



EMOTIONS MOOD



Understanding what are moods and emotions – and their differences – takes time and practice

Emotions are chemicals released in response to our interpretation of a specific trigger. It takes our brains about 1/4 second to identify the trigger, and about another 1/4 second to produce the chemicals. By the way, emotion chemicals are released throughout our bodies, not just in our brains, and they form a kind of feedback loop between our brains and bodies.

Feelings happen as we begin to integrate the emotion, to think about it. The word “feel” can be used for both physical and emotional sensation: we can say we physically feel cold, but we can also emotionally feel cold. This is a clue to the meaning of “feeling”: it’s something we sense. Feelings are more “cognitively saturated”. Feelings are often fueled by a mix of emotions, and last for longer than emotions.

Moods are more generalized. They’re not tied to a specific incident, but a collection of inputs. Mood is heavily influenced by several factors: the environment (weather, lighting, people around us), physiology (what we’ve been eating, how we’ve been exercising, how healthy we are), and finally our mental state (where we’re focusing attention and our current emotions). Moods can last minutes, hours, probably even days or months.

We can experience moods and emotions at the same time, but emotions seem to ‘sit on top’ of moods. For instance, whilst in a bad mood is quite possible to have brief feelings of happiness and joy. Similarly, when a good mood, it is still possible to feel sad or angry feelings. However, it is much more likely that your mood will influence the emotion you feel.

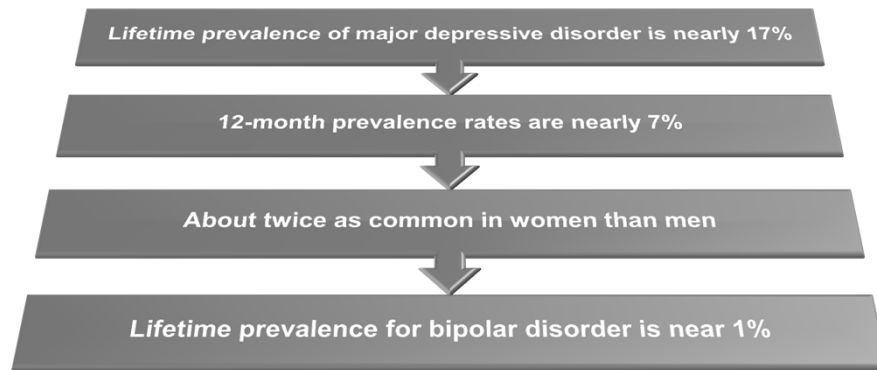
If this happens, the emotion may have the same flavor as the mood. In this way, our emotions are susceptible to the mood we are in, and this also make us more likely to interpret our environment in particular ways and distort our thinking. When we are in a bad mood, it is much easier to misinterpret things in the light of this bad mood.

Depression is a normal emotion

Types of Mood Disorders

Mood Disorder	severe alterations in mood for long periods of time
Depression	feelings of extraordinary sadness and dejection
Mania	intense and unrealistic feelings of excitement and euphoria
Unipolar (Major) Depressive Disorder	experiences only depressive episodes
Bipolar Disorder	experiences both depressive and manic episodes
Depressive Episode	episode in which a person is markedly depressed or loses interest in formerly pleasurable activities (or both) for at least 2 weeks, as well as other changes in sleep or appetite, or feelings of worthlessness
Manic Episode	mood episode in which a person shows a markedly elevated, euphoric, or expansive mood, often interrupted by occasional outbursts of intense irritability or even violence, particularly when others refuse to go along with the manic person’s wishes and schemes
Hypomanic Episode	a person experiences abnormally elevated, expansive, or irritable mood for at least 4 days; in addition, the person must have at least three other symptoms similar to those involved in mania but to a lesser degree

The Prevalence of Mood Disorders

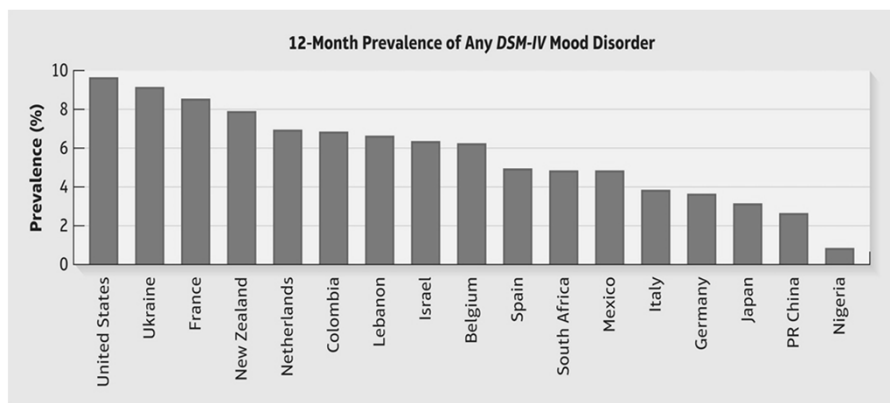


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Figure 7.1 Annual Prevalence of Mood Disorders Around the World

This figure shows the annual (12-month) prevalence of mood disorders using data collected via household surveys in 17 different countries as part of the WHO World Mental Health Survey Initiative (Adapted from WHO World Mental Health Survey Consortium, 2004.)



