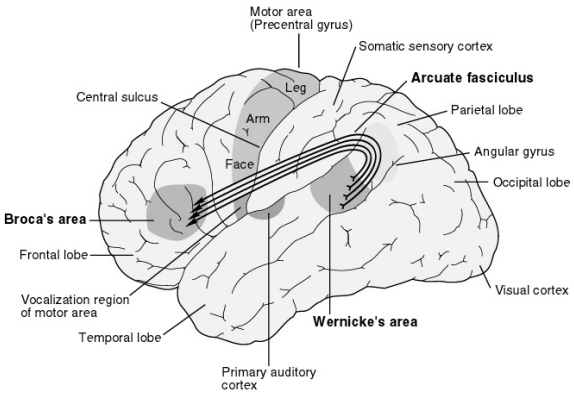
Cellular Mechanisms of Learning and the Biological Basis of Individuality

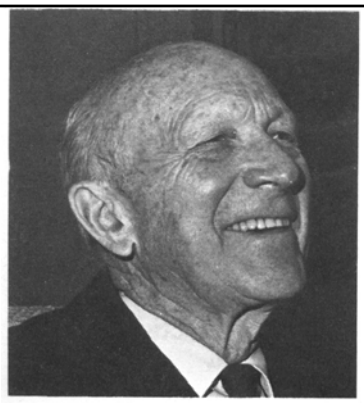
The Study of Memory Has Two Parts:

(1) The *Systems* Problem of Memory:
Where in the brain is memory stored?

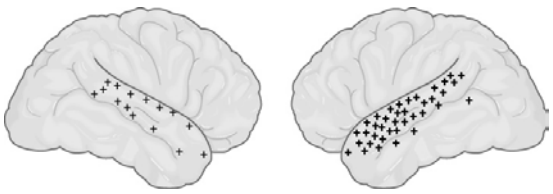
(2) The *Molecular* Problem of Memory:
How is memory stored at each site?

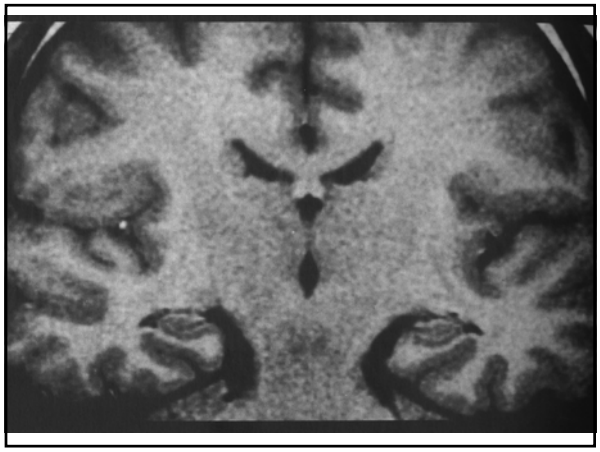


Karl Lashley (1890-1950)

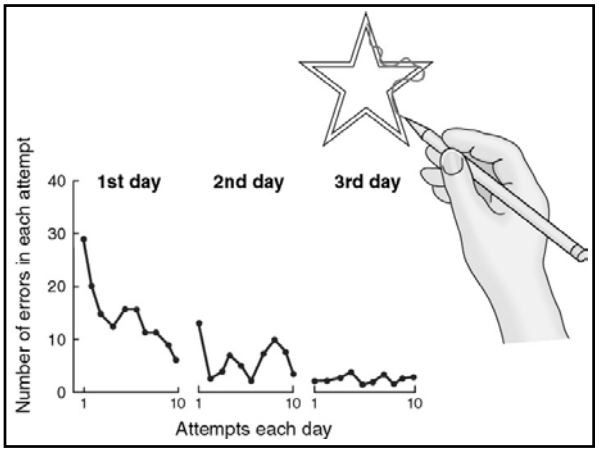


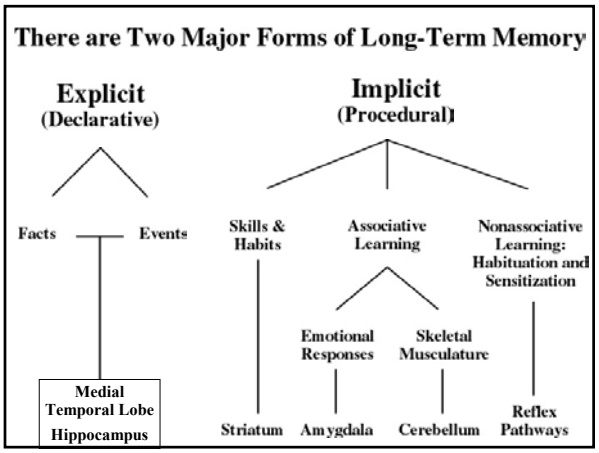
Wilder Penfield (1891-1976)

