Ultraviolet Irradiation of Cerebrospinal Fluid Stimulates Compensatory Processes in Cats with a Unilaterally Damaged Central Nervous System

B. G. Perelygin, V. V. Dulinets, M. A. Danilovskii, and G. A. Vartanyan

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Portions of cerebrospinal fluid (CSF) withdrawn from cats operated upon for unilateral removal of the motor neocortex were exposed to ultraviolet (UV) radiation and then returned to the cats to evaluate the effects of irradiation on the recovery of voluntary movements by the affected limb and the activity of CSF peptide and protein neurohumoral factors during the postoperative period. The exposure of CSF to UV radiation substantially accelerated compensatory processes (the recovery of motor functions) in the animals and activated the biosynthesis of neurohumoral factors.

Key Words: *central nervous system; ultraviolet radiation; cerebrospinal fluid; motor disorders*

As demonstrated in numerous studies, peptide factors displaying lateral tropism to motor centers of the spinal cord and activating their activity appear in the central nervous system early in the course of compensatory processes that develop after unilateral injuries to the motor analyzer [3]. Subsequently these factors lose their activity by forming complexes with the emerging high-molecular protein factors (binding factors), some of which are immunoglobulins [4]. Attempts to stimulate compensatory processes by administering peptide factors or immunomodulators during the acute posttraumatic period have produced encouraging results [5,7]. Continuing the quest for agents capable of stimulating compensatory processes should undoubtedly be on the list of research priorities.

In this study, cerebrospinal fluid (CSF) withdrawn from cats operated upon for unilateral removal of the motor neocortex was exposed to ultraviolet (UV) radiation and then returned to the cats to evaluate the effects of CSF irradiation on the recovery of voluntary movements by the affected limb and the activity of CSF peptide and protein factors during the postoperative period.

I. P. Pavlov Medical Institute; Institute of Experimental Medicine, St. Petersburg

MATERIALS AND METHODS

In 9 male cats, the cortical representation of the right hind limb (motor neocortex) was removed as previously described [1], after which CSF was collected from an occipital cistern (approximately 0.5 ml per kg body weight) and exposed for 2 min to UV radiation predominantly of 254 nm in a quartz cuvette 10 cm^2 in area, the radiation flux density being 2 mW/cm^2; the CSF was then returned to the animal. The irradiation procedure was repeated on postoperative days 3, 5, and 8. The control group consisted of 6 male cats that differed from the test animals only in that their CSF was not irradiated after being placed in a cuvette for 2 min. In both groups, CSF samples were taken from the occipital cistern on days 3, 5, 8, 11, 14, 17, and 21 to determine the activity of peptide and protein factors. In view of the species nonspecificity of the neurohumoral factors under study [2], CSF from operated cats was tested for its ability to induce postural asymmetry in recipient rats before and after heat

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TABLE 1. Recovery of Motor Functions in Cats after Unilateral Removal of the Motor Neocortex and Extracorporeal Exposure of Their Cerebrospinal Fluid to UV Radiation

Behavioral test	Days after start of functional recovery			
	test group		control group	
	50%	100%	50%	100%
1	3	5	8	14
2	8	14	12	19
3	5	7	15	21

Note. 50% and 100% are the percentages of cats able to cope with the respective tests.

treatment (exposure to 100°C for 15 min). Such treatment inactivates the binding (protein) factor(s) while mobilizing the activity of peptide factors so that its measurement can provide an estimate of binding factor activity [2,6]. The activity of peptide factors responsible for postural asymmetry (postural asymmetry factors, PAF) was expressed as the number of minimal active doses contained in 50 μl of CSF and determined by 10 consecutive dilutions with physiological saline of the material under study [5].

The affected limb was observed daily for recovery of motor activity, with evaluation of the cat's ability to restore the natural position of the limb contralateral to the side of brain damage (after moving the limb by the experimenter forward, backward, rightward, and leftward) and to use this limb in walking (Test 1), rearing up with or without the support of the forepaws (Test 2), and jumping on a chair or table (Test 3).

