I. 4/28: Schizophrenia Affective Disorders

A. Schizophrenia Overview

1. Complex disease that affects 1% of world population
2. Symptoms
   a) Negative symptoms: lack of certain behaviors
   b) Cognitive symptoms: disorder of information processing
   c) Positive symptoms: additional abnormal behaviors
   d) Physical traits: finger signatures, larger heads, wide-set eyes
3. Typically onsets during 20s, later than most disorders
   a) Symptoms appear within five years of onset
   b) Positive symptoms appear last

B. Positive Symptoms

1. Positive symptoms may be preceded by short-lived euphoria
2. Examples
   a) Irrational, disorganized thinking
   b) Delusions (grandeur, persecution, etc.)
   c) Hallucinations: malfunctions of sensory perception
3. Dopamine is related to positive symptoms
   a) Dopa antagonist chlorpromazine eliminates positive symptoms
   b) L-dopa, cocaine, and amphetamine (dopa agonists) trigger positive symptoms
   c) Positive symptoms results from dysfunction in mesolimbic dopaminergic system: too much dopamine
      (1) VTA, nucleus accumbens, amygdala

C. Negative Symptoms

1. Absence of certain behaviors such as motivation, unusual facial expressions, eye pursuit, anhedonia, etc.
2. Enlarged ventricles reduces gray matter, particularly third ventricles
3. Loss of brain tissue is progressive after onset
   a) Schizophrenics lose gray matter more quickly with age than control subjects
4. Hypofrontality
a) Decrease of activity in frontal cortex, deficiency of dopamine

5. Induction of schizophrenia symptoms in animals via PCP or ketamine results in inability to change strategies (perseverance of behavior)
   a) Interestingly, no conclusive evidence of schizophrenia in any animals other than humans

D. Relationship Between Positive and Negative Symptoms
   1. Positive symptoms come from too much dopamine, negative symptoms come from not enough dopamine
      a) Makes treatment of both at once very difficult
   2. Hypofrontality (negative symptoms) is alleviated by NMDA agonists
   3. Too much dopamine in nucleus accumbens (positive symptoms) alleviated by D2 antagonists
   4. Effective treatment: partial competitive dopamine agonist
      a) Partial: high affinity for receptors but low efficiency
      b) Competitive: blocks dopamine from reaching receptor
      c) Because of these qualities, acts as agonist in prefrontal cortex and antagonist in nucleus accumbens
      d) Thus alleviates all symptoms of schizophrenia

E. Causes of Schizophrenia
   1. Viral cause
      a) Epidemiology shows multiple links between schizophrenia and viral spread
         (1) Latitude effect: risk grows as birth moves away from equator
         (2) Seasonality: risk is high for births in early months (Jan-Apr)
         (3) Risk higher when birth takes place in cities
      b) Most details still murky
   2. Developmental causes
      a) Lack of sociability and psychomotor skills in youth are associated with schizophrenia
      b) Twin studies: twins who share a placenta are more likely to both develop schizophrenia
   3. Genetic causes
a) Parental schizophrenia increases risk for their children by a factor of 10

b) Multiple genes involved and not all cases come from genetics
   (1) Evidence: Identical twins from schizophrenic parents have lower risk than expected that both develop schizophrenia

F. Cognitive Symptoms
   1. Attention deficits
   2. Slow reaction time
   3. Deficit in learning/memory
   4. Poor planning and problem solving
   5. Deficit in abstract thinking

G. Affective disorders:
   1. Bipolar Disorder
      a) Cycle between mania and depression
      b) Depressive episodes usually longer than mania (average 3x longer)
      c) Depression can be on its own, mania on its own is very rare
   2. Major Depressive Disorder
      a) More likely in women than men
      b) Accompanied by sleep disorder (less SWS sleep, earlier REM onset)
      c) Hereditary effect; more than one gene
      d) Seasonality effect: May/Jun/Jul birth increases risk
   3. Unipolar depression treatments
      a) Monoamine hypothesis
         (1) Lack of monoaminergic activity leads to depression
         (2) MAO inhibitors has 65% success rates treating depression
         (3) Lack of 5-HT and tryptophan related to depressions
         (4) SSRIs and SNRIs: very effective
         (5) Issues with hypothesis: MA levels increase much faster than depression eases, not all MA agonists are antidepressants, lithium does not act on MA
   4. Bipolar treatment
      a) Lithium
(1) Fast and effective treatment for mania
(2) Stabilizes neuromodulatory pathways
(3) Side effects mostly related to weight gain

5. Other treatments
   a) Electroconvulsive therapy (ECT)
      (1) Controlled seizure under anesthesia
      (2) Last line of defense against bipolar disorder
      (3) 50% success rate
   b) Transcranial Magnetic Stimulation (TMS)
      (1) Non-invasive repeated stimulation of prefrontal cortex
   c) Deep brain stimulation
      (1) Direct stimulation of anterior cingulate cortex
      (2) Invasive but fast onset and accumulation of antidepressant effects
      (3) Can also be done by stimulating nucleus accumbens
   d) Vagus nerve stimulation
      (1) Indirect form of deep brain stimulation
      (2) Stimulation of peripheral vagus nerve leads to stimulation of brainstem
      (3) Exact mechanism unknown, but related to seizure prevention