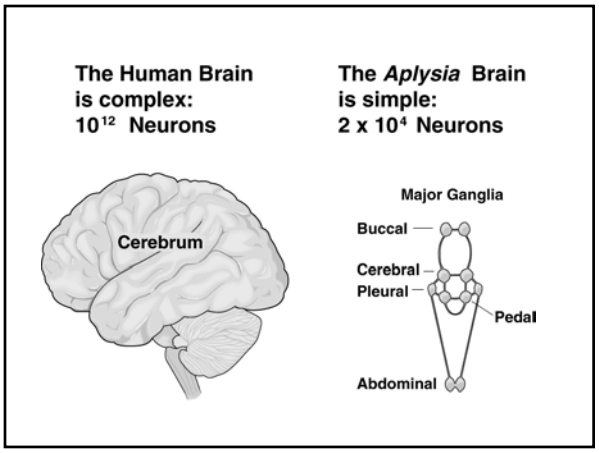


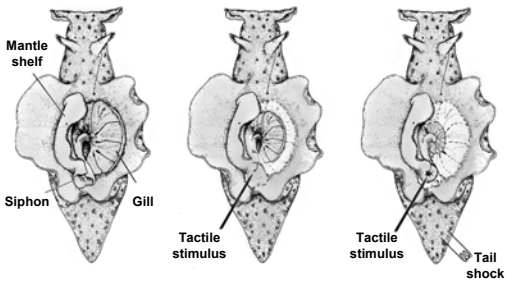


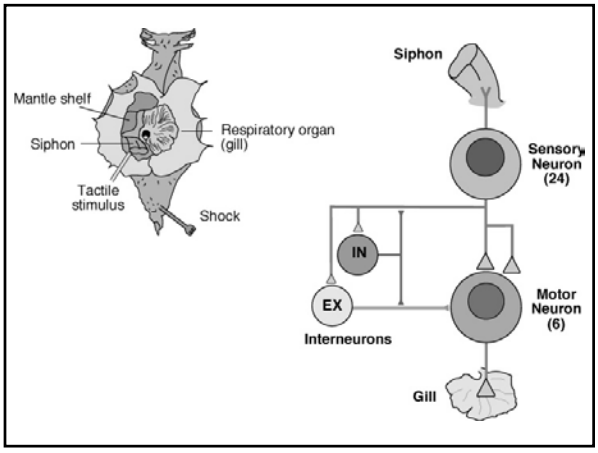
Brenda Milner 1918–

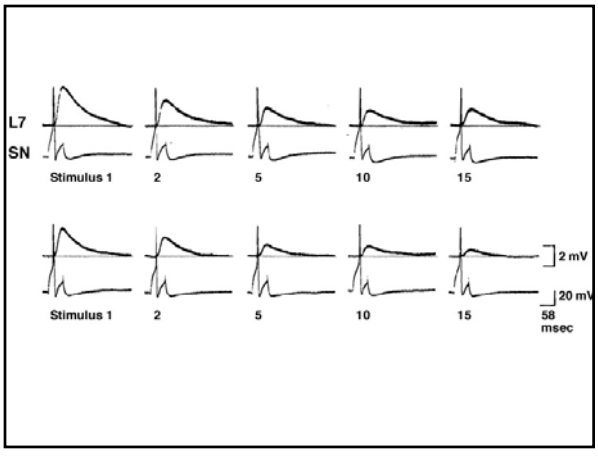

1st day
2nd day
3rd day
Number of errors in each attempt
40
30
20
10
0
1
10
1
10
1
10
Attempts each day

