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 (pentylentetrazol)*: 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.

   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.
c. Specific brain areas involved in Korsakoff’s syndrome:
- draw connections between hippocampus, mamillary body, dorsomedial thalamus, cingulate cortex, and back to hippocampus.

- brain regions affected by thiamin deficiency intimately associated with medial temporal lobe.
- memory dysfunction of Korsakoff’s patients is likewise closely associated (anterograde amnesia for declarative information) with that seen in bilateral medial temporal lobectomies.

d. Treatment:
- high doses of thiamin can improve the motor ataxia and eye movement abnormalities.
- if structural (loss of neurons in mamillary bodies and mediodorsal thalamus) brain damage done, thiamin supplement will not reverse the anterograde memory deficit.
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*:
      - afflicts 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.
Figure 10-1: MR Scans Illustrating Changes as a Consequence of Aging and Disease
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 **APOe4** 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!