

N O T I C E

THIS DOCUMENT HAS BEEN REPRODUCED FROM
MICROFICHE. ALTHOUGH IT IS RECOGNIZED THAT
CERTAIN PORTIONS ARE ILLEGIBLE, IT IS BEING RELEASED
IN THE INTEREST OF MAKING AVAILABLE AS MUCH
INFORMATION AS POSSIBLE

EFFECT OF MEPROBAMATE ON THE VESTIBULO-
SENSORY AND VESTIBULAR SOMATIC REACTION

N.V. Khinchikashvili

Translation of "Vliyaniye priyema
meprobamata na vestibulo-sensornuyu
i vestibulo-somaticheskiye reaktsii".
Fiziologicheskiy Zhurnal, Vol. 25,
No. 5, 1979, pp 507-512



NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON D.C. 20546 MARCH 1980

(NASA-TM-76104) EFFECT OF MEPROBAMATE ON
THE VESTIBULOSENSORY AND VESTIBULAR SOMATIC
REACTION (National Aeronautics and Space
Administration) 13 p HC A02/MF A01 CSCL 06P

N81-22683

Unclas
G3/52 21895

STANDARD TITLE PAGE

| | | | |
|---|--|---|-----|
| 1. Report No. NASA TM 76104 | 2. Government Accession No. | 3. Recipient's Catalog No. | |
| 4. Title and Subtitle EFFECT OF MEPROBAMATE ON THE VESTIBULO-SENSORY AND VESTIBULAR SOMATIC REACTION | | 5. Report Date MARCH 1980 | |
| | | 6. Performing Organization Code | |
| 7. Author(s) N.V. Khinchikashvili | | 8. Performing Organization Report No. | |
| | | 10. Work Unit No. | |
| 9. Performing Organization Name and Address SCITRAN Box 5456 Santa Barbara, CA 93108 | | 11. Contract or Grant No. NASW-3198 | |
| | | 13. Type of Report and Period Covered Translation | |
| 12. Sponsoring Agency Name and Address National Aeronautics and Space Administration Washington, D.C. 20546 | | 14. Sponsoring Agency Code | |
| | | 15. Supplementary Notes Translation of "Vliyaniye priyema meprobamata na vestibulo-sensornuyu i vestibulo-somaticheskiye reaktsii". Fiziologicheskii Zhurnal, Vol. 25, No. 5, 1979, pp 507-512 | |
| 16. Abstract The influence of meprobamate on the vestibular illusion of counter-rotation, movement coordination and "vertical writing" was investigated by a "double blind trial" method and placebo. The obtained results confirm the possibility of the meprobamate application for prophylaxis and correction of vestibular disturbances. | | | |
| 17. Key Words (Selected by Author(s)) | | 18. Distribution Statement This copyrighted Soviet work is reproduced and sold by NTIS under license from VAAP, Soviet copyright agency. No further copying is permitted without permission from VAAP. | |
| 19. Security Classif. (of this report) Unclassified | 20. Security Classif. (of this page) Unclassified | 21. No. of Pages 12 | 22. |

UDC 612.886:615.214.22

EFFECT OF MEPROBAMATE ON THE VESTIBULO-SENSORY AND VESTIBULAR SOMATIC REACTION

By N. V. Khinchikashvili*

The question of illusory reactions and disorders in motor coordination of /507** vestibular origin acquires urgency as a consequence of the increase in the role of intellectual, sensory and sensomotor operations, especially in occupations linked to transportation. Illusory sensations are the sensory component of vestibular sequential reactions reflecting the "internal neurodynamics" of the vestibular function and participating in the general function of perception of space [13]. This function includes also the level of statokinetic stability, also closely linked to the functional state of the vestibular analyzer [3,12]. Distortion of perception of spatial position and disruption in coordination of human voluntary movement drastically impairs the control of the means of motion [30]. Therefore study of the illusory (of vestibular origin) and vestibulo-motor reactions, as well as search for pharmacological methods of suppressing them currently acquire great importance.