RESULTS

Cats of the control group did not stand up during the first 2 postoperative days and made no attempts to correct the unnatural position of the affected (right hind) leg. On days 3-5 they were standing and moving predominantly on the three healthy limbs and made no attempts to rear up so as to get access to the food presented to them. On day 8 they began using the affected limb when walking but its movements were not coordinated. Moving this limb sideward, forward, or backward by the experimenter elicited no response directed at normalizing the posture. Although the animals attempted to rise up on the hind legs with the help of the forepaws, they invariably fell on the side contralateral to the brain damage. On day 14 the cats performed Tests 1 and 2 well, except that they were still unable to rear up without the support of the forelegs. By day 21, the cats successfully performed all three tests (Table 1).

The test cats also failed to stand up during the first 2 days, but, unlike the controls, used all four legs in walking on days 3-5. The coordination of leg movements was more or less satisfactory and responses directed to normalize the posture were elicitable by moving the affected leg in any direction, although the response latency remained increased in those days. Attempts to rise up on the hind legs without the support of the forepaws resulted in the animal falling on the side contralateral to the brain

TABLE 2. Activity of Postural Asymmetry Factors (PAF) in UV-Exposed Cerebrospinal Fluids from Cats with Unilaterally Removed Motor Neocortex

Days after operation	PAF activity			
	in CSF of the test group		in CSF of the control group	
	before heat treatment	after heat treatment	before heat treatment	after heat treatment
3	-	10^4	5	5
5	-	10^4	10	10
8	-	5×10^3	10	10^2
11	-	10^3	5	10^2
14	-	10^3	-	10^3
17	-	10^3	-	10^4
21	-	10^3	-	10^3

Note. PAF activity is expressed as the number of minimal active doses contained in 50 μl of CSF.

damage. On days 8-14 the cats were able to rear up without the use of farepaws. They began jumping freely on the chair by days 5-7 (Table 2).

As can be seen from the above, motor functions were most impaired in the first 8 postoperative days in the control group and in the first 3 days in the test group and had returned toward normal by day 14 in the latter group, i.e., UV irradiation of the CSF resulted in a considerably accelerated recovery of motor functions as assessed by the three tests.

Tests of heat-unexposed CSF samples from the control cats showed the presence of PAF already on day 3; these factors had their highest activity on days 5-8 and had been completely inactivated by day 14 (Table 2). The activity of CSF samples subjected to heat treatment (which inactivated the binding factor) did not differ from that of untreated samples on days 3-5 but rose sharply later to reach its peak on day 17 (when it was 10 times higher than the highest activity in the untreated samples), followed by some decline on day 21.

In the test group, PAF activity in CSF samples was not detectable on the days when it was tested, even on day 3 (Table 2). In contrast, the heat-treated CSF samples showed markedly elevated PAF activities on days 3-11 as compared to the control group. This indicates that the binding factor(s) appeared in the UV-exposed CSF shortly after irradiation.

Analysis of the findings from this study revealed an association between the degree to which motor functions were impaired, on the one hand, and PAF activity in the CSF, on the other. Thus, this activity was higher when motor disorders were at their peak (cats were unable to move on the four paws and did not respond to forced movements of the affected limb) than when motor functions began to recover. The decline in PAF activity was due to the inactivating action of the thermolabile binding factor(s).

The binding factor(s), whose activity was estimated by the difference in PAF activities before and after heat treatment of CSF, was active by day 3 in the test group but only by day 8 in the control group, and it emerged in the CSF at the time when voluntary movements of the affected limb began to be restored.

In summary, the present study indicates that one mechanism by which exposure of CSF to UV radiation promotes the correction of motor deficit may be a modulating influence exerted by this radiation on the biogenesis of both the PAF and binding factor(s). Although the contribution of photochemical changes in plasma and CSF proteins to the therapeutic effect from UV irradiation has not been ascertained [8], the prospects for clinical use of UV radiation are undoubtedly good.

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