Mood (Affective) Disorders

What are moods? _________________________________________
______________________________________________.

What are some examples of enduring moods? ________________
_______________________________________________________.

What are the two main types of mood disorders? ______________

Depression is characterized by ______________________________
_______________________________________________________;

Mania is characterized by ________________________________.

Unipolar disorder refers to the condition in which individuals
experience depressive symptoms only.

Bipolar disorder refers to the condition in which individuals suffer
from bouts of mania and depression (aka manic-depressive disorder).

Incidence of mood disorders: at least ___ of US population are believed
to suffer from mood disorder in any _______ period (underestimate).

Incidence climbs to 6% when people report suffering from a mood
disorder some time during their life:
- unipolar depression is more prevalent (____) than bipolar disorder
  (____) in US during any single year.
- 45-85% of individuals suffering from mood disorders will have a
  recurrence of the disease - treatment helps prevent such relapses.

Diagnostic criteria for Mania

Criterion A
- a distinct period of abnormally and persistently ______________
- abnormally here is defined in relation to the person’s normal
  behavior;
- usually lasts ________________.

Criterion B (requires 3 of the following symptoms, 4 if the mood is
characterized as irritable):
1. ________________________________;
2. ______________________________ (e.g., feels rested after only 3 hours
   of sleep);
3. More talkative than usual or pressure to keep talking;
4. ______________ (jumping to a new line of thought before completing
   the preceding one) or subjective experience that thoughts are
   racing;
5. ______________ (i.e., attention easily drawn by unimportant stimuli);
6. Increase in goal-directed activity (socially, at work or school, or
   sexually) or ______________;
7. Excess involvement in pleasurable activities which have a high
   potential for painful consequences (e.g., person engages in
   unrestrained buying sprees, sexual indiscretions, or foolish business
   investments).
Diagnostic criteria for Mania (continued)

Criterion C (excludes hypomania)
- mood disturbance sufficiently severe to cause marked impairment in
  ________________________________________________________________
  ________________________________________________________________
  ____________________________.
- this criterion is used to distinguish manic episodes from hypomanic
  mood, which is a less severe form of mania that would normally
  NOT produce marked impairments in occupational or social
  functioning.

Criterion D (excludes schizoaffective disorder)
- at no time during the disturbance have there been delusions or
  hallucinations for as long as two weeks in the absence of prominent
  mood symptoms (i.e., before the mood symptoms developed or after
  they have remitted).
  ________________________________________________________________;
- these delusions and hallucinations do not occur ______ of the mood
  disturbance, as they would in schizophrenia.

Criterion E (exclusion criterion)
- should not be superimposed on schizophrenia, schizophreniform
  disorder, delusional disorder, or psychotic disorder NOS (not
  otherwise specified).

Criterion F (exclusion criterion)
- it cannot be established that an organic factor initiated and
  maintained the disturbance (e.g., drug intoxication, vitamin
  deficiency, hormonal imbalance).

Diagnostic criteria for Major Depressive Episode

Criterion A
- (requires at least 5 of the following 9 symptoms during the same
  2-week period and represent a change from previous functioning)
- at least one of the symptoms is either 1. depressed mood, or 2. loss
  of interest or pleasure.

1. __________________ (or can be irritable mood in children and
  adolescents) most of the day, nearly every day, as indicated either
  by subjective account or observation by others;
2. Markedly diminished __________________ in all, or almost all,
  activities most of the day, nearly every day (as indicated either by
  subjective account or observation by others of apathy most of the
  time);
3. _________________________________(e.g., more than
  5% of body weight in a month), or decreased appetite nearly every
  day (in children, failure to make expected weight gains);
4. _________________________________ nearly every day (observable
  by others, not merely subjective feelings of restlessness or being
  slowed down);
5. ____________________________ nearly every day;
6. ____________________________ or excessive or inappropriate guilt (may
  be delusional) nearly every day (not just self-reproach or guilt
  about being sick);
8. Diminished ability to think or concentrate, or indecisiveness, nearly
  every day (subjective account or as observed by others);
9. ____________________________ (not just fear of dying), recurrent
  suicidal ideation without a specific plan, or a suicide attempt or a
  specific plan for committing suicide.
Diagnostic criteria for Major Depressive Episode (continued)

Criterion B (exclusion criterion)
- it cannot be established that an organic factor initiated and maintained the disturbance.
- the disturbance is not a normal reaction to the death of a loved one (this would be termed “________________” which is distinguished from “_______________”, classically defined by the symptoms in criterion A).
- reactive depression could be categorized as major depression if it lasts too long (say two months or more).

