibitors (SSRIs)- e.g., fluoxetine- have made on the treatment of depression, serotonin has become the biogenic amine neurotransmitter most commonly associated with depression.
- Depletion of serotonin may precipitate depression, and some patients with suicidal impulses have low cerebrospinal fluid (CSF) concentrations of serotonin metabolites and low concentrations of serotonin uptake sites on platelets.

Dopamine

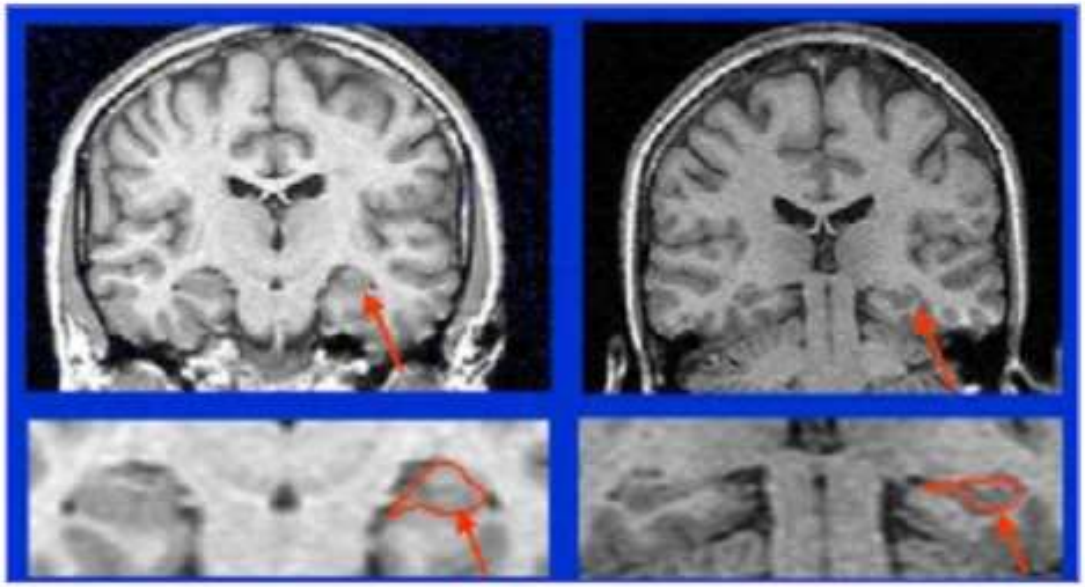
- The data suggest that dopamine activity may be reduced in depression and increased in mania. Drugs that reduce dopamine concentrations (e.g., reserpine) and diseases that reduce dopamine concentrations (e.g., Parkinson's disease) are associated with depressive symptoms.
- In contrast, drugs that increase dopamine concentrations (e.g., bupropion) reduce the symptoms of depression.
- Two recent theories about dopamine and depression are that the mesolimbic dopamine pathway may be disfunctional in depression and that the dopamine D1 receptor may be hypoactive in depression.

Structural changes

- Decreased volume of:
  - frontal lobes
  - parietal lobes
  - hippocampus
  - subcortical nuclei
- Increased volume of:
  - lateral ventricles
  - third ventricle

Brain Atrophy in Depression

Atrophy of the Hippocampus in Depression



Normal Depression

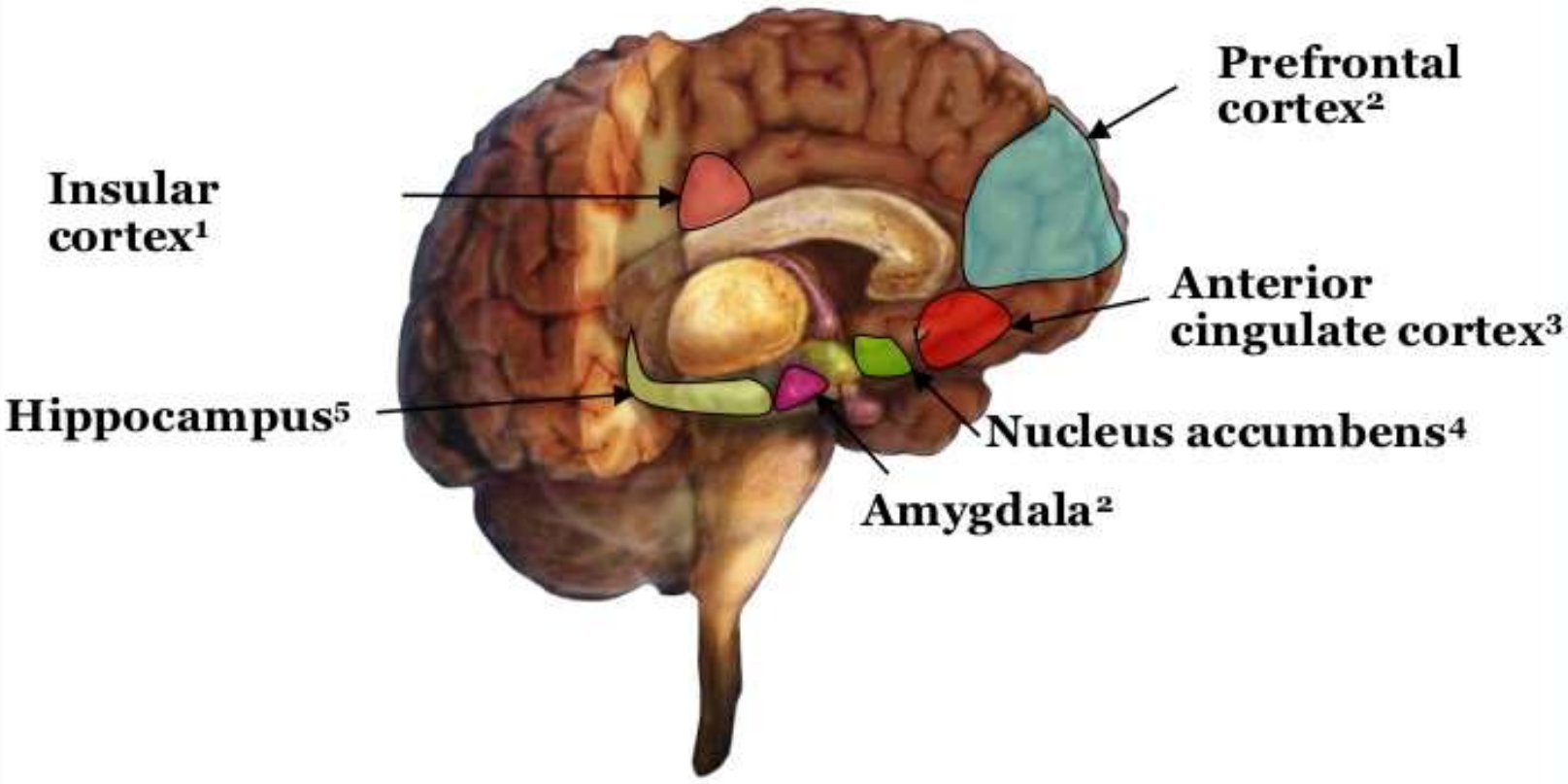
Bremner JD, et al. *Am J Psychiatry* 2000;157(1):115-118.
Reprinted with permission from JD Bremner

Key Replicated Brain Imaging Findings

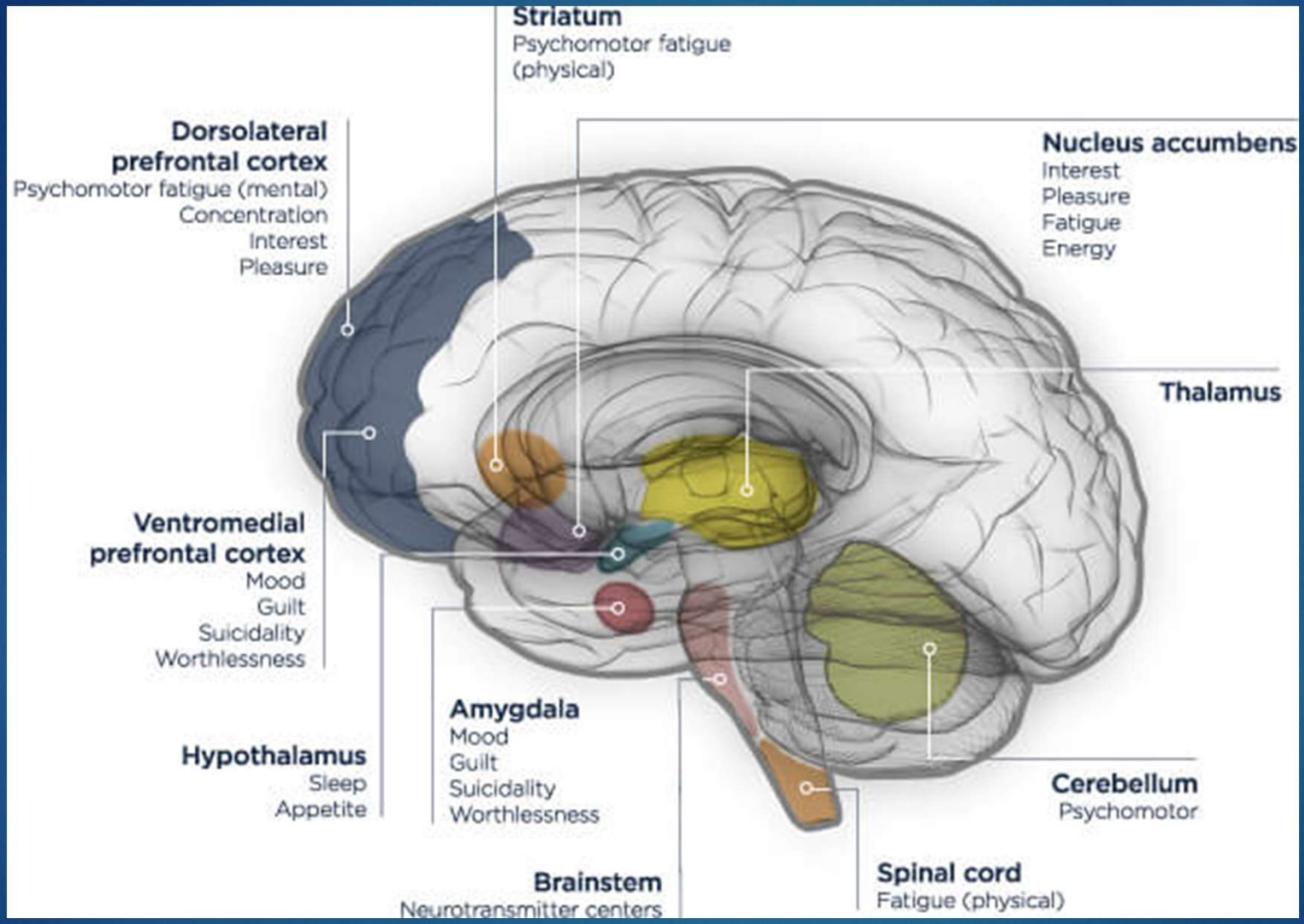
- Most brain imaging studies have shown abnormalities in these key areas: amygdala, hippocampus, prefrontal cortex, anterior cingulate cortex, and orbitofrontal cortex[1–3]
- Many studies have found prefrontal cortical hypoactivity at baseline improved after treatment[4]
- Many studies have found limbic hyperactivity (especially cingulate) at baseline normalized after treatment[4]
- More recent studies have focused on network relationships (limbic, prefrontal) and dynamic changes over time[2,4–6]
- There is great heterogeneity among patients; scanning is not predictive or individually diagnostic