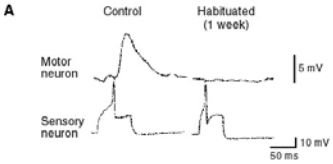

There are Two Major Forms of Long-Term Memory
Explicit
(Declarative)
Implicit
(Procedural)
Facts
Events
Skills &
Habits
Associative
Learning
Nonassociative
Learning:
Habituation and
Sensitization
Emotional
Responses
Skeletal
Musculature
Medial
Temporal Lobe
Hippocampus
Striatum
Amygdala
Cerebellum
Reflex
Pathways


The Human Brain
is complex:
10^12 Neurons
The Aplysia Brain
is simple:
2 x 10^4 Neurons
Cerebrum
Major Ganglia
Buccal
Cerebral
Pleural
Pedal
Abdominal

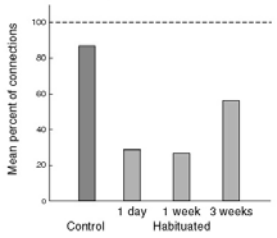

Mantle shelf
Siphon
Gill
Tactile stimulus
Tactile stimulus
Tail shock

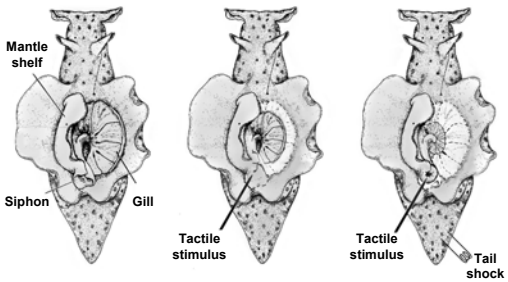

Mantle shelf
Siphon
Respiratory organ (gill)
Tactile stimulus
Shock
Siphon
Sensory Neuron (24)
IN
EX
Interneurons
Motor Neuron (6)
Gill


