Mood disorders

phenomenology, etiology, treatment

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Mood disorders

Mood disorders are clinical conditions, in most cases recurrent and chronic diseases of which the essential feature is a disturbance of mood.

Mood: persistent emotional states that affect how an individual acts, think and perceivel his or her environment The basic abnormalities of mood: depression, mania.

Both occur on a continuum from normal to clearly pathological. The minor symptoms may be an extension of normal sadness or elation, more severe symptoms are associated with discret syndromes which appear to differ qualtitatively from normal processes and which require specific therapy (affective disorders)

Distinguishing normal mood from clinical psychopathology

1. impairments of autonomic body functioning
(indicated by disturbances in sleep, appetite, sexual interest, and autonomic nervous system and gastrointestinal activity)

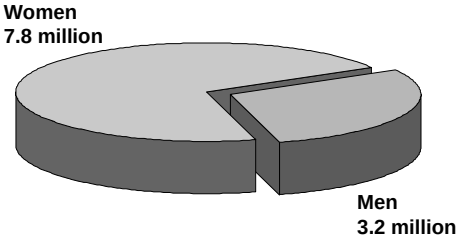
2. reduced desire and ability to perform the usual, expected social roles
(in the family, at work, in marriage, or in school)

3. suicidal thoughts or acts

4. disturbances in reality testing
(manifested in delusions, hallucinations, or confusion)

Depression: A common mood disorder

Total individuals with depression in the US:
11 million (1990)



Depression—A Major Cause of Disability Worldwide

DALYs—2000 and 2020

Rank	2000[1]	2020 (Estimated)[2]
1	Lower respiratory infections	Ischemic heart disease
2	Perinatal conditions	**Unipolar major depression**
3	HIV/AIDS	Road traffic accidents
4	**Unipolar major depression**	Cerebrovascular disease
5	Diarrheal diseases	Chronic obstructive pulmonary disease

1.World Health Report 2001. Mental Health: New Understanding, New Hope. Geneva, World Health Organization, 2001.
2. Murray CJL, Lopez AD, eds. *The Global Burden of Disease*. Boston: Harvard University Press; 1996.
DALYs=disability-adjusted life-years.

History

J. FALRET (1854) described patients who became depressed and elavated in a cyclie fashion : la folie circulaire

K. L.Kahlbaum (1882) called the similar disorder "cyclothymia"

E. KRAEPELIN (1921) called the underlying illness "manic-depressive illness", "psychosis maniaco -depressiva".

S. FREUD emphasized the importance of loss in depression (the repressed anger is turned inward by the depressed person)

A. T.BECK, A.ELLIS - the cognitive approach, importance of the cognitive triad, schemas, distortions

Depression

- Affects all ages and cultures
- Woman; men-ratio (in adults) 2 : 1
- Not related with:
  - education
  - ethnic differences
  - income
  - marital status

Depression

Life time prevalence	4,1 - 19,6%
Point prevalence	5 - 8%
Duration of episode	10 months
Relapse rate	50% (on average 5 episodes)
Death by suicide	15%

→ **A VERY SERIOUS DISEASE!!**

DSM-IV

A: Bipolar disorders:
One or more Mianic or Hyporrianic Episodes are Usually associated with one or more Depressive Episodes

Cyclothymia:
Chronic mood disturbance involving frequent Hypormanic Episodes and frequent periods of depressive mood or anhedonia

B: Depressive disorders:

Major Depression
One or more Depressive Episodes without Manic or Hypomanic Episode

Dysthymia (Depressive Neurosis)
Chronic mood disturbance involving frequent periods of depressive mood and anhedonia during a two-yera period (without Major Depressive Episod)

Major Depression; symptoms

- Depressed mood
- Diminished interest, anhedonia
- Loss of appetite/ weight loss
- Psychomotor retardation
- Loss of energy
- Feelings of worthlessness/ feelings of guilt
- Diminished ability to concentrate
- Suicidal thoughts
- Insomnia
- Anxiety symptoms

Depressive syndrome I.

Dymptoms of DEPRESSION

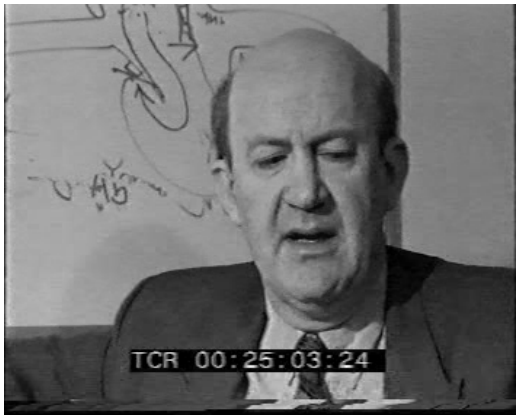
Emotional features
- -.depressed mood "blue"
- irritability, anxiety
- anhedonia loss of interest
- loss of zest' diminished emotional bonds
- interpersconal withdrawal; preoccupation with death

Cognitive features
- self-criticism, sense of worthlessness guilt
- pessimism, hopelessness, despair
- distractible, poor concentration
- uncertain and indecisive
- variable obsessions
- somatic complaints (particularly in the elderly)
- memory impairement
- delusions and hallucinations

Depressive syndrome II.

