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NEUROPATHOLOGICAL EFFECTS OF INJECTION OF TETANUS TOXIN INTO CERTAIN STRUCTURES OF THE RAT BRAIN

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The neuropathological effects of local injection of tetanus toxin (TT) into various structures of the brain were studied in experiments on rats. Definite neuropathological changes were observed in the animals, different from those found after injection of TT elsewhere. As a rule the action of TT in a given region of the brain was local. The experiments confirm the theory of generator mechanisms of neuropathological syndromes, according to which specific manifestations of the corresponding syndrome are determined by the location of a generator of pathologically enhanced excitation in a certain brain structure.

KEY WORDS: subcortical brain structures; lateral geniculate body; tetanus toxin; neuropathological syndromes.

Previous experiments showed that after injection of tetanus toxin (TT) into the lateral geniculate body (LGB) of animals specific pathophysiological effects characterizing a syndrome of photogenic epilepsy arise [1,3,6]. These effects were the result of functional changes evoked by TT in LGB, i.e., they were the result of the formation of a generator of pathologically enhanced excitation (GPEE) in that nucleus [2]. However, in order to explain the role of this mechanism in the formation of the neuropathological syndrome, an answer must be found to the question: Could not these phenomena be the result of spread of TT into other regions of the brain? Data in the literature of the ability of TT to spread in the brain [7, 8] do not provide an unequivocal answer to this question.

It was accordingly necessary to investigate the effects of creation of appropriate GPEE in neighboring structures connected anatomically with LGB. Such experiments would, on the one hand, provide fresh evidence on the character of spread of TT in different regions of the brain and, on the other hand, they would show whether corresponding neuropathological syndromes can be obtained by injection of TT into various structures of the animal brain.

EXPERIMENTAL METHOD

Under hexobarbital anesthesia TT was injected into various subcortical structures of 66 noninbred albino

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TABLE 1. Features of Neuropathological Syndromes Arising After Local Injection of Tetanus Toxin into Various Subcortical Structures

Brain structures*	No. of experimental animals	Mean latent period of development of syndrome, h	Features of neuropathological syndromes											
			photogenic convulsions		compulsive movements		hyperalgesia		hyperesthesia		rotatory movements		fits of agitation	
			%	№	%	№	%	№	%	№	%	№	%	№
AL	1—4	9,8	0	—	0	—	0	—	25	2	0	—	100	1—4
CP	5—7	25,8	0	—	0	—	33	5	100	5—7	100	5—7	33	5
GD	8—28	15,8	86	8—15 17—19 22—28	100	8—28	5	18	14	12—18 23	14	22,19 12	0	—
Hipp. d	29—31	26.3	0	—	0	—	100	29—31	100	29—31	0	—	33	31
VE	32—35	19,7	25	32	50	32,35	25	34	75	33—35	100	32—35	25	34
Zi	36—40	27,2	0	—	20	36	60	36,38	100	36—40	100	36—40	0	—
SN	41—47	18,3	0	—	14	41	0	—	28	41—45	100	41—47	0	—
Hipp. v.	48—53	14,5	0	—	0	—	67	48—51	100	48—53	0	—	67	48—50 53
CS	54—59	9,5	17	58	100	54—59	67	55—57 59	50	56—58	0	—	17	56

*Abbreviations of structures explained in captions to Fig. 1.

rats weighing 250-350 g. The specific toxicity of the TT was $5 \cdot 10^4$ mouse MLD/ml. Micropipets made of Pyrex glass, with an outer diameter of the tip of not more than 100 μ, were used for the local injection of TT. The volume of TT injected was $0.3 \cdot 10^{-4}$-$0.5 \cdot 10^{-4}$ ml (dose about 2 MLD). Stereotaxic coordinates of the cerebral cortex and subcortical structures were taken from an atlas of the rat brain [5].

