

# Aplysia – learning and memory



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Synaptic Plasticity Activity dependent changes in synaptic transmission that can alter the normal circuitry and thus behavioral response

What did Santiago Ramon y Cajal think? Mechanisms underlying learning does not require formation of new neurons, but strengthening connections between existing neurons

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Hebbian Plasticity + what else did Hebb contribute? Neurons that fire together wire together

-Proposed synaptic plasticity as a theoretical mechanism for learning and memory

Synaptic Plasticity leads to change in \_\_\_\_\_ at what two locations?

Circuit Function

Both Pre-and Post synaptic locations

Short-term synaptic plasticity (Time course and how it occurs)-Seconds to minutes

1. Post-translational modification of existing proteins

Long-Term Synaptic Plasticity (Time course and how it occurs)-Hours/Days/Years

1. Changes in Gene expression

2. Protein Synthesis

3. Growth of new synapses

Functional Roles of Synaptic Plasticity

1. Development

2. Learning

3. Memory

4. Motor Control

Molecular Mechanisms of Synaptic Plasticity (6)

1. NMDA Receptor Activation

2. Protein Kinase Activation

3. Phosphatase Activation

4. AMPA Receptor Insertion

5. Gene expression and protein synthesis

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6. Growth/Loss of synapses One major advantage of using Aplysia Huge neurons - over 100 microns in diameter

You can stick an electrode in with your hand Simple Learning Examples

1. Habituation

2. Sensitization

3. Classical Conditioning 2 Neural Mechanisms for Learning and who advocated for them Presynaptic - Kandelians

Postsynaptic - Glanzman What kind of approach was taken with aplysia?

Reductionist!

This is a simpler system with a simpler NS How many neurons are in Aplysia brain? Compared to Human?  $2 \times 10^4$

Human has  $10^{12}$  Describe the Gill Withdrawal Reflex Tactile or electrical stimulation of the siphon or mantle elicits withdrawal of the gill & siphon into the mantle cavity Non-Associative Learning Reflective mechanism - not associating a stimulus with anything

Poke in the eye is going to cause you to reflexively avoid that in the future

Example of non-associative learning Habituation - a meaningless stimulus might startle someone the first time (clap) but get less reaction later What does habituation need? A consistent interval within a short period of time Habituation Reduction of a response with repeated presentation of a stimulus Habituated Gill Withdrawal - what else could be due to? Muscle Fatigue

Change in motor neuron response How do we know that habituated gill withdrawal is not due to those things? A touch on the head (not siphon) produces a full response after habituation has occurred Kandel's Proposed

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mechanism of habituation  
Reduction of synaptic release of NT at some point in the neural network  
How do you experiment on habituation with the gill withdrawal reflex? Keep NS intact, cut away most of body, leave the siphon skin & tail still connected together and to the system

-Map the synaptic connectivity  
What is the system between the siphon skin and the gill? Sensory neuron to interneuron

Interneuron to motor neuron to gill

\*\*Sensory neuron also goes straight to motor neuron  
What is the system between the tail skin and the gill? Sensory neuron to modulatory interneuron

Modulatory neuron to interneuron

Interneuron to motor neuron to gill

\*\*Modulatory interneuron also goes straight to motor neuron  
What was occurring during habituation? Presynaptic Phenomenon

-Depression of NT release between the siphon afferent and the motor neuron

\*\*NOT synaptic fatigue, bc that behavior comes back when you re sensitize the animal

Habituation Experiment - What did the depression do? How long did it last?

Lasts for Minutes

-Presynaptic

-Reduction in strength of excitatory synapses between sensory neuron and motor neuron

-Decrease in number of synaptic vesicles available for

release  
Sensitization  
Generalization of an aversive response elicited by a noxious stimulus to another non-noxious stimuli  
Short Term Sensitization -

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What form of facilitation is this? Presynaptic

-Recruitment of additional synaptic elements that modulate synaptic transmission at sensory neuron-motor neuron synapse

-Enhancement of NT release onto motor neurons  
Sensitization - What is responsible for short and long term? Short - Presynaptic

Long - Becomes both pre and post synaptic  
What does the sensory neuron release on the motor neuron? Glutamate  
How does sensitization happen?

What NT is responsible? Serotonin is released presynaptically & acts through adenylyl cyclase to ultimately close K<sup>+</sup> channels  
How serotonin acts in sensitization (Short Term!)

1. Serotonin binds to receptor on sensory neuron

2. Activates adenylyl cyclase

3. ATP to cAMP

4. cAMP activates PKA

5. PKA closes K<sup>+</sup> channels

6. Depolarizes the cell

7. VG Ca<sup>2+</sup> channels open

8. Ca<sup>2+</sup> comes in

9. Increase in vesicle release

10. Increases response of a motor neuron to the same stimulus  
Describe Long Term Sensitization steps  
1. Same steps with serotonin & eventual PKA activity

2. Sustained PKA activity - gets translocated to the nucleus

3. Ultimately binds to TF in nucleus

4. Activates transcription of genes

5. Some of those are enzymes that keep PKA in activate state

6. Leading to an increase in Ca<sup>2+</sup> concentration & bigger post synaptic

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response What other long term change occurs in sensitization? Structural!

Number of synapse is increasing as well as the efficacy of those

synapses Classical Conditioning Change in responsiveness to one stimulus

(CS) based on association with another stimulus (US) Describe Classical

Conditioning in Aplysia US - Shock

CS - Lightly touching the siphon

Eventually, touching the siphon will lead to a strong withdrawal reflex

Proposed mechanism for classical conditioning Enhanced presynaptic

facilitation

-Ca<sup>2+</sup> channels open bc CS already fired the sensory neuron

-Serotonin effect is enhanced bc Ca<sup>2+</sup> binds to calmodulin - binds to

adenylyl cyclase, etc Which two types of learning depend on presynaptic

facilitation? Classical Conditioning

Sensitization Role of NMDA receptors in classical conditioning in

Aplysia Coincidence Detectors on the motor neuron 3 steps of post synaptic

depolarization 1) LTP

2) Upregulation of AMPA receptor function

3) Stimulation of retrograde signal 2 Parts of Presynaptic Activation 1) Late

Phase presynaptic facilitation

2) Late-Phase hyperexcitability