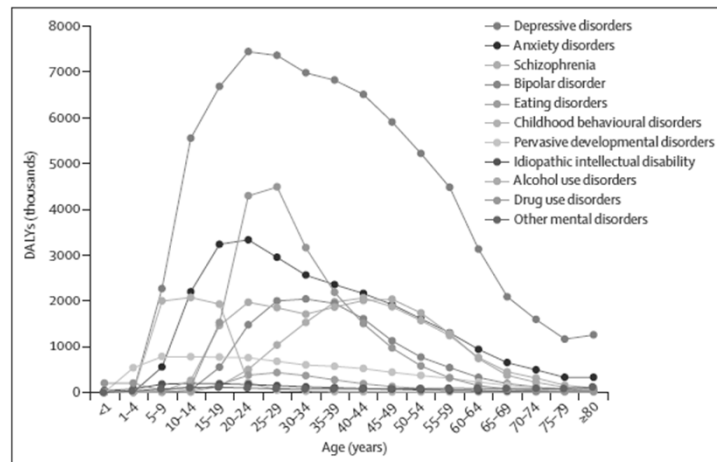
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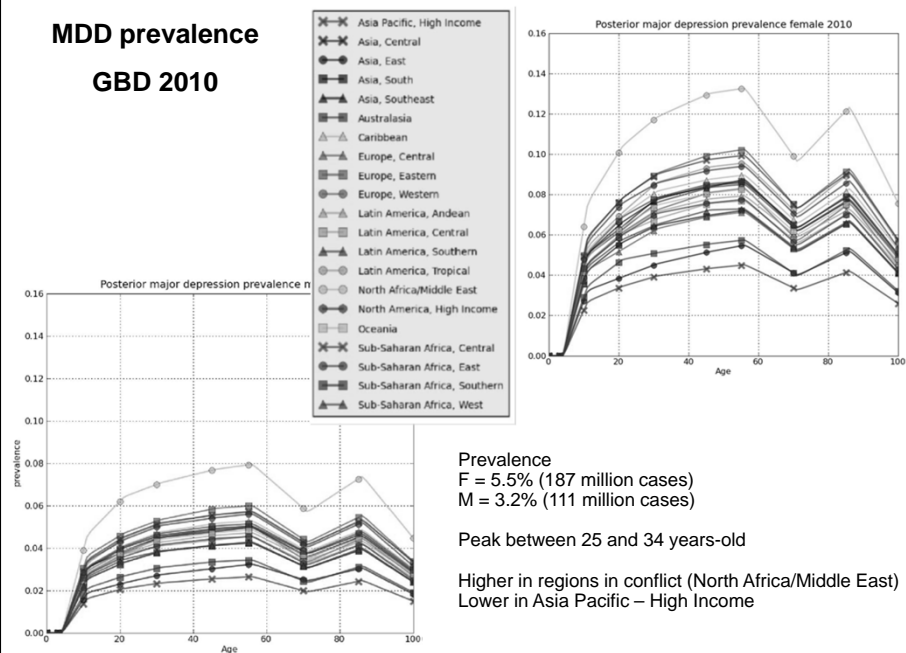
Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010

Harvey A Whiteford, Louisa Degenhardt, Jürgen Rehm, Amanda J Baxter, Alice J Ferrari, Holly E Erskine, Fiona J Charlson, Rosana E Norman, Abraham D Flaxman, Nicole Johns, Roy Burstein, Christopher J L Murray, Theo Vos

Lancet 2013; 382: 1575-86



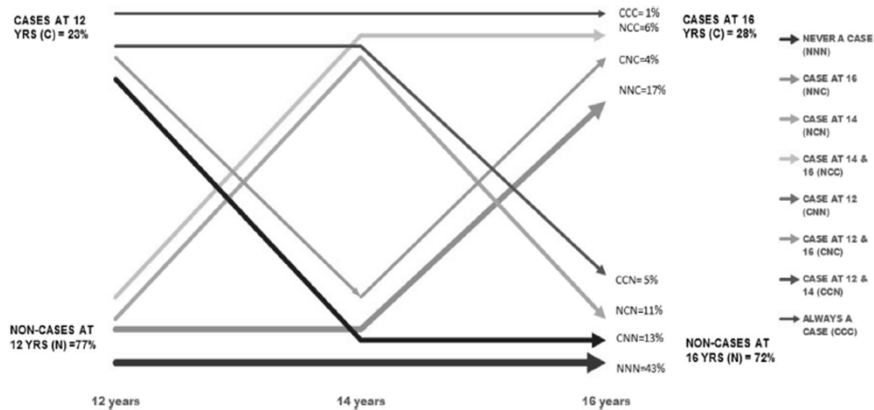
MDD prevalence GBD 2010



Ferrari et al, PLoSOne 2013; 8(7): e69637

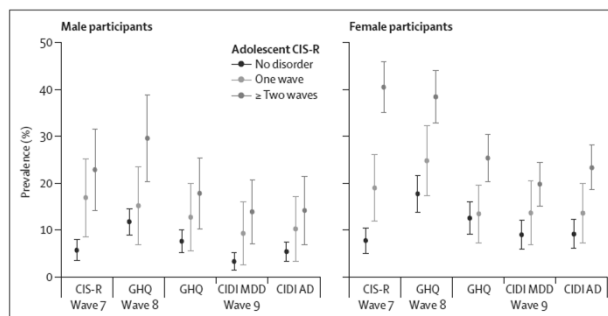
PATHWAYS TO DEPRESSION BY AGE 16

- Most often occurs during late adolescence up to middle adulthood, such reactions may begin at any time from early childhood to old age
- Self-reported symptoms of depression in 1800 individuals at age 12, 14 and 16 years.
- A quarter of young people met criteria for self-rated depression caseness at age 12
- Self-rated caseness increased to nearly a third by age 16, with a greater rise in young females compared to males.



Scott et al, *J Affect Dis* 2018; 230: 1-6

From adolescence to young adulthood



1,943 Australian adolescents followed-up from age 15 to age 30.

At least one episode during adolescence: M=29%, F=54%

60% went on to report a further episode as a young adult: for adolescents with one episode of less than 6 months duration, just over half had no further common mental health disorder as a young adult.

Longer duration of mental health disorders in adolescence was the strongest predictor of clear-cut young adult disorder (OR for persistent young adult disorder vs none 3.16).

Adolescents with a background of parental separation or divorce (OR=1.62) also had a greater likelihood of having ongoing disorder into young adulthood.

Patton et al, *Lancet* 2014; 383: 1404-11

MAJOR (UNIPOLAR) DEPRESSIVE DISORDER

5+ of the following symptoms during the same 2-week period, at least one of which is either (1) depressed mood or (2) loss of interest or pleasure.

Do not include symptoms that are clearly attributable to another medical condition.

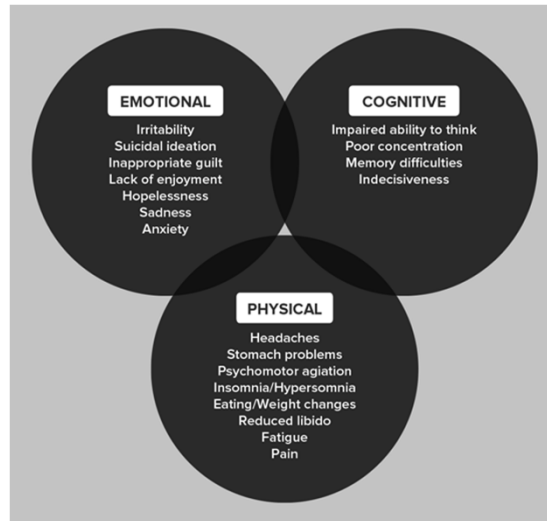
DEPRESSIVE EPISODE

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful).
2. Markedly diminished interest or pleasure in (almost) all activities most of the day, nearly every day
3. Significant weight loss or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day.
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan or a suicide attempt or a specific plan for committing suicide.

