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LONG-LASTING POST-TETANIC POTENTIATION IN HIPPOCAMPAL NEURONS IN TISSUE CULTRUE

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KEY WORDS: long-lasting post-tetanic potentiation; hippocampus; nerve tissue culture.

Long-lasting post-tetanic potentiation (LLPTP) is a characteristic functional property of hippocampal neurons which reflects their plastic properties [2, 7, 10]. LLPTP is known to consist of the long preservation of the focal potential, in response to a single stimulus, enhanced by tetanization. According to some workers [2, 7], LLPTP is one of the phenomena that reflect plastic changes in the structure of synaptic connections that lie at the basis of memory. At the present time an important role in the formation of long-lasting trace processes is ascribed to the monoaminergic systems of the brain [3, 9], which are considered [2, 8] to participate also in the formation of LLPTP. It is evident that hippocampal afferent fibers (including monoaminergic) may become involved in the process of excitation of neurons during tetanization of intrahippocampal systems of interneuronal connections (Schaffer's collaterals, for example), leading to the appearance of LLPTP, for they run in the same bundle with these connections and terminate on the same neurons. During the development of LLPTP, studied on a model of short-limbed hippocampal slices [1, 10], segments of these afferents which evidently function for a certain time *in vitro* may participate in excitation of the neurons. Meanwhile explantation of slices for a longer period under tissue culture conditions inevitably leads to degeneration of the axon terminals belonging to neurons of other brain structures and divided during explantation. Consequently, the appearance of LLPTP in explants in culture may be evidence that it is an internal functional property of the hippocampus and arises without the direct participation of its afferent connections. The object of the present investigation was to study the ability of neurons to undergo LLPTP and to study it in explants of the hippocampus surviving for several days in culture.

EXPERIMENTAL METHOD

Experiments were carried out on 11 explants obtained from C57BL mice aged 9-14 days and cultured for 4-7 days by a method similar to that used to obtain and culture hippocampal explants from newborn mice [4]. The technique for the electrophysiological experiments was the same as that described by the writers previously [6]. Testing stimuli were applied in series of ten pulses with an interval of 10 sec, and the amplitude of the responses evoked by them was averaged on an NTA-1024 analyzer. Intervals between series measured 15 min. Tetanization was carried out with a frequency of 20 Hz for 7 sec.

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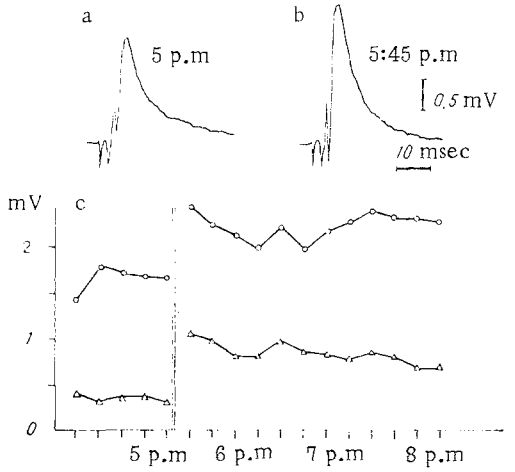

Fig. 1. Evoked responses of neurons in area CA_3 of hippocampus of 12-day old mouse in tissue culture before and after tetanic stimulation of dentate fascia (4 days *in vitro*). a) Before tetanization; b) 25 min after tetanization with a frequency of 20 Hz for 7 sec; c) dynamics of amplitude of positive wave of averaged response (circles) and population spike (triangles): on left — before tetanization (indicated by double verticle line), on right — after tetanization. Abscissa, clock time; ordinate, amplitude (in mV).