1. Sheline YI. *Biol Psychiatry*. 2000;**48**:791–800. 2. Sheline YI. *Biol Psychiatry*. 2003;**54**:338–352. 3. Nestler EJ, et al. *Neuron*. 2002;**34**:13–25. 4. Mayberg HS. *Br Med Bull*. 2003;**65**:193–207. 5. Fales CL, et al. *Biol Psychiatry*. 2008;**63**:377–384. 6. Siegle GJ, et al. *Biol Psychiatry*. 2007;**61**:198–209.

Areas of the Brain Implicated in Depression

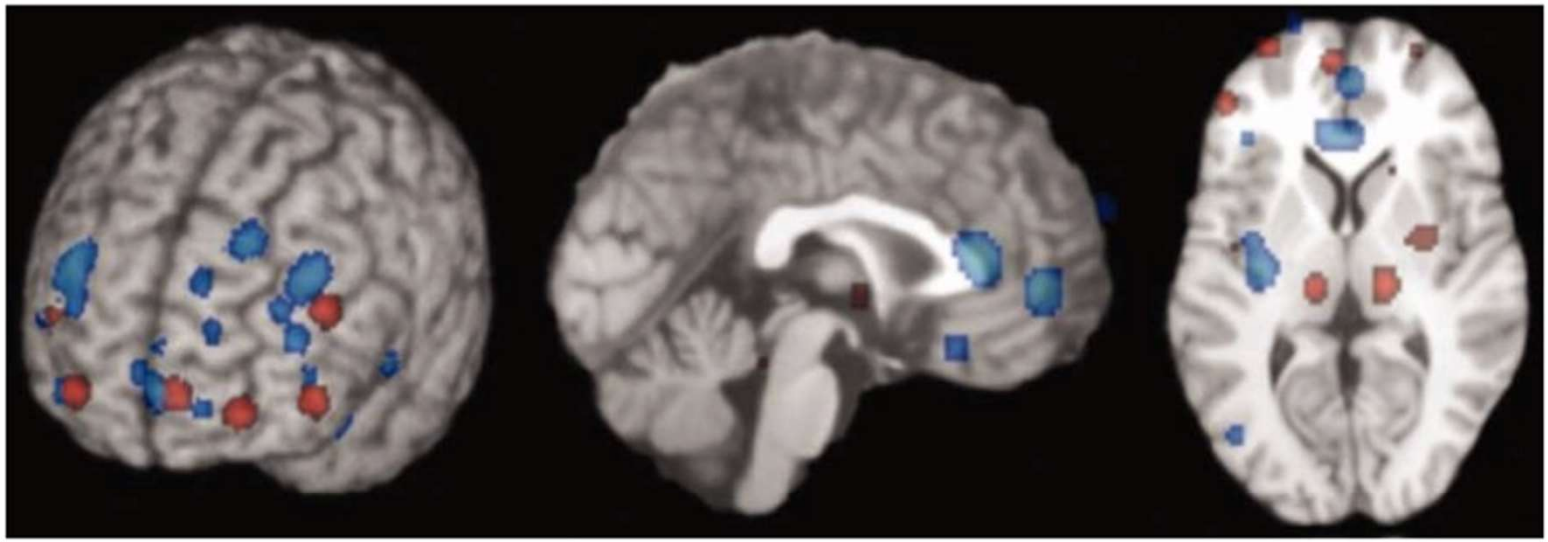


1. Kennedy SE, et al. *Arch Gen Psychiatry*. 2006;**63**:1199–1208. 2. Drevets WC. *Curr Opin Neurobiol*. 2001;**11**:240–249. 3. Whittle S, et al. *Neurosci Biobehav Rev*. 2006;**30**:511–525. 4. Schlaepfer TE, et al. *Neuropsychopharmacology*. 2008;**33**:368–377. 5. Gaughran F, et al. *Brain Res Bull*. 2006;**70**:221–227.


Striatum
Psychomotor fatigue
(physical)
Dorsolateral
prefrontal cortex
Psychomotor fatigue (mental)
Concentration
Interest
Pleasure
Nucleus accumbens
Interest
Pleasure
Fatigue
Energy
Thalamus
Ventromedial
prefrontal cortex
Mood
Guilt
Suicidality
Worthlessness
Amygdala
Mood
Guilt
Suicidality
Worthlessness
Hypothalamus
Sleep
Appetite
Cerebellum
Psychomotor
Brainstem
Neurotransmitter centers
Spinal cord
Fatigue (physical)

Decreased Activity in DLPFC and dACC in Patients with MDD

Areas of increased activation in patients with MDD at rest (red) and decreased activation (blue) compared with controls



Increased activity: lateral orbital prefrontal cortex, ventromedial prefrontal cortex, amygdala, thalamus, caudate

Decreased activity: dorsolateral prefrontal cortex (DLPFC), insula, pregenual and dorsal anterior cingulate cortex (dACC), superior temporal gyrus

Fitzgerald PB, et al. *Hum Brain Mapp*. 2008;**29**:683–695.

Psychoneuroendocrynological factors

Lasting alterations in neuroendocrine and behavioral responses can result from severe early stress. Recent studies in depressed patients indicate that the history of early trauma is associated with increased HPA activity accompanied by structural changes (i.e. atrophy or decreased volume) in the cerebral cortex.

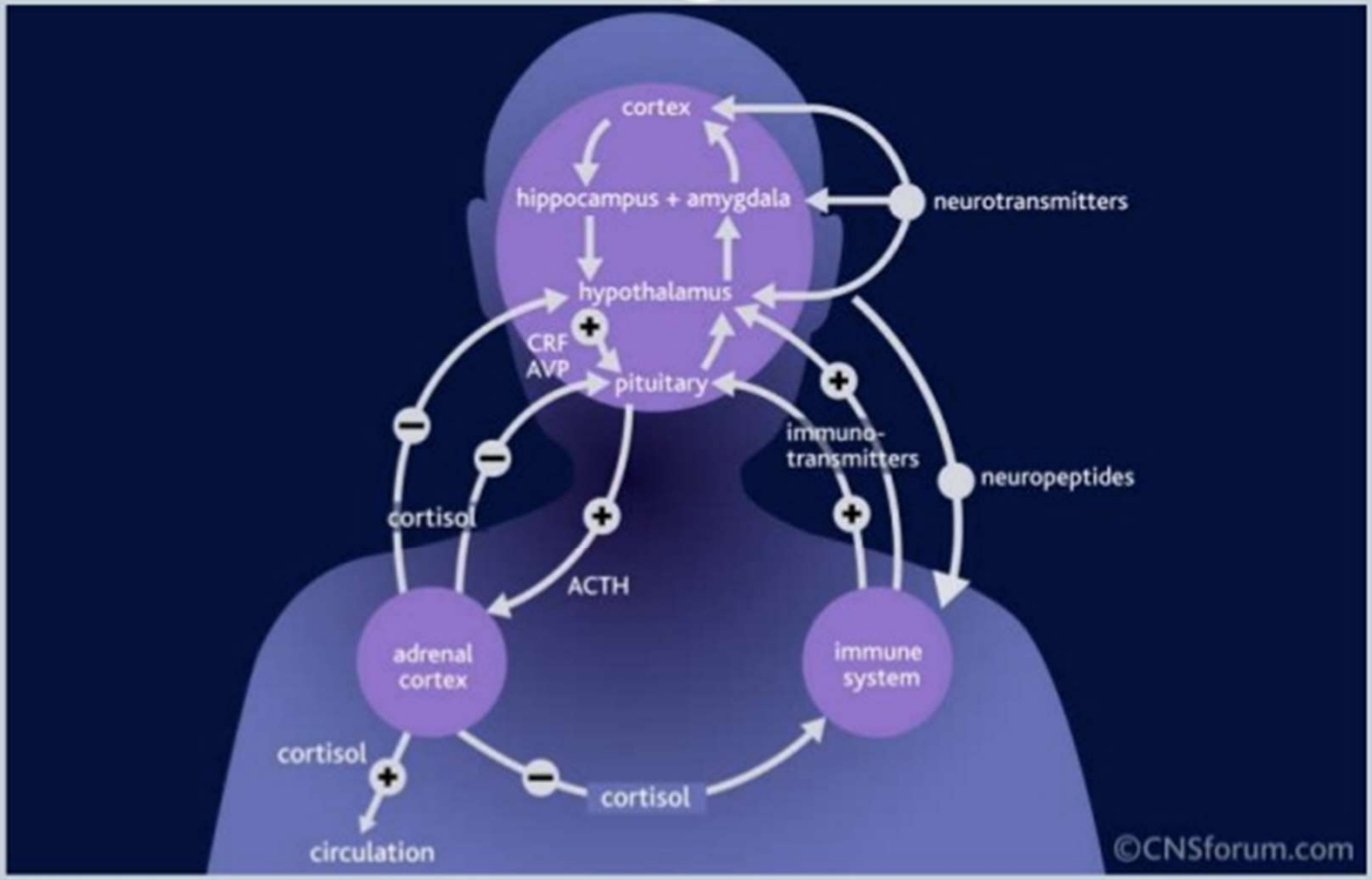
- Disturbances of hypothalamus-pituitary-adrenal axis (HPA):

– ↑ corticotrophin (ACTH), ↑ cortisol,

– ↑ neuropeptides (NPY, SP, TRH, CRH , β-endorphin).

