Neuroscience of Mental Health Disorders Part 3

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BIPOLAR DISORDER
The Brain and Bipolar Disorder

Experts believe bipolar disorder is partly caused by an underlying problem with specific brain circuits and the balance of brain chemicals called neurotransmitters.

Three neurotransmitter (brain chemicals) identified with Bipolar Disorder are:

- Noradrenaline (norepinephrine)
- Serotonin
- Dopamine

- Serotonin is connected to many body functions such as sleep, wakefulness, eating, sexual activity, impulsivity, learning, and memory. Researchers believe that abnormal functioning of brain circuits that involve serotonin as a chemical messenger contribute to mood disorders (depression and bipolar disorder).

- Dopamine is commonly linked with the pleasure system of the brain. Disruption to the dopamine system is connected to psychosis and schizophrenia, a severe mental disorder characterized by distortions in reality and illogical thought patterns and behaviors, thus the reason for confusion in gaining an accurate diagnosis of an individual with Bipolar who is also psychotic and/or delusional.
The Depressed Brain

PET scans show that brain energy consumption rises and falls with manic and depressive episodes.

Depressed state (May 17)  Manic state (May 18)  Depressed state (May 27)
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<th>Mania</th>
<th>Hypomania</th>
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<td>Major depression</td>
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DEPRESSION
Neurobiology of Depression – Depression Is In the Brain

The neurobiology (biology of the brain) of major depression research areas include:

- Psychosocial stress and stress hormones
- Neurotransmitters such as serotonin, norepinephrine, dopamine, glutamate and gamma-aminobutyric acid (GABA)
- Neurocircuitry (neuroimaging)
- Neurotrophic factors
- Circadian rhythms
Emotionally arousing rumination → Over dreaming (REM) and less deep sleep (recuperation) → Tiredness or exhaustion by morning → Depressive thinking styles → Emotionally arousing rumination
CAUSES AND TREATMENT

DEMORALIZED

50% HIGH CORTISOL

STRESS

DEPRESSION

25% ANXIETY
TRAUMA / ABUSE / ILL

4% GENETIC

11% UNKNOWN

6% PMS

4% DRUG ABUSE

CHANGE IN LIFESTYLE

MEDICATION

THERAPY

MEDICATION AND THERAPY

LIMITED OR SLOW RECOVERY
Areas of the brain affected by Depression
How neurons communicate
Brain Diagram with Amygdala
“Neurotransmitter” what does this really mean? Neurotransmitters are chemical messengers within the brain that facilitate communication between nerve cells. Here’s an illustration of serotonin.
Another view of the components of the Brain’s Limbic System involved in Depression
Depression Manifestations

- Major or Clinical Depression: Sever and disrupts ability to perform daily tasks
- Dysthymia: Milder than major depression but persists for at least 2 years
- Double Depression: = Major + Dysthymia
- Atypical Depression: Can temporarily put on a brave face and can appear OK to others
- Melancholia: Unable to even temporarily feel any lift, easy to see in someone
- Depression coupled with Anxiety
- Postpartum Depression
- SAD Winter Blues
Social-Cognitive Perspective

The social-cognitive perspective suggests that depression arises partly from self-defeating beliefs and negative explanatory styles.

- **Biological influences:**
  - genetic predispositions
  - changes in brain chemistry
  - brain damage due to stress and other factors

- **Psychological influences:**
  - negative explanatory style
  - learned helplessness
  - gender differences

- **Social-cultural influences:**
  - traumatic/negative events
  - cultural expectations
  - depression-evoked responses

- **Depressed mood**
Diminished Serotonin Activity

Overactive Deep Limbic System

- Depression
- Negativity
- Moodiness
- Irritability
- Social isolation
- Hopelessness
- Excessive guilt
- Easily offended
The Limbic System & Brain Structures related to it
Brain Circuits and Symptoms in Depression

- More than just a mood circuit for MDD
  - Monoamine pathways hypothetically relate to all symptoms of MDD
- Separate branches of monoamine pathways may independently modulate various malfunctioning brain areas that create a unique portfolio of symptoms
- Modulating separate branches of monoamine pathways with treatment may cause some but not all symptoms to be resolved
Depression and Anxiety are Ultimately About How the Brain Responds to the Environment

“Stressors” (psychological, nutritional, hormonal, medication, drug/alcohol “kindling”)

Genes
- Multiple susceptibility alleles each of small effect;
- Promoters bind RNA polymerase;
- Supressors block phenotypic expression BDNF, Bcl-2