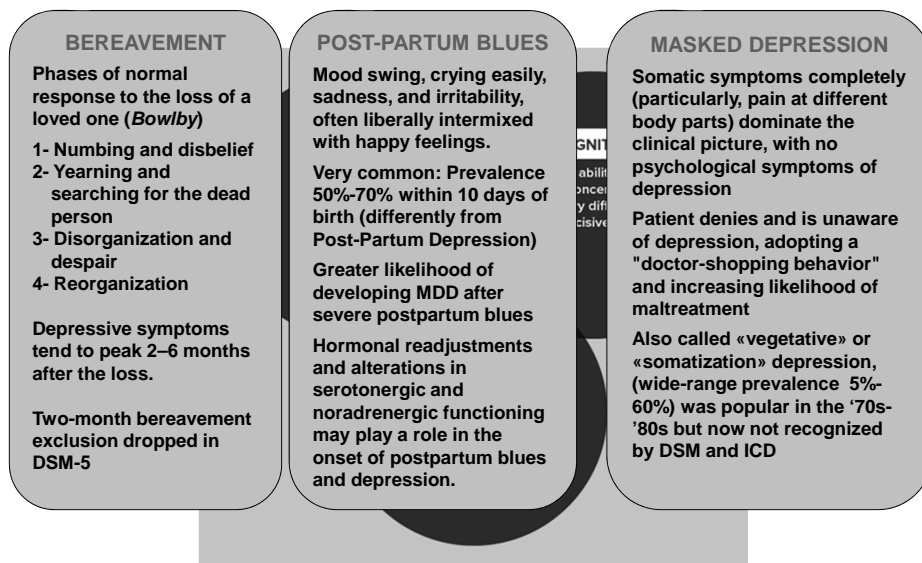
Table 7.1 Specifiers of Major Depressive Episodes

Specifier	Characteristic Symptoms
With Melancholic Features	Three of the following: early morning awakening, depression worse in the morning, marked psychomotor agitation or retardation, loss of appetite or weight, excessive guilt, qualitatively different depressed mood
With Psychotic Features	Delusions or hallucinations (usually mood congruent); feelings of guilt and worthlessness common
With Atypical Features	Mood reactivity—brightens to positive events; two of the four following symptoms: weight gain or increase in appetite, hypersomnia, leaden paralysis (arms and legs feel as heavy as lead), being acutely sensitive to interpersonal rejection
With Catatonic Features	A range of psychomotor symptoms from motoric immobility to extensive psychomotor activity, as well as mutism and rigidity
With Seasonal Pattern	At least two or more episodes in past 2 years that have occurred at the same time (usually fall or winter), and full remission at the same time (usually spring). No other nonseasonal episodes in the same 2-year period

Depression is a constellation of symptoms



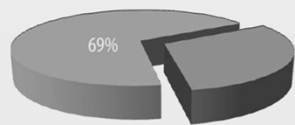
Depression is a constellation of symptoms



Patients With Depression Have a Predominance of Physical Symptoms

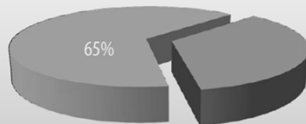


Primary Reason for Clinical Visit
as Reported by Depressed Patients (N=1,146)¹



■ Presented With Only Physical Symptoms
■ Presented With Psychological and Physical Symptoms

Mean Prevalence of Pain Symptoms
Reported by Depressed Patients (N=1,912)²



■ Had MDD and Pain ■ Had MDD and No Pain

1. Simon GE, et al. *N Engl J Med*. 1999;341(18):1329-1335.
2. Bair MJ, et al. *Arch Intern Med*. 2003;163(20):2433-2445.

Other reported rates:

- **76%** of patients with depression or anxiety also made somatic presentations³
- **69%** of primary care patients with depression also had pain⁴
- **43%** of patients with depression also had chronic painful physical conditions⁵
- **66%** of patients with MDD had chronic pain⁶

3. Kirmayer LJ, et al. *Am J Psychiatry*. 1993;150(5):734-741.
4. Bair MJ, et al. *Psychosom Med*. 2004;66(1):17-22.
5. Ohayon MM. *J Clin Psychiatry*. 2004;65(suppl 12):5-9.
6. Arnow BA, et al. *Psychosom Med*. 2006;68(2):262-268.

DEPRESSION RATES IN MEDICAL ILLNESSES

Condition	Rate of depression
Neurologic	
Stroke	30 %
Epilepsy	35 %
Parkinson's disease	40 %
Alzheimer's disease	50 %
Multiple sclerosis	50 %
Migraine	47 %
Other medical	
Cardiovascular disease	35 %
COPD	40 %
Chronic kidney disease	30 %
Cancer	30 %
Rheumatoid arthritis	20 %*
Diabetes	33 %

Strakowski et al, *Curr Psychiatry Report* 2013; 15: 386

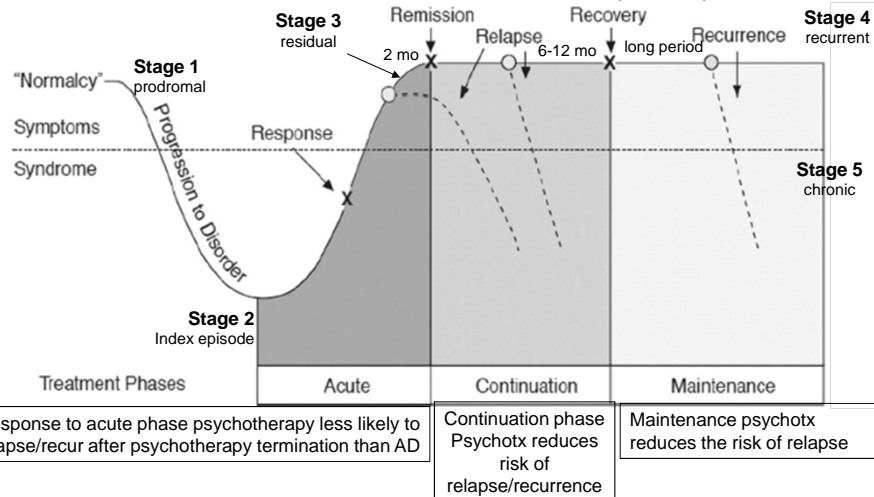
Course of major depression

Probability of recurrence increases with the number of prior episodes and comorbid disorders