- Changes in thyroid hormones, growth hormone and prolactine
- Association with endocrinopathies (hypo- and hyperthyroidism, Cushing's disease, Addison's disease)

HPA Axis


cortex
hippocampus + amygdala
neurotransmitters
hypothalamus
CRF
AVP
pituitary
immuno-
transmitters
neuropeptides
cortisol
ACTH
adrenal
cortex
immune
system
cortisol
cortisol
circulation
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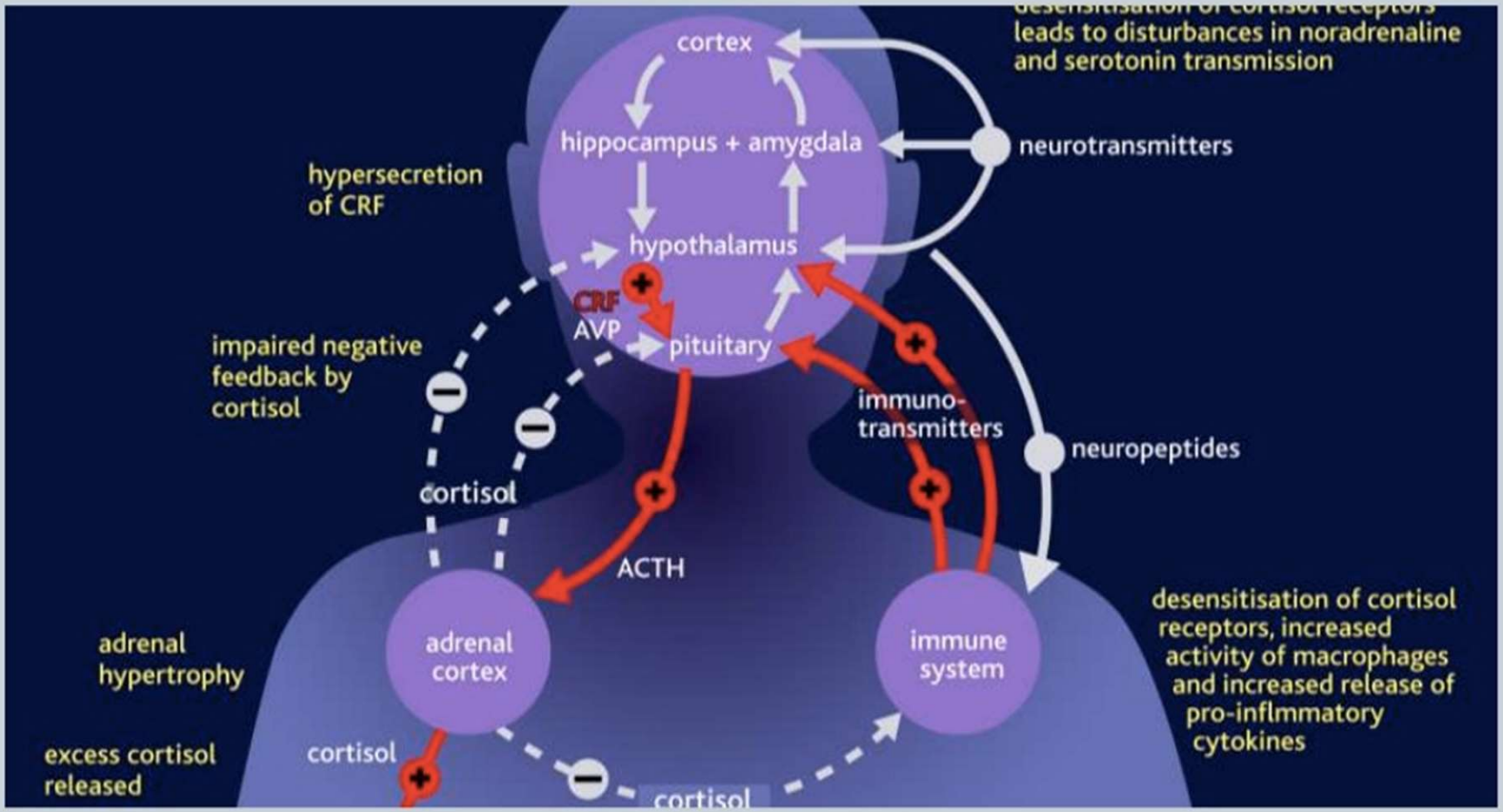
HPA Axis

- HPA axis overactivity is one of the best replicated findings in the neurobiology of depression
- Fifty percent of depressed patients exhibit nonsuppression of cortisol secretion after administration of the dexamethasone ; appears that glucocorticoid receptors may become dysfunctional in depression.
- IV administration of exogenous CRF causes depressed patients to exhibit a blunted ACTH response compared with that in healthy subjects; likely to be due to downregulation of CRF receptors in the pituitary, secondary to persistent increased CRF secretion.
- Hypercortisolaemia is associated with neurotoxicity and reduced hippocampal neurogenesis.

HPA Axis in Depression



Neurotrophic factors

- Volumetric decreases in the hippocampus and other forebrain regions in depressed patients have supported hypothesis for depression involving decrements in neurotrophic factors.
- Main focus has been BDNF
- Support for the 'BDNF hypothesis' has come from a literature showing that several forms of stress reduce BDNF-mediated signalling in the hippocampus, whereas chronic treatment with antidepressants increases BDNF-mediated signalling.

Brain-derived neurotrophic factor

- protein that, in humans, is encoded by the *BDNF* gene
- member of theneurotrophin family of growth factors
- acts on certain neurons of the central nervous system and the peripheral nervous system, helping to support the survival of existing neurons, and encourage the growth and differentiation of new neurons and synapses
- is active in thehippocampus, cortex, and basal forebrain—areas vital tolearning, memory, and higher thinking.

Psychoimmunology

- Interleukins (IL-1→12).
- Tumor Necrosis Factor (TNF).
- Interferons (IFN-α, -β, -γ).
- Other (M-CSF, G-CSF, MG-CSF).

Cytokines in depression

1.Treatment of patients with cytokines can produce depression symptoms;

2. Activation of the immune system is observed in many depressed patients;

3. Depression occurs more frequently in those with medical disorders associated with immune dysfunction;

4. Activation of the immune system, and administration of endotoxin (LPS) or interleukin-1 (IL-1) to animals induces sickness behavior, which resembles depression, and chronic treatment with antidepressants has been shown to inhibit sickness behavior induced by LPS;

5. Several cytokines can activate the hypothalamo–pituitary–adrenocortical axis (HPAA), which is commonly activated in depressed patients;

6. Some cytokines activates cerebral noradrenergic systems, also commonly observed in depressed patients;

Life events

- A long-standing clinical observation is that stressful life events more often precede first, rather than subsequent, episodes of mood disorders.
- The most compelling data indicate that the life event most often associated with development of depression is losing a parent before age 11 years.
- The environmental stressor most often associated with the onset of an episode of depression is the loss of a spouse.
- Another risk factor is unemployment- persons out of work are 3 times more likely to report symptoms of an episode of major depression than those who are employed.

Personality factors

- No single personality trait or type uniquely predisposes a person to depression.
- All humans, of whatever personality pattern, can and do become depressed under appropriate circumstances.
- Persons with certain personality disorders- OCD, histrionic and borderline- may be at greater risk for depression than persons with antisocial or paranoid personality disorder.

DSM-V criteria for Major Depressive Disorder

Must have 1 of these 2

- Depressed mood most of the day, nearly every day for **2 weeks**
- Loss of interest or pleasure in all or almost all activities

Plus these other symptoms to equal 5 total

- Change in weight (+/- 5%) or appetite
- Sleep disorder (insomnia/hypersomnia)
- Psychomotor retardation/agitation
- Fatigue/loss of energy
- Guilt/low self-esteem
- Difficulty concentrating/indecisiveness
- Recurrent thoughts of death or suicide

Special types of Depression

- Melancholic
  - Anhedonia, severly depressed mood
  - Somatic symptoms (worse in the morning, early morning awakening, weight loss, loss of libido, profound feelings of guilt
  - More common in elderly
- Atypical
  - Overeating, oversleeping, anxiety
- Catatonic (extremely rare)
  - Catalepsy, blunted affect, extreme withdrawal, motoric immobility/negativism, echolalia, echopraxia

Masked depression- depression without depression

- atypical depression in which somatic symptoms or behavioural disturbances dominate the clinical picture and disguise the underlying affective disorder

- Somatic manifestations of MD are distinguished by an extreme diversity:

  -headaches,

  - back pain,

  -abdominal pain etc.

