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Insights into Depression

Nik Raju, MD, DABPN
Board-Certified Staff Psychiatrist, Lindner Center of HOPE
Assistant Professor of Clinical Psychiatry
University of Cincinnati College of Medicine

Conflicts of Interest and Caveats

- No conflicts of interest to report
- This presentation is for informational purposes only and is not to be interpreted as medical advice
- This presentation is a brief introduction and not meant to be exhaustive
- This presentation is not meant to provide self-diagnoses or diagnoses to family members – diagnoses should be made by a healthcare professional (general physician, psychiatrist, psychiatric PA/NPs, psychologists, counselors, and social workers)

Today's Objectives

- Outline characteristics of different forms of depression
- Describe treatment options for depression

Introduction to Depression

- Likely a heterogenous group of disorders that appear similar clinically and thus grouped under individual categories
- Definitions and characteristics based on the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders 5th Edition*
- No clinically-validated biomarkers at this time unfortunately
- 280 million people worldwide living with depression in 2019 (per WHO) - one of the leading causes of disability worldwide

Biological Basis of Depression - Theories

- Genetic, inherited component – heritability estimated to be at 37%
- Overactive hypothalamic-pituitary-adrenal (HPA) axis leading to excessive secretion of cortisol
- Thyroid and adrenal gland abnormalities
- Neurotransmitter deficits – serotonin, norepinephrine, dopamine, as well as alterations of glutamate, acetylcholine and GABA levels
- Neural circuit abnormalities
- Immune dysfunction

Neurovegetative Symptoms of Depression

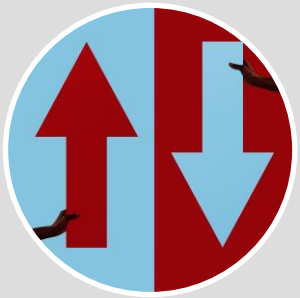
- Low energy (fatigue)
- Inattention/difficulty concentrating
- Sleep difficulties with early morning awakenings
- Low appetite with weight loss
- Decreased libido
- Depression often worse in the morning

Medical Causes of Depression

- Certain medications (e.g. steroids, interferon, specific BP medications, antibiotics, chemotherapy)
- Recreational substances – marijuana, alcohol, cocaine withdrawal
- Endocrine – thyroid, parathyroid, pituitary gland, or adrenal gland abnormalities
- Infectious – mononucleosis, HIV/AIDS, hepatitis, influenza/COVID-19, pneumonia
- Rheumatologic – rheumatoid arthritis, lupus
- Nutritional – anemia, certain vitamin deficiencies
- Neurologic – MS, Parkinson's disease, TBI, stroke, epilepsy, sleep apnea
- Cardiac – heart attacks, heart failure
- Cancer

Mood Disorder Spectrum

Unipolar Depression/Major Depressive Disorder (MDD)



Persistent Depressive Disorder/MDD with Mixed Features/Cyclothymia/Bipolar II Disorder

Bipolar I Disorder

Unipolar

Mixed Features

Bipolar

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Mood Disorders

- Major depressive disorder (“classic depression”) with multiple specifiers
- Persistent depressive disorder (e.g. dysthymia)
- Cyclothymia
- Bipolar II disorder
- Bipolar I disorder

Major Depressive Disorder (Unipolar Depression)

- Episodic in nature but must occur for at least 2 weeks
- Characterized by depressed mood and/or anhedonia (loss of interest or lack of pleasure)
- **5 of the following symptoms**:
  - Sleep disturbances (often including early morning awakenings) or increased drive to sleep
  - Appetite often with accompanying weight changes – decreased or increased
  - Decreased energy
  - Concentration and memory difficulties
  - Psychomotor slowing or agitation/restlessness
  - Decreased motivation
  - Suicidal ideation – either passive or active

Major Depressive Disorder (Unipolar Depression) - Specifiers

- Symptom specifiers
  - With anxious distress
  - With mixed features
  - With melancholic features
  - With atypical features
  - With psychotic features
  - With catatonia
  - With peripartum onset
  - With seasonal onset
- Severity specifiers
  - Mild
  - Moderate
  - Severe
- Course specifiers
  - In full remission (no symptoms for at least 2 months)
  - In partial remission

Persistent Depressive Disorder (Dysthymia)

- Chronic, low-lying depression for at least 2 years in adults and at least 1 year in children/adolescents with less than 2-month period free of depressive symptoms
- Similar symptoms as MDD but can also include low self-esteem and difficulties with decision making
- Symptoms are less severe than a major depressive episode but always persistent
- Major depressive disorder episodes can occur with dysthymia – “double depression”