L7
SN
Stimulus 1
2
5
10
15
2 mV
20 mV
Stimulus 1
2
5
10
15
58 msec

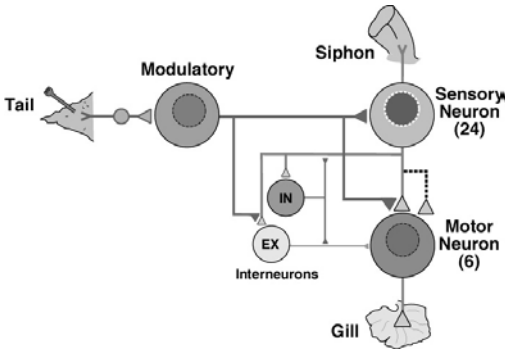


B Inactivation of synaptic connections by long term habituation

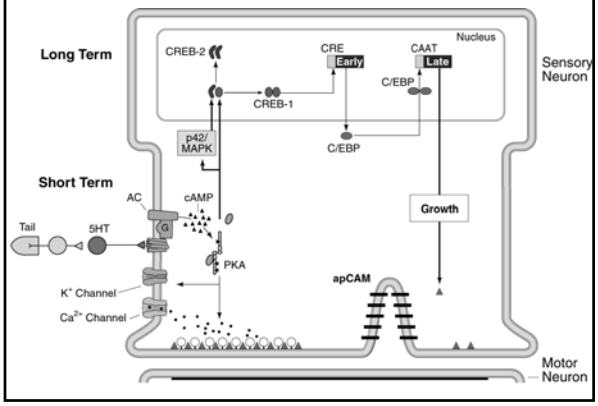


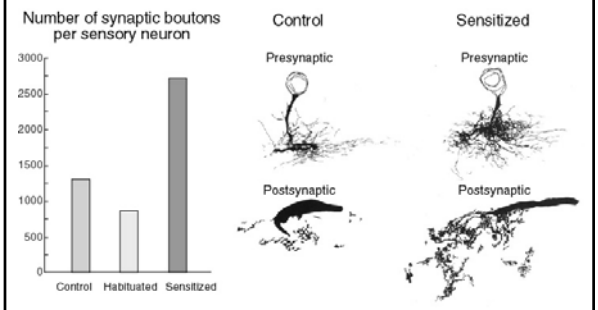


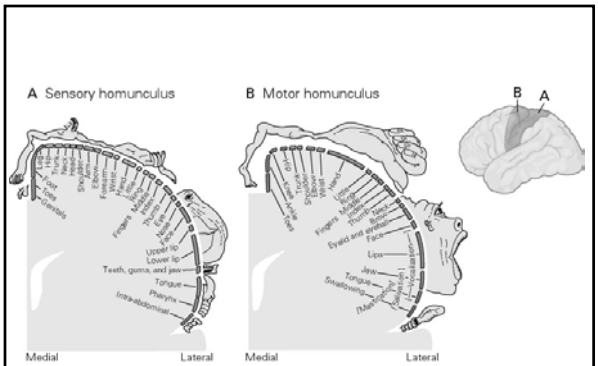
Sensitization Strengthens the Monosynaptic Connection of Gill Withdrawal

