Thursday 12/1/16

Disorders

(Cont. from lecture starting Tuesday)

Infectious Diseases
   -Most common are Encephalitis and Meningitis

Encephalitis
   - “Inflammation of the brain: caused by bacteria, viruses or toxic chemicals” (p.384 of textbook)
   - Symptoms include fever, irritability, nausea, convulsions, delirium, and signs of brain damage.
   - No known treatment

Diseases involved with Encephalitis
   - **Herpes Simplex**: causes cold sores. A virus that lives in the spinal ganglion and breaks out along sensory nerves periodically
   - Encephalitis is caused from the spreading of the outbreak of the herpes virus spreading to the brain
   - **Polio**: (acute anterior poliomyelitis) is the damage to all motor neurons (brain and spinal cord). There, however is a vaccine for it (James Salk)
   - **Rabies**: Fatal viral disease that causes brain damage; usually transmitted through the bite of an infected animal (p.385). Symptoms include fever, headaches, convulsions, seizures and lead to death within a week
   - Affects cerebellum and hippocampus. There is a vaccine to prevent this.
   - **AIDS** (not including HIV): untreated cases find brain damage of up to 75% of victims. Caused by an excess of Calcium through NMDA receptors (excitotoxicity).
   - AIDS dementia complex, common syndrome of disease; forgetfulness in AIDS patients

Meningitis
   - Inflammation of the meninges, cause by bacteria or virus
   - Symptoms include: headache, stiff neck, convulsions, death
   - Most common form usually does not cause major brain damage
   - Can be treated with antibiotics

Schizophrenia
   - Affects 1% of the population. Complex. Not strictly degenerative.
   - 3 types of symptoms
     1.) Negative: lack of some normal behaviors
     2.) Cognitive: disorder of information processing
     3.) Positive: additional abnormal behaviors
- Not really any obvious physical signs of this disorder, except some small differences (larger head, wide-set eyes and differences in the length of finger in males)
- Late onset: usually occurs in people in their 20's
- Symptoms usually occur gradually within a time period of 5 years. Positive symptoms show up last.

**Positive symptoms:** Dopamine
- Positive symptoms sometimes preceded by elation/euphoria
- Thought Disorders: irrational, disorganized thinking
- Delusions: non-factual beliefs (persecution, contact with Aliens, grandeur [irrational belief about the self as being highly superior in all traits])
- Hallucinations: sensory perception malfunctions
- Treatment: Chlorpromazine blocks D2 receptors and eliminated positive symptoms
- L-Dopa, cocaine, amphetamine: Agonists that increase positive symptoms
- A dysfunction of the meso-limbic dopaminergic system. “too much dopamine”
- The more D2 receptors blocked, the larger the anti-psychotic effect

**Negative symptoms:** Brain Damage
- Flat effect, flat motivation, unusual facial expression, social inhibition, anhedonia (inability to feel pleasure), poor eye pursuit, deficit in eye-blink reflexes
- Enlarged ventricles: large lateral (and 3rd ventricles)-less gray matter (temporal, frontal lobes)

Evidence from Anatomy: loss of brain tissue (cortical gray matter)

Hypofrontality: evidence from physiology
- Decrease of activity in (dorso-lateral) frontal cortex
- Due to decrease in dopamine reuptake
- Reduced frontal lobe activity

Hypofrontality: animal studies
- PCP “angel dust” or Ketamine produce schizophrenic-like symptoms: Indirect NMDA antagonists → decrease neural activity. Dopamine modulation in prefrontal cortex
- Lack of prefrontal activity. Dopamine results in persevering behaviors
- Clozapine increases dopamine in prefrontal cortex and alleviates symptoms

**Treatment**
- Step 1: Hypofrontality. Less NMDA and DA release in prefrontal cortex → less PFC activity. Negative symptoms. Alleviated by indirect NMDA agonists
- Partial Competitive Dopamine agonists: high affinity, less efficient than DA atypical antipsychotic drugs (clozapine, aripiprazole). Agonist in PPC. Antagonist in Nucleus Accumbens. Alleviates all symptoms of Schizophrenia
Causes

- **Viral**
  - Epidemiology: study of disease at population level
  - Latitude effect: increase risk if birth is far from the equator
  - Seasonality effect: higher if born in later winter/early spring
  - Births after a flu epidemic on second trimester of pregnancy
- **Other risk factors**
  - Vitamin D deficiency (lack of sunlight or milk)
  - Smoking and alcohol consumption during pregnancy
- **Developmental causes**
  - Lack of sociability and psychomotor skills in childhood associated with schizophrenia
  - Monozygotic twin studies: if twinning occurs before day 4, separate placentas: decrease likelihood of developing in both twins
- **Genetic Cause**
  - Parents with Schizophrenia increases the risk of a child by a factor of 10
  - Twin fingerprints correlate with concordance for Schizophrenia
  - Identical twins from two schizophrenic parents only have a 45% chance of developing the disorder. This should be 75%, but other genes and factors come into play

Cognitive Symptoms

- Attention deficits
- Slow reaction times
- Poor planning and problem solving
- Deficit in abstract thinking
- No clear neural correlates or mechanisms found in brain yet

Affective Disorders

- **Bipolar**: cycle between depression and Mania, but cycles of depression last 3x longer than mania
  - Cases of just mania alone are rare.

**Depression**: “Major Depressive Disorder”

- 2-3x more common in women than in men (7% of occurrences in women and 3% of occurrences in men)
- Symptoms include: feelings of unworthiness, guilt, low energy and difficulty falling asleep (and sometimes difficulty waking up)
  - suicide attempts: 15% unipolar (normally depression by itself). 30% bipolar (both mania and depression)
- accompanied with sleep disorder: less slow wave sleep, more stage 1 sleep and earlier onset of REM sleep.
- Hereditary: one direct parent → 10x increase of risk. No single genes
- Seasonality effect: birth in May/June/July → high risk for suicide