10. L. S. Lozovskaya, Defensive and Pathological Reactions of Immunity in Children in Connection with Virus Infection [in Russian], Moscow (1973).
11. O. V. Smirnova and T. A. Kuz'mina, Zh. Mikrobiol., No. 4, 8 (1966).
12. V. D. Solov'ev and T. A. Baktemirov, Interferon in the Theory and Practice of Medicine [in Russian], Moscow (1970).
13. V. D. Solov'ev, T. A. Baktemirov, and A. E. Gumennik, Vopr. Virusol., No. 5, 531 (1967).
14. M. Masugi, Beitr. Path. Anat., 91, 5 (1933).

CROSS-REACTING THYMUS AND BRAIN ANTIGENS IN THE CEREBRAL CORTEX

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Rabbit antisera against antigens of whole mouse, rabbit, guinea pig, and human brain were found to have a cross cytotoxic action on lymphocytes of the thymus, lymph nodes, and spleen of the animals of these species. Mouse thymus cells were the most sensitive (index of cytotoxicity 63-100%); the cells of other mouse lymphoid organs and lymphocytes of the other species of animals and man were more resistant. Bone marrow cells were not injured by any serum. Antigens responsible for the cytotoxic properties of the sera were found to be located in the human cerebral cortex and to be absent from the white matter and the brain stem.

KEY WORDS: thymus; cerebral cortex; cross-reacting antigens.

Species-specific O-antigenic correlations between the mouse brain and thymus were first described by Reif and Allen [12]. Later similar correlations were discovered in rats [13]. We now know that species-specific and cross-reacting antigens are present in the brain and thymus of many species: rats [4, 11, 13-15], mice [4, 6, 12, 14, 15], and birds [5]. The brain of most species of animals contains antigens in common with antigens of mouse thymocytes [7]. Meanwhile the problem of which brain components, i.e., the gray or white matter, are more closely connected with these antigens has so far received little study [3, 9].

The object of this investigation was to examine this problem.

EXPERIMENTAL METHOD

Antisera against whole brain tissue of CBA mice, guinea pigs, and man and also of the various parts (cortex, brain stem, white matter) of the adult human brain were obtained from rabbits weighing 2-2.5 kg after immunization with brain homogenates together with Freund's complete adjuvant [2]. Titers of antibrain antibodies were determined by the complement fixation test in the cold [1] with the antigens used for immunization. Sera with titers of 1/160-1/320 were used. The sera thus obtained were heated to 56°C for 30 min and absorbed with liver homogenates and erythrocytes [5] of the species of animal or man relative to which the cytotoxic activity of the sera was subsequently to be tested. The tests were carried out by the method of Niederhuber and Möller [10] against thymus, lymph node, spleen, and bone marrow cells of the corresponding species of animal or against human lymph nodes, spleen, and bone marrow cells. The cell population of human lymphocytes before testing was enriched with T cells by passage through a cotton wool column (1 g:200 mg), previously washed with medium No. 199. The viability of the cells was estimated with a 0.2% aqueous solution of Trypan Blue.

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TABLE 1. Comparative Characteristics of Cytotoxic Activity of Antisera against the Brain of Different Species of Animals and Man

Source of lymphocytes	Cytotoxic index of anti-brain sera (1:10)				
	mouse		human		guinea pig
	expt. 1	expt. 2	expt. 1	expt. 2	expt. 1
Thymus					
mouse	95±1,54	100	82±2,71	86±2,82	63±3,41
guinea pig	35±1,99	40±3,46	41±3,48	—	68±3,30
rabbit	22±2,93	28±3,17	22±2,93	—	—
Lymph nodes					
mouse	66±3,34	79±3,70	48±3,53	45±3,45	40±3,46
guinea pig	36±3,39	36±3,39	42±3,49	—	67±3,32
rabbit	25±3,06	25±3,06	23±3,24	—	—
human	20±2,80	22±2,91	20±2,82	18±2,71	3±1,51
Spleen					
mouse	40±3,46	43±3,50	48±3,53	42±3,41	20±2,83
guinea pig	21±2,88	25±3,06	23±2,98	—	26±3,10
rabbit	20±2,82	22±2,93	20±2,81	—	—
human	9±1,52	8±1,41	7±1,72	7±1,75	5±1,53
Bone marrow					
mouse	5±1,54	9±2,03	9±2,02	7±1,76	4±1,39
guinea pig	0	0	7±1,80	—	1±0,70
rabbit	0	0	0	—	—
human	0	0	0	0	0

Legend. Viability of cells from mouse, human, and rabbit lymphoid organs in all experiments of the control series (with normal serum) was 80-90%, but the viability of guinea pig lymphocytes was 70%.