Risk of relapse is 2-fold after each of new episode

Recurrence = 40-50%

Bochting et al, *Clin Psychol Rev* 2015; 41: 16-26
Cosci & Fava, *Psychother Psychosom* 2013; 82: 20-34



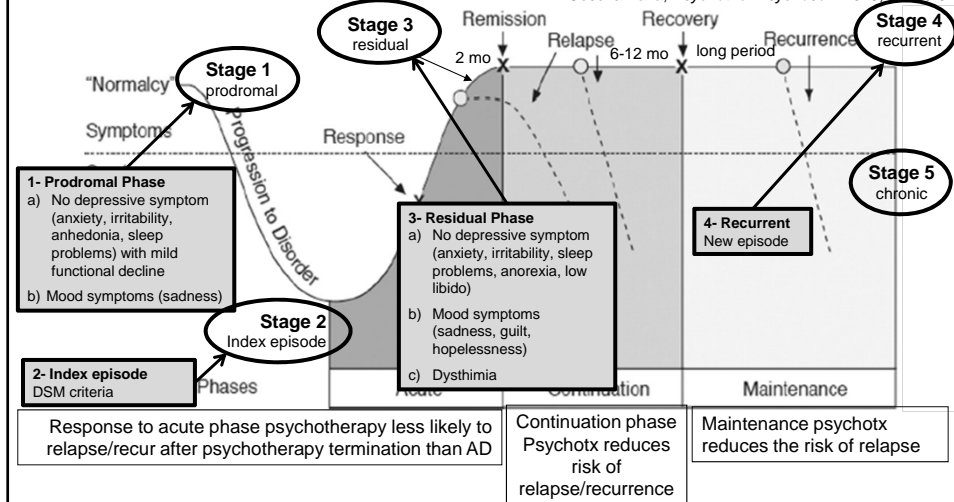
Course of major depression

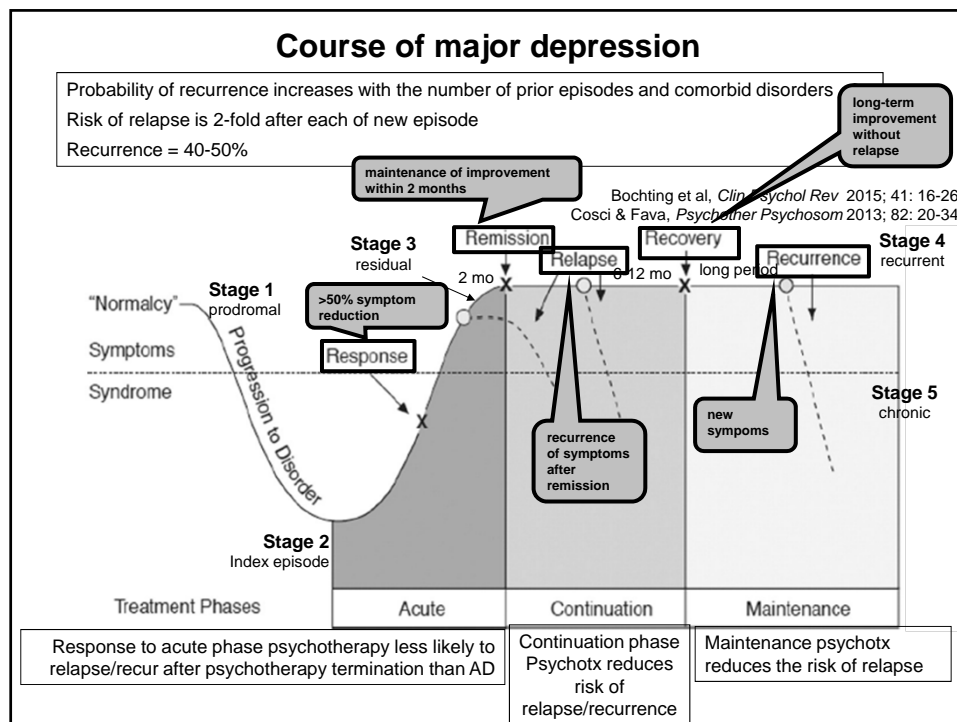
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Cosci & Fava, *Psychother Psychosom* 2013; 82: 20-34





Persistent Depressive Disorder (former Dysthymic Disorder)

Mild to moderate version of depression

- Persistently depressed mood most of the day for at least 2 years
- Intermittent normal moods occur briefly (most important characteristics differentiating from MDD)
- Lifetime prevalence of 2.5 to 6%
- Average duration is 4-5 years
- «Double Depression»: co-occurring PDD and MDD in the same person

**DSM-5
Other Specified Depressive Disorder**

Recurrent Brief Depression	Concurrent presence of depressed mood and at least 4 other symptoms of depression for 2-13 days at least once per month (not associated with the menstrual cycle) for at least 12 consecutive months in an individual whose presentation has never met criteria for any other depressive or bipolar disorder and does not currently meet active or residual criteria for any psychotic disorder.
Short-duration Depressive Episode (4-13 days)	Depressed affect and at least 4 of the other 8 symptoms of a major depressive episode associated with clinically significant distress or impairment that persists for more than 4 days, but less than 14 days, in an individual whose presentation has never met criteria for any other depressive or bipolar disorder, does not currently meet active or residual criteria for any psychotic disorder, and does not meet criteria for recurrent brief depression.
Depressive Episode with Insufficient Symptoms	Depressed affect and at least 1 of the other 8 symptoms of a major depressive episode associated with clinically significant distress or impairment that persist for at least 2 weeks in an individual whose presentation has never met criteria for any other depressive or bipolar disorder, does not currently meet active or residual criteria for any psychotic disorder, and does not meet criteria for mixed anxiety and depressive disorder symptoms.