Criterion C (excludes schizoaffective disorder)
- at no time during the disturbance have there been delusions or hallucinations for as long as two weeks in the absence of prominent mood symptoms (i.e., before the mood symptoms developed or after they have remitted).

Criterion D (exclusion criterion)
- not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder NOS.

Generally excluded from Major Depression is a mild, less severe, form of depression called ________________.

_______________ is a condition referring to a milder form of bipolar disorder, in which the manic and depressive episodes are usually milder than those categorized in full blown bipolar disorder.

Diagnostic criteria for Melancholic Depression

often argued to be different from reactive depression. It is called melancholic depression (interchangeable with endogenous depression).

To be diagnosed with melancholic depression, the same criteria as major depression need to be observed, in addition to the following:

Melancholic criterion (require 5 of the following 9 symptoms)
1. _________________________ in all, or almost all, activities;
2. ____________________________ (does not feel much better even temporarily, when something good happens);
3. Depression regularly worse in the ____________;
4. ____________________________ (at least 2 hours before usual time of awakening);
5. ____________________________ (not merely subjective complaints);
6. Significant _________________ (e.g., more than 5% of body weight in a month);
7. No significant personality disturbance before first Major Depressive Episode;
8. One or more previous Major Depressive Episode followed by complete or nearly complete recovery;
9. Previous good response to specific and adequate somatic antidepressant therapy (e.g., tricyclics, ECT, MAOI, lithium).
Incidence of Major Depression

- Estimated that _____ of men and _______ of women in the U.S. will suffer from a major depressive episode at some time in their life.

- Interestingly, children’s incidence of depression is not influenced by sex (equally likely in boys and girls).

- Age of onset normally vary between __________________________ _____.

- Depression is life-threatening: up to ____ of depressed individuals commit suicide each year.

- In 1996 the Centers for Disease Control and Prevention listed suicide as the _____ leading cause of death in the U.S. (slightly behind infection with the AIDS virus), taking the lives of 30,862 people (note that although this number is very likely underestimated, not all suicides are associated with depressive illnesses).

- More than _____ of individuals will suffer more than one episode of major depression in their life (relapse).

- Experimental evidence indicates a link between ________ and mood disorders (not just depression).

Incidence of Bipolar Disorder

- Men and women are _____________ to develop bipolar disorder (no sex differences).

- It afflicts approximately ___ of Americans.

- Bipolar disorder, which tends to run in families, typically emerges in ____________ and continues to flare up across an individual’s lifetime.

- More than half of individuals will suffer more than one episode of manic depression in their life (relapse).

Etiology of Mood Disorders

- Stress has been associated in prospective studies with the occurrence of Mood Disorders, more so with Major Depression.

Question: What is the difference between a prospective and a retrospective study?

- Mood Disorders are observed in several different cultures and societies, so the stress experienced in industrialized nations may not be to blame.

- Mood Disorders tend to run in families, suggesting a genetic link, which is stronger in __________________________. 
Etiology of Mood Disorders (continued)

- In relation to Depression, twin studies have reported concordance rates for identical twins of roughly ____.
- This concordance drops dramatically for fraternal twins to approximately ________.
- These results suggest a ______________________ that is strongly modulated by environmental factors; otherwise, concordance should be closer to 100% in monozygotic twins.
- The concordance in monozygotic twins for bipolar disorder is much higher, approximately ____ when reared together, and still above ______ when reared apart.
- Chromosomes 11, 18, and 21 have been linked to mood disorders in some studies, to be later disproved. The roles of these putative genes in mood disorders have never been established.

________________________________________________________________________ remain some of the best predictors of Mood Disorders:
- examples of stressful life events particularly associated with depression include ____________________________;
- examples of traumatic childhood events also include _______.

Biological hypothesis of Depression

Because depression affects so many aspects of one’s life (eating, sleeping, pleasure, thoughts, emotions), the major regulatory neurotransmitters, involved in ______, have been implicated early on in the research on the biological basis of depression.
- of the major modulatory systems, ______________________ have received the most attention and experimental involvement in the development and course of depressive illnesses.

Noradrenergic (norepinephrine) and serotonergic systems

- the link with monoamines came in the 1950’s when it was observed that hypertensive patients treated with ______ developed a high incidence (____) of depressive symptoms.

Question: What does reserpine do in the brain (clue-Parkinson’s disease)?

- at about the same time, researchers found that a drug used to treat tuberculosis ( _______ ) appeared to elevate the mood of these patients - this drug acts by __________________ of monoamines impregnating buttons (__________________).