Vegative, autonomic features
- fatigabilityn no energy
- insomnia or hypersomnia - anorexia or hyperrexia - weight loss or gain
- psychomotor retardation, impaired libido frequent diurnal variation

Sign of depression:
stooped and slow movement ; tearful , sad facies; dry mouth and skin constipation



Major affective disorders

Major depression (unipolar)

The depressive symptoms and signs can vary from profound retardation and withdrawal to irritable, unrelieved agitation. The most severe symptoms early in the day.

Thought disorder is occasionally present. Delusions are affect-laden and mood congruent (self-condemning)

Hallucinations are uncommon

Depressed elderly may present memory impairement and mild disorientation (pseudodementia) Median age of onset is 37 with the majority of adult females Family and twin studies suggest a genetic factor

(depressive spectrum disorders: alcoholism, antisocial personality disorder in relatives)

Prevalence in the general population: 1-3 %
in first degree relatives: 13 %
in identical twins . 30-40 %

Minor affective disorders

Dysthymia (depressive neurosis)

Patients are depressed, have difficulty falling asleep, feel best in the morning and despondent in the afternoon/evening Symptoms must have been present for two or more years

More common in women in the late 2o's or 3o's Predisposition to depression:

- major loss in childhood (parents'); recent loss: health, job, spouse; chronic stress: medical disorder

- personality disorders (drug abuser) dependent, hystrionic

Cyclothymia (mild depression and hypomania over 2-year period) Onset: in the 2o's, more females

Job instability, occasional suicide attempts, markedly risk of drug and alcohol abuse

Criteria for Manic Episode

A. A distinct period of abnormality and persistently elevated, expansive, or irritable mood (at least 1 week)

B. During the period of mood disturbance, three (or more) of the following symptoms:

(1) inflated self-esteem or grandiosity
(2) decreased need for sleep
(3) more talkative than usual
(4) flight of ideas
(5) distractibility of attention
(6) increase in goal-directed activity (social, work, sex)
(7) excessive involvement in pleasurable activities that have a high potential for painful consequences

C. The symptoms do not meet criteria for a mixed episode

D. The mood distarbance is sufficiently severe to cause marked impairement in functioning (social, occupational)

E. The symptoms are not due to the direct physiological effect of'

Gender differences in depressive symptomatology

Typical (classical) Depressive symptoms ⟷ **Depr. Mood, insomnia**

anhedonia, anxiety,

females

Atipical Deprsessive symptoms ⟷ **irritability,aggression, alcohol, drugs, e.g.**

males

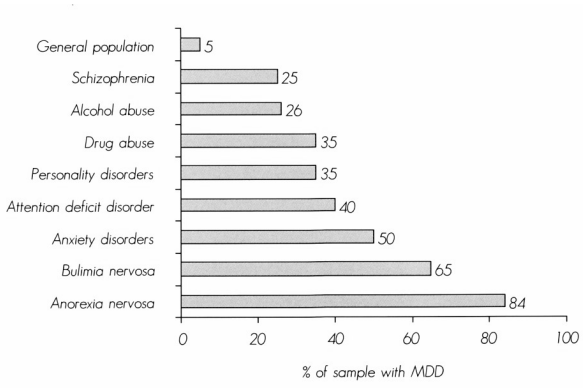


Figure 13.1 Prevalence of MDD in other Axis I disorders.

Causes/background

- Genetic predisposition
- Neg. life events, stresses
- Personality traits, cognitive-, psychodynamic formulations - losses, cognitive distortions learned helplessness- early traumas – psychol.predisposition
- Early traumas+genetic vulnerable - CRH+NE hyperresponsivity, long term potentiation, devastating hippocampus cells, decreasing feedback control- so minor stresses will cause max CRH and cortisol response – biological predisposition

Background, etiology II.

