IMMUNOGENESIS AND AXOPLASMATIC TRANSPORT IN WISTAR RATS

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Specialists working in the field of neuroimmunology [1] are studying the following problems: a) the mechanisms of induction of the nervous system in the process of immunogenesis [2]; b) the principles and mechanisms of regulation of immunity by the efferent part of the nervous system [3]; c) the causes of similarity of the immune and nervous systems [4]. In other words, facts concerning the principal aspects of interaction and integration of the immune and nervous systems are accumulating. At the same time, it must be said that there is as yet no information in the literature on interdependence of immunogenesis and axoplasmatic transport in experimental animals. Yet axoplasmatic transport is one of the most important processes characterizing the functional state of the nervous system [5]. The aim of this investigation was to determine the parameters of this process in Wistar rats at different times after injection of an antigen.

EXPERIMENTAL METHOD

Experiments were carried out on Wistar rats weighing 150-200 g (altogether 35 animals were used). The rats were immunized by a suspension of sheep's red blood cells (SRBC) in a dose of 1.0 ml of the 20% suspension intraperitoneally. Control animals were given an injection of the corresponding volume of medium 199. Next, at intervals of 5, 24, 48, 72, and 96 h after injection of the antigen, the parameters of rapid axoplasmic transport (RAT) along the motor fibers of the sciatic nerve were determined [7]. The intensity of RNA and protein synthesis in different parts of the nerve tissue was determined as follows. Pieces of spinal cord and visual cortex (80-100 mg) were immersed in medium 199 and cut into small pieces measuring 1.0 × 0.5 × 0.5 mm. The slices were cultured at 37°C in Petri dishes 40 mm in diameter, in medium 199 with the addition of 20% bovine serum, 70 μg of vitamin C, and 5 mg glucose to 1 ml of medium [8]. After culture for 30-40 min, some slices from each organ were incubated with ^{3}H-uridine (0.2 MBq/ml) and some with ^{3}H-leucine (0.3 MBq/ml) for 15 min. The slices were then washed with cold (4°C) medium with an excess of the unlabeled nucleoside or amino acid, and treated in graduated vials with 5% TCA at 4°C for 90 min. The slices were rinsed with 70° alcohol, replaced in the graduated vials, and dissolved in a 1 M solution of Hyamine, Scintillator was added to the vials and radioactivity of the acid-soluble (S) and acid-insoluble RNA or protein fraction (I) was determined on a counter. Next, the total labeled uridine or leucine was calculated (R), equal to the total radioactivity of the two fractions (R = S + I) for each type of macromolecule, and the relative incorporation was determined with a correction for permeability of the cells for the precursor:

$$I/(S + I) \times 100.$$

The calculation was based on specific radioactivity of the slices (in cpm/mg wet weight). Antibody-forming cells (AFC) in the mesenteric, inguinal, and popliteal lymph nodes (LN) was determined by Cunningham's method [10]. The numerical results were subjected to statistical analysis by Student's test [6].

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TABLE 1. Rapid Axoplasmic Transport (RAT) of Proteins along Motor Fibers of Sciatic Nerve of Wistar Rats and Formation of AFC in Regional Lymph Nodes at different Times after Immunization with SRBC

Number of animals	Time after immunization, h	Rate of transport (mm/day)	Level of radioactivity of transported material, conventional units	Number of AFC in lymph nodes (10^2)		
				mesenteric	inguinal	popliteal
8	Control	400,5±15,8	6,83±1,26	0	0	0
5	5	388,8±13,4	25,5±3,1**	0	0	0
4	24	423±17,2	9,17±3,18	0	0	0
3	48	396±20,7	22,3±2,39**	0	0	0
6	72	396±9,2	15,4±4,2*	0	0	0
5	96	352±13,4*	11,4±3,5	5,6	1,5	0
4	168	—	—	0	0	0

Legend. Level of radioactivity of transported material calculated as mean value of total of three segments of peak of transported material. A dash means that no investigation was carried out, *$p < 0.05$; **$p < 0.01$.

