Memory Disorders

I. Types of memory:
   A. Declarative memory:

   1. Episodic: memory for time and places.
   2. Semantic: memory for facts and knowledge (language, numbers, etc).

   B. Procedural memory:

   - examples: mirror drawing, playing piano, riding a bicycle.

II. Duration of memory:
   A. Short-term memory:

   - examples: retain a phone number while dialing; remembering what you had for lunch yesterday but not a week ago.

   B. Long-term memory:

   - examples: childhood memories, language vocabulary.

III. Memory disorders:
   A. Amnesia: severe memory loss.

   1. Retrograde amnesia: cannot recall events that occurred prior to the brain trauma.
   2. Anterograde amnesia: cannot recall events that occur after the brain trauma.

   B. The Search for the Neural Trace of Memory (the Engram):

   1. Engram:

   2. Karl Lashley’s studies:
      a. Principle of mass action:
      b. Principle of equipotentiality:

   3. Donald Hebb’s contributions:
      a. Cell assemblies:
3. Donald Hebb’s contributions (continued):
   b. **Reverberation**: ______________________________________
   _________________________________________________________
   ________________________________________________________.
   - provided the neural basis for consolidation: strengthening of
   short-term memories into long-term memories.

4. Evidence for neural consolidation process:
   a. **Electroconvulsive therapy (ECT)**: used for therapeutic relief of
   several psychological symptoms, a very common side-effect is
   retrograde amnesia.
   b. **Seizure-inducing drugs (pentylenetetrazol)**: produced retrograde
   amnesia in animals.
   - thus, interference with normal neural processing shortly after an
   experience causes amnesia for this experience.

C. Human Amnesia:
1. H.M.: sustained bilateral temporal lobe removal (lobectomy),
   which included: ______________________________________
   ________________________________________________________.
   - milestone case in the history of the neurobiology of learning and
   memory.
   - suffered no loss of intelligence (IQ).
   - suffered only mild retrograde amnesia.
   - suffered devastating anterograde amnesia.

   What kind of memories were most affected? ____________________.
   - H.M.’s procedural memories appeared relatively normal.

What did H.M.’s case tell us about memory?
   a. medial temporal lobe structures involved in memory processes.
   b. challenged the view of diffuse memory processes.
   c. supports distinct short-term and long-term memory.
   d. suggested a role for medial temporal lobe in consolidation.
   e. demonstrated the distinction between declarative vs procedural
   memories.

No treatment has been reported to improve H.M.’s severe memory
dysfunction.

2. **Korsakoff’s syndrome (aka Wernicke-Korsakoff’s)**: described by
   Russian physician Sergei Korsakoff in 1889.
   a. **Symptoms**:
      - ____________________________________________________
      - unawareness of memory defect.
      - memory problems often preceded by ataxia (difficulty to walk
        and keep posture, and muscle control of eye movements).

   b. **Etiology**:
      - prevalence - approximately 1 million Americans.
      - ____________________________________________________
      - alcohol increase the need for vitamin B1, and at the same time
        reduce the need for caloric intake.
      - no known predisposition.
      - lack of thiamin produces degeneration of vulnerable neurons,
        particularly in the dorsomedial thalamus and mamillary bodies.
3. Dementias
   a. Symptoms:
      i. Amnesia: impairments in memory (more severe than normally seen in normal aging), usually the identifying sign.
      ii. Agnosia: _________________.
      iii. Apraxia: ______________________ (most likely to appear after amnesia).
      iv. Aphasia: _________________.
   b. Etiology:
      - some genetic associations, but mostly unknown.
      - rarely strikes before 40 years of age.
      - _________________.
      - this figure rises to between 20 – 50% in people over the age of 85.
      - 50% of dementias can be attributed to Alzheimer’s disease.

4. Alzheimer’s disease
   a. Symptoms: similar to those described for general Dementias.
   b. Etiology:
      - affects approximately 2.5 million Americans.
      - Alzheimer’s disease of early-onset (as early as 40 years of age) associated with specific genes.
      - some genes are also associated with late-onset Alzheimer’s.
      - late-onset AD accounts for > 99% of all AD diagnosed.
      - progression of disease is variable, with some patients dying within 8-10 years of diagnosis, while others live 20+ years.
4. Alzheimer’s disease (continued)

c. Brain abnormalities associated with Alzheimer’s disease:

i. ________________________________________________
   __________________________________________________
   ______________________________.
   - normal form is cleaved to produce a protein with 40 amino-acids (Aβ40);
   - mutation leads to ________________________________;
   - long form clusters together and form plaques in patients
     with AD, called ___________________; 
   - unknown how APP mutation produces plaques.
   - plaques lead to neural degeneration beginning in
     hippocampus, but generalizes to all of neocortex.
   - some people with mutation do NOT develop AD.
4. Alzheimer’s disease (continued)

ii. Massive neuronal death:

____________________________________________________________________

____________________________________________________________________


4. Alzheimer’s disease (continued)

iii. Another gene on chromosome 19 associated with AD:

- two copies of this allele increases the risk to develop AD to ________________
- individuals with two APOE alleles have measurable differences in brain blood flow even before AD symptoms.

iv. Additional genes associated with AD have been found on chromosome 1 and 14.
- presenilin-1 (chromosome 14) and presenilin-2 have been associated with approximately 5% of patients with AD.
- unknown how presenilin mutation may produce AD defect
- other protein, Tau, also associated with neural tangles.
4. Alzheimer’s disease (continued)

d. Treatment:
- nothing has been found that can cure disease.
  i. drugs are given to improve acetylcholine neurotransmitter functions:
     - give precursor – choline and lecithin;
     - give acetylcholinesterase inhibitors to reduce breakdown – physostigmine;
     - give agonist – drugs that mimic acetylcholine, especially at the muscarinic type 1 receptor or nicotinic agonists (work on nicotinic receptors).
     - all cholinergic manipulations have resulted in poor symptom relief

  ii. drugs given to improve neurotrophic factors that promote neuronal survival, growth, or differentiation – nerve growth factor (NGF), a large protein that does not cross the blood-brain-barrier.

  iii. recently, the use of a vaccine against Aβ42 has shown some promises in a mouse model of AD.
     - in the same mouse model, injections of small amounts of Aβ42 early during development leads to significantly reduced behavioral and brain signs of AD!