EXPERIMENTAL RESULTS

During the electrophysiological study of the explants, high-amplitude focal potentials were recorded in the pyramidal layer of area CA_3 in response to stimulation of the dentate fascia and area CA_1 and to stimulation of Schaffer's collaterals. A positive wave with an amplitude of about 2 mV, with population spikes superposed on it, can be seen in Fig. 1a. After tetanic stimulation an increase in amplitude of the focal response was observed in 8 of 11 experiments and it lasted for 0.5-4 h. In the experiment whose results are illustrated in Fig. 1 tetanization led to an increase of about 1.5 times in the amplitude of the wave, whereas the population spike was more than doubled in amplitude (b). The enhanced responses shown on the trace and graph (Fig. 1c) on application of testing stimuli after tetanization were observed in this experiment for 3 h.

The character of changes in focal responses and the time course of LLPTP in the present experiments were similar to those observed *in situ* [5, 7] and in hippocampal slices [1, 8, 10]. At the same time, it must be pointed out that LLPTP could be recorded in hippocampal explants when slices obtained from animals aged 9-14 days were used for culture. In tissue cultures from the hippocampus of newborn mice, despite the formation of organotypical functional systems of interneuronal connections in the explants during the first two weeks, stable high-amplitude focal potentials did not arise, and the ability of the neurons to give trace responses was poorly developed [6]. Differentiation of neurons in the hippocampus isolated immediately after birth of the animal takes place *in vitro* in the absence of afferent influences from other brain structures and may be due primarily to realization of their genetically determined program of development. However, a specific functional property of hippocampal neurons such as ability to undergo LLPTP is evidently formed in the course of their postnatal differentiation in situ, under conditions of the modulating influence of maturing synaptic afferent connections of the hippocampus which have not developed in newborn mice.

The ability of neurons of the intact hippocampus to undergo LLPTP, it can be tentatively suggested, is formed in the early stages of postnatal development *in situ*, and it is subsequently preserved also under tissue culture conditions, during prolonged isolation of the hippocampus from surrounding brain structures. Activation of monoaminergic fibers is thus not an obligatory condition for the appearance of LLPTP, which can be evoked in the hippocampus irrespective of external afferent influences. However, this does not rule out the possibility that monoaminergic brain systems participate in its development, for results obtained in experiments on short-lived slices, using propranolol, a β-adrenoreceptor blocker [8], testify to the possible modulating influence of noradrenergic nerve fibers on the duration of LLPTP.

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EFFECT OF HYDROCORTISONE ON FORMATION OF THE OSMOTIC CONCENTRATION FUNCTION IN ALBINO RATS

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During ontogeny physiological systems pass through special "critical" periods of development, the most characteristic features of which are nowadays considered to be the accelerated formation of the developing structure or function and increased sensitivity to controlling factors [11, 14]. During these periods realization of the genetic program may be substantially modified by various factors which exert their action through the endocrine system. A transient disturbance of the steroid hormone balance in prenatal or early postnatal ontogeny leads to changes in behavioral responses, functions of the endocrine system, and responses to hormonal and stressor influences in the adult stage [2, 4], which are evidently based on changes in the activity of certain inducible enzymes [3].

In mammals of species born unable to see, morphological and functional maturation of the kidney takes place in the postnatal period. It was accordingly decided that it would be interesting to study the potential ability of certain hormones to influence the course of ontogeny of the concentrating function of the kidney.

In the investigation described below the modifying effect of a single increase in the blood hydrocortisone level in rats was studied during the first few days after birth.

EXPERIMENTAL METHOD

Experiments were carried out on Wistar albino rats of both sexes aged from 5 to 60 days. On the 5th day after birth, during the period when intensive formation of the structures of the concentrating mechanism of the kidney begins [7], physiological saline was injected into control rats in a volume of 100 µl. The experimental rats received an intraperitoneal injection of a suspension of microcrystalline hydrocortisone (from Gedeon Richter, Hungary) in a dose of 1 µg/g body weight. From the 7th day of life until two months, with different age intervals (Table 1), rats of the various subgroups were tested for manifestation of an antidiuretic response. For this purpose, half of the animals of each age subgroup received an

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