EARLY POSTNATAL DEVELOPMENT OF THE RECURRENT INHIBITION SYSTEM OF HIPPOCAMPAL AREA CAI

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Although the hippocampus has been the target for much electrophysiological research, data on the functional development of this structure are very limited [1, 2, 4-7]. There have been virtually no electrophysiological studies of development of hippocampal inhibition in the early stages of postnatal development (PND). According to data obtained on cats [6], during intracellular recording of hippocampal pyramidal neurons, in the early stages of PND the principal form of neuronal response to all stimulated inputs is the IPSP. Meanwhile, experiments on hippocampal slices from rabbits and rats [4] indicate that maturation of the hippocampal recurrent inhibition system takes place later than development of excitatory connections. Electron-microscopic studies of synaptogenesis in area CAI of the rabbit hippocampus have now been undertaken, and, in particular, it has been shown that synapses of symmetrical type do not begin to appear on the bodies of pyramidal neurons in area CAI before the second week of life [8].

Consideration of all these facts suggests that the recurrent inhibition system of hippocampal area CAI is formed to a large extent postnatally.

The aim of this investigation was to determine the time of development of the recurrent inhibition system in area CAI of the mouse hippocampus in the postnatal period.

EXPERIMENTAL METHOD

Experiments were carried out on hippocampal slices from mice of different ages (from 4 days to 1 month). A salt solution of the following composition was used (in mM): NaCl 124, KCl 4.5, $NaHCO_3$ 26, $CaCl_2$ 2, $MgSO_4$ 2, NaH_2PO_4 1.25, and glucose 10. The slices were incubated at 30-32°C. Field potentials were recorded in area CAI in response to stimulation of Schaffer's collaterals. To determine the degree of maturity of the recurrent inhibition system, the following technique was used. Conditioning stimulation (the region through which pass axons of pyramidal cells in area CAI) induces activation of inhibitory interneurons, producing recurrent inhibition on pyramidal cells. The magnitude of the inhibition thus developing was judged by inhibition of the orthodromic population spike to testing stimlation of Schaffer's collaterals. The strength of testing stimulation was chosen so that the amplitude of the population spike was one-third of the maximal value. The strength of conditioning stimulation of the alveus varied from 0 to 80V with a step of 10V. The interval between conditioning stimulation of the alveus and testing stimulation was 15-20 msec. Graphs of amplitude of the orthodromic population spike as a function of strength of conditioning stimulation of the alveus were plotted. Altogether 9 litters (20 animals) were studied.

EXPERIMENTAL RESULTS

Field potentials (FP) recorded in the animals before the 9th-10th days of PND had a number of features distinguishing them from FP of more adult animals. For instance, the population spike of FP of the young animals was lower in amplitude, longer in duration, and had a longer latent period. Another marked difference was the absence of the late positive wave of FP, following the population spike (Fig. 1). Considering the coincidence between the time of this component and of the appearance of IPSP in the pyramidal neurons, it can be tentatively suggested that the late positive wave reflects, at least partially, inhibitory processes arising in the pyramidal cells, and that its low amplitude in the early stages of

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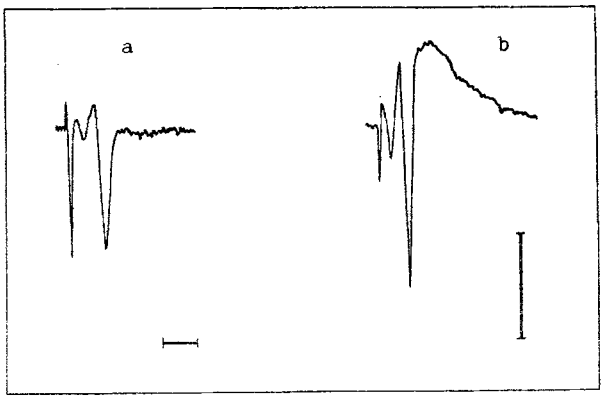

Fig. 1. Example of orthodromic FP to stimulation of Schaffer's collaterals in hippocampal area CAI for animals aged 8 (a) and 14 (b) days. a) Stimulus duration 200 μsec, 60V; b) 100 μsec, 30V. Calibration: 5 cm, 1 mV.

PND may be due to immaturity of inhibition.

Unlike the orthodromic type, antidromic population spikes recorded in young (4-6 days) and adult (1 month) animals to conditioning stimulation of the alveus (CSA), possessed similar parameters (latent period 3-5 msec, duration 2-3 msec), but the maximal amplitude of this potential was much lower in young than in older animals. Starting with the 7th-8th day of PND the amplitude of these population spikes rose and was commensurate with the population spikes of more adult animals.