After the end of the operation and recovery of the animals from the anesthetic, their behavior was studied visually and by means of tests. The tests used included photic and acoustic stimulation, a puff of air, and touching with a soft brush. After the end of the experiments the location of the micropipet tip was verified morphologically. For this purpose, the water-insoluble dye carmine was added in powder form to the solution of TT. The zone of localization of the dye was determined in photographs of brain sections as a region of increased optical density.

EXPERIMENTAL RESULTS

The points of injection of TT into the various brain structures are shown on the schemes of brain sections (Fig. 1). The main results of the experiments are given in Table 1, and they show that after local injection of TT into different regions of the rat brain definite pathophysiological effects and syndromes developed. For instance, after injection of TT into the anterior thalamic nuclei (AL) characteristic behavioral disturbances developed: The rats responded inappropriately to external stimuli, ran and jumped chaotically, and developed a state of agitated motor excitation.

As a result of injection of TT into nuclei of the extrapyramidal system (CDP, VE, SN) and into an undefined zone of the thalamus (Zi) a syndrome developed which was mainly accompanied in the rats by characteristic postural asymmetry, turning movements of the "head — tail" type in the contralateral direction relative to the localization of TT, and ipsilateral rotatory movements relative to the longitudinal axis of the trunk. In most cases these features were accompanied by hyperesthesia of the contralateral part of the trunk.

The syndrome which the animals developed after injection of TT into the hippocampus (Hipp. d., Hipp. v.) and amygdala (LA) was accompanied chiefly by generalized hyperesthesia and hyperalgesia: Slight touch or a puff of air evoked stereotyped scratching of localized regions of the back and sometimes vocal responses in the animals. Similar bouts of scratching movements appeared spontaneously, without any external stimulation. This response of the animals could be described as nociceptive.

Of special interest from the standpoint of differentiation between the effects of manifesting the neuropathological syndromes arising after injection of TT into LGB was the syndrome observed in the rats as a result of injection of TT into the superior colliculus (CS). The main symptom found in the animals in this case was photogenic compulsive movements, which usually appear a few hours earlier than when TT was injected into LGB, and were of a more marked nociceptive character: The animals went into a state of general excitation, and individual compulsive movements were accompanied by vocal responses. Unlike this picture, when TT was injected into LGB the syndrome which developed was associated with the appearance of photogenic compulsive motor responses in the rats without any marked nociceptive component, and with photogenic convulsions. It can tentatively be suggested that the appearance of such a symptom (photogenic compulsive

