Effect of Interferon on the Development of Parkinsonism Induced by the Administration of 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine (MPTP) in C57Bl/6 Mice

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The administration of reaferon, a recombinant α-interferon preparation, hampers the development of parkinsonism caused by MPTP administration in C57Bl/6 mice.

Key Words: *MPTP; parkinsonism; reaferon*

Immunological processes have been found to play an important role in the mechanisms of development of parkinsonism caused by MPTP administration, as was established previously in experiments in C57Bl/6 mice. It was shown that adoptive transfer of lymphocytes from mice with pronounced parkinsonian symptoms to healthy mice caused the main parkinsonian symptom, oligokinesia, to develop in the latter [3]. In view of the fact that lymphokines are regulators of the immune system, a study of their effect on the development and course of parkinsonism is of undoubted interest. One of these immunoregulatory lymphokines, α-interferon, participates in the modification of different immune reactions. It regulates the immune response, inhibits its antibody production, and boosts the activity of natural killers [4]. In addition, the recently discovered neurotropic activity of α-interferon is now being actively studied [5]. Data have been obtained indicating that a-interferon can modify the effect of administered substances by directly interacting with opiate receptors [1,6]. These properties of α-interferon underlie the assumption that it may prevent the development of parkinsonism. In the present study the effect of reaferon (RF), a recombinant α-interferon preparation, on the origin and development of parkinsonian symptoms caused by systemic administration of MPTP was studied in C57Bl/6 mice.

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MATERIALS AND METHODS

Experiments were carried out on male C57Bl/6 mice aged 10 months weighing initially 25-30 g. Parkinsonism was simulated by administration of the neurotoxin MPTP [7]. Immediately before the experiment MPTP was dissolved in physiological saline and then injected into animals at 20 mg/kg body weight twice a day at 12-hour intervals during 6 days.

Manifestation of the main parkinsonian symptoms, namely of oligokinesia and muscle rigidity, indicated the presence and characterized the development of parkinsonism. Oligokinesia was assessed from 3-min locomotor activity of animals in an automated test using AutoTrack software in the Opto-Varimex system (Columbus Instruments). Muscle rigidity, displayed in a decrease of the neck — to-tail linear measurement, was assessed in points (1-3). In addition, the speed of movement (in cm/sec) was calculated on the basis of the distance covered and the time of movement. The locomotor activity was recorded twice: before MPTP adminis-

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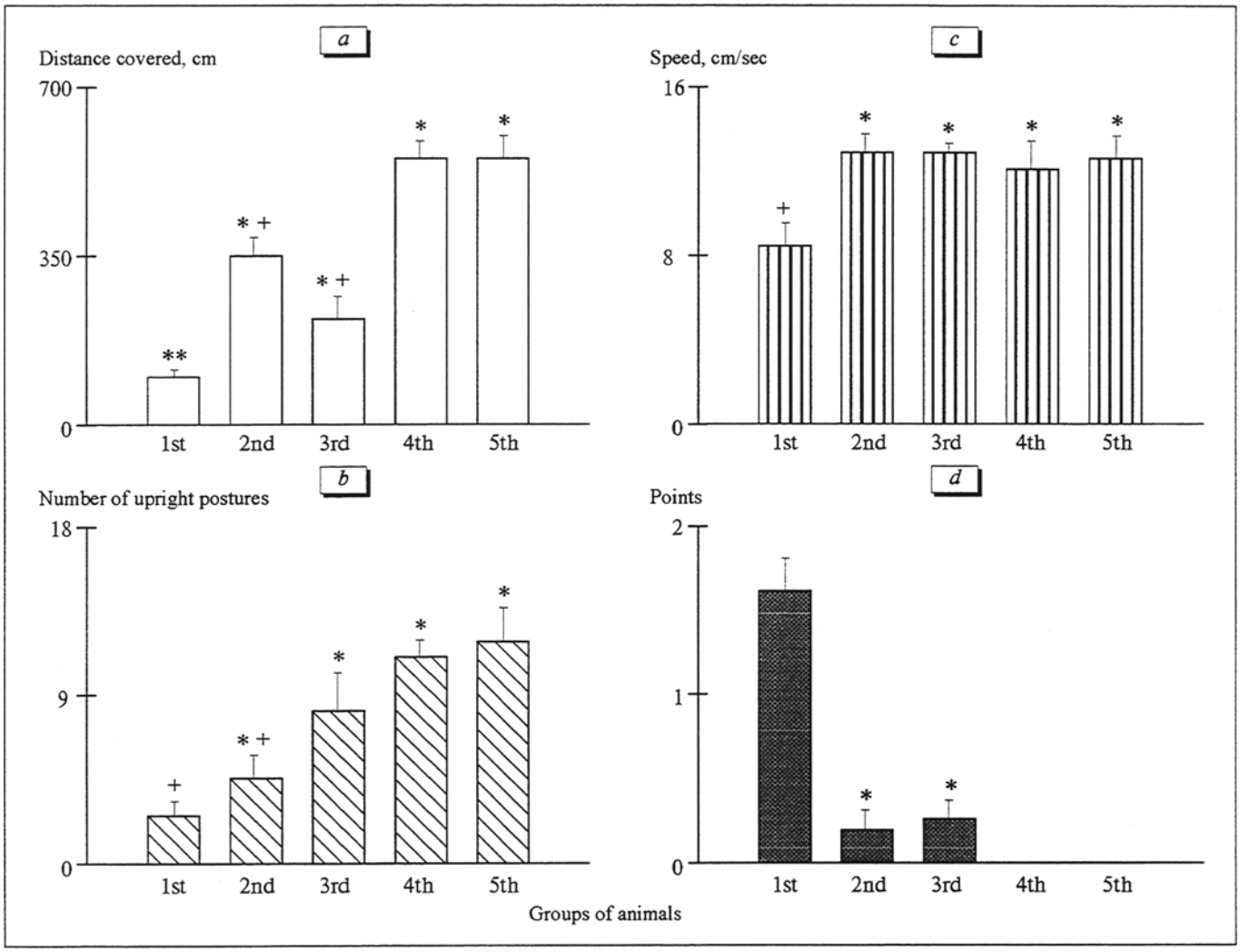

