Affective Disorders: Mania and Depression

Unipolar Treatments:
The monoamine hypothesis states that depression is due to a lack of monoaminergic activity.

Drugs known to affect depression (broadest to most specific):

<lower 5HT specificity>
- MAO inhibitors (increase levels of NE, DA, 5HT). 65% success.
- Reserpine (monoamine antagonist) induce depression.
- Tricyclic antidepressants (inhibits reuptake of NE and 5HT).
- Levels of 5-HT in blood lower in suicidal depressive patients.
- Tryptophan depletion induces depression.

- Selective/Specific Serotonin Reuptake Inhibitors (prozac, celexa, paxil...)
  High treatment success.
- Serotonin and Norepinephrine Reuptake Inhibitors.

<higher 5HT specificity>

Bipolar Treatments:
Lithium
Treats bipolar (80%), not unipolar. Acts quickly and effectively on Mania.
Side effects include weight gain, increase in fluid intake and excretion, diabeter, could lead to fatal overdose.
What it does: Stabilizes neuromodulatory pathways. Valproate (increase GABA, affects Mania).

Drawbacks with the monoamine hypothesis:
- Lithium does not act on monoamines.
- Increase in monoamine levels is fast, but effects of the drugs are slow.
- Cocaine inhibits reuptake of monoamine, but is not an antidepressant.

Electro Convulsive Therapy
Controlled seizures, anesthetized, under curare (muscle paralysis).
- It is for bipolar patients, when everything else fails.
- Fast; 50% success rate in responding.
Side effects are memory loss, risk of focal seizures.
Acts by increasing GABA and neuromodulators.

Transcranial Magnetic Stimulation (TMS) of prefrontal cortex (new technique).
- Effective in prefrontal cortex.
- Needs repeated treatments
- Non-invasive.
- Long-lasting effects with repeated TMS.

Deep Brain Stimulation
- Direct stimulation of (subgenual) Anterior Cingulate Cortex, or stimulation of nucc. Accumbens.
- Invasive
- Fast onset of antidepressive effect. Effects accumulate (after 6 months; 35% remission, 60% improvements).

**Vagus Nerve Stimulation**
- Indirect form of deep brain stimulation is by stimulating the periphery.
- Indirect stimulation of the brain stem
- Exact mechanisms are unknown, but it is related to seizure prevention.

**Bipolar Disorders: Mania**
Occurs due to hyperactivity in the **Anterior Cingulate Cortex (ACC)**.

- ACC normally regulates emotions (inhibition effect).
- Mostly involved in the manic phase.
- Most effective treatments of depression result in decreased activity in ACC.

![Depressed state (May 17) Manic state (May 18) Depressed state (May 27)](also see fig 15.10 in textbook)

**Fragmentation of Sleep**
People who have depression have it reflected in their sleep pattern.
Major depression leads to less stages 3 and 4 of sleep, more sleep fragmentation, REM sleep occurs earlier and is more intense.
(Also see fig 15.18 in textbook)

**Sleep therapy:**
**Different types-**
1) Delaying, or preventing, REM sleep. Slow but effective; a common side effect of antidepressants.
2) Slow Wave Sleep deprivation: Effective quicker (1-2 nights).
3) Total Sleep Deprivation

**Depressogenic hypothesis:** A depression-inducing substance is secreted at night, and is cleared during the awake state.
Total sleep deprivation has fast effects, but not for everyone:
Works best for patients with fluctuating daily moods.
Not long-lasting.

4) Partial/intermittent sleep deprivation helps the effects of antidepressants.

Other Affective Disorders

Seasonal Affective Disorders (SAD): related to hypothalamus?
Depression dependent on seasonal changes.
-is a Unipolar depression.
-short days, long nights (winter) ? can lead to depression. Summer depression is rare.
-genetic basis (melanospin gene).
-Treatments: Phototherapy, light therapy and exercise.

END OF CHAPTER