It has been established that the directed effect on the emotional sphere by prescribing tranquilizers can increase the human performance capacity [4,7,15,24].

*Department of Otorhinolaryngology and Pharmacology of Odessa Medical Institute.

**Numbers in margin indicate pagination in original foreign text.

The works of many researchers have covered an extensive and comprehensive study of the mechanisms for the effect and influence of tranquilizers (including meprobamate) on different functions of the organism. Good endurance and absence of side effects and the depressing effect of therapeutic doses of tranquilizers (including meprobamate) on the psychic and psychomotor reactions are practically important [2,6,26,27]. This justifies the interest in studying the effect of tranquilizers on the vestibular reactions.

We studied the effect of a number of different tranquilizers on the vestibulo-spinal reflexes occurring during centrifuging of albino mice. Here it was found that the duration and degree of pronouncement of these reflexes are lowest in animals treated with meprobamate. This also determined the selection of the preparation for this study.

Technique of Studies

Eighty-three men of the flight staff in age from 21 to 30 were under observation. The medical commission concluded that all of them were practically healthy, including in an otorhinolaryngological respect, and possessed high vestibular stability. To exclude the phenomena of training and from a more objective evaluation of the effect of the preparation, the subjects were divided into three groups, each of which participated only in one series of observations. The effect of meprobamate on the vestibulo-sensory reaction was studied in 33 people (first series); the effect on the vestibulo-somatic--in 50 people: of them, in 25 people in a test for coordination of movements (second series) and in 25 people in a test of "vertical writing" (third series). The subjects received a single generally /508 accepted and prescribed average therapeutic dose of meprobamate--0.2 g [17]. To

eliminate the subjective factors in evaluating the effect of the preparation and for a quantitative evaluation of the psychogenic factor linked to intake of the medicine, in all these studies the "double blind" method and placebo were used [14,16,25]. The placebo tablets completely simulated the meprobamate tablets we used (0.2 g each from the firm Germed, GDR) and contained talc, starch and sucrose. The technique of recording the vestibulo-sensory reaction consisted of determining the duration of the vestibular illusion of counter-rotation (VIC) in the modified test according to Barany—after 20-fold rotation for 40 s. The subjects were rotated in a darkened room (with closed eyes). The duration of the sensory reaction after cessation of rotation was noted according to the time of subjective feeling of counter-rotation by the subjects themselves by pressing a knob installed in the right armrest of the Barany chair and linked to a writing instrument. According to the recording on the tape with rotation of movement of 3.3 mm/s, VIC duration was defined in seconds. In order to obtain objective information about the true duration of the reaction, the subjects were instructed that the findings would not affect their further activity and are only of scientific interest. In the given series of observations the VIC was recorded three times with an interval between the rotations of 1 hour. Forty minutes before the second and third effect the subjects took meprobamate or placebo.

In order to study the effect of meprobamate intake on the vestibular-somatic reactions two procedures were used: study of the coordination of arm movements according to [9] and the "writing" test [22] in modification [5]. In the first case, as an adequate stimulant of the vestibular apparatus, the anterior frontal otolith reaction of V. I. Voyachek (OR) was used. The "vertical writing" test was implemented before and after the caloric test according to [1]. The basis for inclusion of the given test in the method section was the results of studies

confirming its great diagnostic value during vestibulometry [3,8,28]. In the second and third series of observations we held to the following program: first the vestibular-somatic reactions were recorded at rest and after stimulation of the vestibular analyzer. In 24 hours the subjects took a tablet of meprobamate or placebo.

After taking the tablet, always at the same time (40 minutes) the reactions were again recorded at rest and after vestibular test. Within 48 h, subjects who received meprobamate took a placebo, and those who took a placebo--meprobamate, and the studies were repeated in the same sequence. Thus each subject was examined six times.

The studies were conducted always at the same time (10-13 h) and no earlier than within 1.5-2 h after eating. A total of 398 experiments were done. The statistical processing of the findings was carried out with the use of Student's criterion.