BIOLOGICAL CAUSAL FACTORS

Genetic liability

- 2-3 times higher among blood relatives than gen.pop.
- 2-times higher among monozygotic than dizygotic twins
- Genetic studies suggest 30-40% of variance
- Short alleles of 5-HTTLPR transporter and GxE studies

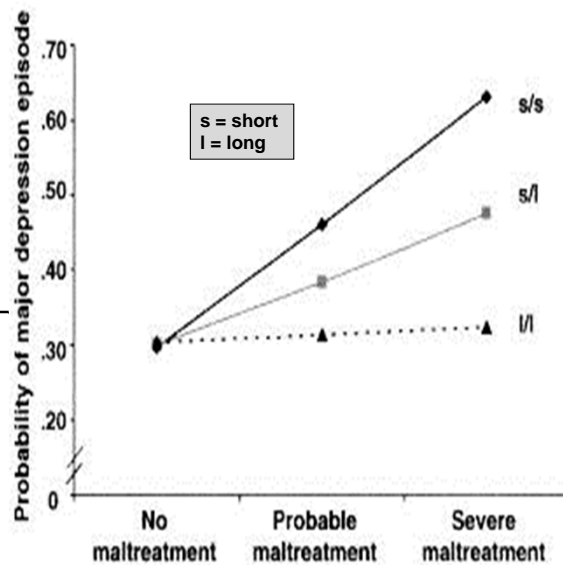
Neurotransmitter system

- Monoamine theory: partial or total depletion of 5-HT and/or NE
- Failure of research to support monoamine hypothesis
- A number of integrative theories have been proposed that include a role for neurotransmitters, not alone but rather as they interact with other disturbed hormonal and neurophysiological patterns and biological rhythms

Hormonal system

- HPA axis
- HPA-secreted blood cortisol 20-40% in outpts and 60-80% in inpts with MDD
 - Recent evidence suggests that dexamethasone (exogenous steroid that provides negative feedback to the pituitary gland to suppress the secretion of ACTH) non-suppression may be a general indicator of mental distress rather than specific to depression
- Hypothalamic-pituitary-thyroid axis
- People with hypothyroidism often become depressed and up to 70% of MDD patients have dysfunctional axis

GxE study: childhood maltreatment, genetics, adult antisocial behavior



N = 1037 (M = 52%)

Individuals assessed at age 3, 5, 7, 9, 11, 13, 15, 18, 21 and 26

Maltreatment (at age 3-11):

- Severe: 8%
- Probable: 28%
- None: 64%

Interaction between the short/long allele polymorphism of the serotonin transporter gene and childhood maltreatment



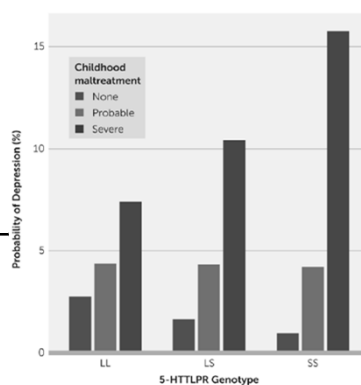
Vulnerability to adult depression

Alleles = alternate forms of DNA sequencing at a specific locus
Genotype = combination of alleles at a given locus

Caspi et al, *Science* 2003; 301: 386

CHILDHOOD MALTREATMENT AND ADULT DEPRESSION: ROLE OF 5-HTTLPR

- Replication of Caspi's study in a different socio-cultural context
- Pelotas (Brazil): 5,249 children born in 1993 and followed-up at age 11, 15 and 19 (2012)

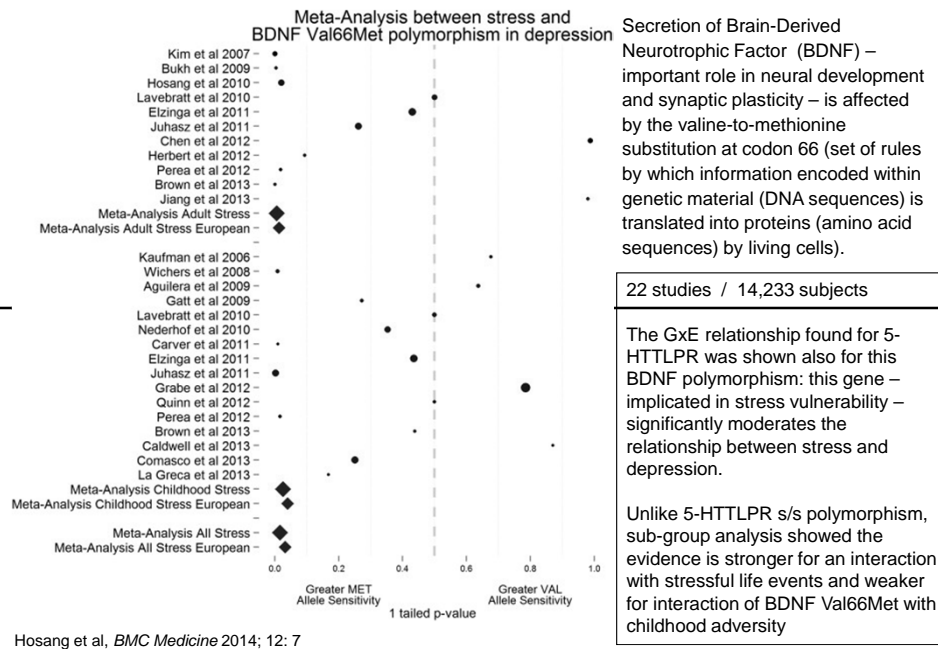


Parameter	Caspi et al. 2003	This Study
Sample size	847	2,392
Design	Prospective cohort	Prospective birth cohort
Retention rate	96% at 26 years	81.3% at 18 years
Male	52%	45.7%
Ethnicity	100% Caucasian	69.7% white
Genotype assessment	Biallelic	Biallelic and triallelic
5-HTTLPR genotype distribution ^a		
SS	17%	19.8%
LS	51%	47.8%
LL	31%	32.4%
Environmental assessment	Five items (mother-child interaction observation, parent harsh discipline checklist, disruptive caregiver changes, retrospective assessment for physical and sexual abuse)	Seven retrospective questions (two on child neglect, three on emotional abuse, one each on physical and sexual abuse)
Childhood maltreatment exposure		
None	64.9%	70.8%
Probable	26.4%	17.7%
Severe	8.7%	11.5%
Outcome measurement	Dichotomous and quantitative	Dichotomous
Major depression prevalence	17% (12-month)	3.3% (point)
Temporal order assessment ^b	Yes	Yes
G×E specificity evaluation	No	Yes

