

Long-Term Potentiation

Definition: "Long-term potentiation (LTP) occurs on any occasion when a presynaptic cell fires (once or more) at a time when the postsynaptic membrane is strongly depolarized (either through recent repetitive firing of the same presynaptic cell or by other means)."^[1]

NMDA Channels

Most of the depolarizing current for excitatory PSP (Post-synaptic potential) is carried in the ordinary way by ligand-gated ion channels that bind glutamate. During LTP development, a second distinct subclass of channel-linked glutamate receptors - NMDA receptors (named so because they are selectively activated by the artificial glutamate analog N-methyl-D-aspartate). The NMDA-receptor channels are doubly-gated, opening only when two conditions are satisfied simultaneously:

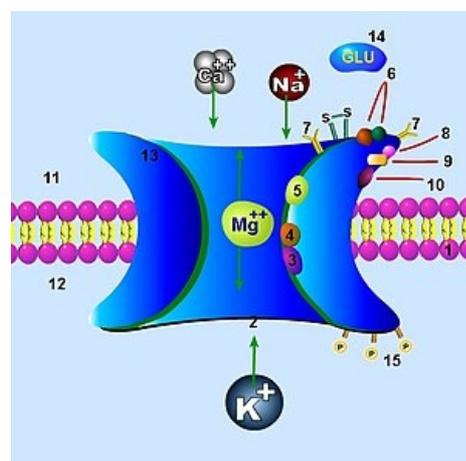
1. The membrane must be strongly depolarized (the channels are subjected to a peculiar form of voltage gating that depends on extracellular Mg^{2+})
2. The neurotransmitter glutamate must be bound to the receptor (on the contrary, when NMDA-receptors are blocked with a specific inhibitor, LTP does not occur, even though ordinary synaptic transmission continues)

An animal treated with an NMDA inhibitor fails to learn/remember information of the type thought to depend on the hippocampus (declarative/reflexive type), but behaves almost normally otherwise.

NMDA channels, when opened, are highly permeable to Ca^{2+} , which acts as an intracellular messenger, triggering the local changes responsible for long-term potentiation. On the contrary, LTP is prevented when Ca^{2+} levels are held artificially low in the postsynaptic cell (by injecting EDTA into it) and can be induced by transiently raising extracellular Ca^{2+} levels artificially high. The nature of the long-term changes triggered by Ca^{2+} is uncertain, but they are thought to involve structural alterations in the synapse.

The entry of calcium (after successful activation of NMDA-receptor channel) triggers number of events:

1. Protease activation → results in cytoskeletal (morphological) changes, such as change in the shape of dendritic spines.
2. Lipase activation → breakdown of fats → arachidonic acid formation → arachidonic acid exits the postsynaptic cell and bind on the presynaptic membrane → promoting even more glutamate release → thus behaving as a retrograde messenger.
3. Production of second messengers:
 1. IP3 (inositol triphosphate):
 1. Stimulates release of calcium from intra-synaptosomal stores →
 2. Ca^{2+} -calmodulin complex activates the Ca^{2+} -calmodulin-dependent kinase → cAMP production → cAMP activates cAMP-dependent kinases by phosphorylating them → the activated kinases phosphorylate and activate transcription factors.
 2. Diacylglycerol (DAG) as second messengers →
 1. Activation of Protein Kinase C →
 2. Further activation of transcription factors that enable serotonin and acetylcholine-enhanced neuronal excitation associated with memory tasks.^[2]



NMDA receptor

Memory Consolidation

For memory consolidation, this process requires certain time: 5-10 minutes for minimal consolidation, 1 hour for stronger consolidation. This can occur by the rehearsal technique (as proven by psychological studies):

- Brain has a natural tendency to rehearse newfound information
- Rehearsal causes the mind to accelerate the process of consolidation
- Progressively over time, more and more information is fixed in memory spaces.
- This explains why a person can better remember in depth information on a single subject, rather than superficial information on vast amounts of different subjects.
- This also explains why a person who is wide awake can consolidate memories better than a person who experiences mental fatigue.

Links

Related articles

- Learning and Memory

References

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2. RANG, H. P. – DALE, M.M.. *Pharmacology*. 5. edition. Edinburgh : Churchill Livingstone, 2003. ISBN 0-443-07145-4. Page 187

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