LONG-LASTING POTENTIATION
OF SYNAPTIC TRANSMISSION IN THE DENTATE AREA

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for long-lasting potentiation: (a) an increase in the efficiency of synaptic

transmission at the perforant path synapses; (b) an increase in the excitability of the granule cell population.

INTRODUCTION

These experiments arose from an observation made during a study of the phenomenon of frequency potentiation in the dentate area of the hippo-campal formation (Lømo, 1966). It was noticed that the response evoked

synaptic contacts of the *en passage* type with dendritic spines (Blackstad, 1958), each

fibre making contact with many granule cells. The synapses are restricted to the middle third of the molecular layer, and account for nearly 40 % of the total synaptic population in that region (Nafstad, 1967); the origin of the remainder is not known.
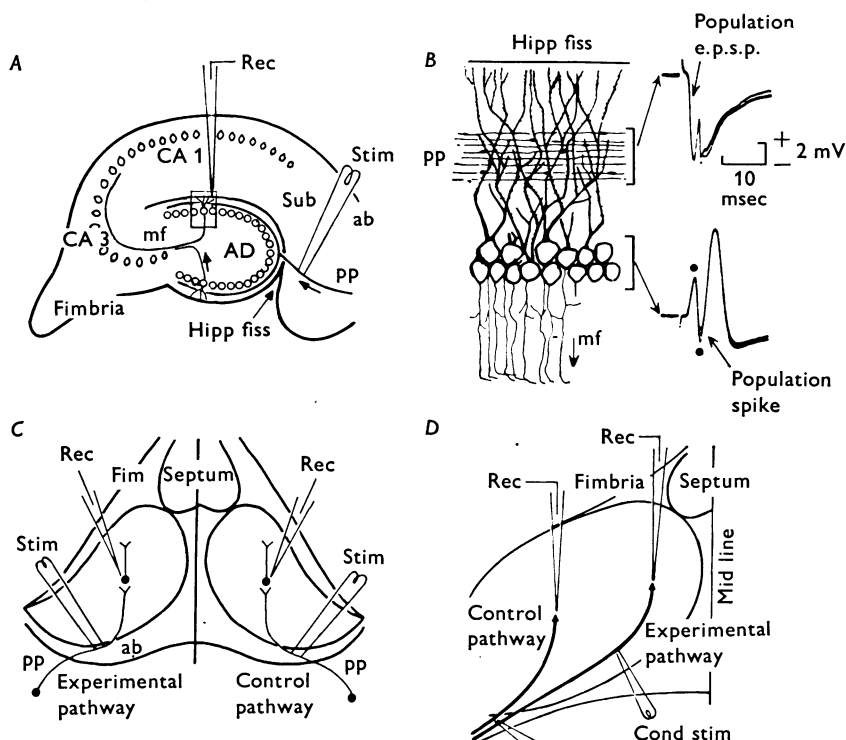

Fig. 1. *A*, diagrammatic parasagittal section through the hippocampal

formation, showing a stimulating electrode placed beneath the angular bundle (ab) to activate perforant path fibres (pp), and a recording micro-

Population potentials

Fig. 1 *B* shows the population potentials recorded at two levels in the dentate area.

course of an experiment frequent checks were made to ensure that the responses

if they were not. Adjustments of this sort were more frequently necessary when

conditioning train.

    3. A phase of spike depression lasting from a few seconds to more than a minute.

    4. A phase of potentiation, sometimes lasting for several hours, and in many cases involving synaptic as well as spike components of the response.

of the traces caused by the continuously moving film, and these values are

and 45 min after the train have been superimposed in Fig. 3*E*. The

layer where the active current sink is located, but was equally pronounced in the region of the passive source in the cell body layer. No similar potentiation occurred in the control pathway, where the slope of the early part
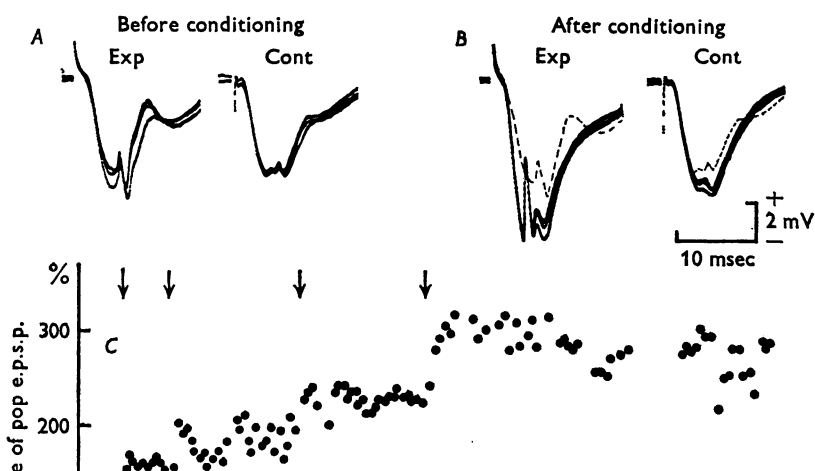
of the population e.p.s.p. was the same after conditioning as it was before.