Fig. 1. Effect of reaferon on parkinsonian symptoms caused by MPTP administration in C57Bl/6 mice. *a*) horizontal motor activity; *b*) vertical motor activity; *c*) speed of movement in open field; *d*) muscle rigidity. $p<0.01$: *as compared to the 1st group; +as compared to the 5th group.

tration and 6 days after neurotoxin treatment according to the indicated scheme.

The experimental mice were divided into 5 groups. The 1st group was treated with MPTP for 6 days. The 2nd group received RF for 3 days at 150 IU/g i.p. [6] and then MPTP for 6 days (the group with RF pretreatment). Animals of the 3rd group were injected RF at the same dose 2 h after MPTP administration for 3 days and for the next 3 days treated with MPTP alone (the group with synchronous administration of RF). The 4th and 5th groups were controls, with a 3-day administration of RF at 150 IU/g in the 4th group and 6-day injection of physiological saline in the 5th group. Physiological saline and RF were administered to the test and control animals in a volume of 0.2 ml.

MPTP (Research Institute of Pharmacology, Russian Academy of Medical Sciences) and RF (Sanitas, Lithuania) were used in the study.

The results were processed statistically with the Student *t* test.

RESULTS

The findings are given in Fig. 1. Six days after the start of MPTP administration, C57Bl/6 mice manifested marked parkinsonian symptoms such as oligokinesia, bradykinesia, and muscle rigidity. Both horizontal (distance crossed) and vertical (the number of upright postures) motor activity were significantly lowered and the speed of movement in the open field was reduced. Muscle rigidity comprised on average 1.5-2 points.

The development of oligokinesia and muscle rigidity was substantially decreased in the groups with RF pretreatment or synchronous administration. Muscle rigidity was noted in 20% of animals and did not exceed 1 point. Horizontal and vertical

motor activity in RF-treated mice was higher as compared with only MPTP-treated animals, but did not attain the values of the control group administered physiological saline. The speed of movement in the open field in RF-treated mice did not slacken and was the same as the control values.

Reaferon administration to intact animals did not cause any changes in horizontal and vertical motor activity or in the speed of movement in the open field.

Thus, it may be assumed that preliminary or synchronous administration of RF, a preparation of α-recombinant interferon, with MPTP results in less pronounced parkinsonian manifestations in C57Bl/6 mice. RF had the greatest effect on muscle rigidity and also prevented the slowing of open-field movement (probably reflecting a weakening of bradykinesia). Horizontal and vertical motor activity increased but did not reach the control level with RF administration. The effect of RF on the development of MPTP-induced parkinsonism may be related both to the immunoregulatory properties of α-interferon and to its neurotropic activity. It was noted previously that anti-dopamine antibodies can have a damaging effect and cause the development of parkinsonism when injected in the caudate nucleus [2]. Probably, α-interferon inhibits the production of antibodies against dopamine, the level of which is elevated in parkinsonism, and thereby discourages the development of parkinsonism. α-Interferon may also act upon parkinsonian manifestations via the opiate system.

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