- Pathological behaviour masking:

  -compulsive gambling

  -compulsive work,

  -changes in arousal or orgasmic function,

  -decreased libido

  -impulsive sexual behaviour

  -alcoholism,

  -drug addiction

Special types of Depression

- Seasonal Affective Disorder SAD (also known as "winter depression" or "winter blues")
  - Some people have a seasonal pattern of mood disorders.
  - They tend to experience depressive episodes during particular seasons, most commonly in winter.
  - The pattern has become known as SAD, although this term is not used in DSM-V.
  - SAD is more prevalent in people who are young and typically affects more females than males. It is characterized by: increased appetite (carbohydrate craving), weight gain and excessive sleep.
  - Treatment- phototherapy
- Postpartum onset

Psychotic Symptoms

- Hallucinations & delusions in depression or mania

- mood congruent:
  - in depression (inadequacy, guilt, disease, death, nihilism, punishment)
  - in mania (inflated worth, power, knowledge, identity, special relationship to deity or famous person)
- mood incongruent:
  - in depression and mania (eg. paranoid)

- Poorer prognosis,
- Higher risk of suicide
- Usually requires hospitalization

Physical Symptoms

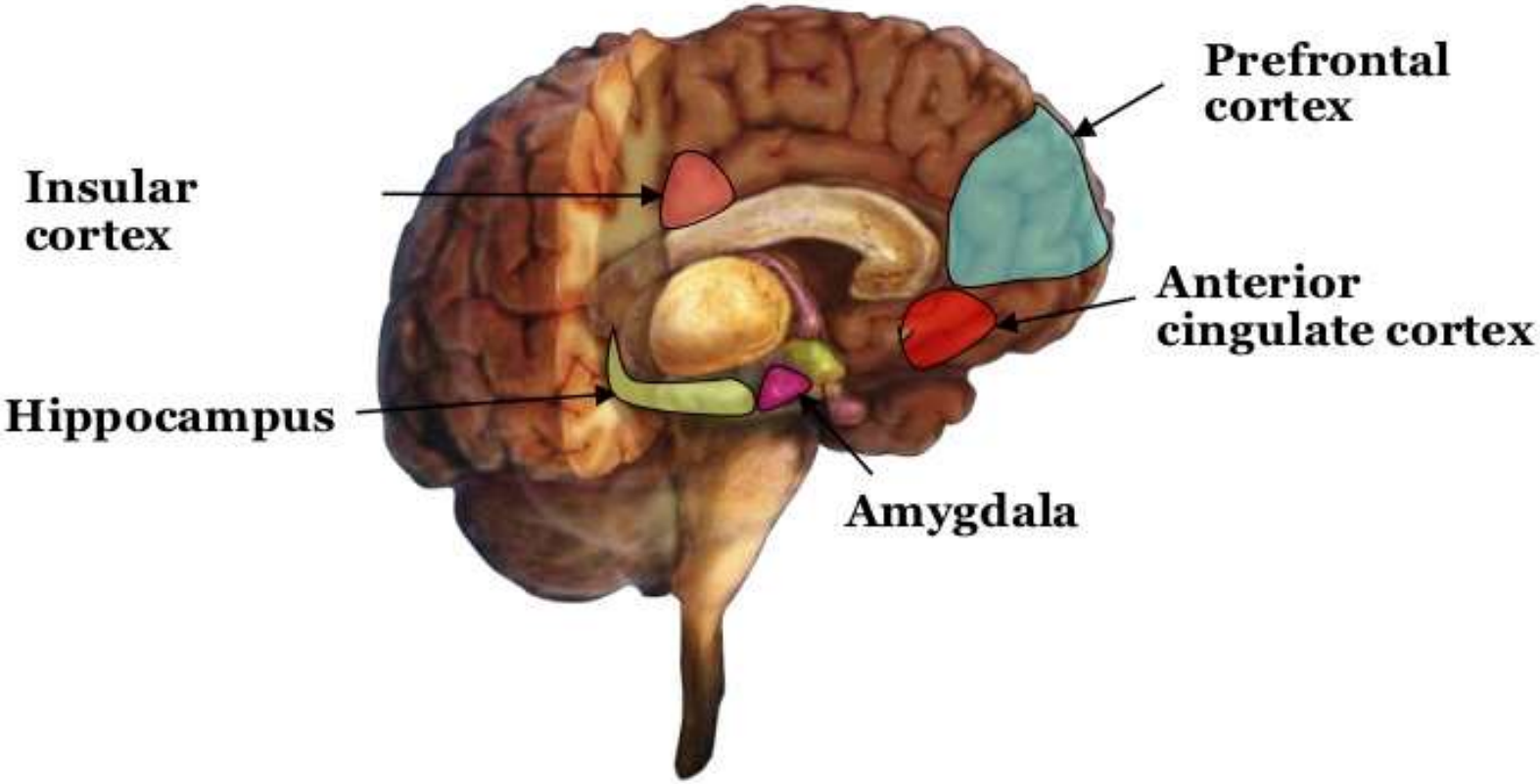
- Headache
- Vague
- Sleep disturbances
- Fatigue
- Aches and pains
- Back pain
- Significant change in appetite resulting in weight loss or gain
- Constipation

Physical Symptoms in Psychiatric Patients

Symptom	Psychiatric Patients %	Healthy Subjects %
Tiredness, lack of energy	85	40
Headache, head pains	64	48
Dizziness or faintness	60	14
Feeling of weakness in parts of body	57	23
Muscle pains, aches, rheumatism	53	27
Stomach pains	51	20
Chest pains	46	14

Data from Kellner R, Sheffield BF. The one-week prevalence of symptoms in neurotic patients and normals. Am J Psychiatry 1973;130:102–105

Some Key Areas of the Brain that May Play a Role in Both MDD and Pain



Remission

In partial remission:

- symptoms of the immediately previous major depressive episode are present, but full criteria are not met, or
- there is a period lasting less than 2 months without any significant symptoms of a major depressive episode following the end of such an episode.

In full remission:

- during the past 2 months, no significant signs or symptoms of the disturbance were present

Severity

Severity is based on the number of criterion symptoms, the severity of those symptoms and the degree of functional disability.

- **Mild**: Few, if any, symptoms in excess of those required to make the diagnosis are present, the intensity of the symptoms is distressing but manageable, and the symptoms result in minor impairment in social and occupational functioning.
- **Moderate**: The number of symptoms, intensity of symptoms, and/or functional impairment are between those specified for "mild" and "severe".
- **Severe**: The number of symptoms is substantially in excess of that required to make the diagnosis, the intensity of the symptoms is seriously distressing and unmanageable, and the symptoms markedly interfere with social and occupational functioning.

Secondary mood disorders

1. Caused by a general medical condition:

- neurological disorders (dementia, stroke, SM)
- hormonal changes (thyroid abnormalities, Addison's disease, Cushing's disease)
- cancer
- cardiovascular diseases (heart attack)
- gastrointestinal diseases (cirrhosis)
- pulmonary diseases (chronic pulmonary obstructive disease)
- autoimmune diseases (lupus, rheumatoid arthritis)

Secondary mood disorders

2. Substance-induced mood disorder

- Alcohol dependence frequently coexists with mood disorders. Both patients with major depressive disorder and those with bipolar I disorder are likely to meet the diagnostic criteria for an alcohol use disorder.
- Substance-related disorders other than alcohol dependence are also commonly associated with mood disorders. The abuse of the substances may be involved in precipitating an episode of illness or, conversely, may represent patient's attempts to treat their own illnesses.
- Although manic patients seldom use sedatives to dampen their euphoria, depressed patients often use stimulants, such as cocaine and amphetamine, to relieve their depression.

Treatment of depression

Treatment guidelines recommend that initial treatment should be individually tailored based on factors including:

- severity of symptoms
- co-existing disorders
- prior treatment experience
- patient preference

Treatment of depression

- Pharmacotherapy
- Psychotherapy
- Electroconvulsive therapy
- Phototherapy
- Vagal Nerve Stimulation (VNS)
- Transcranial Magnetic Stimulation (TMS)
- Sleep Deprivation

Pharmacotherapy

- TCAs
- MAOIs
- SSRIs
- SNRIs
- SARI

Pharmacotherapy

- The available antidepressants do not differ in overall efficacy, speed of response or long-term effectiveness.
- Antidepressants, however, do differ in their pharmacology, drug-drug interactions, short- and long-term side effects, likelihood of discontinuation symptoms and ease of dose adjustment.
- Failure to tolerate or to respond to one medication does not imply that other medications also fail.

Pharmacotherapy

Selection of the initial treatment depends on:

- symptoms severity
- chronicity of the condition
- course of illness
- family history of illness
- prior treatment response
- concurrent general medical and other psychiatric conditions
- potential drug-drug interactions
- patient preference

Pharmacotherapy

- The use of specific pharmacotherapy approximately doubles the chances that a depressed patient will recover in 1 month.
- All currently available antidepressants may take up to 3 to 4 weeks to exert significant therapeutic effects, although they may begin to show their effects earlier.
- Choice of antidepressant is determined by the side effect profile least objectionable to a given patient's physical status, temperament and life style.
- Although the first antidepressant drugs, the monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs), are still in use, newer compounds have made the treatment of depression more "clinician and patient friendly".

Pharmacotherapy

- Antidepressant treatment should be maintained for at least 6 months or the length of a previous episode, whichever is greater.
- Depressive episodes that have involved significant suicidal ideation or impairment of psychosocial functioning indicate the need of prophylactic treatment.
- Prophylactic treatment with antidepressants is effective in reducing the number and severity of recurrences.
- When antidepressant treatment is stopped, the drug dose should be tapered gradually over 1 to 2 weeks, depending on the half-life of the particular compound.

Psychotherapy

- cognitive-behavioral therapy
- psychoanalytic psychotherapy
- interpersonal therapy
- family and group therapy

PHOTOTHERAPY (light therapy)

- It typically involves exposing the affected patient to bright light in the range of 1.500 to 10.000 lux (the unit of illuminance), typically with a light box that sits on a table or a desk.
- Patient sit in front of the box for approximately 1 to 2 hours before dawn each day although some patients may also benefit from exposure after dusk.
- Usually for 1 to 2 weeks but longer treatment durations may be associated with greater response.
- In addition to seasonal depression the other indications may include:
  - sleep disorders (also in geriatric patients)
  - irritability and diminished functioning associated with shift work
  - jet lag (fatigue caused by the time zone difference)
  - OCD that has a seasonal variation

Vagal Nerve Stimulation (VNS)

- Experimental simulation of the vagus nerve in several studies designed for the treatment of epilepsy found that the patients showed improved mood.
- This observation led to the use of left VNS stimulation using an electric device implanted in the skin, similar to a cardiac pacemaker.
- The mechanism of action of VNS to account for improvement is unknown.
- The vagus nerve connects to the enteric nervous system and, when stimulated, may cause the release of peptides that act as neurotransmitters.
- Extensive clinical trials are being conducted to determine the efficacy of VNS.