In this experiment there was a decrease in the size of the late components

of the response in both experimental and control pathways: a change

seen in several experiments (Fig. 4*B*).

A   Before conditioning   B   After conditioning

Exp   Cont   Exp   Cont

2 mV

10 msec

%   ↓   ↓   ↓   ↓

300   C

of pop e.p.s.p.

200

twenty-four out of the thirty-five conditioned pathways showed long-lasting

potentiation. Potentiation of all three parameters was observed in nine of

Fig. 5*A*, far right, the potentiated response obtained after 6 hr may be

compared with that obtained before conditioning (stippled trace). Again

(as in Figs. 3, 7 and 11), potentiation of the population e.p.s.p. can be seen

not only in the synaptic layer (Fig. 4*A* and *B*) but also in the cell body

layer, as an increase in the slope of the initial positive wave. In *B* the

in spite of the increase in the population e.p.s.p. (Fig. 4C). It was not until

after the fourth train that the spike became clearly larger than it had been before conditioning.

The latency of the spike also varied, as can be seen both from the superimposed records of Fig. 5A and from the plot of individual latency measurements in Fig. 5C. Two separate phenomena underlie the latency changes

latency which occurred after each conditioning train: the other is the

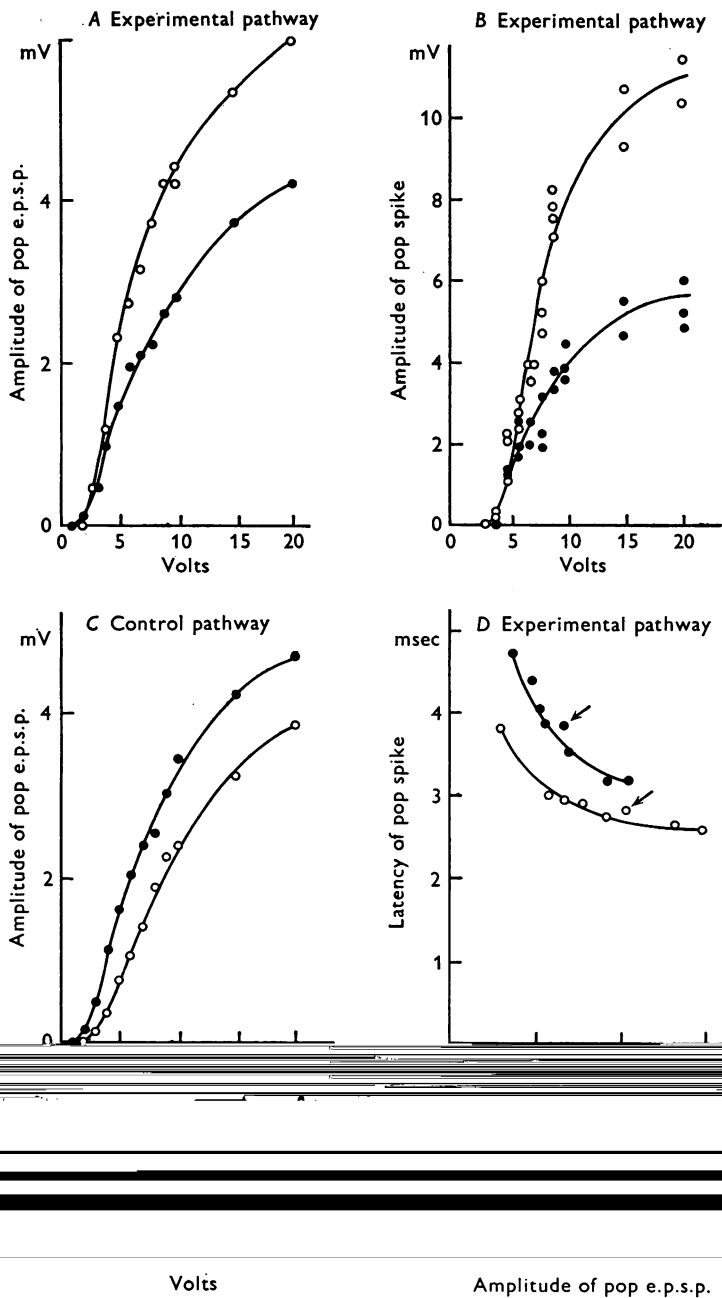tendency of the spike to jump, from one stimulus to the next, between an

