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CORRECTION OF DISTURBANCES OF IMMUNITY ARISING AFTER HEAD INJURY

A. P. Romodanov, N. I. Lisyanyi, and L. V. Kurganova

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Head injuries, like any other type of trauma, act as extremely strong stress stimuli and are accompanied by the release of hormones, neuropeptides, catecholamines, and other biologically active substances into the circulation, giving rise to cellular depopulation of the lymphoid organs and forming a secondary immunodeficiency syndrome [1, 3, 4, 9, 10]. Meanwhile it has been shown that immune disturbances arising in such cases in the posttraumatic period can be largely corrected by the use of immunostimulators such as T-activin, myelopide or, which is particularly important, small doses of serum from traumatized animals [8]. In this connection it is important to study the immunostimulating action of the humoral factor isolated from the blood serum of animals subjected to craniocerebral trauma (CCT) on the development of posttraumatic immunodeficiency.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 150-190 g. A closed head injury was inflicted by means of a spring-operated hammer in the left fronto-parietal region of the head in rats [8]. The animals were immunized with sheep's red blood cells (SRBC) in a dose of 5×10^8 1 h after CCT and on the 1st, 3rd, 5th, and 7th days. The number of antibody-forming cells (AFC) in the spleen was determined on the 5th day by the method in [12]. A local delayed-type hypersensitivity reaction (DTHR) was induced by the method in [2], by sensitizing the animals 1 h after CCT.

A typical index was used as indicator of post-stress changes in the immune system, namely the ratio of the weight of the thymus to the animal's body weight [1, 3]. The immunostimulating humoral factor (IHF) was isolated by the writers' own method, by acetic acid extraction with selective fractionation on ultrafiltration membranes [5]. IHF was injected intramuscularly into the experimental animals in a dose of 1-10 mg/kg body weight depending on the experimental conditions.

Laboratory of Neuroimmunology, Research Institute of Neurosurgery, Ministry of Health of the Ukrainian SSR, Kiev.

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TABLE 1. Effect of IHF on Thymic Index of Rats after CCT

Experimental conditions	Dose of IHF, mg	Thymic index			
		on 1st day	p	on 5th day	p
Intact animals	—	2,17±0,09 (11)	<0,05	2,17±0,09 (11)	<0,01
CCT	—	1,20±0,04 (13)		1,34±0,13 (15)	
CCT + IHF	1	2,16±0,21 (13)	<0,05	2,16±0,04 (10)	<0,01
CCT + IHF	5	2,48±0,27 (15)	<0,05	2,52±0,87 (15)	<0,05
CCT + IHF	10	2,62±0,40 (11)	<0,05	2,72±0,19 (10)	<0,01
CCT + CF	5	1,64±0,15 (10)	>0,05	1,69±0,31 (10)	>0,05

Legend. Here and in Table 2, number of animals given in parentheses. CF) Control factor.

TABLE 2. Effect of IHF on Antibody Formation in Rats after CCT

Experimental conditions	Dose of IHF, mg	Number of AFC per 10^6 karyocytes	p
Intact animals	—	415±21,7 (14)	<0,05
CCT	—	36±3,3 (15)	
CCT + IHF	1	428±13,8 (13)	<0,05
CCT + IHF	5	545±31,1 (15)	<0,05
CCT + IHF	10	1091±82,4 (11)	<0,05
CCT + CF	5	254±22,2 (10)	<0,05

EXPERIMENTAL RESULTS

The results were subjected to statistical analysis by Montsevichute-Eringene's method [7]. In the experiments of series I the effect of the humoral factor isolated from the blood serum of traumatized animals on the development of post-traumatic cellular depopulation of the thymus was studied 1 and 5 days after CCT. Injection of IHF into the rats 1 h after CCT prevented cellular depopulation of the thymus, as shown by an increase in the thymic index on the 1st and 5th days after CCT (Table 1). Of all the doses from 1 to 10 mg/kg studied, a dose of 10 mg/kg gave the strongest immunostimulating activity, whereas the factor obtained from the serum of healthy animals had no stimulating action. In some animals, after correction with IHF the thymic index exceeded that of intact animals.

