ELECTROENCEPHALOGRAPHIC EFFECTS OF INTRACENTRAL INJECTION OF ANTIBODIES AGAINST BRAIN-SPECIFIC S-100 ANTIGEN

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UDC 612.82.017.1-087.87

The effects of intracentral injection of antibodies against brain-specific S-100 antigen (S-100 protein) were studied by an electroencephalographic method with estimation of the power of the EEG rhythms by analog computer. Intracerebral injections of antibodies against S-100 protein caused an increase in power of the principal EEG rhythms in the hippocampus, caudate nucleus, and mesencephalic reticular formation, followed by the development of epileptiform activity in these same structures.

KEY WORDS: electroencephalogram; brain-specific S-100 antigen.

Hyden and Lange [8, 9] showed in 1970 that intraventricular injection of antibodies against brain-specific S-100 antigen (S-100 protein) has a proactive, inhibitory action on the ability of rats to acquire skills during training.* This behavioral effect of injection of antibodies developed during the first 4 days, but the main results of the injection could be observed as early as on the first day. An immunofluorescence control (by the indirect Coons' method) showed that antibodies against S-100 protein were located mainly in the cytoplasm of the gliocytes and in the nuclei of pyramidal and granule cells of Ammon's horn and the fascia dentata of the hippocampus. The result of the injection was considered by these workers to be due entirely to the adsorption of antibodies by S-100 protein, although this interpretation has been criticized [10].

The absence of any information on the physiological (bioelectrical) effects of antibodies against S-100 protein in the literature adds substantially to the difficulty of exhaustive analysis of the behavioral and histochemical studies of Hyden and co-workers [8, 9].

The object of this investigation was a computer analysis of the electroencephalographic effects of intracentral injection of antibodies against S-100 protein and it is a part of a combined investigation of the physiological role of brain-specific antigens being conducted in the authors' laboratory [1, 6, 7]. Its aims were: a) to study the dynamics of changes in rhythms of the EEG in rats when recorded over a long period in unanesthetized animals after injection of antibodies against S-100 protein into the lateral ventricle; b) to assess the temporal characteristics of development of the effects of antibodies in different brain structures.

EXPERIMENTAL METHOD

The methods of the electrophysiological investigations [2] and of isolation, purification, and identification of S-100 protein [4] were fully described previously. Protein was isolated from bovine brain. It was purified in ammonium sulfate and by chromatography on DEAE-cellulose, DEAE-Sephadex, and preparative electrophoresis in polyacrylamide gel. When the isolated and purified S-100 protein was used as an antigen, a

*An effect of antibodies arising in response to their injection before the training session.

Laboratory of Neurophysiological Mechanisms of Adaptation, Institute of Clinical and Experimental Medicine, Academy of Medical Sciences of the USSR, Siberian Branch, Novosibirsk. (Presented by Academician of the Academy of Medical Sciences of the USSR V. P. Kaznacheev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 84, No. 8, pp. 158-160, August, 1977. Original article submitted March 9, 1977.

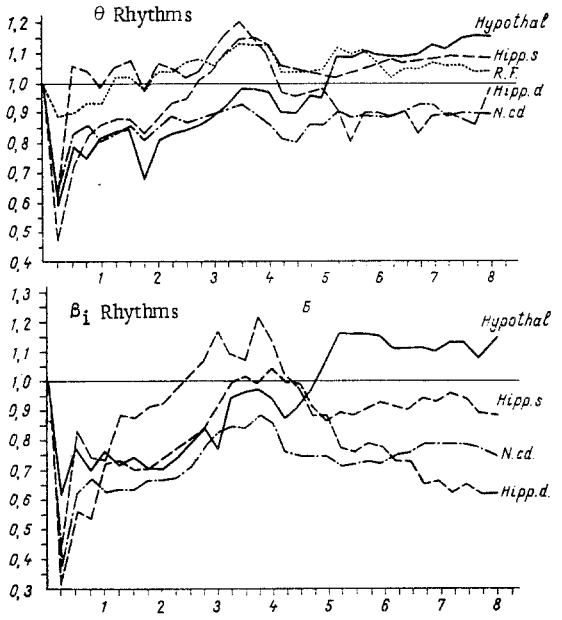

Fig. 1. Dynamics of changes in power of θ (A) and β rhythms (B) in various brain structures after intracentral injection of S-100 protein. Hypothal) Posterior hypothalamus; hip. d, s) right and left hippocampus, respectively; N. cd.) caudate nucleus; R.F.) reticular formation, gigantocellular nucleus.

complex of it with methylated bovine serum albumin was made and this was injected into rabbits in accordance with the usual scheme of immunization. Antiserum against S-100 protein gave only one band with brain extract in the precipitation test.

Antiserum against S-100 protein, dissolved before use in distilled water (0.05 ml), was injected into the left lateral ventricle. The orientation of the microcannula and electrodes was taken from stereotaxic coordinates of Marsala and Fifkova's atlas. Electrical activity of the right and left hippocampus, the head of the caudate nucleus, the posterior hypothalamus, gigantocellular nucleus of the mesencephalic reticular formation, and the cerebral cortex. The isolated α, β, θ, and Δ rhythms of the EEG were integrated with respect to the modulus of function on an analog computer. The results of integration were displayed as graphs on a real time scale by the USChl-03 instrument. The analog signal was recorded simultaneously on a "Talana" tape recorder. Curves showing the dynamics of the integral of the modulus of the EEG rhythms were processed manually. The resulting sets of numbers were processed on a Hewlett-Packard 9820A calculator in order to determine the mean values of the dispersions and confidence intervals (by Student's t test for P = 0.1).

EXPERIMENTAL RESULTS

Control experiments with intracentral injection of nonimmune rabbit serum and of distilled water, just as previously [2], caused no systematic or unidirectional changes in the EEG. The most typical effect of intracentral injection of antibodies against S-100 protein was an increase in the amplitude of the θ and β EEG rhythms, most marked in the hippocampus contralateral to the site of injection, and recorded 3-4 h after the injection. This was followed by deep depression of the EEG rhythms (Fig. 1).

The dynamics of the changes in the rhythms in the hypothalamus was rather different. After depression of activity for a short time, a substantial increase in power of the EEG rhythms and their stabilization at a high level for the remainder of the time were recorded in this region. In eight of the 10 experiments of this series the increase in power of the principal EEG rhythms "degenerated" into epileptiform activity (synchronous and hypersynchronous θ waves), which first appeared in the caudate nucleus and right hippocampus and then became generalized in other brain structures.

A uniform increase in power of the EEG rhythms and the development of epileptiform activity thus were discovered in these experiments as a result of intracentral injection of antibodies against S-100 protein.* This effect is basically similar to that described by the writers previously [2] and it is evidently specific for the action of brain antibodies on cerebral electrogenesis [1, 2, 6, 10, 11]. The most likely cause of this effect is a prolonged depolarization shift [1, 3], recently described for antiserum against S-100 protein, developing in response to application of the antibodies. The depolarization shift, once it has arisen, can equalize the excitability of the various neuron pools and so lead to epileptiform changes in the EEG [3].

It can be suggested on the basis of these results that the affect of antibodies against S-100 protein on learning in rats, described by Hyden and Lange [8], is based on the "obliterating" proactive mechanism of seizure electrogenesis that has already been investigated.

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*Monospecific serum against S-100 protein was kindly provided by Candidate of Biological Sciences S. M. Sviridov from the Laboratory of Developmental Genetics, Institute of Cytology and Genetics, Siberian Branch, Academy of Sciences of the USSR, to whom the authors are grateful.