- **Genetic factors:**

  a/ an X-linked dominant pattern of inheritance in families with histories of bipolar ilness; autosomal dominant transmission (inherited abnormality of membrane lithium-transport) - contradictory results

  b. chromosoma 11 and bipolar disease - not replicated

  c/ *no* markers have clearly been discovered for major depression

  Chronobiological factors:

  a/ disruption of human circadian rhytms might explain several features of mood disorders (sleep-disturbances,

  delayed REM-latency, higher densitiy of REM-sleep)

  b/ seasonal mood disorders: relationship between sunlight and mood: light therapy of depression

Genotypes and "Emotional" Symptoms in Specific Pathways

- **Genotype for the serotonin transporter (serotonin reuptake "pump")**
  - **Two** alleles: short (s) and long **(l)**
- **The relationships between 5-HT transporter genotypes and symptoms of fear or depression, or the diagnosis of an anxiety disorder or an affective disorder, are only partly consistent**
- **Carriers of the s allele are more likely to have**
  - **Abnormal activation of the amygdala during exposure to provocative visual stimuli**
  - **Affective illnesses when exposed to numerous stressors**

Background, etiology III.

3. Biogenic amin theory – norepinephrine, serotonin, dopamin hypothesis

   Levels of Ne and serotonin vary with mood: Dysregulation of synaptic transmission rather then a deficieny or excess of neurotransmitters

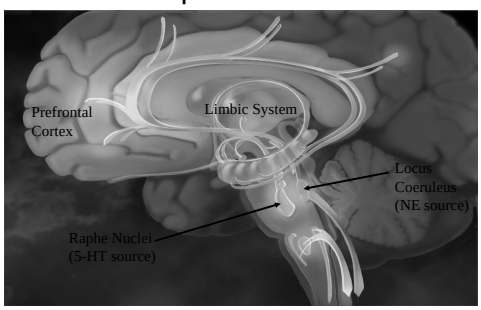
   Gene polimorphisms, modified gene expression

4. Psychological and sociocultural variables:

Loss and the effect of loss on the individual

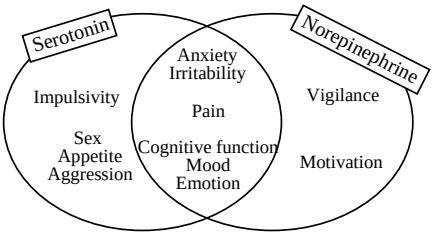
Cognitive distortions, social support or isolation

Serotonin and Norepinephrine in Depression



Kaplan and Sadock, eds. *Comprehensive Textbook of Psychiatry 6th ed.* Baltimore: Williams & Wilkins; 1995; p 27-28.

Serotonin and Norepinephrine: Effect on Depressive Symptoms



⇨ Dual action agents may provide the broadest spectrum of therapeutic effect across the full range of emotional and physical symptoms of depression

Delgado, unpublished.

Outlook

- Untreated one episode of depression lasts an average of 10 months
- About 50 per cent of individuals who experience one episode of depression will have a further attack
- The average number of recurrences in a life time is 5

The chronicity of major depressive disorder

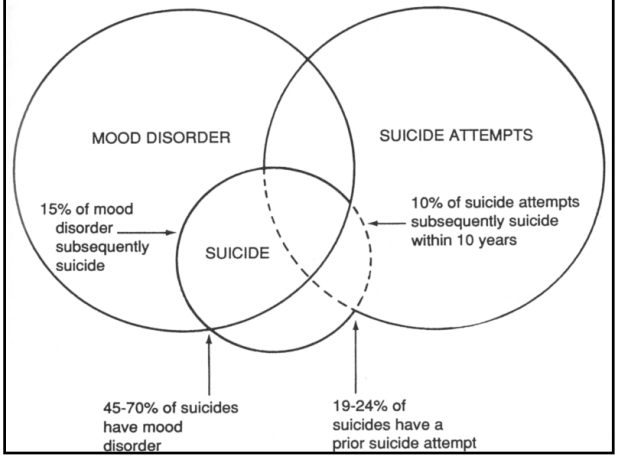
- 50% chance
  that a second depressive episode will follow the first
- 80–90% chance
  that a third depressive episode will follow the second
- Major depressive disorder tends to be a chronic condition
- Treatment of major depressive disorder should also be viewed as chronic

Specifiers of major depression (DSM IV)

- With melancholic features
- With atypical features
- With psychotic features
- With seasonal pattern
- With postpartum onset

Mood disorders and suicide

- **Depression is the most highly correlated disorder associated with suicide**
- **Approximately 60%-80% of all suicides occur in persons with a mood disorder.**
- **Schizophrenia and schizoaffective disorder- approximately 10% of individuals commit suicide.**



Underdiagnosis and undertreatment of depression

- Stigma
- Lack of public knowledge
- Patients do not always complain of depressed mood
- Depressive symptoms are often masked by somatic anxiety or other medical conditions
- Poor compliance with therapy

Development of the various pharmacological classes of AD's

- **1957 - 1970 TCA's (tricyclic antidepressants)**
  MAO's (non selective monoamine oxidase inhibitors)
- **1970 - 1980 NARI's (noradrenaline reuptake inhibitors)**
- **1980 - 1990 SSRI's (selective serotonin reuptake inhibitor)**
- **1990 - 2000 RIMA's (reversible inhibitors of mono amine oxidase)**

