Unipolar treatments:

- The monoamine hypothesis: depression is due to a lack of monoaminergic activity.
  - 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

Bipolar treatment: Lithium

- Treat bipolar (80%), not unipolar. Fast and effective on Mania.
- Side effects include weight gain, increase in fluid intake and excretion, diabetes, fatal overdose.
- Stabilize neuromodulatory pathways. Valproate (increase GABA, effect on Mania)

Problems 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 re-uptake of monoamine, but is not an antidepressant.

Affective disorders: treatments
Electro Convulsive Therapy.
- Controlled seizures, anesthetized, under curare (muscle paralysis)
- For biopolar patients, when everything else fails.
- Fast, 50% success in responding.
- Side effects: 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 treatments
- Non-invasive

Deep brain stimulation
- Direct stimulation of (subgenual) anterior cingulate cortex
- Invasive
- Fast onset of antidepressive effect. Accumulating effects (after 6 months: 35% remission, 60% improvements)
- Also: direct stimulation of nucc. Accumbens.
- Indirect form 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 regulates emotions (inhibition)
- Mostly involved in the manic phase
- Most effective treatments of depressions 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 of antidepressants

**Other Affective Disorders**

Seasonal Affective Disorders (SAD): hypothalamus?
- Unipolar depression
- Short days, long nights (winter) -> depression
- Summer depression is rare
- Genetic basis (melanopsin gene)
- Treatments: Phototherapy, light therapy and exercise.