Immunization of the animals with SRBC 1 h after trauma, against the background of injection of IHF (experiments of series II) induced stimulation of humoral activity, which was recorded as a dose-dependent increase in the relative and absolute numbers of AFC in the spleen (Table 2). Injection of humoral factor obtained from intact serum, unlike injection of IHF, caused only a very small increase, not significant, in the intensity of immunogenesis in the traumatized animals and did not increase the number of cells in the spleen in the post-traumatic period.

In the experiments of series III the effect of IHF was studied on the development of the response of cellular immunity in the post-traumatic period on a model of local DTHR. Injection of a sensitizing dose of SRBC and IHF 1 h after CCT intensified DTHR (Fig. 1). Consequently, injection of IHF in the early stages after experimental CCT increased the intensity of the cellular and humoral immune response and prevented post-traumatic cellular depopulation of the lymphoid organs, especially the thymus and spleen, i.e., corrected the development of the post-traumatic immunodeficiency syndrome arising after head injury [8, 9].

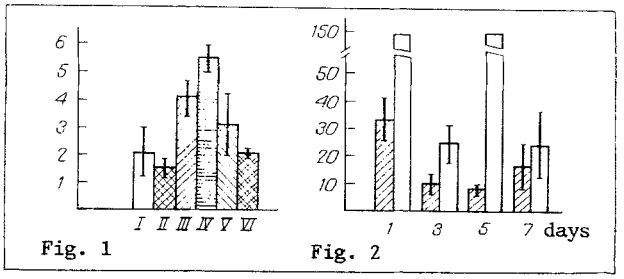

Fig. 1. Effect of IHF on development of DTHR in rats. I) Intact animals, II) rats with CCT, III) rats with CCT after injection of 1 mg IHF, IV) with CCT after injection of 5 mg IHF, V) with CCT after injection of 10 mg IHF, VI) with CCT after injection of 5 mg CF. Ordinate, difference in weight of control and experimental lymph nodes.

Fig. 2. Effect of IHF (5 mg, intramuscularly) on immune response in rat spleen at different times after CCT. Abscissa, times of investigation (in days); ordinate, number of AFC per 10^6 karyocytes; shaded columns denote control, unshaded — experiment.

The next step was to study whether IHF may have an immunostimulating action in the later stages after trauma. In the experiments of series IV the effect of injection of IHF 1, 3, 5, and 7 days after head injury on the humoral immune response induced at these times was studied. As will be clear from Fig. 2, injection of IHF led to an increase in the intensity of AFC formation at different times after trauma, i.e., IHF not only prevented the post-traumatic disturbance of immunogenesis, but also stimulated immune responses during secondary immunodeficiency. In animals receiving IHF 1, 3, 5, and 7 days after CCT, a larger number of nucleated cells was found in the lymphoid organs and the thymic index was much higher than in animals not receiving IHF. Consequently, the humoral factor studied has a dose-dependent immunostimulating (possibly immunomodulating) action on specific (AFC production) and general (the number of cells in the lymphoid organs, increase in weight of the thymus) immune responses. These changes in the immunity system after injection of IHF suggest that it can influence both the central and the peripheral organs of immunity. Essentially, IHF not only has immunostimulating properties, but it can also prevent the development of disturbances in the immunity system and, in particular, the depopulation of the thymus following injection in the early stages after trauma.

The humoral factor obtained from the blood serum of animals undergoing head injury thus affects the circulation and distribution of lymphoid organs in the post-traumatic period and intensifies their cooperative interaction, as is manifested by an increase in the intensity of humoral and cellular immunity. The mechanism of the immunostimulating action has not been fully explained. It may perhaps be connected with both a direct and an indirect effect through other regulating systems, especially the neuroendocrine and neuropeptide systems, which is a characteristic feature of immunostimulators of the myelopide type [6, 11]. Meanwhile, unlike T-activin, which potentiates the immune response in the post-traumatic period but does not affect the number of cells in the lymphoid organs in the early stages after trauma, IHF prevents cellular depopulation of the thymus, and in the late stages after trauma it restores the cell composition of the gland.

These investigations show that disturbances in the immune system arising after head injury are reversible and can be largely corrected by the use of a serum humoral factor isolated from blood serum, which has an immunostimulating and immunoprotective action.

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