生物物理学 II　Handout No. 8

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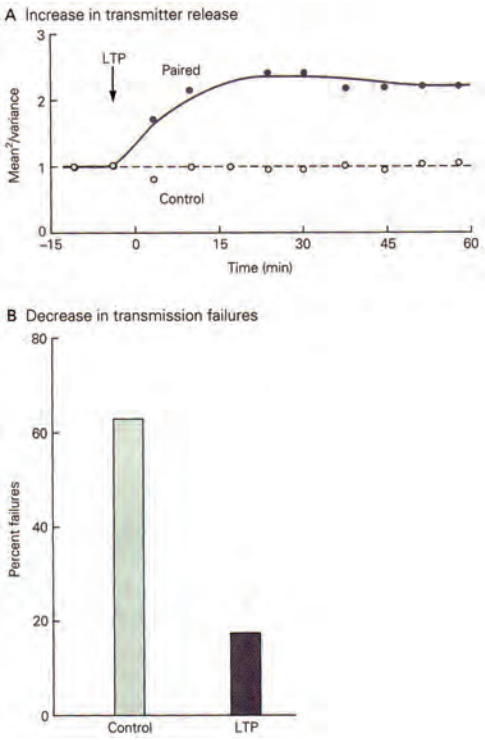

Figure63-11 Maintenance of the early phase of LTP in the CA1 region of the hippocampus depends on an increase in presynaptic transmitter release. Quantal analysis of LTP in area CA1 is based on a coefficient of variation of evoked responses. This analysis assumes that the number of quanta of transmitter released follows a binomial distribution, where the coefficient of variation (mean squared/variance) provides an index of transmitter release from the presynaptic terminal that is independent of quanta) size. (From Malinow and Tsien 1990.)
A. With LTP the ratio of mean squared to variance increases, indicating an increase in transmitter release. This increase occurs only in the pathway that is paired with depolarization of the postsynaptic cell. It does not occur in a control pathway that is not paired.
B. At normal rates of stimulation the number of failures in transmission is significant (60%). After LTP the percentage of failures decreases to 20%, another indication that LTP is presynaptic.

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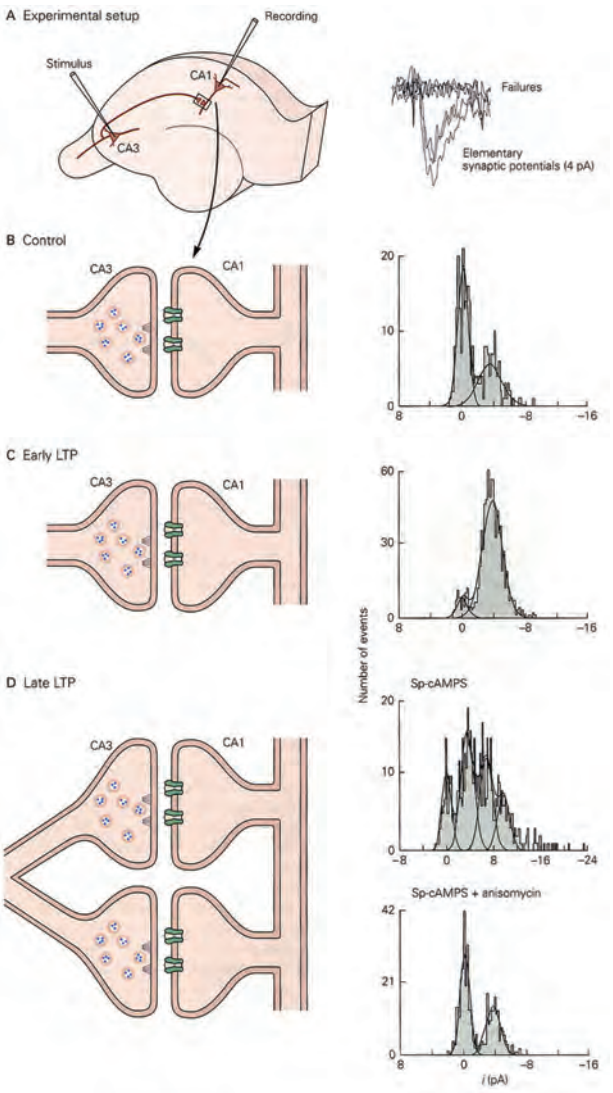