Fig. 6. Effect of conditioning on stimulus–response curves. Same experiment as in Figs. 4 and 5. The two sets of points in *A* give the values of the population e.p.s.p. for the experimental pathway, as a function of stimulus strength before conditioning (filled circles), and almost 10 hr later (open circles) which was 3 hr after the last of six conditioning trains. Similar

In the majority of cases for which we have adequate data, the potentia-

potentiation of the e.p.s.p. In Fig. 6D the data from A and B have been

replotted to show the latency of the population spike as a function of the

e.p.s.p. amplitude, before and after conditioning. The two arrows point to

values obtained at the normal test strength of 9V. Before conditioning, an

e.p.s.p. of 2·7 mV was associated with a spike latency of 3·9 msec, while

after conditioning the same e.p.s.p. (obtained with a weaker stimulus)

mean, the variability fell from 0·35 to 0·09. In the control pathway (D),

the changes were restricted to a general reduction of both e.p.s.p. and

spike amplitudes, with the disappearance after conditioning of the un-

seen in the superimposed averaged records shown in *B*. Conditioning had

no obvious effect on the population e.p.s.p. (*B* and *E*) or the population

spike (*B* and *F*), on either side. It is worth noting that a later experiment
on a more lateral and previously unstimulated segment of the dentate area
in the same animal produced potentiation of all three parameters (Fig. 2).
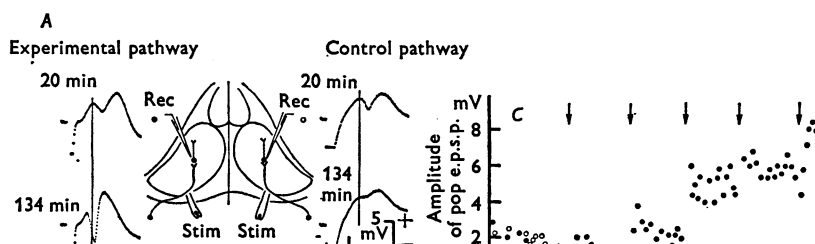
The result of one of these experiments is shown in Fig. 11. The increase in
slope and in the peak amplitude of the population e.p.s.p. after conditioning

is apparent in the superimposed records in *A*, obtained from the synaptic

trains indicated in *B*. As in other experiments the e.p.s.p. potentiation

was present both in the cell body and synaptic layers. The time course

Duration of the after-effect

The longest after-effects we observed are illustrated in Fig. 12. The complete time course of the increase in amplitude of the population spike, for the experiment on Figs. 4–6, is shown in Fig. 12A. By the sixth

induced. Thereafter, the spike remained undiminished until its sudden

further increases. Six to eight hr after the last train the amplitude began to

amplitude of the extracellular potential, V_e, is related to the evoked membrane depolarization, ΔV_m, by the expression

$$V_e = -\frac{r_e}{r_i + r_e} \Delta V_m + K, \qquad (1)$$

where r_i and r_e are the resistances per unit length of the internal and external media respectively. K is a term containing constants of integration

excitability of the population, and this could be controlled either by intrinsic factors, such as those which determine threshold, or by the extrinsic modulation of tonic excitatory and inhibitory afferent activity.

Again, either mechanism might be available for long term modification. We now examine our results in the light of these various possibilities.

Evidence against an increase in the size of the perforant path volley

We were not able to detect a presynaptic compound action potential, and thus to obtain a direct measure of the size of the presynaptic volley. It is, however, unlikely that the number of perforant path fibres excited by the test volley increased significantly after conditioning, since there was

no reduction in the threshold for evoking an e.p.s.p. after conditioning, and

since the potentiated response could not be mimicked by increasing the size of the afferent volley with stronger shocks before conditioning. It seems

spike was usually narrower at its base, suggesting that the increase in

discharge, resulting, presumably, from a more rapid approach to threshold

Variability of the effect

A conspicuous feature of these experiments was the great variation in

The interest of these results derives both from the prolonged duration

of the effect, and from the fact that an identifiable cortical pathway is

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