**Depression**

Unipolar treatments:
- The **monoamine** hypothesis: Depression is due to a lack of monoaminergic activity

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 the blood lower in suicidal depressive patients
- Tricyclic antidepressants (inhibits reuptake of NE and 5HT).
- Level 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**

-Bipolar treatment: lithium
- treats bipolar (80%), not unipolar. Fast and effective on Mania.
- side effects include weight gain, increase in fluid intake and excretion. diabetes, fatal overdose
- stabilize neuromodulator pathways. Valproate (increase GABA, effect on Mania).

-Problem with the monoamine thy
  - lithium does not act on monoamines.
  - increase in monoamine levels is fast, but effects of the drugs are slow.
  - Cocaine inhibits re-uptake

**Effective disorders: treatments**
- Electro convulsive therapy
  - controlled seizure, anesthetized, under curare (muscle paralysis)
For bipolar patients, when everything else fails,
fast, 50% success in responding
side effect: memory loss. Risk of focal seizures
acts by increasing GABA and neuromodulators

-New technique, Transcranial Magnetic Stimulation of prefrontal cortex
  - Effective in prefrontal cortex
- Need repeated treatment
- Non-invasive

- Deep brain stimulation
- Direct stimulation of (subgenera) Anterior Cingulate Cortex
- Invasive
- Fast onset of antidepressive effect. Accumulating effects (after 6 months: 35% remission, 60% improvements).
- Also: Direct stimulation of nucc.Accumbens.

- Vagus nerve stimulation

- Indirect from of deep brain stimulation by stimulating the periphery
- Indirect stimulation of the brain stem
- Exact mechanisms unknown, but related to seizure prevention

**Bipolar disorders: mania**

- due to hyperactivity in the anterior cingulate cortex (ACC)
- ACC normally regulate emotions (inhibition).
Mostly involved in the manic phase.
Most effective treatments of depression result in decrease in activity in ACC

Fragmentation of sleep
Other treatments of bipolar disorders

Fact: major depression - less stages 3 and 4, more sleep fragmentation, REM occurs earlier and is more intense.

Sleep therapy:
- Delaying or preventing REM sleep, Slow, but effective. A common side effect of antidepressants.
- Slow Wave Sleep deprivation: effective faster (1-2 nights)
- Total sleep deprivation
  ■ Depressogenic hypothesis:
    A depression-inducing substance is secreted at night, and is cleared during the awake state.
  ■ Fast effects, but not for everyone:
    Works best for depressed patients with fluctuating daily moods.
  ■ Not long lasting.

Partial intermittent sleep deprivation helps the effect

Other Affective Disorders

**Seasonal Effective Disorders (SAD):** hypothalamus?
- Unipolar depression.
- Short days, long nights (winter) → depression.
- Summer depression is rare.
- Genetic basis (melanospin gene)
- Treatments: phototherapy, light therapy and exercise.