Cellular Mechanisms of Learning and the Biological Basis of Individuality

The Study of Memory Has Two Parts:

1. The Systems Problem of Memory:
   Where in the brain is memory stored?

2. The Molecular Problem of Memory:
   How is memory stored at each site?
Brenda Milner 1918–
There are Two Major Forms of Long-Term Memory

Explicit (Declarative) - Facts, Events
Implicit (Procedural) - Skills & Habits, Associative Learning, Nonassociative Learning: Habitation and Sensitization

Medial Temporal Lobe
Hippocampus

Striatum - Emotional Responses
Amygdala - Skeletal Musculature
Cerebellum - Reflex Pathways

The Human Brain is complex: $10^{12}$ Neurons
The *Aplysia* Brain is simple: $2 \times 10^4$ Neurons
Sensitization Strengthens the Monosynaptic Connection of Gill Withdrawal
Long-Term Memory Requires a CREB1-Mediated Transcriptional Cascade

Number of synaptic boutons per sensory neuron

Control

Presynaptic

Sensitized

Presynaptic

A Sensory hamarculus

B Motor hamarculus

A
Expression of R(AB) Transgenic Construct Leads to a Defect in Late LTP

Contextual Conditioning

Context Conditioning is Selectively Impaired in R(AB) Mice
Relating Molecular Signaling to the Cognitive Map for Space: The Hippocampal Pyramidal Cells Recruited In LTP Encode Space

Place Cell Examples in Mouse

Place Cell Map Stability is Dependent Upon PKA and Protein Synthesis

Three Degrees of Attention

No Task
- Not hungry
- No food

Foraging
- Hungry Mouse
- Pellets drop randomly

Spatial Task
- Bright lights and noise "On"
- Mouse runs to goal to turn off lights and noise
Optimal stability

Place Field Stability is Dependent on Attention

Average Similarity

Optimal stability

No Task  Foraging  Spatial Task

Dopamine as a Candidate Mediator of Attention

Both Explicit and Implicit Memory Storage Use Modulatory Transmitters and a CREB-Mediated Transcriptional Switch for Converting Short-Term to Long-Term Memory

Aplysia (bottom up modulation)  Hippocampus (top down modulation)
Three Methods of Regulating Synaptic Strength

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