The Biology of Memory

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Memory

• Registration
  – **Attention** sufficient to start storage
• Encoding - creates the memory: occurs with ‘quality’ sleep
• Consolidation - time to set up storage: needs intact brain structures
• Retrieval: Slows down with age-**normal**
Attention is Key

- Not interested
- Medications
- Poor sleep
- Jet lag
- Alcohol
- Impaired hearing or sight
- Depression
- Pain
Medications

• Chemotherapy “chemobrain”
• Antihistamines
• Sleep medications
• Anticholinergics, i.e. medication for bladder spasticity
• Anti anxiety medications
• Narcotics
Phrenology
The science of the ‘bumps’
Structures

• Frontal lobes: judgement, personality, social behavior
• Temporal lobes: hearing, speech, short term memory
• Occipital lobes: vision, reading, colors, shapes
• Parietal lobes: sensation, localization, recognizing
• Brain stem: automatic behaviors, breathing eye movements, balance, hearing
An adult brain contains about 100 billion nerve cells. Branches connect the nerve cells at more than 100 trillion points. Scientists call this dense, branching network a "neuron forest."
Synapses
Neurotransmitters

• Dopamine: stimulus, feel good, emotion, movements

• Serotonin: ten different sub types, involve depression, mood, migraine, etc

• Acetylcholine: triggers muscle activity, decreased in Alzheimer’s

• Norepinephrine: stimulates multiple systems, helps sleep, dreams

• GABA: pain modulation, inhibits other neuron connection

• Glutamate: excitatory, helps memory

• CGRP: pain and muscle activity

• Endorphins: pain modulation, sense of well being
How does speech work?

• We hear it
• We remember it
• We organize it
• We sing it (different pathway)
Speech

• Tone
• Modulation
• Accents
• Loudness
• Cadence
• Emotion
Anatomy of speech
Creativity

• Music
  • Stored in multiple locations
  • Interacts with emotional brain
  • Triggers motor activity
  • Triggers remote memory
  • Independent of most speech pathways
Creativity

• Art
  • Involves color perceptions
• Shape
• Recognition of familiar objects (sometimes)
• Three dimensional
• Geometric i.e., quilts
Creativity

- Taste
  - Five senses in different proportions
- Smell
  - 10,000 (or more) individual smells we can perceive
  - Connect with memory, emotion, people, places
What makes a GREAT Meal?
(Unable to test in rats)

- Food
- Taste
- Smell
- Texture
- Temperature
- Company
- Lighting
- Background sounds, pace, setting, etc.
Loss of taste and smell is devastating!

- Common early sign of neurodegenerative conditions
  - Parkinsons
  - Alzheimer’s
- Leads to weight loss
- Can also be from trauma, infections, toxic fumes
The chemistry of memory

- Oxygen
- Glucose - a double edge sword
- Ketones
- Vitamins
- Minerals

- The brain is energy dependent 24/7. It does NOT slow down during sleep
How does memory fail?

• Structural damage interrupts pathways (traumatic brain injuries)
• Lack of oxygen (strokes, drowning, heart attacks)
• Frequent trauma creates cumulative damage (boxers, football players)
• Toxic chemicals (lead, mercury)
• Degenerative processes
Football players/Boxers

Normal Brain

Advanced CTE
Progressive cognitive decline equals dementia

- Dementia is progressive and a change from previous status
- It can have multiple causes such as alcohol, drugs, strokes
- It effects multiple systems including memory, judgement, orientation, mood, executive function, speech and language
Alzheimer’s disease is a specific type of dementia

- Described by Alois Alzheimer in 1907
- Based on a 51 year old woman he follow for a number of years with progressive memory loss and personality changes
- Neuropathology studies showed
  - Amyloid plaque
  - Neurofibrillary tangles
Normal  vs  Alzheimer's

Neuron  vs  Neurofibrillary tangles

Amyloid plaques
Clinical diagnosis until recently was “best guess”

• Every gradually progressive dementia was considered likely Alzheimer’s
• Positive diagnosis could only be made at autopsy
• We were right about half the time
We can identify Alzheimer’s disease in real time using PET imaging

Amyloid specific imaging
Figure 1 Theoretical portrayal of the temporal development of pathologic and clinical events leading to Alzheimer disease dementia

Hypothetical Model of Dynamic Biomarkers of the Alzheimer’s Pathological Cascade

Ronald C. Petersen Neurology 2018;91:395-402
Treatment

- Vaccines to reduce amyloid formation have failed
- Nerve growth stimulators have failed
- Antioxidants have failed
- Estrogen-like medications are in testing phases
- Anti-inflammatory meds, i.e., ibuprofen have failed
Genetic risks:
The APOE question

- We all have two copies of the APOE gene.
- They can be easily measured, if you want to.
- It is marker of how rapidly you metabolize lipids, including amyloid.
- It gives a RELATIVE RISK of Alzheimer’s disease and cardiovascular disease.
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<tbody>
<tr>
<td>Disease Risk</td>
<td>40% less likely</td>
<td>40% less likely</td>
<td>2.6 times more likely</td>
<td>Average risk</td>
<td>3.2 times more likely</td>
<td>14.9 times more likely</td>
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Research observation

• People with more education have less AD
• People who exercise more have less AD
• Ex-smokers have less AD than those who never smoked
• Using ibuprofen frequently is associated with less AD
• People with diabetes have more AD
• People with strokes have more AD
• People with gum and tooth disease get more AD
Acting on the observations

• Keeping your brain active delays dementia
• Starting smoking is still bad for you
• Taking ibuprofen to ‘fix’ memory loss hasn’t worked
• Exercise is good for the brain
• Maintaining good blood pressures is important
• None of the vitamins or supplements have helped
• Dental care is important
Research questions

• If we can get amyloid out of the brain will it cure Alzheimers?
• If we can prevent the formation of amyloid in the brain will it prevent Alzheimer’s?
• Are there other chemicals/drugs that can recover lost memory? (Hint: music works)
Results of most recent studies

- Slowing the formation of amyloid did NOT change the course of the illness
- Dissolving amyloid plaque did NOT change the illness
- Tau-reducing drugs are just starting to be tested
- Low carbohydrate diets seem to help
Dr Alzheimer may have been wrong!

- His patient was younger than the ones we are treating
- Amyloid may not be a cause, but rather a secondary effect of some other process
- Inflammation or infection, possibly a virus may be the trigger
- Stress management may be a potential modifying factor, but you can’t patent it