Transcranial Magnetic Stimulation (TMS)

- Transcranial Magnetic Stimulation (TMS) shows promise as a treatment for depression.
- It involves the use of a very short pulses of magnetic energy to stimulate nerve cells in the brain.
- The patient do not require anesthesia or sedation and remain awake and alert.
- It is a 40-minute outpatient procedure that is prescribed by a psychiatrist and performed in psychiatrist's office.
- The treatment is typically administered daily for 4 to 6 weeks.
- The most common adverse event related to treatment was scalp pain or discomfort.
- TMS therapy is contraindicated in patients with implanted metalic devices or nonremovable metalic object in or around head.

Sleep Deprivation

- Approximately 60% of depressive patients exhibit significant but transient benefits from total sleep deprivation.
- The positive results are typically reversed by the next night of sleep.
- Several strategies have been used in an attempt to achieve a more sustained response to sleep deprivation.
- A number of studies have suggested that total or partial sleep deprivation followed by immediate treatment with an antidepressant or lithium sustains the antidepressant effects of sleep deprivation.
- Several studies have revealed that sleep deprivation accelerates the response to antidepressant medications.

Course of depression

Onset:

- The first depressive episode occurs before age 40 years in about 50% of patients.
- A later onset is associated with the absence of a family history of mood disorders, antisocial personality disorder and alcohol abuse.

Duration:

- An untreated depressive episode lasts 6 to 13 months, most treated episoded last about 3 months.
- The withdrawal of antidepressants before 3 months has elapsed almost always results in the return of the symptoms.
- As the course of the disorder progresses, patients tend to have more frequent episodes that last longer.
- Over a 20-year period, the mean number of episodes is 5 or 6.

Prognosis

- Major depressive disorder tends to be chronic and patients tend to relapse.
- Patients who have been hospitalized for a first episode of major depressive disorder have about 50% chance of recovering in the first year.
- About 25% of patients experience a recurrence of major depressive disorder in the first 6 months after release from hospital, about 30 to 50 % in the following 2 years and about 50 to 75% in 5 years.
- The incidence of relapse is lower in patients who continue prophylactic psychopharmacological treatment and in patients who have only 1 or 2 depressive episodes.

Prognostic indicators

Good prognosis:

- mild episodes
- the absence of psychotic symptoms
- a short hospital stay
- psychosocial factors:
  - friendships during adolescence
  - stabile family functioning
  - generally sound social functioning for the 5 years preceding the illness
- the absence of a comorbid psychiatric disorder or personality disorder
- advanced age of onset

Prognostic indicators

Poor prognosis:

- comorbidity of:
  - dysthymic disorder
  - abuse of alcohol or other substances
  - anxiety disorder
- a history of more than one previous depressive episode

Depression in the old age

Epidemiology

- Of 35 million seniors in the US
  - An estimated 2 million have a depressive illness
  - 5 million have subsyndromal depression
  - Less than 10% are treated
  - 1 in 10 Americans over 65 will be depressed
- 19% of all suicides are by patients over 65
  - Seniors comprise 13% of the population
  - The highest suicide rates in the U.S. are found in white men over age 85.
- Seniors have 50% higher health care costs if depressed

What are the differences between older and younger persons with depression?

- **Assessment is different:** e.g., cognitive assessment needed, recognize sensory impairments, allow more time
- **Symptoms of disorders may be different:** e.g., different symptoms in depression
- **Treatment is different:** e.g., different doses of meds, different psychotherapeutic approaches

Depression is the most frequent cause of emotional suffering in later life and frequently diminishes quality of life.

A key feature of depression in later life is **COMORBIDITY**

e.g., with physical illness such as stroke, myocardial infarcts, diabetes, and cognitive disorders (possibly bi-directional causality)

Epidemiology

- 16.2% of US population report at least one lifetime episode
- More than half of patients have first episode by age 40
- 25% of older cancer patients
- 25-50% of post-stroke patients
- 1/3 of Alzheimer's patients
- 50% of Parkinson's patients
- 30% of post-MI patients

Predisposing risk factors for depression

- Female sex.
- Widowed or divorced status.
- Previous depression.
- Brain changes due to vascular problems.
- Major physical and chronic disabling illnesses.
- Polypharmacy.
- Excessive alcohol use.
- Social disadvantage and low social support.
- Caregiving responsibilities for person with a major disease (e.g., dementia).
- Personality type

Screening for depression should be undertaken :

- any recently bereaved individual with unusual symptoms

(active suicidal ideation, guilt not related to the deceased, psychomotor retardation, mood congruent delusions, marked functional impairment more than 2 months after loss, or a reaction seemingly out of proportion to the loss).

- bereavement continuing 3 to 6 months after the loss,
- social isolation,
- persistent complaints of memory difficulties,

Screening for depression should be undertaken :

- chronic disabling illness,
- recent major physical illness (e.g., within 3 months),
- persistent sleep difficulties,
- significant somatic concerns or recent onset of anxiety,
- refusal to eat or neglect of personal care,
- recurrent or prolonged hospitalization,
- diagnosis of dementia,
- diagnosis of Parkinson disease,
- diagnosis of stroke
- recent placement in a nursing home or other long-term care facility.

A full assessment for depression in the elderly includes the following:

- Review of diagnostic criteria according to DSM-V.
- Estimation of severity, including presence of psychotic or catatonic symptoms.
- Suicide risk assessment.
- Review of psychiatric comorbid illnesses.
- Review of medical illnesses.
- Personal and family history of mood disorder, as well as other psychiatric illnesses.
- Review of current medications and allergies.
- Review of substance use.
- Review of current stresses and life situation.

A full assessment for depression in the elderly includes the following:

- Level of functioning/disability.
- Review of support system, family situation, and personal strengths.
- Mental status examination, including an assessment of cognitive functioning.
- Physical examination and laboratory investigations in order to identify any medical problems that could contribute to or mimic depressive symptoms (e.g., hypothyroidism and anemia, leading to TSH, B12, and Hb testing being part of the workup).
- Review of collateral information when available

Major Depression

Similar across lifespan but there may be some differences. Among older adults:

- **Psychomotor disturbances** more prominent (either agitation or retardation),
- Higher levels of **melancholia**(symptoms of non-interactiveness, psychological motor retardation or agitation, weight loss)
- Tendency to talk more about **bodily symptoms**
- **Loss of interest** is more common
- **Social withdrawal** is more common
- **Irritability** is more common
- **Somatization** (emotional issues expressed through bodily complaints)is more common

Pseudodementia—"depression with reversible dementia" syndrome: dementia develops during depressive episode but subsides after remission of depression.

Mild cognitive impairment (MCI) in depression ranges from 25% to 50%, and cognitive impairment often persists 1 year after depression clears.

Even if depression and cognitive problems clear, they may be prodromal for eventual irreversible dementia (40% on 3-year follow-up).

History of depression, especially in later life, even without cognitive impairment, is a risk for eventual dementia.

Psychotic depression

A problem in the elderly:

- 20-45% of geriatric psychiatric inpatients
- 4% of depressed elders in the community

Presentation:

- Primarily delusions, hallucinations less so
- Guilt, hypochondriasis, nihilism, persecution, jealousy
- Highly systematized, mood-congruent delusions
- Delusion often frightening or catastrophic
- Needs treatment for depression and psychosis
- These patients require antipsychotic treatment
- Often require electroconvulsive therapy (ECT)

Course of Geriatric Depression

- More chronic than early onset depression
- Adult rate for chronic depression is 20%
- Geriatric rate for chronic depression near 30%
- 13-19% relapse at one year
- Risks for relapse after age 65
  - Frequent episodes
  - Late age at onset
  - Dysthymia
  - Medical illness
  - High severity of first episode
  - Hospitalization, suicide attempt
- Rationale for long term use of antidepressants in this population

Treatment of Depression in Older Adults

- Use same antidepressants as younger patients—however, start low, go slow, keep going higher, and allow more time(if some response has been achieved, may allow up to 10-14 weeks before switching meds).
- Older patients may have a shorter interval to recurrence than younger patients. Thus, they may need longer maintenance of medication.
- Data are not clear if the elderly are more prone to relapse.

What do we know about elderly suicide?

- Elderly suicides are characterized by a higher rate than the general population, higher lethality, greater determination and fewer warning signs
- They are consistently associated with a number of risk factors, e.g. past history of suicide, physical illness, psychiatric illness and certain personality traits (Conwell et al, 2002)
- Some of these factors are modifiable, e.g. depressive illness
- The majority of elderly who eventually commit suicide would make contact with a primary care physician one month before their suicide (but not necessarily for a mood problem) and most remain undetected (Chiu et al, 2004)

Bereavement (loss of a loved one through death)

Grief (psychosocial reaction to any loss such as depression, anxiety, guilt, anger, etc)

Approximately 800,000 older Americans are widowed each year.

Acute grief: traumatic distress

- separation distress,
- guilt/remorse,
- social withdrawal,
- preoccupation with images of dead person

Lasts approximately 6 months leads to **Integrated Grief** as a background state

- reestablishment of interests,
- accessibility of memories of deceased
- no preoccupations
- more positive emotions

- In contrast to the DSM-IV-TR, in which a diagnosis of major depressive disorder was not made within 2 months of the loss of the loved one, except when marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms or motor retardation was present, in DSM-V, a diagnosis of major depressive disorder can be made at any time following the loss, even without the preceding symptoms.

- This change reflects the understanding that grief typically lasts 1 to 2 years, rather than 2 months, and that major depressive disorder may occur in the presence of grief at any time after loss.

Depression in Children and Adolescents

- Depression is not always easy to recognize in children. In children, symptoms of depression are often hidden by other behavioral and physical complaints.
- Many young people who are depressed will also have a second psychiatric condition at the same time which can complicate diagnosis.

