edema test showed that it causes not only edema, but also death of the animals. After injection of LPS in a dose of 4 μg the animals did not die, and the extent of edema of the paws was similar to its extent after injection of an equal dose of heated enterotoxin concentrate. LPS in a dose of 0.04 μg produced no appreciable paw edema. Considering that the content of LPS in the enterotoxin concentrate does not exceed 1% and that this amount does not cause edema of the paws, it can be concluded that the activity of the heated enterotoxin concentrate is in fact attributable entirely to the presence of thermostable toxin.

The mouse paw edema method can therefore detect activity of both the thermolabile and the thermostable enterotoxins of E. coli.

To this it must be added that the mouse paw edema test is simple, reproducible, and sensitive.

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STUDY OF COMPENSATION AFTER UNILATERAL LOSS OF VESTIBULAR FUNCTION

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The dynamics of compensation of the after-effects of unilateral destruction of the labyrinth was studied in rabbits. Destruction of the labyrinth was followed by nystagmus, an increase in the external respiration and heart rates, and EEG activation. The investigations revealed differences in the rate of extinction of these reactions with time. In the late stages after labyrinthectomy marked asymmetry of the nystagmic response of the eyes to angular accelerations of equal intensity but opposite direction was observed. Stimulation of the intact otolith apparatus was accompanied by the appearance of positional nystagmus. The results point to imperfection of the mechanisms of compensation after total unilateral loss of vestibular function.

KEY WORDS: vestibular system; deprivational and positional nystagmus; compensation of disturbed functions.

Clinical observations and experimental investigations on animals of different species have shown that a whole series of sensory, motor, and autonomic disorders develops after trauma to or surgical removal of one

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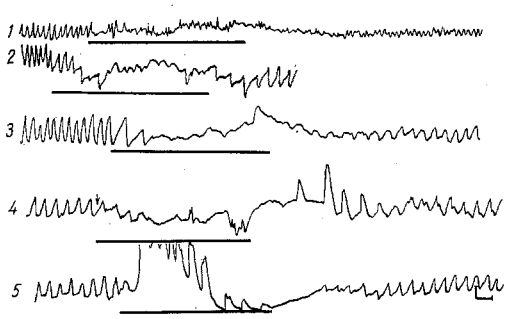

Fig. 1. Effect of horizontal negative angular accelerations of 40 deg/sec^2 on deprivational nystagmus in a rabbit at various times after destruction of right labyrinth: 1) increase in frequency of deprivational nystagmus in response to negative angular acceleration in clockwise direction (45th minute); 2, 3, 4, 5) inhibition of deprivational nystagmus and appearance of reversed nystagmic jerks in response to negative angular acceleration in the anticlockwise direction 50 min and 4, 8, and 16 h after labyrinthectomy. Bold straight lines below curves show duration of acceleration. Calibration: 1 sec, 100 μV.

labyrinth. With time these disorders gradually subside and partly disappear through the development of central regulatory processes of compensation [3, 6, 10, 11]. Meanwhile, the principles governing the development of compensation, especially during the first day when the after-effects of unilateral labyrinthectomy are most substantially weakened, have been inadequately studied and data in the literature concerning the stability of the resulting compensation are contradictory [3, 5, 8].

The object of this investigation was to study the dynamics of compensation of various responses arising after destruction of one labyrinth and to assess the degree of compensation during stimulation of the intact labyrinth.

EXPERIMENTAL METHOD

Experiments were carried out on 12 adult waking rabbits of the same sex. The labyrinth (usually the right) was stimulated mechanically through the cavity of the middle ear under local anesthesia. The completeness of exclusion of the labyrinth was verified by morphological investigation of the side of the operation after the animals were killed. As responses to be used for analysis and quantitative determination of the compensatory processes, nystagmic eye movements, the blood pressure, and the external respiration and heart rates were recorded [2]. During the experiments the animals were fixed in a natural posture by means of a special device. Before and after labyrinthectomy they were subjected to cupular and otolithic stimulation. In the first case the animals were placed on the platform of a turntable so that their head was at the center of rotation at an angle of 40-45° to the horizontal plane for stimulation of the horizontal semicircular canals. Rotations were trapezoidal in shape (speed of rotation 360 deg/sec, angular acceleration 40 deg/sec^2) and were either clockwise or anticlockwise. Postrotational nystagmus was recorded. To stimulate the otoliths the animals were rotated around the longitudinal body axis through 90°, and were kept in that position for up to 1 h. The experiments were carried out in darkness. All the physiological parameters were recorded on the Elema–Schonander Mingograph before labyrinthectomy, immediately after the operation, and then every 15 min for the first 2-3 h, and subsequently at hourly intervals for several days.

EXPERIMENTAL RESULTS

Immediately after labyrinthectomy nystagmic eye movements in the direction of the intact labyrinth began. The initial frequency of the deprivational nystagmus averaged 3.5 ± 0.24 jerks/sec. The response weak-

TABLE 1. Number of Nystagmic Jerks in Rabbits in Response to Negative Horizontal Angular Acceleration of 40 deg/sec^2 at Different Times after Right-Sided Labyrinthectomy and before the Operation (M ± m)

Time of examination	Total number of nystagmic jerks	
	rotation to the right	rotation to the left
Before labyrinthectomy	89,9±7,8	84,2±8,0
After labyrinthectomy		
0,5 months	42,0±5,1	9,1±1,1
12 "	51,2±5,8	15,0±1,5
24 "	65,9±7,6	19,1±2,0

TABLE 2. Frequency of Positional Nystagmus in Rabbits during Rotations to the Left through 90° at Various Times after Right-Sided Labyrinthectomy (M ± m)