Result of Studies and Their Discussion

In the first series the intake of meprobamate had a noticeable effect on the pronouncement of the vestibulo-sensory reaction and reliably ($P < 0.01$) reduced its duration (table 1) to 20 s after intake of meprobamate--in 71.9% of the individuals and only in 45.4% before intake of the preparation. It is important that of the 18 people in whom in the control studies two phases of reactions were observed, after intake of meprobamate the second phase was missing in six of those examined.

The intake of placebo induced only a psychologically governed unreliable trend towards reduction in duration of the VIC. A reaction before 20 s was revealed only in 51.5% of those studied. In the same way as before intake, the placebo

TABLE 1. EFFECT OF INTAKE OF PLACEBO AND MEPROBAMATE ON DURATION OF ILLUSION OF COUNTER-ROTATION IN EXAMINED INDIVIDUALS DURING CONDUCTING ROTATING BARANY TEST

| Statistical indices | Duration of illusion of counter-rotation (in s) | | |
|-----------------------|---|-------------------------|-----------------------------|
| | Before intake (control) | After intake of placebo | After intake of meprobamate |
| <i>n</i> | 33 | 33 | 32 |
| <i>a-b</i> | 1,8-60,0 | 2,4-60,0 | 0-33,9 |
| <i>M±m</i> | 24,3±2,36 | 22,6±2,11 | 16,9±1,29 |
| <i>p</i> ₁ | | >0,5 | <0,01 |
| <i>p</i> ₂ | | | <0,05 |

Note: a-b--maximum and minimum values; *p*₁--relative to control; *p*₂--relative to intake of placebo.

yielded a sensory reaction above 40 s in 15.1% of the studied.

Processing of the results of the second series of observations indicated that in the overwhelming majority of subjects (88%) after OR a stable disorder was revealed in the fine coordination of movements. In this respect the average value of the post-rotating tremor (PRT) reliably rose ($p < 0.01$). As is apparent from table 2, the placebo intake did not have a significant effect on spontaneous tremors (ST) as on the post-rotating indices of tremor. Despite the fact that after the otolith test the pronounced nature of the vestibular-somatic reactions in individuals who took the placebo was lower than before intake, the reliability of the differences between the amounts of PRT and ST was preserved ($p < 0.05$). After intake of meprobamate the PRT in 76% of the subjects was manifest to a lesser degree than in the control, in 8%--was preserved and only in 16%--was intensified. This was reflected in the sharp decrease in the average amount of PRT (16.7 ± 1.51 versus 23.2 ± 1.46 in the control). Here one should also note that the reliability of differences between the indices of PRT and ST that occurred in the control studies

and after intake of the placebo was lacking in individuals who took meprobamate ($p > 0.05$). As for the time for fulfillment of movements on these tasks, then under the influence of OR as well as the preparations, it practically was not changed, and all the findings were statistically unreliable.

TABLE 2. NUMBER OF UNNECESSARY CONTACTS IN TEST FOR COORDINATION OF MOVEMENTS

| Time of study | Spontaneous tremor | Post-rotating tremor | P2- |
|-----------------------------|--------------------|----------------------|--------|
| | M ± m | M ± m | |
| Before intake (control) | 16,7 ± 1,38 | 23,2 ± 1,46 | < 0,01 |
| After intake of placebo | 14,5 ± 1,19 | 18,8 ± 1,47 | < 0,05 |
| After intake of meprobamate | 12,6 ± 1,34 | 16,7 ± 1,51 | > 0,05 |

The results of the third series of observations are presented in table 3, from which it is apparent that intake of placebo and meprobamate did not affect the spontaneous indices of "vertical writing." The use of the caloric test sharply altered the nature of "vertical writing" after increasing the degree of its deviation by more than 3-fold.