Symptoms of Major Depressive Disorder in Adults	Signs of Depression Frequently Seen in Youth
Depressed mood most of the day	Irritable or cranky mood
Decreased interest/enjoyment in once-favorite activities	Boredom, loss of interest in sports, video games; giving up favorite activities
Significant weight loss/gain	Failure to gain weight as normally expected; overeating and weight gain especially in teens
Insomnia or hypersomnia	Changes in sleep patterns; delays in going to or falling asleep; refusal to wake for school; early morning awakening
Psychomotor agitation/retardation	Difficulty sitting still, pacing, or very slowed down with little spontaneous movement
Fatigue or loss of energy	Persistently tired, feels lazy

Symptoms of Major Depressive Disorder in Adults	Signs of Depression Frequently Seen in Youth
Low self-esteem; feelings of guilt	Self-critical; blaming oneself for things beyond one's control; "no one likes me, everyone hates me"; feels stupid
Decreased ability to concentrate; indecisiveness	Decline in performance in school due to decreased motivation and ability to concentrate; frequent absences
Recurrent suicidal ideation or behavior	Frequent thinking and talking about death; writing about death; giving away favorite toys or belongings

Depression before puberty occurs equally in boys and girls. After puberty, depression is more common in girls.

Treatment

- The American Academy of Child and Adolescent Psychiatry practice parameters, as well as a consensus of experts who developed the Texas Children's Medication Algorithm Project (TMAP) made evidence-based recommendations for the treatment of children and adolescents with depressive disorder.
- These include psychoeducation and supportive interventions for youth with mild forms of depression.
- For youth with moderate to severe depression or recurrent episodes of major depression, with significant impairment and with active suicidal ideation or behaviours, or psychosis, optimal intervention includes both pharmacotherapy and cognitive behavioral therapy (CBT).
- CBT or interpersonal therapy (IPT) alone may be effective for moderate depression, especially when treatment is continued for 6 months or longer.

Pharmacotherapy

Fluoxetine and **escitalopram** have Food and Drug Administration (FDA) approval in the treatment of major depression in adolescents.

FDA Warning and Suicidality

- In September 2004, the FDA received information from their Psychopharmacological Drug and Pediatric Advisory Committee indicating, based on their review of reported suicidal thoughts and behaviour among depressed children and adolescents who participated in randomized clinical trials with 9 different antidepressants, an increased risk of suicidality in those children who were on active antidepressant medications.
- Although no suicides were reported , the rates of suicidal thoughts and behaviours were 2% for patients on placebo versus 4% among patients on antidepressant medications.

FDA Warning and Suicidality

- The FDA, in accordance with the recommendation of their advisory committees, instituted a "black-box" warning to the health professional label of all antidepressant medication indicating the increased risk of suicidal thoughts and behviours in children and adolescents being treated with antidepressant medications, and the need for close monitoring for these symptoms.
- Several reviews since 2004, concluded that the data do not indicate a significant increase in the risk of suicide or serious suicide attempts after starting treatment with antidepressive drugs.

„Baby blues"

- Many women experience some affective symptoms during the postpartum period - 4 to 6 weeks following delivery.
- Most of these women report symptoms consistent with "**baby blues**" a transient mood disturbance characterized by:
  - mood lability
  - sadness
  - dysphoria
  - subjective confusion
  - tearfulness

„Baby blues"

- These feelings may last several days.
- They have been ascribed to rapid changes in women's hormonal levels, the stress of childbirth and the awareness of the increased responsibility that motherhood brings.
- No professional treatment is required other than education and support for the new mother.
- If the symptoms persist longer than 2 weeks, evaluation is indicated for postpartum depression.

Postpartum depression

- Coded as a subtype of major depressive disorder in DSM-V and is characterized by:
  - depressed mood
  - excessive anxiety
  - insomnia
  - change in weight
- The onset is generally within 12 weeks after delivery.
- Treatment of postpartum depression is not well studied because of the risk of transmitting antidepressants to newborns during lactation.

Characteristic	Baby Blues	Postpartum Depression
Incidence	30-75% of women who give birth	10-15% of women who give birth
Time of onset	3 to 5 days after delivery	Within 3 to 6 months after delivery
Duration	Days to weeks	Months or years, if untreated
Associated stressors	No	Yes, especially lack of suport
Sociocultural influence	No, present in all cultures and socioeconomic classes	Strong association
History of mood disorder	No association	Strong association
Family history of mood disorder	No association	Strong association
Tearfulness	Yes	Yes
Mood lability	Yes	Often present, but sometimes mood is uniformly depressed
Anhedonia	No	Often
Sleep disturbance	Sometimes	Nearly always
Suicidal thoughts	No	Sometimes
Thoughts of harming the baby	Rarely	Often
Feelings of guilt, inadequacy	Absent or mild	Often present and excessive

Postpartum depression

- Mood episodes can have their onset during pregnancy or postpartum.
- Between 3% and 6% of women will experience the onset of major depressive episode during pregnancy or in the weeks following delivery.
- 50% of "postpartum" major depressive episodes actually begin prior to delivery.
- Thus, these episodes are referred to collectively as *peripartum* episodes.

Postpartum depression

- Women with peripartum major depressive episodes often have severe anxiety and even panic attack.
- Prospective studies have demonstrated that mood and anxiety symptoms during pregnancy, as well as the "baby blues", increase the risk for postpartum major depressive episode.

Postpartum depression

- Peripartum-onset mood episodes can present either with or without psychotic features.
- Infanticide is most often associated with postpartum psychotic episodes that characterized by command hallucinations to kill the infant or delusions that the infant is possessed.
- Sometimes extended suicide is commited
- Psychotic symptoms can also occur in severe postpartum mood episodes without such specific delusions or hallucinations

Postpartum depression

- Postpartum mood (major depressive or manic) episodes with psychotic features appear to occur in from 1 to 500 to 1 in 1000 deliveries and may be more common in primiparous women.

- Once woman has had a postpartum episode with psychotic features, the risk of recurrence is between 30% and 50%.

Postpartum depression

- The postpartum period is unique with respect to the degree of neuroendocrine alterations and psychosocial adjustments, the potential impact of breastfeeding on treatment planning and the long-term implications of a history of postpartum mood disorders on subsequent family planning.

Postpartum depression in men?

- A syndrome described in fathers is characterized by mood changes during their partners' pregnancies or after the babies are born.
- These fathers are affected by several factors:
  - added responsibility
  - diminished sexual outlet
  - decreased attention from his wife
  - the belief that the child is a binding force in an unsatisfactory marriage

Bipolar Disorder

Epidemiology of bipolar disorder

- Annual incidence: **<1%**
- **M=F**

- M: more common manic episodes
- F: more common depressive, mixed episodes, more often rapid cycling

Genetics of bipolar disorder

Genetics (susceptibility):

- polygenic (many genes)

Environment (triggers):

- rough times/stress
- alcohol and drugs
- big changes
- poor nutrition

Chromosome 18	**Data suggest the preference of as many as four different loci on this chromosome. Studies have found linkage to 18q to preferentially occur in families in which affective illness was transmitted through the mother, suggesting a possible parent-of origin effect.**
Chromosome 21q	Regions have shown linkage or association to both schizophrenia and bipolar disorder.
Chromosome 22q	The breakpoint cluster region (BCR) gene is located on chromosome 22q11. The BCR gene encodes an activating protein, which is known to play important roles in neuron growth and

Genetics of bipolar disorder

- Twin study– concordance rates of 67% for MZ twins, 20% for DZ for bipolar disorder

- Neurotransmitter deficiencies –catecholamines (norepinephrine and serotonin)

- Monoamine hypothesis – shortage of NE, D, 5-HT

Patterns of inheritance

If you have…

identical twin with bipolar:

- 50-60% chance of bipolar
- 75% chance of depression

1st degree relative (child, parent, sibling) with bipolar:

- ~8% chance of bipolar
- ~10% chance of depression

two parents with bipolar:

- 30-75% chance of bipolar

2nd degree relative (aunt, uncle,cousin, grandparent) with bipolar:

- **1%** chance of bipolar
- **5%** chance of depression

no affected relatives with bipolar (gen. population.):

- **1%** chance of bipolar
- **5%** chance of depression

Types of bipolar disorder
DSM-V

- Bipolar I (Mania and Depression)
- Bipolar II (Hypomania and Depression)
- Cyclothymic Disorder
- Bipolar Disorder Due to Substance/Medication or Another Medical Condition

Bipolar Spectrum Disorder

- Until recently, it was believed that bipolar disorder occurred in 1% of the general population. This figure pertains to what is known as bipolar I disorder.
- However, the current bipolar schema in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), also includes bipolar II, cyclothymia, and bipolar disorder due to substance/medication or another medical condition.
- Thus, it should not come as a surprise that, in a wave of new epidemiologic studies, the prevalence of the entire spectrum has been revised up to at least 5% of the general population.
- Although the DSM-V does not use the construct of "bipolar spectrum," its bipolar subtypes implicitly adhere to such a broad schema.

Bipolar Spectrum Disorder

The leader in the realm of bipolar disorder and subtyping is **Hagop Akiskal**, an Armenian-American psychiatrist best known for his research on temperament and bipolar disorder.

Akiskal divided bipolar disorder into **6 primary subtypes** which include:

- Bipolar I: full mania
- Bipolar Ia: depression with mania
- Bipolar II: depression with episodes of hypomania
- Bipolar IIa: cyclothymia
- Bipolar III: antidepressant-caused hypomania
- Bipolar IIIa: depression and/or hypomania caused by substance use
- Bipolar IV: depression caused by hyperthymic attitude
- Bipolar V: recurrent depression and dysphoric hypomania episodes
- Bipolar VI: depression that progressives to a dementia-like disorder

Manic Episode

- A distinct period of abnormally and persistently **elevated**, **expansive** or **irritable mood** and abnormally and persistently **increased goal-directed activity** or **energy**
- Lasting at least **1 week** and present most of the day, nearly every day (or any duration if hospitalization is necessary)
- At least **3** of the following symptoms must be present with the "elevated, expansive, or irritable" mood; if the mood is only irritable, **4** symptoms must be present.

Manic Episode

1. inflated self-esteem or grandiosity
2. decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
3. more talkative than usual or pressure to keep talking
4. flight of ideas or subjective experience that thoughts are racing
5. distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
6. increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
7. excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

Manic Episode

- The mood disturbance is sufficiently severe to cause marked impairment in social or occupational functioning or to necessitate hospitalization to prevent harm to self or others or there are psychotic features.

