ACB 4451A

*Integrative Neuroscience*

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Synaptic Plasticity & Learning

Learning enables an individuum to adapt its behaviour according to changing environments.

declarative (explicit)

facts ↔ events

Non-declarative (implicit)

procedural

imprinting

associative

non-associative

classical and operant conditioning,

habituation, sensitization,

...

Where do we learn?

How do we learn?
Different Concepts

Proteins/Macromolecules
(900,000 different proteins)

„Grandmotherneuron“
(up to 100 billion neurons, 1,000 billion glia cells)

Synaptic plasticity
(1 million kilometres nerve fibres, 1 million billion synapses)
Synaptic Plasticity and Learning

Donald Olding Hebb (1904-1985)
Synaptic Plasticity in Development and Disease
LONG-LASTING POTENTIATION
OF SYNAPTIC TRANSMISSION IN THE DENTATE AREA
OF THE ANAESTHETIZED RABBIT FOLLOWING
STIMULATION OF THE PERFORANT PATH

BY T. V. P. BLISS AND T. LØMO

From the National Institute for Medical Research, Mill Hill,
London NW7 1AA and the Institute of Neurophysiology,
University of Oslo, Norway

(Received 12 February 1973)

SUMMARY
Long-term Potentiation (LTP)
The Experiment

(b) Control

Pyr - Recording EPSP

Tetanus

No recording

Post-tetanus (30°)

Recorded EPSP

Control EPSP

Stim

Tetanus

Stim

Post-tetanic EPSP

LTP
LTP is Synapse Specific

(a) Whole-cell patch clamp recording

Control EPSP

S1

S2

60' after tetanus on S1

LTP

EPSP1

EPSP2

Tetanus on S1

Field EPSP slope (mV / ms)

LTP

EPSP1

EPSP2

no LTP

Time (min)

2 4 6

0 30 60
LTP is (not always) NMDAR Dependent
LTP is Calcium Dependent

(a) \( \text{CO}_2^-\cdot\text{CO}_2^- \) \( \text{CO}_2^-\cdot\text{CO}_2^- \) \( \text{CO}_2^-\cdot\text{CO}_2^- \) \( \text{CO}_2^-\cdot\text{CO}_2^- \) 

\( \text{N} \) \( \text{N} \) \( \text{N} \) \( \text{N} \) 

C=O C=O 

HC=N\text{\textsubscript{2}} HC=N\text{\textsubscript{2}} 

K\text{\textsubscript{d}} = 89 \mu\text{M} 

(b) 2.5 - 4 s flash delay

Time (min)

(b) 2.5 - 4 s flash delay

Time (min)

(c) \( \text{CH}_2\)\text{\textsuperscript{+H\textsuperscript{+}}} \) \( \text{CH}_2\)\text{\textsuperscript{+H\textsuperscript{+}}} 

K\text{\textsubscript{d}} = 0.55 \mu\text{M} 

1 s flash delay

EPSP slope (%)

Time (min)

EPSP slope (%)

Time (min)
LTP at CA1 Pyramidal Neurons

(a) An axon terminal of Schaffer collaterals

Before tetanus

- A post-synaptic spine of a CA1 pyramidal cell
- Non NMDA receptors
- NMDA receptors (blocked)
- Metabotropic receptors
- Voltage-dependent Ca^{2+} channels (closed)

Single shock

K^+ → Na^+

Glu

Ca^{2+}

Glutamine
During tetanus

Tetanus

Glu

Glu

Glu

Ca^{2+}

Glu

K^{+}

Na^{+}

Ca^{2+} - dependent processes

Na^{2+}, Ca^{2+} → [Ca^{2+}]_i

Ca^{2+}

Glutamine
Associative LTP

Pairing protocol – depolarization of pre- and postsynaptic cell at the same time

control

potentiated

2 mV

50 ms

100 ms

20 mV
Mechanisms of LTP and LTD

- Mg$^{2+}$
- NMDA
- AMPA
- VGCC
- Ca$^{2+}$
- Ca$^{2+}$ stores
- IP$_3$
- PLC$ightarrow$ DAG$ightarrow$ Protein kinases
- Phosphatases
- LTP
- LTD
Different phases of LTP

Early phase LTP
Fast, biochemical processes
  Activation of metabotropic processes
  Phosphorylation of receptors
  Recruitment of additional receptors from extrasynaptic sites
  Enhancement of transmitter release probability (retrograde messenger)

Late Phase LTP
Irreversible changes
  \emph{De novo} protein synthesis
  Structural changes at the synapse
  Morphological changes
LTP – Learning???
Invertebrate Models

Problem: behaving animal – little access to single cell level brain preparation – no behaviour, no learning

solution: low evolved animals with simple neuronal structures and simple behaviour

- Aplysia: gill withdrawal reflex - Habituation, facilitation (dishabituation), sensitization, conditioning
- Hermisenda: Phototaxis – conditioning
- Drosophila: genetic approach
- C. elegans: genetic approach, ablation of neurons
Vertebrate Models

Problem: complex Learning, complex brains

- Imprinting in chicken: Macromolecules in thelencephalon
- Song learning in birds: immediate early genes in the forebrain
- Lesion studies/ neuropharmacology studies in rats and mice: role of the hippocampus, prefrontal cortex, amygdala and cerebellum
- Imaging studies

- LTP and LTD (hippocampus, amygdala, cortex)
- Short-term plasticity
  - Odor memory in mice (Bruce effect)
  - Fear conditioning in rats and mice
  - Habituation of the acoustic startle response in rats
  - Eyeblink conditioning in rodents
  - (..?)
Eric Kandel  
(Nobel prize for physiology, 2000)
The Acoustic Startle Response

- easy to elicit
- quantifiable
- short pathway
- can be modulated by learning

Habituation is an intrinsic modulation

Nucleus cochlearis/ Cochlear root
Nucleus reticularis Pontis caudalis
In Vitro Electrophysiology

Interaural -1.04, Bregma -10.04
I am learning all the time. The tombstone will be my diploma. ~Eartha Kitt