The Long-Term Facilitation of Neuronal Activity Produced by Repeated Pairing of an Orthodromic Stimulus and Antidromic Stimuli in the Sliced Hippocampal Formation

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Long-term facilitation in extracellularly recorded population spikes was demonstrated by repeated paired stimulation (RPS) in CA1 neurons of the guinea pig hippocampal slices. Paired stimulation, consisting of a single orthodromic "test" stimulus and a train (5 pulses at 200 Hz) of antidromic stimuli with an interstimulus interval (ISI) of 20, 500 msec or 1 sec was repeated every 5 sec over a 250 sec period. The amplitude of the population spike in response to the test stimulus increased gradually after RPS and reached a plateau level 30-50 min after RPS. The plateau value was dependent on ISI; the shorter the ISI the greater the increase of responses. In contrast, no facilitation was observed when either the test stimulus or the antidromic stimuli were applied separately, without pairing.

Long-lasting synaptic modifications after the manipulation with various methods such as the brief tetanic stimulation of inputs (Bliss and Lomo 1973) have attracted much attention because underlying mechanisms of them could be the basis of learning and memory in the brain. In this report, a new type of stimulation paradigm has been demonstrated to produce a long-term facilitation in CA1 neurons of the hippocampal formation.

Thin hippocampal slices were prepared from guinea pig and maintained in vitro (Miyakawa et al. 1985). Extracellular recordings were obtained from the CA1 cell body layer with a glass microelectrode. An orthodromic "test" stimulus and antidromic stimuli were applied through two stimulating electrodes placed in the stratum radiatum and in the alveus, respectively.

After observing a constant amplitude of the population spike (arrow in the inset of Fig. 1A), the test stimulus was followed by a short train of 5 antidromic stimuli with a frequency of 200 Hz. This pairing was repeated 50 times once every 5 sec (RPS; shaded area in Fig. 1A). Thereafter the test stimulus alone was given successively to monitor the amplitude of the population spike.

Fig. 1A shows the mean amplitude changes of the population spike following RPS with three different interstimulus intervals (ISIs) between the test stimulus and the first stimulus.

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of antidromic stimuli.

The amplitude of the response to the test stimulus gradually increased after RPS and reached a plateau level 30-50 min after RPS with a mean plateau value of 172±3% (n = 9), 127±3% (n = 5), and 103±4% (n = 5), for ISI of 20, 500 msec, and 1 sec, respectively, with a significant difference depending on the ISI (t-test, p<0.01).

For control experiments, we adopted two stimulation paradigms (Fig. 1B): (1) a single orthodromic test stimulus applied once every 5 sec (filled circles, n=5); and (2) a train of 5 antidromic pulses alone repeated 50 times at 5 s intervals (open circles, n=5). As shown in B, no significant increases were observed in two controls.

Thus we conclude that RPS produces the long-term facilitation in the test response depending on the temporal relationship of the antidromic stimuli to the orthodromic test stimulus.

These results suggest that the temporal contiguity of pre-and postsynaptic activities of neurons may play an important role for producing the long-term facilitation.

References