- The episode is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication)

Hypomanic Episode

- Lasts at least **4** consecutive days.
- The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization.
- No psychotic features are present (if there are psychotic features, the episode is, by definition, manic).
- The episode is associated with an unequivocal change in functioning that is uncharacteristic of the individual when not symptomatic.
- The disturbance in mood and the change in functioning are observable by others.
- The episode is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication).

Depressive episode

Must have 1 of these 2

- Depressed mood most of the day, nearly every day for **2 weeks**
- Loss of interest or pleasure in all or almost all activities

Plus these other symptoms to equal 5 total

- Change in weight (+/- 5%) or appetite
- Sleep disorder (insomnia/hypersomnia)
- Psychomotor retardation/agitation
- Fatigue/loss of energy
- Guilt/low self-esteem
- Difficulty concentrating/indecisiveness
- Recurrent thoughts of death or suicide

Mixed affective state

- The criteria are met **for both** a manic and major depressive episode nearly every day for at least a **1 week**
- a state wherein features unique to both depression and mania—as despair, fatigue, morbid or suicidal ideation; racing thoughts, pressure of activity, and heightened irritability—occur either simultaneously or in very short succession
- In current (DSM-V) nomenclature, however, a "mixed episode" no longer stands as an episode of illness unto itself; rather, the symptomology specifier "with mixed features" can be applied to any major affective episode (manic, hypomanic, or depressive)
- Causes marked impairment in social, occupational or interpersonal functioning
- May be with psychotic features
- May require hospitalization
- Use of antidepressants in BD increases the risk of mixed episodes

Rapid cycling

- At least **4 episodes** of a mood disturbance in the previous **12 months** that meet criteria for a major depressive, manic, hypomanic or mixed episode

- 2 months interval between similar episodes or switch to an episode of opposite polarity

Treatment of bipolar disorder Mood stabilizers

First generation

- Lithium
- Valproate
- Carbamazepine

Second generation

- Atypical Antipsychotics
- Lamotrigine

Lithium

- Lithium has numerous pharmacological effects, but its precise mechanism of action in the treatment of psychiatric illnesses is uncertain.
- Efficacy: 49-70%
- Onset of action: 5-21 days
- Therapeutic lithium levels are between 0.6 and 1.2 mEq/L
- Tolerability: weight gain, neurocognitive, renal, gastrointestinal, endocrine side effects

Valproate

- Efficacy: 49-65%
- Onset of action: 3-10 days
- Therapeutic plasma levels are between 50 and 120 µg/mL
- Tolerability: gastrointestinal, neurocognitive side effects, weight gain, rare hepatotoxicity with liver failure

Carbamazepine

- Efficacy: 27-63%
- Onset of action: 7-14 days
- Therapeutic plasma levels are between 4 and 12 µg/mL
- Oxcarbazepine the derivative form of carbamazepine may possess similar antimanic properties (higher doses are required)
- Tolerability: neurocognitive, dermatologic, hematopoietic side effects

Atypical Antipsychotics

- Olanzapine
- Risperidone
- Quetiapine
- Ziprasidone
- Aripiprazole

Apart from their antipsychotic feature they have also demonstrated antimanic efficacy and are approved by the FDA for this indication.

Other Anticonvulsants

- **Lamotrigine**: open trial suggest mood-stabilizing effects as add-on or monotherapy; antidepressant effect confirmed in placebo-controlled trial
- **Gabapentin**: open trials suggest mood-stabilizing effects as add-on; not confirmed in double-blind, controlled trials
- **Topiramate**: open trials suggest mood-stabilizing effects as add-on; no data from controlled trials; anorexia may be a positive side effect

Course of bipolar I disorder

- Bipolar I disorder most often starts with depression (75% of the time in women and 67% in men) and is a recurring disorder.
- Most patients experience both depressive and manic episodes, although 10 to 20% experience only manic episodes.
- The manic episode typically have a rapid onset (hours or days) but may evolve over a few weeks.
- An untreated manic episode lasts about 3 months, therefore, clinicians should not discontinue giving drugs before that time.
- Of persons who have a single manic episode, 90% are likely to have another.
- As the disorder progresses, the time between episodes often decreases.

Bipolar I disorder in children

- The incidence of bipolar I disorder in children and adolescents is about 1% and the onset can be as early as age 8 years.
- Common misdiagnoses are schizophrenia and oppositional defiant disorder.
- Bipolar I disorder with such an early onset is associated with a poor prognosis.

Prognosis

- About 40 to 50% of patients with bipolar I disorder may have a second manic episode within 2 years after the first episode.
- Patients may have from 2 to 30 manic episodes, although the mean number is about 9.
- On long-term follow-up:
  - 15% of all patients with bipolar I disorder are well
  - 45% are well, but have multiple relapses
  - 30% are in partial remission
  - 10% are chronically ill
- 1/3 of all patients with bipolar I disorder have a chronic symptoms and evidence of significant social decline

Prognostic indicators

Good prognosis:

- short duration of manic episodes
- advanced age of onset
- few suicidal thoughts
- few coexisting psychiatric or medical problems

Prognostic indicators

Bad prognosis:

- premorbid poor occupational status
- alcohol dependence
- psychotic features
- depressive features
- male gender

Course of bipolar II disorder

- The course and prognosis of bipolar II disorder indicate that the diagnosis is stable because there is a high likelihood that patient with bipolar II disorder will have the same diagnosis up to 5 years later.

- Bipolar II disorder is a chronic disease that warrants long-term treatment strategies.

Clinical features predictive to bipolar disorder

Early age at onset
Psychotic depression before 25 years of age
Postpartum depression, especially with psychotic features
Rapid onset and offset of depressive episodes of short duration (<3 months)
Recurrent depression (more than 5 episodes)
Depression with marked psychomotor retardation
Atypical features
Seasonality
Bipolar family history
Trait mood lability (cyclothymia)
Hyperthymic temperament
Hypomania associated with antidepressants
Repeated (at least 3 times) loss of efficacy of antidepressants after initial response
Depressive mixed state (with psychomotor excitement, irritable hostility,

Dysthymia

Also known as "persistent depressive disorder„

- The presence of a depressed mood most of the time for at least **2 years**

(in children and adolescents mood can be irritable and duration must be at least 1 year)

- Plus 2 or more of the following:

1. Poor appetite or overeating
2. Insomnia or hypersomnia
3. Low energy or fatigue
4. Poor concentration or difficulty making decisions
6. Feelings of hopelessness

- The symptoms are not as severe as those for major depressive disorder

Dysthymia

- Dysthymia is distinguished from major depressive disorder by the fact that patients complain that they have always been depressed. Thus, most cases are of early onset beginning in childhood and adolescence.

- Early vs. Late Onset Dysthymia

– Early Onset (before 21 years of age):

1) greater chronicity,

2) poorer prognosis,

3) greater likelihood of familial transmission.

Dysthymia - Epidemiology

- 5-6 % of population
- F=M
- Frequently coexists with:
  - major depressive disorder
  - anxiety disorders (especially panic disorder)
  - substance abuse
  - borderline personality disorder
- An estimated 40% of patients with major depressive disorder also meet the criteria for dysthymia
- A combination often referred to as **double depression**

Dysthymia - Treatment

- Pharmacotherapy:
  - SSRIs
  - venlafaxine
  - bupropion
- Psychotherapy:
  - Cognitive-behavioral therapy (CBT)
  - Psychoanalytic psychotherapy
  - Interpersonal therapy
  - Family and group therapies

Dysthymia - Prognosis

- About 50% of patients with dysthymia experience an insidious onset of symptoms before age 25 years.
- Studies of patients with the diagnosis of dysthymia indicate that about:
  - 20% progressed to major depressive disorder
  - 15% to bipolar II disorder
  - <5% to bipolar I disorder
- About 25% of all patients with dysthymia never attain a complete recovery.

Cyclothymia

- Chronic (>2 years) instability of mood
- Numerous episodes of hypomania and mild depression
- 1% of the population
- F>M (3:2)
- Frequently coexist with:
  - borderline personality disorder
  - substance dependence

Cyclothymia- Treatment

- Mood stabilizers (lithium, valproate, carbamazepine)
  - Doses and plasma concentrations of these agents should be the same as those in bipolar I disorder
- Antidepressant treatment of depressed patients with cyclothymic disorder should be done with caution because these patients have increased susceptibility to antidepressant-induced hypomanic or manic episodes.
- Psychotherapy

Cyclothymia- Prognosis

- The onset of symptoms of cyclothymic disorder often occurs insidiously in the teens or early 20s.
- About 1/3 of all patients with cyclothymic disorder develop a major mood disorder, most often bipolar II disorder.

Premenstrual dysphoric disorder (PMDD)

- PMDD is a severe and disabling form of premenstrual syndrome (PMS) affecting 3–8% of menstruating women.
- PMDD was added to the list of depressive disorders in the DSM-V in 2013.
- The disorder consists of a "cluster of affective, behavioral and somatic symptoms" that recur monthly during the luteal phase of the menstrual cycle.
- The hormonal changes that occur during the menstrual cycle are probably involved in producing the symptoms, although the exact etiology is unknown.

Premenstrual dysphoric disorder (PMDD)

DSM-V

A. In the majority of menstrual cycles during the past year, at least 5 symptoms must be present in the final week before the onset of menses, start to *improve* within a few days after the onset of menses, and become *minimal* or absent in the week postmenses.