TABLE 2. Comparative Characteristics of Cytotoxic Activity of Sera against White and Gray Matter of the Human Brain

Source of lymphocytes	Cytotoxic index of sera (1:10) obtained by immunization with homogenates of different parts of the brain							
	cortex			white matter			brain stem	
	expt. 1	expt. 2	expt. 3	expt. 1	expt. 2	expt. 3	expt. 1	expt. 2
Thymus								
mouse	85±2,52	83±2,66	84±2,59	17±2,66	7±1,80	7±1,80	5±1,54	4±1,39
guinea pig	15±2,52	16±2,59	18±2,72	7±1,80	9±2,02	7±1,80	8±1,92	6±1,69
rabbit	25±3,37	22±2,93	24±3,10	2±9,99	3±1,21	4±1,39	3±1,21	2±0,99
Lymph nodes								
mouse	20±2,83	29±3,21	57±3,53	10±2,12	8±1,92	8±1,92	6±1,68	6±1,68
guinea pig	17±2,66	25±3,06	18±2,72	7±1,80	10±2,12	9±2,02	5±1,54	7±1,80
rabbit	22±3,30	20±2,90	22±3,30	3±1,21	5±1,54	3±1,21	4±1,39	5±1,54
human	15±2,70	18±2,72	19±2,68	3±1,21	3±1,21	1±0,70	2±0,99	1±0,70
Spleen								
mouse	21±2,81	24±3,01	28±3,17	11±2,21	5±1,54	10±2,12	4±1,39	6±2,89
guinea pig	13±2,38	15±2,52	16±2,59	3±2,21	9±2,02	9±2,02	5±1,54	7±1,80
rabbit	25±2,54	23±2,90	28±3,17	5±1,54	4±1,39	5±1,54	3±1,21	4±1,39
human	12±2,18	11±2,34	7±1,78	3±1,21	3±1,21	0	2±0,98	0
Bone marrow								
mouse	10±2,12	6±1,68	5±1,54	1±0,70	0	0	0	2±0,99
guinea pig	8±1,92	5±1,54	7±1,80	0	1±0,70	1±0,70	1±0,70	2±0,99
rabbit	9±2,02	3±1,21	4±1,39	0	0	0	0	0
human	0	0	0	0	0	0	0	0

EXPERIMENTAL RESULTS

As Table 1 shows, antisera against mouse and human brain tissue had a marked cytotoxic action on mouse lymphocytes. The cytotoxic index was highest for thymus cells, lower for lymph node and spleen cells, and bone marrow cells were not damaged by the sera tested. This order of sensitivity corresponds to the content of O-positive cells in these organs [6]. Guinea pig, rabbit, and human lymphocytes also were sensitive to the sera, but by a much lesser degree in every case than mouse lymphocytes.

Antibodies against guinea pig brain also reacted differentially with lymphocytes from the different lymphoid organs, but the sensitivity of mouse and guinea pig cells to that serum in most cases was identical. Human lymphocytes were resistant to the action of that serum also.

Rabbit sera against human cerebral cortex (Table 2) had the same action on lymphocytes as the sera against whole brain homogenate (Table 1). Antisera against white matter of the brain and against antigens of the brain stem were virtually inactive against lymphocytes (Table 2).

The cytotoxic indices of the sera, incidentally, did not correlate with titers of complement-fixing antibodies against the corresponding brain antigen.

The results confirm others published previously [4, 6, 11, 13-15] on the existence of cross-reacting thymus and brain antigens in animals of various species. The present writers found that the cross-reacting antigens were located in the cerebral cortex, which differs in its functions and, evidently, antigenically also, from other parts of the brain.

The results of the present experiments are in agreement with observations by other workers [6, 11, 16] that mouse lymphocytes are more sensitive to the action of antibrain antibodies than lymphocytes of other species of animals.

According to data in the literature, human thymocytes are the least sensitive [8] or even resistant [16] to the action of homogous and heterologous antibrain sera. The results of the present experiments show that other human lymphoid organs also have low sensitivity to antibrain sera. The reason for this phenomenon requires further study.

LITERATURE CITED

1. V. I. Ioffe and K. M. Rozental', Zh. Mikrobiol., No. 12, 65 (1943).
2. P. V. Osipova and Yu. L. Zhitnukhin, Vest. Akad. Med. Nauk SSSR, No. 1, 66 (1971).
3. G. Birnbaum, Brain Res., 84, 111 (1975).
4. J. Clagett, H.-H. Peter, J. D. Feldman, et al., J. Immunol., 110, 1085 (1973).
5. E. Feiglova, L. Pichlikova, and K. Nouza, Folia Biol. (Prague), 18, 256 (1972).
6. E. S. Golub, Cell. Immunol., 2, 353 (1971).
7. E. S. Golub, J. Immunol., 109, 168 (1972).
8. M. F. Greaves and G. Brown, Lancet, 1, 455 (1974).
9. M. J. Moore, P. Dikkes, A. E. Reif, et al., Brain Res., 28, 283 (1971).
10. J. E. Niederhuber and E. Möller, Cell Immunol., 3, 559 (1972).
11. H.-H. Peter, J. Clagett, J. D. Feldman, et al., J. Immunol., 110, 1077 (1973).
12. A. E. Reif and M. V. Allen, J. Exp. Med., 120, 413 (1964).
13. H. G. Thiele and R. Stark, Lancet, 2, 878 (1971).
14. H. G. Thiele, R. Stark, and D. Keeser, Europ. J. Immunol., 2, 524 (1972).
15. H. G. Thiele, R. Stark, and M. Földi, Naturwissenschaften, 59, 221 (1972).
16. H. G. Thiele, R. Stark, D. Keeser, et al., Lancet, 2, 1447 (1973).