Epigenetics
- Gene and Protein Expression, e.g., BDNF* levels reduced during depression, mania

Cells:
- Glial and neuronal abnormalities; mitochondrial dysfunction

Systems:
- Abnormal function and information processing in multiple, interacting circuits

Behavior:
- Complex interactions affecting emotional, psychomotor, cognitive, visceromotor function

*BDNF promotes the growth and survival of brain cells, promotes learning, memory, higher thinking; Bcl-2 exerts pro-and anti-apoptosis via mitochondria membrane
3-D Active SPECT Healthy Brain vs Anxiety and Depression

3-D Active SPECT of a Healthy Brain


3-D Active SPECT of Brain With Anxiety and Depression – increased anterior cingulate and deep limbic activity.

Depression is a real, biochemical brain dysfunction.

A PET Scan measures vital functions such as blood flow, oxygen use, and blood sugar (glucose) metabolism.

Source: Mark George, M. D. Biological Psychiatry Branch Division of Intramural Research Programs, NIMH 1993
Color PET scan of brain showing depression
Elevated Levels of MAO in Depression

**Healthy Subjects**

- Monoamine Neurotransmitters
  - Orange: Serotonin
  - Green: Norepinephrine
  - Blue: Dopamine

**Depressed Subjects**

- Additional MAO-A enzymes

Elevated levels of MAO-A may be the primary monoamine lowering process in MDD.

MAO = monoamine oxidase.
MDD = major depressive disorder.
*MAO exists as 2 forms: MAO-A and MAO-B.
Neurotransmitters & Depression

A reduction of norepinephrine and serotonin has been found in depression.

Drugs that alleviate mania reduce norepinephrine.
Prozac: How It Works

Normal:
Serotonin is released into the synapse to aid in the transmission of nerve impulses.

Depressed:
The pre-synaptic nerve reabsorbs the serotonin from the synapse too quickly. The low concentration of serotonin in the synapse prevents the traveling of the impulse to the post-synaptic nerve.

On Prozac:
Prozac blocks serotonin reuptake receptors, keeping the concentration of serotonin in the synapse high enough to carry nerve impulses across the synapse.
THOUGHTS

CBT

BEHAVIORS

EMOTIONS

or

Lexapro
escitalopram oxalate

Equivalent to 10 mg escitalopram
100 Tablets
Rx only
Selenium
Integral part of regulatory proteins (selenoproteins) in the brain; Supplementation trials are promising; May alleviate postpartum depression.

Magnesium
Deficiency damages NMDA (N-methyl-D-aspartate) receptors in the brain, which regulate mood; Well-documented antidepressant effects.

Chromium
Elevates serotonin (feel-good neurotransmitter) levels in the brain; May be particularly effective on eating symptoms of depression such as carbohydrate craving and increased appetite, due to its effect on blood sugar regulation.

Vitamin B12
Depression may be a manifestation of B12 deficiency; Repletion of B12 to adequate levels can improve treatment response; B12 deficiency common in psychiatric disorders.

Vitamin B6
Cofactor for serotonin and dopamine production (feel good chemicals); Studies indicate that low levels may predispose people to depression.

Vitamin B2
Law B2 has been implicated in depression due to its role in methylation reactions in the brain.

Biotin
Part of the B-vitamin complex, biotin deficiency has induced depression in animal and human studies.

Inositol
Influences signaling pathways in the brain; Particularly effective in SSRI (selective serotonin reuptake inhibitor) sensitive disorders.

Carnitine
Increases serotonin and noradrenaline which lift mood; In trials, carnitine alleviates depression with few, if any, side effects.

Antioxidants
Oxidative stress in the brain alters neurotransmitter function; Antioxidants protect our brain, which is very sensitive to oxidation; Several antioxidants – Vitamins A, C and E, Lipoic Acid, CoQ10, Glutathione and Cysteine – play a key role in prevention and treatment of depression.

Selenium
Zinc
Improves efficacy of antidepressant drugs; Particularly useful for treatment resistant patients; Regulates neurotransmitters.

Serine
Regulates brain chemistry; Involved in NMDA receptor function; Acts as a neurotransmitter; Low levels correlate with severity of depression.

Inositol
Vitamin D
Clinical trials suggest increasing blood levels of vitamin D, which is actually a hormone precursor, may improve symptoms of depression.

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How talk therapy and antidepressant medications add up

Untreated depression

Amygdala is too active → PFC is not active enough

with ADM alone → with talk alone

Amygdala has 'cooled down' → The effect of both

ADM → talk

PFC has 'heated up'

Depression abated