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EFFECT OF ANTISYNAPTOSOMAL ANTIBODIES ON SYNAPTOSOMAL PROTEIN METABOLISM

V. I. Lokhmatov and V. A. Levchenko

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In recent years highly specific immunologic methods have been used on an increasingly wide scale to study mechanisms of brain function [1, 3, 4, 8, 9]. However, the molecular mechanisms of action of brain antibodies have not been adequately studied.

In the investigation described below the effect of intracerebral injection of antisynaptosomal antibodies on synaptosomal protein metabolism was studied.

EXPERIMENTAL METHOD

Rabbits were immunized by subcutaneous injection of a suspension of synaptosomes from rat cerebral cortex [6] in physiological saline (75 mg protein per animal in 2 ml of solution) with Freund's complete adjuvant. The animals were reimmunized 3 times with intervals of 1 month, without adjuvant. Blood was collected 7-12 days after each reimmunization. The antibody titer in the serum was determined by Ouchterlony's method of microprecipitation in agar [2]. The γ-globulin fraction was isolated by the method in [2].

The γ-globulin fraction for control experiments was isolated from nonimmune rabbit serum.

Experiments were carried out on male laboratory albino rats weighing 180 g, divided into three groups: control group 1) animals not receiving γ-globulin, control group 2) animals receiving nonimmune γ-globulin, experimental group 3) animals receiving injections of immune antisynaptosomal γ-globulin for 3 days (45 μl of dialysate in 1 min into the lateral ventricle).

Labeled precursor of protein synthesis, namely [^{14}C]protein digest of Chlorella (30 μl/min per animal) also was injected into the lateral ventricle of the rats. The animals were killed 2 h and 3 days after injection of the labeled precursor. In the first case the label was injected immediately after the antibodies, in the second case three daily injections of antibodies were given after the label. The synaptosomal fraction was isolated [6] from the brain of the decapitated animals and radioactivity counted in a dioxane scintillator system [5] on an Intertechnique SL-30 liquid scintillation counter. The significance of differences between the values was calculated by Student's test.

EXPERIMENTAL RESULTS

Values of specific radioactivity of synaptosomal proteins from the brain of the control animals and animals receiving nonimmune γ-globulin, when sacrificed 2 h and 3 days after injection of labeled Chlorella digest, were similar (Table 1). Meanwhile it was found that intraventricular injection of antisynaptosomal γ-globulin into the rats caused a significant increase in specific radioactivity of the proteins studied 2 h after, and a decrease in

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TABLE 1. Specific Radioactivity of Synaptosomal Proteins from Rat Cerebral Cortex (in cpm/mg protein) after Intraventricular Injection of Antisynaptosomal Antibodies (M ± m) into Animals

Groups of animals	Time after injection of ^{14}C-digest of Chlorella	
	2 h	3 days
Control 1	16528±390	8142±318
Control 2	16355±319	7698±417
Experimental 3	19473±717*	5438±439*

Legend. *$P < 0.05$ compared with control group.

those studied 3 days after injection of the labeled precursor (compared with values in the control animals and in animals receiving nonimmune γ-globulin).

It can be postulated that the specific radioactivity of the synaptosomal proteins 2 h after injection of the labeled precursor characterizes mainly local protein synthesis [7], whereas radioactivity 3 days after injection of the labeled precursor, considering the known rates of protein synthesis in the groups compared, characterizes mainly the degree of protein degradation. However, the role of axonal flow in the changes in protein synthesis at this particular time point cannot be ruled out. The increase in specific radioactivity of synaptosomal proteins observed in response to injection of the antibodies 2 h after injection of labeled Chlorella digest was evidently associated with increased protein synthesis of brain synapses. A possible cause of this phenomenon is revealed by values of specific radioactivity of the synaptosomal proteins 3 days after injection of the labeled precursor. At this time the specific radioactivity of the synaptosomal proteins was depressed after injection of the antibodies. Interaction between antibodies and the corresponding accessible antigenic groups in the region of the brain synapses gradually led to rapid destruction of the protein antigens blocked by the antibodies, thereby reducing the specific radioactivity of the synaptosomal proteins 3 days after injection of the labeled precursor.

Intensive breakdown of antigen proteins probably led to their increased synthesis, manifested as an increase in specific radioactivity of the synaptosomal proteins 2 h after injection of the [^{14}C]protein Chlorella digest. It can be tentatively suggested that the molecular mechanisms of the action of the various brain antibodies closely resemble the mechanisms of action of antisynaptosomal antibodies we have discussed.

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