Time of examination, months	Frequency of positional nystagmus (in jerks/sec) during rotations of different duration		
	1 min	30 min	1 h
0,5	2,0±0,4	1,5±0,3	0,4±0,1
3	2,0±0,5	1,3±0,4	0,3±0,09
8	1,8±0,3	0,6±0,1	0,3±0,1
12	2,2±0,4	0,5±0,2	0,4±0,2

ened in accordance with a definite rule: During the first 6-7 h the frequency of the deprivational nystagmus fell by half. A statistically significant change was observed at the 75th minute after labyrinthectomy (2.7 ± 0.23 jerks/sec; $P < 0.05$). For many hours the response then remained at virtually the same level, with slight fluctuations. Further weakening of the response began after 22 h, but this followed a much slower and more uniform course, so that after 48-70 h the deprivational nystagmus had usually disappeared.

Unilateral destruction of the labyrinth caused a sharp increase in the respiration rate: on average from 59.7 ± 9.8/min before labyrinthectomy to 124.3 ± 14.0/min 15 min after labyrinthectomy ($P < 0.05$). The respiration rate fell after 1 h to 80.5 ± 12.3/min and the original pattern of the pneumogram was restored after 6 h. Next day the respiration rate was a little slower. The heart rate of the intact rabbits at rest averaged 254.0 ± 11.9 beats/min. Destruction of the labyrinth was followed by an increase in the heart rate. The maximal response was observed 30 min after labyrinthectomy (294 ± 15.6 beats/min). Toward the end of the first day the heart rate fell almost to its initial level. Destruction of the labyrinth also was followed by a fall of the blood pressure on average by 15 mm Hg, returing to normal after 3 h. Significant changes also were observed in the EEG. In cortical derivations from both hemispheres potentials were recorded with a frequency of 4-6 waves/sec and an amplitude of 50-80 μV. This picutre of EEG activation was observed for a long time and the normal EEG usually was restored on the 3rd day after labyrinthectomy.

Negative angular accelerations during clockwise rotations (i.e., toward the side of labyrinthectomy) as a rule led to intensification of the deprivational nystagmus. Slowing of anticlockwise rotation, on the other hand, depending on the time elapsing after labyrinthectomy, was accompanied by a reduction in the frequency or complete suppression of the deprivational nystagmus or the appearance of nystagmus in the opposite direction. For instance, 1 h after destruction of the right labyrinth, in response to negative anticlockwise acceleration the frequency of the nystagmus fell sharply, the slow phase of individual nystagmic jerks was appreciably lengthened, and the nystagmus then disappeared completely for 4-6 sec. The response after 4 h to the same accelerations was different: Not only was the deprivational nystagmus completely inhibited, but a single nystagmic jerk whose fast phase was opposite to that of the deprivational nystagmus and was directed toward the side of labyrinthectomy, appeared. After 8 h several (up to 5) reversed nystagmic jerks had developed, and after 16 h their number increased to 8-10 (Fig. 1). In the late stages after labyrinthectomy distinct asymmetry of the postrotational

nystagmus was observed during right- and left-sided rotations. The response to negative anticlockwise acceleration was only 1/3-1/5 as strong as the response to clockwise rotation. With time, some increase in the strength of postrotational nystagmus was observed in response to rotation in both directions, but marked asymmetry persisted throughout the period of investigation (Table 1). It must be emphasized that throughout 2 years of observation, the head of all the experimental animals remained distinctly rotated toward the side of labyrinthectomy, and the eyes remained deviated.

Rotations around the longitudinal body axis toward the intact labyrinth as a rule were accompanied by the appearance of positional nystagmus. As Table 2 shows, positional nystagmus developed at all stages of the investigations. It was always directed toward the intact labyrinth, and during long rotations a well-marked decrease in its frequency was observed. Rotations to the right, i.e., toward the side of labyrinthectomy, did not cause nystagmic eye movements. In normal animals with intact labyrinths, during rotations around the longitudinal body axis, as a rule nystagmus was absent and only a response of counterrotation of the eyes was observed.

Evocation of responses after unilateral loss of vestibular function is based on the Högyes–Bekhterev balanced centers principle and the compensatory processes are directed toward restoration of the background unit activity of the vestibular nuclei on the deafferented side [1, 7, 9, 12]. The mechanisms of this phenomenon are not clear. Restoration of activity may take place both as a result of an increase in the sensitivity of the vestibular neurons, deprived of their principal input, to other sources of impulsation and as a result of the formation of new synaptic connections. The sudden extinction of deprivational nystagmus during the first few hours and the appearance of reversed nystagmic jerks in response to stimulation of the intact labyrinth 4 h after unilateral labyrinthectomy indicate the very rapid onset of plastic changes in the structures of the vestibular system. The rate of development of compensatory processes differed for different responses to destruction of the labyrinth. Changes in the RNA content and succinate oxidase activity in neurons of the vestibular nuclei and cerebellum after unilateral labyrinthectomy in animals are manifestations of plastic changes [4]. However, these changes evidently did not lead to complete restoration of equilibrium between the activity of the vestibular nuclei on both sides. Evidence in support of this conclusion is given by the asymmetry of the nystagmic response of the eyes constantly observed to stimulation of the horizontal semicircular canal of the intact labyrinth by angular accelerations of equal intensity, but opposite direction, and the appearance of positional nystagmus in response to stimulation of the intact otolith apparatus, and also the persistence of distinct deviation of the eyes and rotation of the head for a long period after labyrinthectomy. The results are evidence of the fragility and imperfection of the compensatory mechanisms after unilateral loss of vestibular function.

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