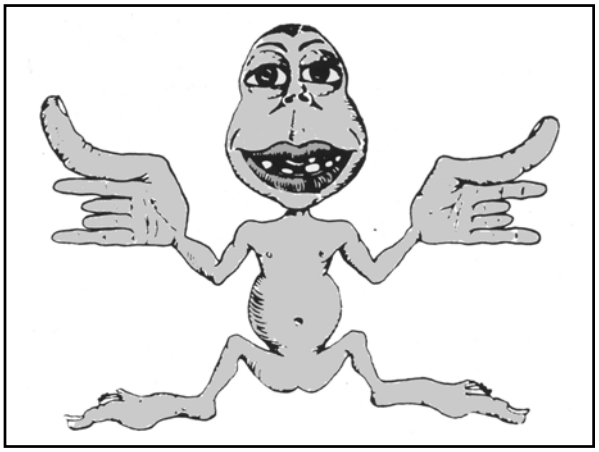


Long-Term Memory Requires a CREB1-Mediated Transcriptional Cascade

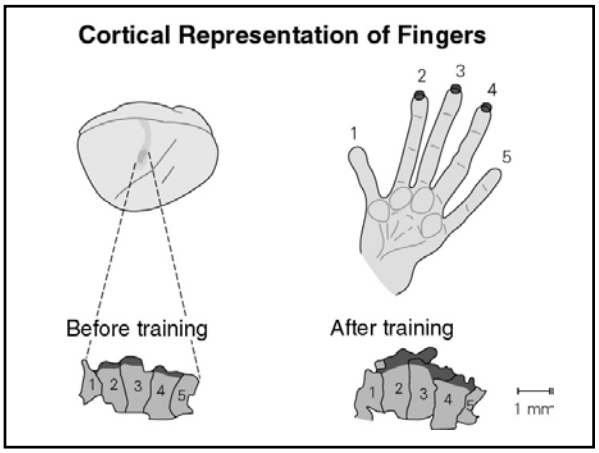


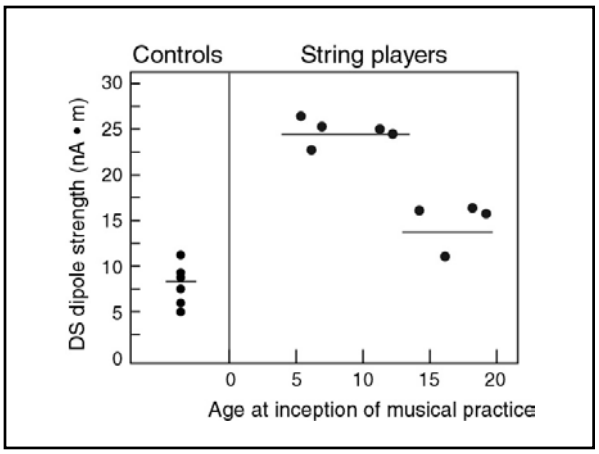


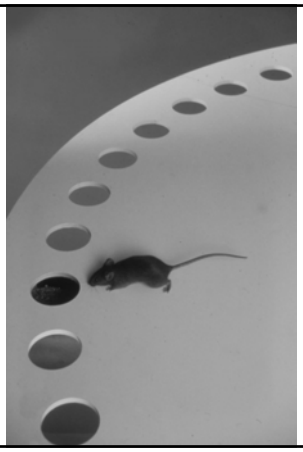




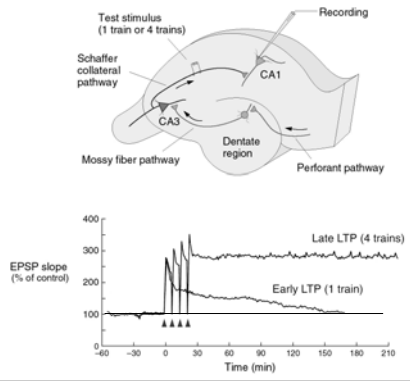
Cortical Representation of Fingers



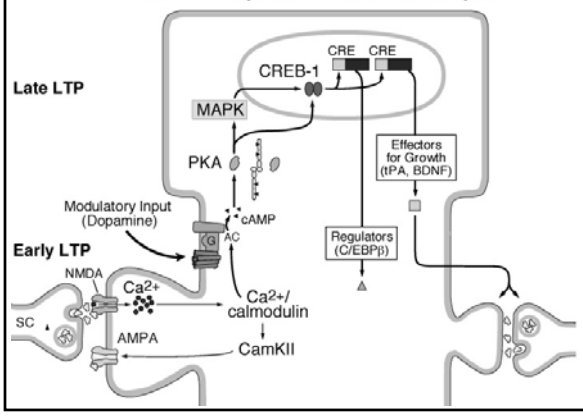




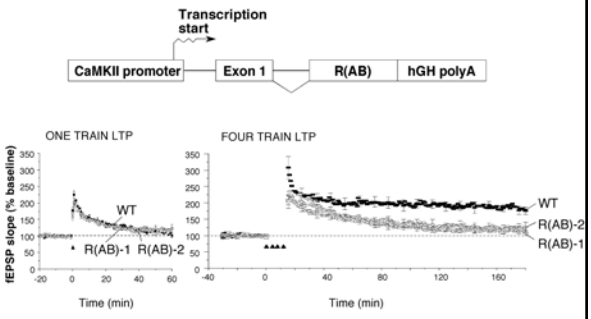
Long-Term Potentiation Has Both an Early and a Late Phase



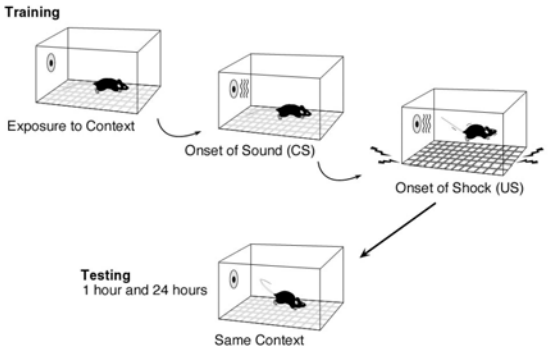
Late LTP Requires PKA and Transcription



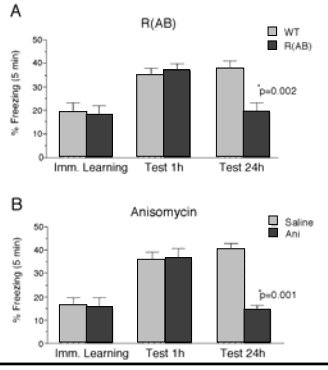
Expression of R(AB) Transgenic Construct Leads to a Defect in Late LTP



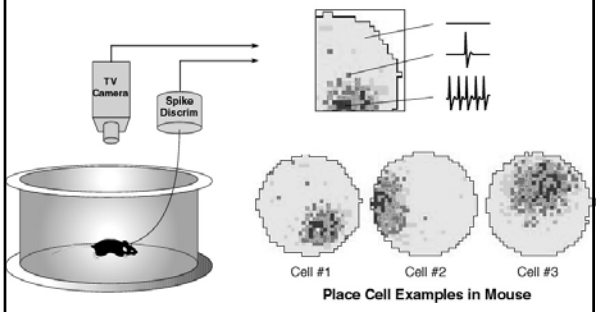
Contextual Conditioning



Context Conditioning is Selectively Impaired in R(AB) Mice

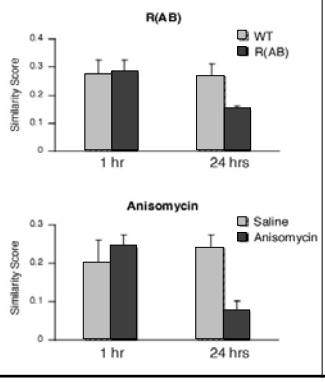


Relating Molecular Signaling to the Cognitive Map for Space: The Hippocampal Pyramidal Cells Recruited In LTP Encode Space