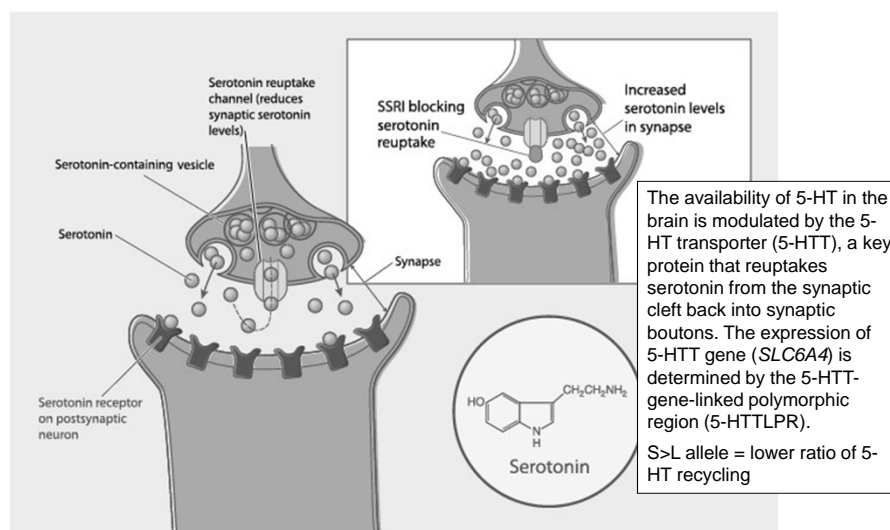
- Small allele carriers w/ severe maltreatment were only 8%, they accounted for >28% of the total cases of depression
- The association btw childhood maltreatment and depression was related to the number of S alleles carried, w/ progressively higher risk for individuals w/ more copies of the short variant.

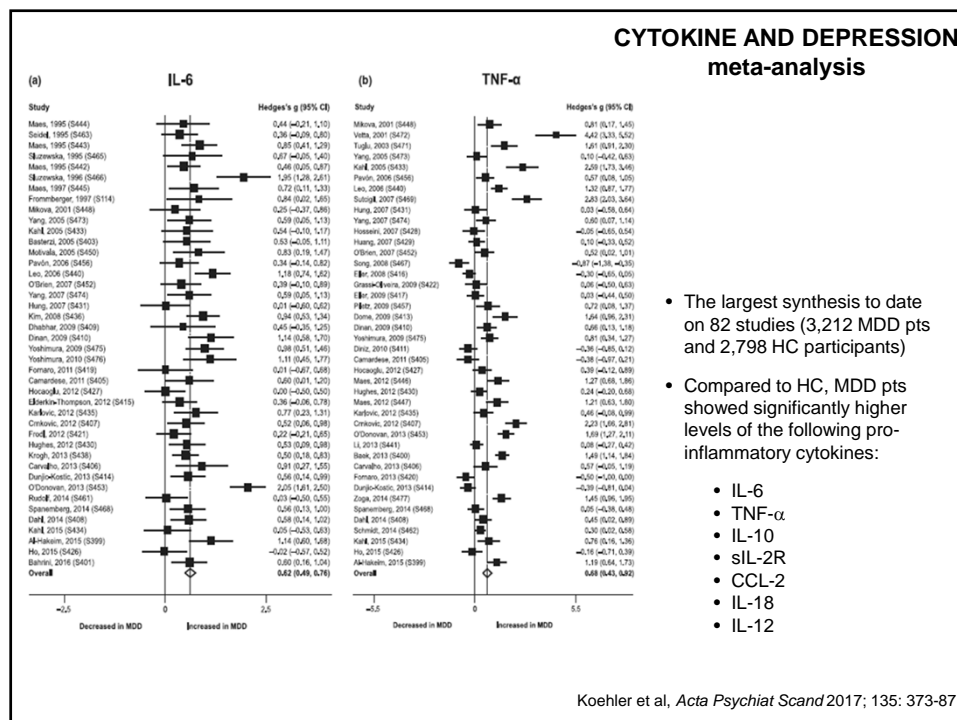
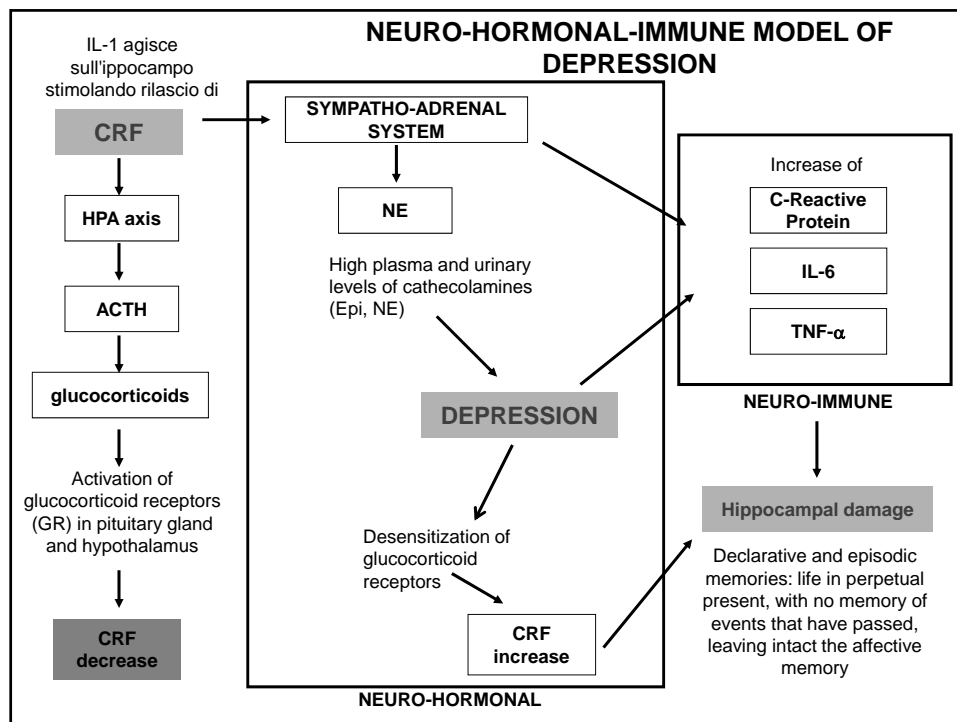
Rocha et al, *Am J Psychiatry* 2015; 172: 978-85