Figure 63-12 The early and late phases of LTP are evident in the synaptic trans- mission between a single CA3 cell and a single Cat cell. (From Bolshakov et al. 1997.)
A. A single CA3 cell can be stimulated selectively to produce a single elemen- tary synaptic potential in a CA1 cell. When the CA3 cell is stimulated repeat- edly at low frequency, it gives rise to either an elementary response of the size of a miniature synaptic potential or a failure.
B. In control cells there are many fail- ures; the synapse has a low probability of releasing vesicles. The distribution of the amplitudes of many responses can be approximated by two Gaussian curves, one centered on zero (the fail- ures) and the other centered on 4 pA (the successful responses). These histo- grams are consistent with the type of synapse illustrated here, in which a sin- gle CA3 cell makes a single connection on a CA1 cell. This connection has a single active zone from which it releases a single vesicle in an all-or-none manner (failures or successes).
C. With the early phase of LTP the prob- ability of release rises significantly, but the two Gaussian curves in the distri- bution of responses is consistent with the view that a single release site still releases only a vesicle but now with a high probability of release.
D. When the late phase of LTP is in- duced by a cAMP analog (Sp-cAMPS), the distribution of responses no longer fits two Gaussian curves but instead requires three or four Gaussian curves, suggesting the possibility that new pre- synaptic active zones and post-synaptic receptors have grown. These effects are blocked by anisomycin, an inhibitor of protein synthesis.

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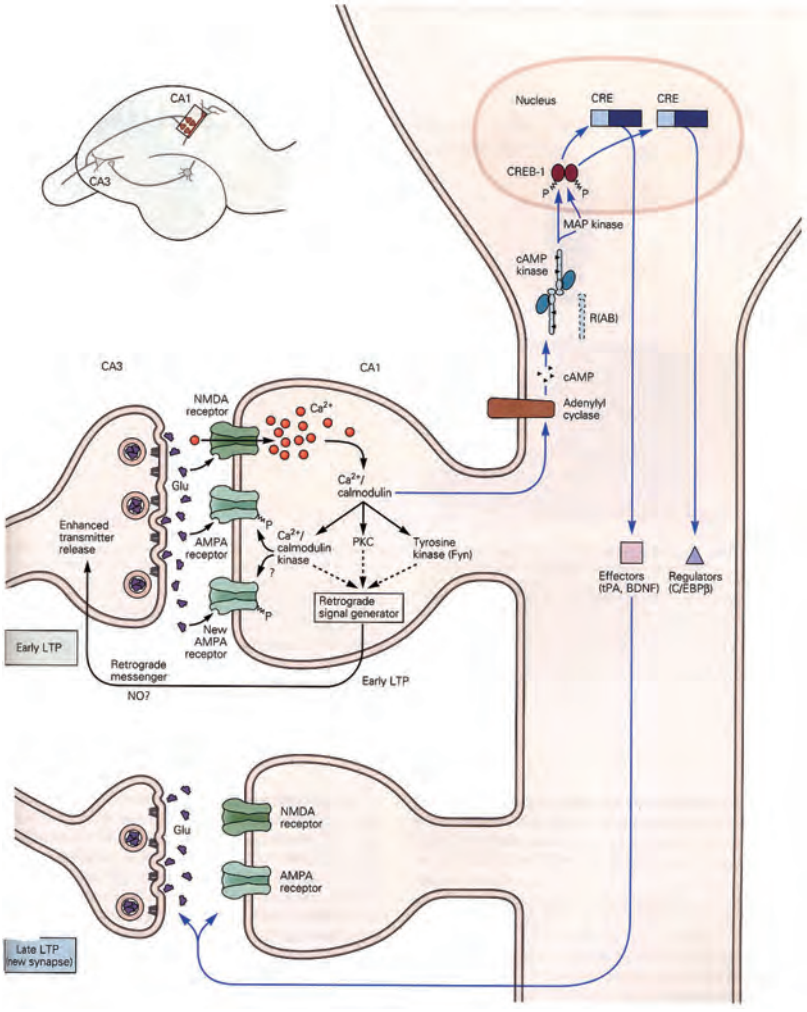

Figure 63-13 A model for the early and late phase of LTP. A single train of action potentials leads to early LTP by activating NMDA receptors, Ca^{2+} influx into the postsynaptic cell, and a set of second messengers. With repeated trains the Ca^{2+} influx also recruits an adenylyl cyclase, which activates the cAMP-dependent protein kinase (cAMP kinase) leading to its translocation to the nucleus, where it phosphorylates the CREB protein. CREB in turn activates targets that are thought to lead to structural changes. Mutations in mice that block PKA or CREB reduce or eliminate the late phase of LTP. The adenylyl cyclase can also be modulated by dopaminergic and perhaps other modulatory inputs. BDNF = brain-derived neurotrophic factor; C/EBPb = transcription factor; P = phosphate; R(AB) dominant negative PKA; tPA = tissue plasminogen activator.