EXPERIMENTAL RESULTS

The rate of RAT of proteins along motor fibers of the sciatic nerve during immunogenesis was shown not to undergo any significant change, especially in the initial stages after injection of the antigen (Table 1). Not until the end of the 4th day was a small but significant degree of inhibition of this process observed ($p < 0.05$). Meanwhile the level of radioactivity of the transported material, characterizing the intensity of the parameter studied, changed highly significantly in the course of development in the immune response. For instance, only 5 h after injection of the antigen, an almost fourfold increase was observed, A relative decline of radioactivity took place 24 h after the beginning of immunogenesis, giving way by the 48th hour to a fresh increase in this parameter. By the end of the 4th day there was a gradual decrease in the intensity of RAT along the sciatic nerve of the immunized animals. Consequently, immunogenesis in Wistar rats is accompanied by significant changes in the parameters of rapid axoplasmic transport.

Intraperitoneal injection of SRBC into the experimental animals led to a change in the intensity of RNA and protein synthesis in different parts of the nerve tissue. For instance, an increase in protein synthesis was observed in the visual cortex during formation of the immune response. Meanwhile, in the spinal cord a heterogeneous situation was observed (at different times of immunogenesis both inhibition and stimulation of this process were identified). The relative fall in the level of radioactivity of the material transported with RAT 24 h after injection of the antigen may perhaps be connected with this phenomenon.

However, in the first place, on the basis of these results we can consider that modulation of the parameters of RAT and of protein and RNA synthesis in the different parts of the nervous system is observed during immunogenesis, and second, there is a possible role of substances migrating with RAT in the regulation of the developing immune response. Evidence in support of this conclusion also is given by information on the trans-synaptic passage of these substances into the innervated tissues [5]. Meanwhile, there is sufficient evidence of innervation of the stroma and parenchyma of lymphoid organs from different parts of the nervous system and of close contact between nervous structures and immunocompetent cells [9].

We studied parameters of the immune response (relative to AFC formation) in a group of lymph nodes located near the sciatic nerve. A successive (after a change in the intensity of RAT in the sciatic nerve) increased in the number of AFC was found in the lymph nodes studied (Table 1). It can be tentatively suggested that this is indirect evidence of the involvement of RAT in regulation of the immune response.

We thus determined for the first time a state of interdependence between immunogenesis and axoplasmic transport in experimental animals (Wistar rats). In this way we identified yet another, previously unstudied, channel of interaction between the immune and nervous systems.

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THE NEUROENDOCRINE SYSTEM AND SPECIFIC FACTORS OF IMMUNITY IN PESTICIDE POISONING

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The problem of neuroendocrine regulation of immunologic functions has been the subject of study by Soviet [3, 4, 7, 8] and Western [16, 18] workers. However, we could find no information in the accessible literature on the neuroendocrine regulation of immunogenesis studied in chronic pesticide poisoning. Nevertheless, there is evidence in the literature that pesticides have a harmful action on factors of immunity, including the toxic action of small doses of pesticides [2, 6, 17].

Investigations into the effect of organophosphorus compounds (OPC) on the state of the hypothalamo-hypophyseal neurosecretory and hypothalamo-hypophyseal-adrenocortical systems (HHNS and HHACS) conducted previously in the writers' department revealed phasic changes in the above-mentioned systems with activation of their functional state after 1 and 3 months of poisoning. In chronic experiments an increase in the content and a change in the relative content of 11-hydroxycorticosteroids, hydrocortisone, and corticosterone were found in the peripheral blood after poisoning with small doses of OPC [5, 11-13].

The aim of this investigation was to compare the effect of chronic poisoning with the OPC Antio (Formathion) on the state of the specific factors of immunity and on the blood level of corticosterone (CS), a glucocorticoid hormone.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 160-220 g, receiving Antio in a dose of 0.01 LD_{50} (3.5 mg/kg) daily perorally for 2 months. Animals of the control group received an equal volume of the solvent.

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