B. One (or more)of the following symptoms must be present:

1.Marked affective lability (e.g., mood swings, feeling suddenly sad and tearful or increased sensitivity to rejection)

2.Marked irritability or anger or increased interpersonal conflicts

3.Markedly depressed mood, feelings of hopelessness

4.Marked anxiety and tension

Premenstrual dysphoric disorder (PMDD)

DSM-V

C. One (or more) to reach a total 5

1.Decreased interest in usual activities (e.g., work, school, friends, hobbies)

2.Subjective difficulty in concentration

3.Lethargy and marked lack of energy

4.Marked change in appetite (e.g., overeating or specific food cravings)

5.Hypersomnia or insomnia

6.Feeling overwhelmed or out of control

7.Physical symptoms (e.g., breast tenderness or swelling, joint or muscle pain, a sensation of 'bloating' and weight gain)

D. The symptoms are associated with clinically significant distress or interference with work, school, usual social activities or relationshipes with others

Premenstrual dysphoric disorder (PMDD)

- Pharmacologic treatment of PMDD is indicated for women with severe and debilitating symptoms.
- Selective serotonin reuptake inhibitors (SSRIs) are the first-line medication.
- The U.S. Food and Drug Administration (FDA) has approved four SSRIs for the treatment of PMDD:
  - Fluoxetine
  - Sertraline
  - Paroxetine
  - Escitalopram
- Additional treatment is symptomatic and includes:
  - analgesic for pain
  - sedatives for anxiety and insomnia
  - diuretics for fluid retention

Suicide

Suicide - Epidemiology

- Ranked as the **8th** leading cause of death in the USA and the **3rd** leading cause of death in the 15-24 age group.
- Suicide kills more than 30,000 Americans each year (6000 a year recorded in Poland).
- A person is nearly twice as likely to die by suicide than by homicide in the United States.
- 1/2 of the persons who commit suicide saw a physician in the preceding month
- 1/3 were being treated for a mental illness at the time of their suicide.

Suicide - Epidemiology

- 80 % of suicides are in males, but females make more attempts
- Majority not in mental health treatment

- No.1 method – hanging (Poland), firearms (USA)
- No.1 suicide site in the world – Golden Gate Bridge, San Francisco

Suicide - Epidemiology

- **90 %** of cases – presence of a psychiatric disorder:

  - **50 %** - major depression
  - **25 %** - alcohol abuse
  - **10 %** - delusional psychosis (schizophrenia)
  - **5 %** - personality disorders

Suicide - Risk Factors

- Sex
- Age
- Race
- Employment
- Marital status
- Religion
- Family history
- Living alone
- Access to guns and other lethal means
- Physical disease
- Feelings
- Recent mental hospitalization
- Financial difficulty
- Talking about suicide
- Suicide of others
- Previous suicide attempt

Suicide - Warning Signs
Talking, reading, or writing about suicide/death.
Talking about feeling worthless or helpless.
Saying ''I'm going to kill myself," "I wish I was dead," or "I shouldn't have been born."
Visiting or calling people to say goodbye.
Giving things away or returning borrowed items.
Self destructive or reckless behavior.
Significant change in behavior.
Running away.

Clinical Evaluation

- Discussing ideas about or plans for suicide may relieve patients of the anxiety and guilt they may have and help establish a safe environment for full assessment and treatment.
- Evaluating a patient for suicide risk does not predict its happening; rather, it is a judgment of the current likelihood of a suicide attempt.
- Directly assessing the suicide risk of a patient allows for appropriate interventions that may be lifesaving.
- The physician should not hesitate to directly ask an at-risk patient about suicidal thoughts.

Recognition

- Familiarity with the risk factors allow to recognize at-risk patients and complete a thorough assessment that includes nonverbal and verbal cues as well as the patient's current quality of life.

- Nonverbal cues, including:
  - downcast eyes,
  - psychomotor retardation of speech or movement,
  - decline in attention to appearance

- should alert the physician to the possibility of depression and the need for prompt follow-up.

- Comments such as, "*I notice you seem sad today*," or "*Something else seems to be troubling you today*," may help start a conversation.

Recognition

- Verbal cues are easily overlooked in the press of time or the discomfort that often follows a patient's response.
- Statements such as, "*I am under a lot of pressure*," or "*My nerves are shot*," offer the physician the opportunity to address the patient's emotional state.
- Good eye contact, empathetic responses, and direct invitations such as, "*Tell me more*," or "*Please tell me why you are feeling that way*," will often prompt a revealing response from the patient.
- Connecting the patient's other illnesses and experiences with the current problem may clarify the severity of his or her feelings, and asking about the patient's family life, school, work, and relationships may allow the patient the opportunity to reveal suicidal thoughts.

Questions for Assessing Suicidality
Other people with similar problems sometimes lose hope; have you?
This must be a hard time for you; what do you think about when you're feeling down?
Do you ever consider running away from your problems?
With this much stress, have you thought of hurting yourself?
Have you ever thought of killing yourself?
How would you do it?
What would happen to your family or significant others if you did that?
What has kept you from acting on these thoughts?

- Simply asking about suicidal intent does not put ideas into a patient's head.

- All patients being evaluated psychiatrically should be assessed for suicide (and homicide) risk

Interview

- Asking the patient to talk about his or her plan or thoughts will allow to ascertain whether the patient has the intent and the means to commit suicide.
- During the clinical assessment, additional information about mood, the presence of anxiety or psychotic symptoms, and any indication of substance misuse (e.g., alcohol, cocaine, marijuana, heroin, prescription medications) should be gathered.
- The psychiatric and social history should include identifying previous suicide attempts or treatment for a psychiatric disorder, and clarification of the patient's current social supports and stressors.

Interview

- Given the likelihood that suicidal ideation occurs within the context of a mental illness, interventions to reduce the risk of suicide must include treating the underlying illness.
- The formal examination should include a mental status assessment that includes current cognition, mood, thought process and content, and the patient's ability to cooperate with and reveal information to the physician.
- Physical signs of substance use or withdrawal, restlessness, and agitation are important findings in the evaluation of a potentially suicidal patient.

Management of suicidal ideation

- At first, management of suicidal ideation should focus on establishing safety, possibly through hospitalization. For patients at high, although not imminent, risk of suicide, aggressive treatment of the underlying psychiatric illness is imperative and should involve a combination of pharmacotherapy and psychotherapy.

- A significant aspect of intervention involves contacting the patient's family or support network to assist in the elimination of the patient's access to potentially lethal means of suicide.

- If an imminent risk of suicide is present, hospitalization is indicated.

Summary of Assessment and Treatment of the Suicidal Patient

Identify predisposing factors (e.g., psychiatric illness, previous suicide attempts, substance abuse).
Identify contributing factors (e.g., family history, current life crises, medical illnesses, access to lethal means, demographic factors).
Conduct a specific suicide inquiry, identifying if a suicide plan or psychiatric symptoms (e.g., depression, anxiety, hopelessness, hallucinations) are present.
Develop a diagnosis formulation that encompasses the current level of suicide risk.
Identify available interventions, including family and social supports.
Begin a thorough and organized treatment that targets the identified psychiatric illness.
Document the assessment and plan.

CASE 1

- A 79-year-old man is brought to the emergency department by his family. Although the patient is essentially mute, his family members report that he has had a history of numerous episodes of depression, the last occurring 6 years ago.

- At that time, he was hospitalized and treated with sertraline. He has been hospitalized a total of four times for depression, but the family denies that he has ever been treated for mania. The patient's only current medication is hydrochlorothiazide, although he has refused to take it for the past 2 days.

- This current episode of depression, similar to previous ones, began 3 weeks prior to the emergency department visit. The patient has had frequent crying episodes and has complained of a decrease in energy. He has lost at least 15 lb in the 3 weeks and for the past 2 days has refused to eat anything at all.

CASE 1 cont.

- Three days ago, the patient told his family that he was "sorry for all the pain and suffering I have caused you" and that "it would be better if I were not around any more." Two days ago, he stopped speaking and eating, and for the past 24 hours he has refused to take anything by mouth, even water.

- After rehydration in the emergency department, the patient was admitted to the psychiatry service. The results of his physical examination were essentially normal, although his blood pressure was 150/92 mm Hg, and he exhibited psychomotor slowing. The patient refused all attempts to feed him by mouth. When asked if he was suicidal, he nodded his assent, as well as nodding to the question, "Are you hearing voices?"

CASE 1 cont.

- What is the most likely diagnosis?
- What is the best plan of action for this patient?

CASE 2

- A 27-year-old man is brought to the emergency department by his friends and his roommate. The friends state that the patient had not slept for the past 3 or 4 weeks. They have noticed that he stays up all night cleaning his apartment. He has bought new computer equipment and a digital video disc player, although his roommate claims that the patient cannot afford these kinds of items.

- The patient has also been bragging to his friends that he has slept with three different women in the past week, behavior very unlike his usual self, and he has been very irritable and explosive. He has been drinking a "lot of alcohol" for the past 2 weeks, which is uncharacteristic. The friends state that they have not seen the patient using drugs, and they do not think he has any medical problems or takes any prescription medication.

- They are not aware of any family history of medical or psychiatric disorders. They state that the patient is a graduate student in social work.

CASE 2 cont.

- On a mental status examination, the patient is noted to be alternately irritable and elated. He is wearing a bright-orange top and red slacks, and his socks are mismatched. He paces the room and refuses to sit down when asked to do so by the examiner. His speech is rapid and loud, and it is hard to interrupt him. He claims that his mood is "great," and he is very angry with his friends for insisting that he come to the emergency department.

- He states that they have probably insisted that he come because "they are jealous of my success with women." He states that he is destined for greatness. He denies having any suicidal or homicidal ideation, hallucinations, or delusions.

CASE 2 cont.

- What is the most likely diagnosis?
- What is the best initial treatment?

CASE 3

- A 34-year-old man visits a psychiatrist with a chief complaint of a depressed mood lasting "for as long as [he] can remember." The patient states that he never feels as if his mood is good. He describes it as being 4 on a scale of 1 to 10 (10 being the best the patient has ever felt).

- He states that he does not sleep well but has a "decent" energy level. His appetite has fluctuated for the past several years, although he did not lose any weight. He feels distracted much of the time and has trouble making decisions at his job as a computer operator. He notes that his self-esteem is low, although he denies thoughts of suicide.

- He notes that he was hospitalized once 5 years ago for major depression and was treated successfully with an antidepressant, although he does not remember which one. He notes that he has felt depressed for at least the last 10 years and that the feeling is constant and unwavering. He denies manic symptoms, psychotic symptoms, or drug or alcohol abuse. He has no medical problems.

CASE 3 cont.

- What is the most likely diagnosis for this patient?
- Should this patient be given any medication?