ROLE OF CHOLINERGIC STRUCTURES IN DISTURBANCES OF CEREBELLAR FUNCTION DURING EXPOSURE TO CENTRIPETAL ACCELERATION

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Experiments on rats showed that injection of atropine (2.5 mg/kg) or gangleron* (7.5 mg/kg) 30 min before spinning animals on a centrifuge prevents the depression of evoked activity of the cerebellar cortex developing during exposure to acceleration. Meanwhile injection of atropine has no effect on inhibition of evoked activity of the cerebellar cortex due to high-frequency stimulation of the mesencephalic reticular formation. It is postulated that the normalizing effect of cholinolytics on evoked potential generation in the cerebellar cortex during exposure to radial acceleration is due to blocking of intercerebellar cholinergic mechanisms.

Exposure to centripetal acceleration causes a disturbance of the receptive function of the cerebellum, as is shown by the sharp decrease in the electrical response of its cortex to peripheral stimulation [3, 4]. An important mechanism of the action of overloading on the central nervous system, especially in the case of radial acceleration, is an excess of incoming afferent impulses [2, 8, 10]. Chlorpromazine, which has adrenolytic properties, does not prevent the inhibition of evoked cerebellar cortical activity during exposure to acceleration, but at the same time it substantially reduces the inhibitory effects of high-frequency stimulation of the mesencephalic reticular formation and hypothalamus [5, 6]. These facts for practical purposes eliminate the question of the determining role both of the nonspecific structures of the rostral portions of the brain stem and of other central adrenergic structures in reducing the excitability of the cerebellar cortical afferent systems during exposure to acceleration.

In the investigation described below the role of cholinergic structures in the development of this phenomenon was investigated. The drugs atropine, with mainly muscarine-like cholinolytic action, and gangleron, blocking mainly nicotine-like cholinergic structures, were used.

EXPERIMENTAL METHOD

Experiments were carried out on 120 albino rats anesthetized with nembutal (40 mg/kg, intraperitoneally). The animals were exposed to radial acceleration (along the spine – chest axis) of a magnitude of 10 g for 4 min on a turn-table with radius of rotation 4.2 m. The drugs were injected intraperitoneally 30 min before the beginning of spinning: atropine in a dose of 2.5 mg/kg as the 0.1% solution, gangleron in a dose of 7.5 mg/kg as the 0.15% solution. Before, during, and after spinning the electrical responses of the

*1,2-dimethyl-3-diethylaminopropyl-p-isobutoxybenzoate hydrochloride.

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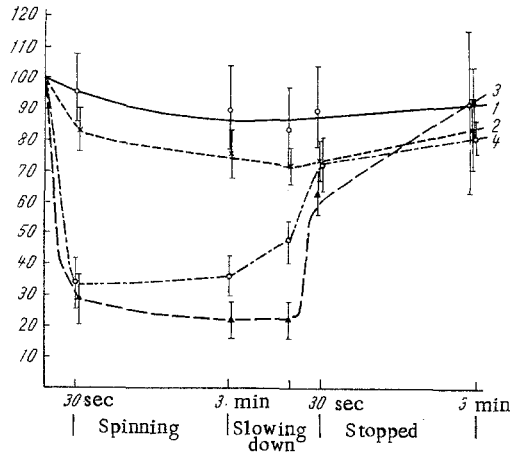

Fig. 1

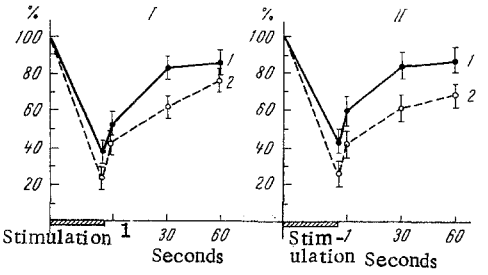

Fig. 2

Fig. 1. Changes in amplitude of cerebellar cortical evoked potentials during exposure to acceleration of 10 g. Here and in Fig. 2, abscissa: time of recording; ordinate: amplitude (in percent of initial value); 1) after injection of atropine; 2) after injection of gangleron; 3) after injection of chlorpromazine; 4) control.

Fig. 2. Change in amplitude of cerebellar cortical evoked potentials during stimulation of the mesencephalic reticular formation: I) before injection of atropine; II) after injection of atropine; 1) stimulation 5 V; 2) stimulation 10 V.