  SNRI's (serotonin and noradrenalin reuptake inhibitors)

  NaSSA's (noradrenergic and specific serotonergic antidepressants)

Efficacy of pharmacotherapy: Acute and continuation phase

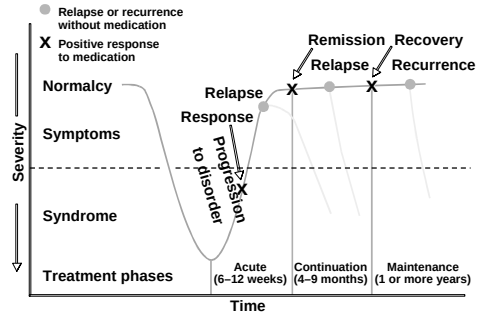
Acute treatment (up to 12 weeks)

- λ **65–70% response rates with adequate trial**
- λ **High response rates with different agents in non-responders**

Continuation (4–9 months)

- λ **Relapse rates of 10–20% in continuation therapy**

Phases of treatment



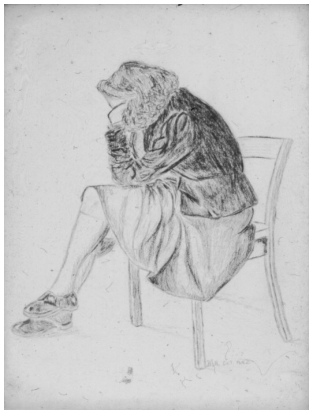
Kupfer DJ. J Clin Psychiatry 1991;52(suppl 5):28–34

Treatment of bipolar disorder, manic

1. Hospitalization (agitated behavior, protective environment, financial disaster)
2. Medication:
   a/ Lithium carbonate (0,8-1,5 mEq/L/) with neuroleptics
   b/ Carbamazepine (600-1200 mg/day)
   c/ Valproic acid 600-1800 mg/day

Treatment of depression

1. **Hospitalization (suicide risk or impulsive behavior, psychotic form**
2. **Out-patient treatment: frequent contact, support system of family,**
3. **Medication**
   a/ Tricyclic antidepressants b/ Tetracyclics c/ MAO Inhibitors
   D/ SSRI (paroxetin, sertalin, fluoxetin, citalopram)
   E/ SNRI (reboxetin) F/ dual action (venlafaxin)
   F/ NaSSa (mirtazapin)
4. **Psychotherapy (cognitive psychotherapy, dynamic-, and family)**
5. **ECT, Sleep deprivation, Light therapy**



Modern antidepressants

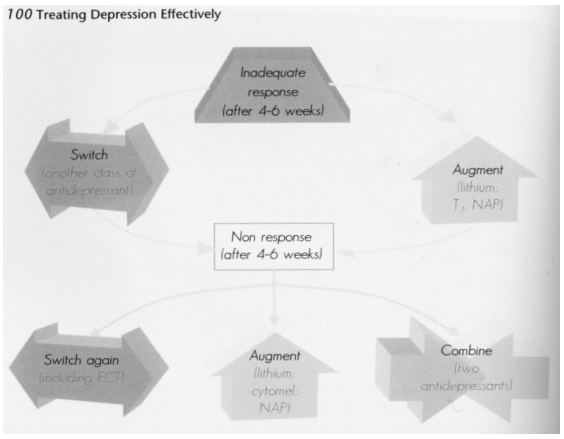
α2- antagonist + 5 HT2 antagonism:
- Remeron

RIMA:
- moclobemide

5-HT reuptake inhibition + 5-HT2 antagonism:
- trazodone
- nefazodone

SSRI's:
- paroxetine
- fluoxetine
- sertraline
- citalopram
- fluvoxamine

SNRI's, dual action
venlafaxin, reboxetine



- In general, depressive illnesses, particularly those that are recurrent, will require medication
- Psychotherapies that research has shown helpful for some forms of depression are interpersonal and cognitive/behavioral therapies.
- Interpersonal therapists focus on the patient's disturbed personal relationships that both cause and exacerbate (or increase) the depression.
- Cognitive/behavioral therapists help patients change the negative styles of thinking and behaving often associated with depression.
- Psychodynamic therapies which are sometimes used to treat depressed persons, focus on resolving the patient's conflicted feelings.

Table 9.1 Suggested psychotherapy targets and interventions in treatment-resistant depression

Targets	*Interventions*
Demoralization and hopelessness	Set short-term goals
Dependency and other neurotic traits	Learn to tolerate loneliness; recognize effect on others
Inactivity/anergia	Participate in some activity
Inadequate social support	Educate the family; re-establish existing relationships
Symptom distress	Specific interventions for anxiety, insomnia and poor concentration

Adapted with permission from *Thase and Howland 1994.*