BDNF Val66Met polymorphism, life events and depression

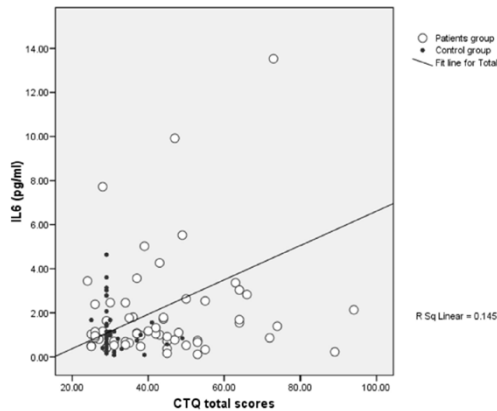


Depression is just a disorder of neurotransmission?





IL-6 as a possible link between MDD and childhood abuse



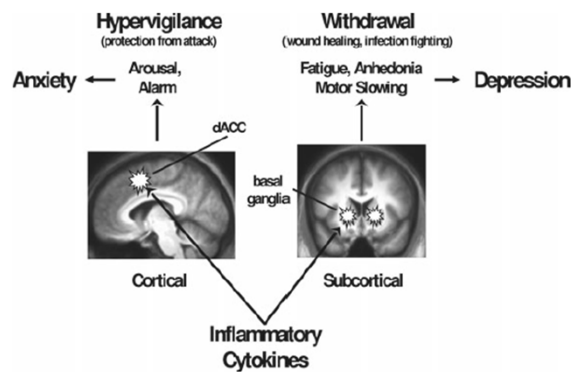
64 MDD inpatients and 53 healthy controls assessed with CTQ

Concentrations of IL-6 and CTQ scores were significantly higher in patients with MDD compared to HC

Significant correlation between total CTQ scores and IL-6 concentrations in the entire sample ($r=0.38$)

CTQ scores of patient clinical subscales concerning physical and emotional abuse, as well as physical neglect also significantly correlated with IL-6 serum levels, indicating that persons who were physically abused, physically neglected, and emotionally abused had higher levels of IL-6.

Munijza et al, *Psychiatry Res* 2018; 264: 26-30



EFFECTS OF INFLAMMATORY CYTOKINES ON THE BRAIN

evolutionary advantages and psychiatric costs

Findings from neuroimaging studies in humans indicate that inflammatory cytokines can alter the function of key subcortical and cortical circuits that lead to conservation/withdrawal (basal ganglia) and hypervigilance (dACC).

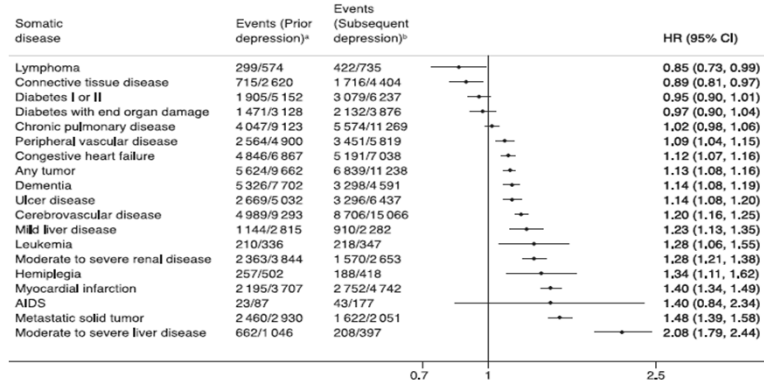
These behavioral responses have evolved to play an essential role in the highly integrated behavioral and immune response to infectious challenge and/or physical trauma.

However, in the modern world, chronic activation of these responses can contribute to the development of disorders of depression and anxiety

Miller et al, *Depr Anx* 2013; 30:297-306

Mortality in MDD before / after chronic somatic diseases

Danish general population followed up for about 20 years (n = 4,984,912)

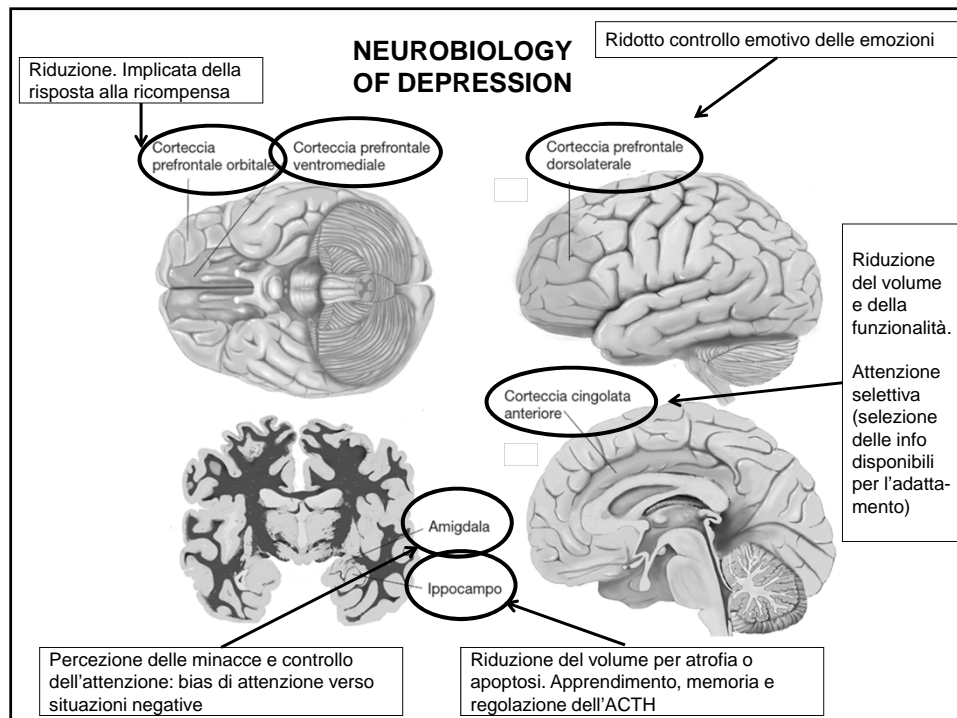


Compared to isolation disease (=no MDD comorbidity), mortality risk was

- higher if with comorbid depression, regardless of the temporal association;
- higher particularly with prior diagnosis of depression than subsequent depression;
- similar for current/prior depression.