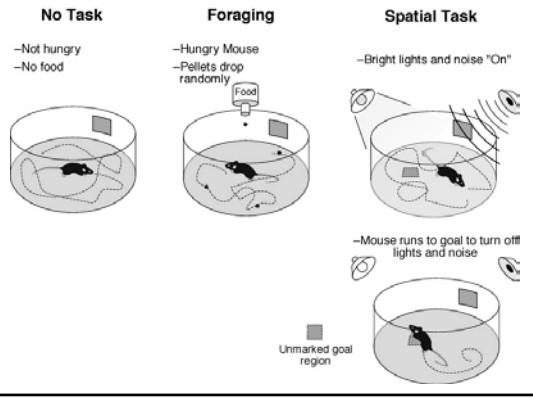


Place Cell Examples in Mouse

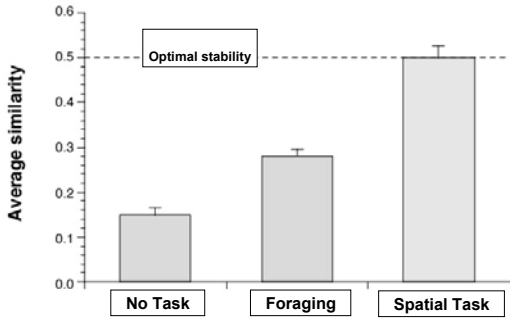
Place Cell Map Stability is Dependent Upon PKA and Protein Synthesis



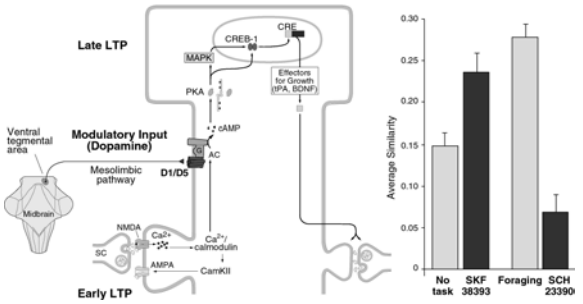
Three Degrees of Attention



Place Field Stability is Dependent on Attention



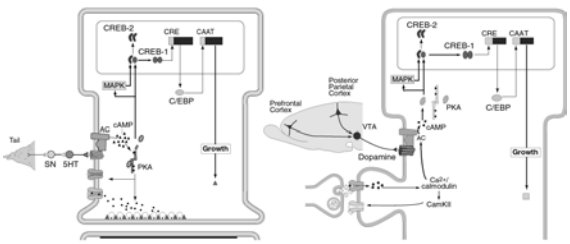
Dopamine as a Candidate Mediator of Attention

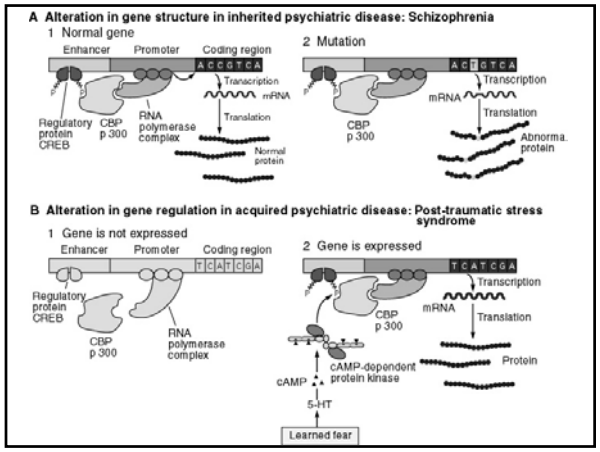


Both Explicit and Implicit Memory Storage Use Modulatory Transmitters and a CREB-MediatedTranscriptional Switch for Converting Short-Term to Long-Term Memory

Aplysia
(bottom up modulation)

Hippocampus
(top down modulation)





Three Methods of Regulating Synaptic Strength

Period	Effect on Synapse	Mechanism
1. Development	Initial Synapse Formation	Molecular Cues
2. Critical Period	Synaptic Fine Tuning	Activity
3. Adult Learning	Synaptic Modulation	Learning