Common Co-morbidities of Unipolar Depression

- Alcohol abuse/dependence and other substance use disorders
- Anxiety disorders
- Obsessive-compulsive disorder (OCD)

Clues to bipolar spectrum depression

- Early age of onset (especially in childhood or early adolescence)
- Psychotic depressive episode occurring prior to age 25
- Atypical features of depression
- Seasonality of depression
- Multiple depressive episodes during a one-year span
- Family history of bipolar disorder
- Hypomania or increased irritability with trial of antidepressants
- Loss of efficacy of antidepressants despite initial efficacy (at least 3 times)

Bipolar I Disorder

- Historically known as manic-depressive disorder
- Characterized by at least 1 manic episode lasting for 1 week or that leads to hospitalization - 3-4 of the following symptoms must be present for mania:
  - Abnormally elevated or irritable mood (required)
  - Decreased need for sleep (e.g. feeling rested after 3 hours of sleep)
  - Increased activity (e.g. working on multiple projects)
  - Increased talkativeness – speech content as well as speed
  - Racing thoughts
  - Grandiosity
  - Impulsivity (e.g. shopping sprees, impulsive decisions)
  - Distractibility
- Mania is an observable change in behavior from others – family and friends are often the first to notice
- Treatment with standard antidepressants alone - without a mood stabilizer medication - can worsen this condition

Bipolar II Disorder

- Most of the time is spent in major depressive episodes
- Characterized by at least 1 hypomanic episode lasting for at least 4 days - 3-4 of the following symptoms must be present for hypomania:
  - **Abnormally elevated or irritable mood** (required)
  - Decreased need for sleep (e.g. feeling rested after 3 hours of sleep)
  - Increased activity (e.g. starting multiple projects at once)
  - Increased talkativeness – increased speech content as well as faster speed
  - Racing thoughts
  - Grandiosity
  - Impulsivity (e.g. shopping sprees, impulsive decisions)
  - Distractibility
- Hypomania is not significant enough to impair functioning or lead to hospitalization
- Hypomania is an observable change in behavior from others – family and friends are often the first to notice
- Treatment with standard antidepressants alone - without a mood stabilizer medication - can worsen this condition

Cyclothymia

- Cycling mood for at least a 2-year period for adults and for at least a 1-year period in children/adolescents
- Elevated mood phases do not meet full criteria for hypomania/mania and depressive phases do not meet full criteria for a major depressive episode

Treatment of Depression – Psychotherapy

- Behavioral therapy
- Cognitive behavioral therapy (CBT)
- Interpersonal therapy
- Psychoanalysis/psychodynamic therapy
- Family therapy

Reasons to Hospitalize

- Danger to self – active suicidal plan with intent and/or preparatory behavior
- Danger to others or society
- Unable to take care of self, including basic activities of daily living

Treatment of Unipolar Depression – Antidepressant Medications

- SSRIs – Prozac, Zoloft, Lexapro, Celexa, Luvox
- SNRIs – Cymbalta, Effexor, Pristiq, Fetzima
- NDRIs – Wellbutrin and related medication, Auvelity
- Atypical Antidepressants – mirtazapine, trazodone, vilazodone, vortioxetine
- MAO-inhibitors
- TCAs

* All these medications often require 2-3 months at an adequate dose to see full benefit

* These medications above can precipitate hypomania, mania, or a mixed depressive episode in individuals with susceptibility to underlying bipolar spectrum depression – mood stabilizer is also required in these individuals

Treatment of Bipolar Depression – Mood Stabilizer Medications

- Lithium
- Antiepileptic Medications
  - Depakote (valproic acid)
  - Tegretol (carbamazepine)
  - Trileptal (oxcarbazepine)
  - Lamictal (lamotrigine)
- Antipsychotic medications
  - Abilify (aripiprazole)
  - Caplyta (lumateperone)
  - Geodon (ziprasidone)
  - Risperdal (risperidone)
  - Seroquel (quetiapine)
  - Vraylar (cariprazine)
  - Zyprexa (olanzapine)

Pharmacogenetic Testing

- Main use is to determine how the medications will be metabolized in the liver or excreted in the kidneys, which can lead to higher or lower blood levels compared to the dosage prescribed
- Can help predict how one will tolerate the medication
- Not generally predictive of which medication will work best for the patient

Neuromodulation Treatments

- Electroconvulsive Therapy (ECT) – major depression, bipolar depression, mixed depressive episode, hypomania, mania, catatonia
- Transcranial Magnetic Stimulation (TMS) – FDA approved for unipolar depression only for both adolescents and adults
- Spravato ® (esketamine) nasal spray – FDA approved for treatment resistant depression and acute suicidality
- Light Therapy – for seasonal major depression, bipolar depression
- Vagal Nerve Stimulation

References

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Questions?