Suicide has little if any influence on the mortality risk

Koyanagi et al, *Acta Psychiat Scand* 2018; 138:500-8



Psychological Causal Factors Diathesis-Stress Model

Loss of a loved one, serious threats to important relationships or occupations, or severe economic or health problems, events involving humiliation, caregiver of a spouse with debilitating disease such as Alzheimer's

Minor stressful events may play a role in relapses rather than onset

Stressful events Chronic Stress
Risk-related vulnerability factors

Vulnerability
in response
to stress

Living in poverty, chronic stressful environment, family turmoil, parental psychopathology, physical or sexual abuse, and other forms of intrusive, harsh, and coercive parenting, neuroticism (negative affectivity), introversion

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MANIC EPISODE

- A. 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).
- B. During the period of mood disturbance and increased energy or activity, three (or more) of the following symptoms (four if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:
 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), as reported or observed.
 6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (i.e., purposeless non-goal-directed activity).
 7. Excessive involvement in activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

HYPOMANIC EPISODE

Same criteria but less duration

... lasting at least 4 consecutive days and present most of the day, nearly every day

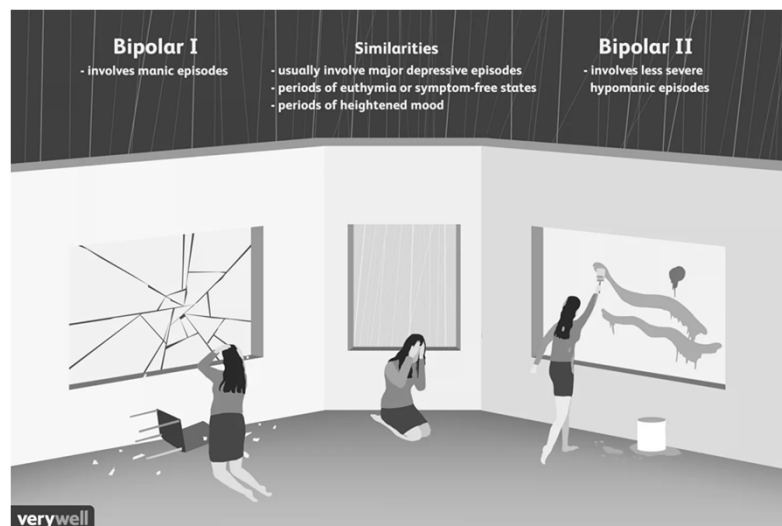
CYCLOTHYMIC DISORDER

Less serious version of the full-blown bipolar disorder; refers to the repeated experience of hypomanic symptoms for a period of at least 2 years.

Individuals with this disorder are at greatly increased risk of later developing full-blown bipolar I or II disorder.

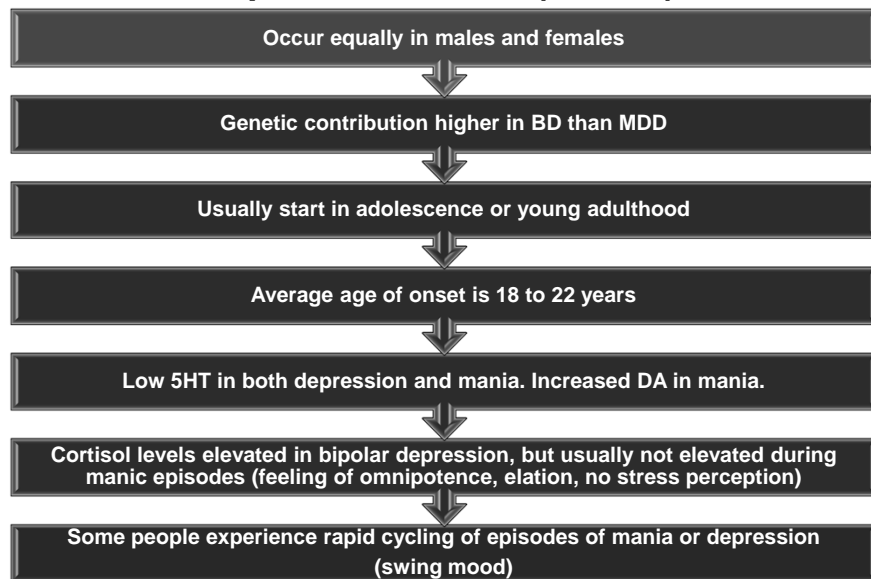
MIXED EPISODE

Symptoms of both full-blown manic and major depressive episodes for at least 1 week, either intermixed or alternating rapidly every few days



The depressive episodes are similar between BD-I and BD-II.
But with BD-I, the mania is more severe than it is with BD-II.

Bipolar Disorders (I and II)



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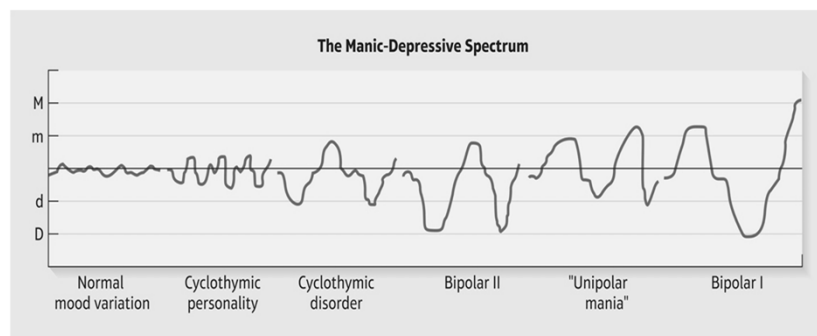
The Manic-Depressive Spectrum

There is a spectrum of bipolarity in moods. All of us have our ups and downs (normal mood variation).

People with a **cyclothymic personality** have more marked and regular mood swings, and people with **cyclothymic disorder** go through periods when they meet the criteria for **dysthymia** (except for the 2-year duration) and other periods when they meet the criteria for **hypomania**.

Unipolar mania is an extremely rare condition.

People with **bipolar disorder I and II** have both periods of **major depression** and periods of **hypomania** but those with **BP-2** have less severe hypomanic episodes



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