- in the mid-1960s Joseph Schildkrut proposed the noradrenergic hypothesis of depression, in which _______ norepinephrine release is associated with depression, and _______ norepinephrine release is associated with mania.

- the same argument was made for the serotonergic system by Arthur Prange.
Noradrenergic and serotonergic pathways in the brain

The discovery of tricyclic antidepressants (first – imipramine), further suggested that symptoms of depression could be ameliorated.
- imipramine also works on the monoamine system by ____________.
- interestingly, most initial tricyclic antidepressants ____________.

Question: What is the role of neurotransmitter reuptake in the monoamine system? ________________________________

The search for “Biological markers of Depression”

In order to determine if NA or 5-HT are altered in depressed patients, need to look at their breakdown products found in the cerebrospinal fluid.
Why? ________________________________

- breakdown product for NA is 3-methoxy-4-hydroxyphenylglycol (MHPG).
- breakdown product for 5-HT is 5-hydroxyindoleacetic acid (5-HIAA).
- patients with ________________ (i.e. reduced central NA activity) respond better to tricyclic antidepressant drugs than depressed patients with ________________ of the metabolite.
- MHPG level increases as these patients respond to drug therapy.
- In contrast, patients with normal MHPG levels, but low 5-HIAA levels – respond better to drugs that increased the level of 5-HT.
Problems with monoamine hypothesis of depression
- most antidepressant drugs immediately begin to increase levels of neurotransmitters but it takes __________ for clinical effects to be observed in depressed patients;
- some patients do not display observable signs of monoamine deficiencies; some might even show evidence of increased monoamine levels;
- about ____ of depressed patients respond to drug therapy.

Obviously, the primary mechanism of action of antidepressant drugs (block NT reuptake - and therefore, increase NT levels of monoamines) _____________________________________________.

Another hypothesis of depression concerns the involvement of hormonal abnormalities associated with the hypothalmo-pituitary-adrenocortical (HPA) axis.

CRF = __________________
ACTH = __________________

Hypothalamo-pituitary-adrenocortical (HPA) axis and Depression

In normal individuals, the HPA axis shows a normal cycle of activity such that cortisol levels are relatively high in the morning, and become increasingly lower throughout the day until a trough is reached late in the evening.

- stimuli that normally increase cortisol secretion via the HPA axis include _______________________________________________.
- a relatively large number of patients displaying signs of major depression have ___________, especially in the evening, when the levels should be at their lowest.
- abnormally high levels of cortisol in patients with major depression have been associated with an ___________, as measured by CRF levels in the cerebrospinal fluids of patients and in animal models of depression (rats and monkeys).
- patients who ultimately attempt suicide also show the highest cortisol levels.
Further evidence of HPA axis abnormality in depressed patients is in response to the ________________________________________.

- DXM is a powerful analog of cortisol and, like cortisol, acts at the level of the _____________________________________________

- when normal people are given DXM, cortisol levels remain low up to 24 hrs after ingestion (see below).

- however, at least 50% of depressed patients show ______________

HPA axis abnormality may be causally implicated in some neurotransmitter (5-HT) alterations:

- chronic unpredictable stress ____________________________

- interestingly, these changes can be ________ by treatment with chronic antidepressant treatments.

- successful antidepressant treatments in humans have also been shown to reverse HPA axis abnormalities (cortisol and CRF).
HPA axis and Depression (continued)

Direct injection of CRF in animals produces many of the same symptoms as those observed in Major Depression:
- __________________________________________;
- _____________________________________________________
- ________________________________________
- in humans, sleep disturbances are mostly associated with the ______
  _______ of sleep (reduced latency to reach REM sleep).
- __________________ has been associated with the initiation of REM sleep.
- ______________, particularly during the second half of the night,
  when more REM sleep is experienced, has been shown to temporarily relieve symptoms of depression!

Stress-diathesis hypothesis of depression (Charles Nemeroff)
- diathesis = inborn predisposition;
- because depressive illnesses run in families, it is very likely that
  genetic factors _________ individuals for depression.
- these genetic factors make up a __________________________ that, if
  achieved, expresses depressive symptoms.
- traumatic events in childhood (stressful) may alter this threshold
  such that it will be made easier to reach, and thus produce depressive
  illness more readily, even when confronted with relatively mild
  challenges (stressors) in adulthood.

At least two animal models in which early experiences change HPA
activity (increased CRF release) throughout the animals life have been
demonstrated.
- ______________________________________________________;
- ______________________________________________________
- ________________________________________