Starting with the 15th day of PND, CSA of average strength caused inhibition of the orthodromic population spike by 40-80%. Separate examples of testing stimulation (TS, top row) and of TS with CSA (bottom row) for animals aged 7, 9, and 12 days of PND, are given in Fig. 2a-c. Clearly CSA of average strength (40-60V) caused marked inhibition of the population spike to TS in an animal aged 9 days (Fig. 2b), whereas the analogous inhibition in the animal aged 7 days was virtually absent, despite the well marked antidromic population spike. Incidentally, in the group of animals from the 9th to the 11th day of PND, with an increase in the animal's age inhibition increased, and this was accompanied by a simultaneous lowering of activation thresholds of the inhibitory system (Fig. 2c, 12 days). The graph in Fig. 3 shows average values for dependence of the amplitude of the orthodromic population spike on the strength of CSA for animals of two age groups: 1) 6-8 days, and 2) 9-11 days. Clearly in the animals aged 9-11 days, with an increase in the strength of CSA there was a significant decrease in amplitude of the population spike to stimulation of Schaffer's collaterals, whereas the corresponding inhibition in animals aged 6-8 days was insignificant. It was also observed that the activation threshold of the recurrent inhibition system was significantly lower in the more adult animals than in the young animals (first points on the graph, CSA 10V).

There is evidence in the literature that differentiated hippocampal inhibitory interneurons may be observed as early as at birth [8] and that activation of both direct and recurrent inhibition can take place through the same type of interneurons [3]. In the light of these data, the absence of inhibition of the orthodromic population spike to TS, in the presence of a well marked antidromic population spike, in animals aged 6-8 days may be connected with the fact that there are no axon collaterals of pyramidal neurons at these times, and that the late development of the recurrent inhibition system (efficacy, activation threshold) may take place on account of this link.

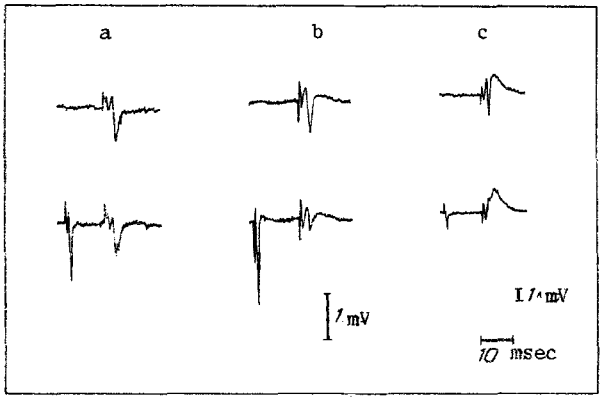

Fig. 2

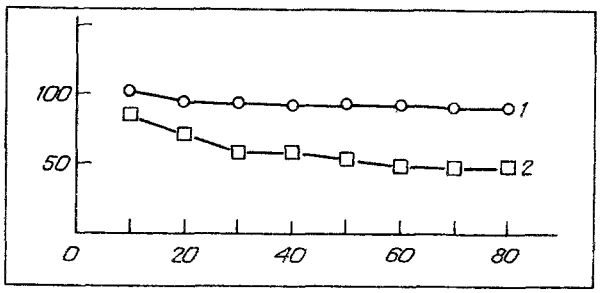

Fig. 3

Fig. 2. Example of inhibition of orthodromic population spike in response to stimulation of Schaffer's collaterals during CSA for animals aged 7 (a), 9 (b), and 12 (c) days of PND. Amplitude of population spike in control was one-third of maximal value. Strength of CSA 40V (a), 50V (b), 30V (c). Calibration: 1 mV, 10 msec.

Fig. 3. Amplitude of inhibition of orthodromic population spike as a function of strength of CSA for two age groups. 1) Group of animals aged 6-8 days of PND; 2) 9-11 days of PND. Abscissa, strength of CSA (in V); ordinate, inhibition of orthodromic population spike to TS of Schaffer's collaterals (CS) (in per cent of control response). Population spike of control response to TS of SC was one-third of maximal amplitude. Error of mean lies within limits of magnitude of the sign.

It was thus shown that recurrent inhibition of hippocampal area CAI is formed entirely postnatally and that the critical period for its development is the middle of the second week of life. During this period of PND there is a significant increase in the level of inhibition, accompanied by a general lowering of activation thresholds. The development of the late positive wave of the orthodromic FP coincides in the times of its formation with the formation of recurrent inhibition, indicating a possible role of the IPSP induced by it in the genesis of global activity.

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