TABLE 1. Amplitude (in μV) of Evoked Potentials of Cerebellar Cortex Before and After Injection of Cholinolytics (M ± m)

Drug	No. of rats	Before injection of drug	15 min after injection of drug
Atropine	26	167.8 ± 10.6	173.7 ± 9.7
Gangleron	12	153.1 ± 8.0	163.1 ± 9.3

cerebellar cortex of the rats to maximal stimulation of the sciatic nerve were recorded. The ipsilateral nerve was stimulated by single square pulses (0.5 msec) from a type MSE-3R Nihon Kohden electronic stimulator with isolation unit at its output. For unipolar recording of evoked potentials from the anterior portions of the vermis cerebelli a steel needle was introduced through the occipital bone and the potentials were recorded on a VC-6 Nihon Kohden oscilloscope. For analysis of the results the amplitude of the two chief phases of the potential were measured together from peak to peak. The mesencephalic reticular formation was stimulated by a bipolar method through buried nichrome electrodes (diameter of tip 0.1 mm, interelectrode distance 1 mm) with square pulses (0.1 msec, 300/sec, 5 and 10 V, 30 sec). Evoked potentials of the cerebellar cortex were recorded before, during, and 1 min after stimulation.

EXPERIMENTAL RESULTS

Injection of atropine and gangleron did not affect the amplitude of the cerebellar cortical potential evoked by sciatic nerve stimulation (Table 1).

The results obtained by administration of cholinolytics and exposure to acceleration are shown in Fig. 1. In the control rats, which did not receive the drugs before spinning, during exposure to acceleration of 10 g the amplitude of the cerebellar cortical evoked potential was reduced to 34.1-35.0% of its initial value, and it gradually recovered after slowing down of the turntable. The effect of acceleration was slightly increased after injection of chlorpromazine (10 mg/kg). The amplitude of the cerebellar cortical evoked potential after spinning for 3 min and during the slowing down period was 20.8-21.4% of its initial level ($P < 0.05$). In the rats receiving gangleron the effect of acceleration was much weaker: the amplitude of the responses was reduced during exposure only to 82.9-75.5%. After injection of atropine, inhibition of the cerebellar cortical evoked potentials during exposure to acceleration was virtually absent: the amplitude

TABLE 2. Frequency of Facilitation of Cerebellar Cortical Evoked Potentials (in percent) During Exposure to Acceleration of 10 g

Group of animals	No. of animals	Period of investigation		
		spinning	slowing down	stopped
Control	18	5.3	5.3	27.7
Receiving atropine	13	38.4	22.2	46.1

of the responses was 95.0-87.9% of its initial level. During spinning and slowing down of the turntable the effects of acceleration in the animals receiving the cholinolytics were significantly different from those in the control ($P < 0.02$).

Analysis of the individual data shows that weakening of the acceleration effect after administration of the cholinolytics was due not only to a decrease in or removal of the inhibitory action, but also to the development of facilitation effects. This last factor is particularly characteristic of atropine. In the control rats the increase in amplitude of the cerebellar cortical evoked potentials during exposure to acceleration was observed extremely rarely, and in the after-period the recovery of evoked activity took place in about one-third of all the animals with a phase of exaltation. As Table 2 shows, in the rats receiving atropine the frequency of the facilitatory effects increased by more than seven times during spinning, by four times during slowing down of the turntable, and by 1.6 times in the after-period compared with the control. This special feature distinguishing the effect of atropine also explains the high value of m (Fig. 1) compared with the value of this parameter in the other series of experiments.

The results in Table 2 show that blocking of the cholinergic synapses abolished the inhibitory effect of acceleration on the cerebellar cortical afferent systems. The localization of the cholinergic structures responsible for this phenomenon is an extremely difficult problem. In a special series of experiments the effect of atropine on inhibition of the cerebellar cortical evoked potentials arising during high-frequency stimulation of the mesencephalic reticular formation was studied. Preliminary injection of atropine in a dose abolishing the acceleration effect did not alter the effect of high-frequency stimulation of the mesencephalic reticular formation (Fig. 2). Both before and after injection of atropine stimulation of the mesencephalon led to marked inhibition of cerebellar cortical evoked activity.

This neurochemical analysis of two outwardly similar phenomena of inhibition of cerebellar cortical evoked activity during high-frequency mesencephalic stimulation and during exposure to acceleration thus indicates that they differ in nature. The nonspecific reticular effects on the cerebellar cortex are evidently based on adrenergic mechanisms, as is shown by the blocking effect of chlorpromazine [6] and the ineffectiveness of atropine. During exposure to acceleration the opposite picture is observed: injection of atropine or gangleron prevents inhibition of cerebellar evoked activity, while injection of chlorpromazine potentiates it slightly. It can be postulated that the normalizing effect of the cholinolytics on the generation of cerebellar cortical evoked potentials during exposure to acceleration is due to blocking of intercerebellar cholinergic mechanisms possibly belonging to the system of inhibitory interneurons. All the elements of the cholinergic mediator system – acetylcholine, cholinesterase, and choline-acetylase [1, 7, 9, 11, 12, 14, 16, 17] – are found in the cerebellar cortex, especially in the granular layer, and both muscarine-like and nicotine-like cholinergic neurons have been detected there [13, 15, 18]. Cholinergic properties have been ascribed with the greatest probability to individual groups of mossy fibers and to Golgi cells [12, 13, 17].

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