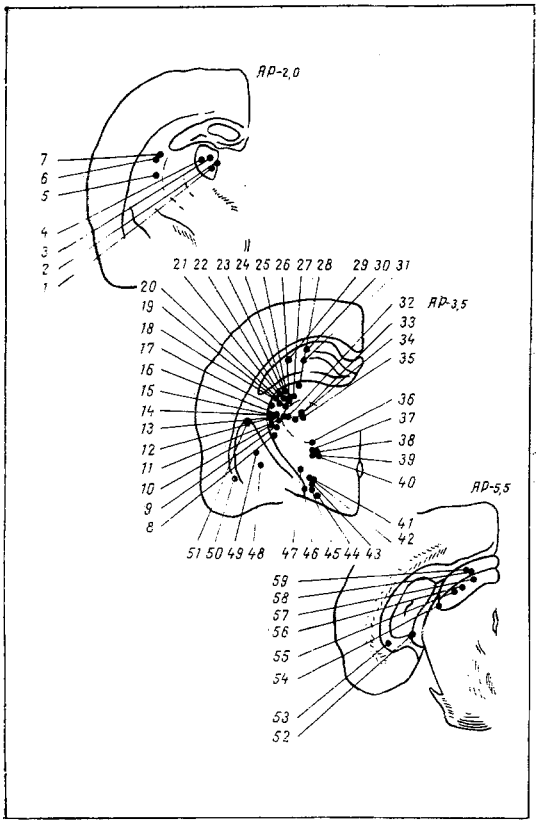

Fig. 1. Localization of regions of infection of TT into various subcortical structures of rat brain. 1-4) Nucleus lateralis anterior thalami (AL), 5-7) caudate-putamen complex (CP), 8-28) corpus geniculatum laterale (LGB), 29-31) hippocampus dorsalis (Hipp. d.), 32-35) nucleus ventralis thalami (VE), 36-40) zona incerta (Zi), 41-47) substantia-nigra (SN), 48,49,51,53) hippocampus ventralis (Hipp. v.), 50) gyrus dentatus (GD), 52) nucleus lateralis amygdalae (LA), 54-59) colliculus superior (CS).

movements) in rats after injection of TT into LGB and CS is connected with the action of TT on different components (the ventral nucleus of LGB and the superior colliculus) of the same visuomotor system [4, 9], and not with the spread of TT from one structure into another along projection fibers, for besides the common features mentioned above, differences also were observed in these phenomena: The appearance of photogenic convulsions after injection of TT into LGB and the occurrence mainly of nociceptive responses after injection of TT into CS.

As a result of injection of TT into the visual cortex of the animals, elements of stereotyped behavior were observed: running, standing for a long time on the hind limbs. Furthermore, no specific motor or sensory disturbances could be observed in the animals before death. Consequently, changes in evoked potentials in the visual cortex on the side of injection of TT into LGB [3], as the results of this series of experiments show, likewise cannot be explained by the spread of TT from the thalamic nucleus along the fibers of the optic radiation, for no features similar to the symptoms of photogenic epilepsy developed in the animals as a result of the direct action of TT on the cortical projection area. The same result has been described for the visual cortex of rats after local injection of TT into that area.

Besides specific systems arising in the majority of animals after injection of TT into various parts of the brain, additional features were observed in some of them (Table 1; animals Nos. 12, 18, 22, 23, 32, 41, and 44). These "nonstandard" effects can be explained by the possible spread of TT into brain regions bordering on the particular structure.

After local injection of TT into various structures of the rat brain, as a rule the action of the toxin is local (see also [7]) and it leads to the appearance of specific neuropathological features in the animals. This

property of TT may be important when it is used for the creation of an experimental model of neuropathological syndromes. The results also confirm the theory of generator mechanisms of neuropathological syndromes [2], according to which specific manifestations of the corresponding syndrome are determined by the localization of a GPEE in a certain brain structure.

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STATE OF THE VASCULAR TONE AND SOME BLOOD BIOCHEMICAL INDICES IN EXPERIMENTAL ATHEROSCLEROSIS AND SENSITIZATION

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The study of the state of tone of the hind limb vessels and some blood indices of lipid metabolism in rabbits with experimental atherosclerosis and sensitization revealed an increase in vascular resistance in the region studied and a disturbance of lipid metabolism in animals of the two experimental groups. The results confirm previous observations that the allergic component is a factor which complicates the course of atherosclerosis.

KEY WORDS: atherosclerosis; sensitization; vascular tone.

The role of the allergic factor in the pathogenesis of atherosclerosis is well known [4-6,13]. Since one of the manifestations of atherosclerosis is a change in vascular reactivity [2,7], the role of allergy in the changes in the state of vascular tone is of great importance. Data in the literature on this matter are highly contradictory. For instance, the possibility of protracted hypertension in sensitized animals has been demonstrated [10]. At the same time, other work has shown that the allergic component lowers the rise in arterial blood pressure produced experimentally [9] or leaves it unchanged [3]. The contradiction between these results, it can tentatively be suggested, is due to some extent to the fact that the vascular tone was assessed by these workers indirectly.

It was accordingly decided to undertake the present investigation in order to compare the level of vascular tone under conditions of sensitization and alimentary atherosclerosis, with the aim of elucidating the role of the allergic component in the changes in vascular reactions in atherosclerosis.

Some indices of lipid metabolism were determined in parallel tests on the animals of all groups.

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