TABLE 3. DEGREE OF DEVIATION IN "VERTICAL WRITING" TEST

| Statistical indices | Spontaneous deviation | Deviation after caloric test (in degrees) | | |
|---------------------|-----------------------|---|-------------------------|-----------------------------|
| | | Before intake (control) | After intake of placebo | After intake of meprobamate |
| M ± m | 5,5 ± 0,81 | 16,9 ± 1,31 | 16,6 ± 1,26 | 12,9 ± 1,16 |
| P ₁ | | | > 0,8 | < 0,05 |
| P ₂ | | | | < 0,05 |

In individuals who received meprobamate, the pronounced nature of the vestibulo-spinal reflexes after calorization was reliably reduced. The angle of deviation was decreased in 64% of the subjects; its average value for the entire group became noticeably lower and was $12.9 \pm 1.16^\circ$ (in the control $16.9 \pm 1.31^\circ$; $p < 0.05$). The placebo does not create such an effect ($p > 0.8$). The figure serves as an illustration of this.

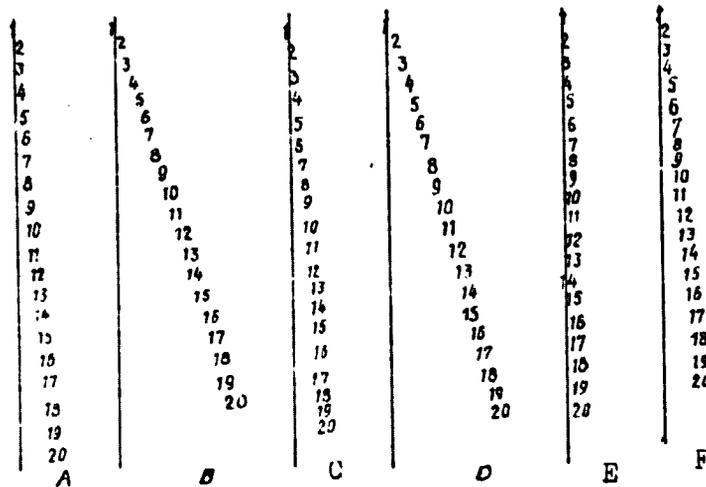


Figure. Study of Vestibular-Somatic Reaction ("Vertical Writing Test") After Intake of Placebo and Meprobamate in Subject S.

Key:

- | | |
|--|--|
| A. Spontaneous deviation of "vertical writing" | D. Deviation after intake of placebo during conducting of caloric test |
| B. Deviation after caloric test | E. Spontaneous deviation after intake of meprobamate |
| C. Spontaneous deviation after intake of placebo | F. Deviation after intake of meprobamate during conducting of caloric test |

The results of our studies clearly demonstrate that upon judging the employed tests meprobamate has a precise and significant effect on the intensity of the vestibulo-sensory and vestibular-somatic reactions of man. By considerably reducing the pronounced nature of the sensory component, the cortical reflection of the vestibular

reactions, and by reducing the discoordination of movements the preparation promotes stabilization of perception of the spatial position, disrupted during stimulation of the vestibular analyzer.

Starting from existing ideas on the intracentral mechanisms for the effect of /510 tranquilizers [2,20,29], and taking into consideration that the state of the spatial-postural orientation is controlled by integration of neural processes in a number of converging subsystems: vestibular visual-oculomotor, proprioceptive-muscular-skeletal, in the coordinating role of the higher sections of the CNS [13,18,21,30], one can propose the following. Evidently, in the given case separation by meprobamate of the intracentral bonds of both the vestibular analyzer and the motogenic zones is observed. As a result the stimulation of the sensory zone is attenuated, and the functioning of the motor zones of the cortex linked to it is disrupted to a lesser degree. Thus, the neural-muscular apparatus, realizing the finely coordinated work, to a certain degree is guarded from unusual effects on the part of the stimulated vestibular analyzer.

This positive effect of meprobamate, evidently can be used for preventive /511 treatment and correction of illusory and spatial-coordination disorders linked to stimulation of the vestibular apparatus in the process of human labor activity.

Conclusion

1. Intake of meprobamate in a dose of 0.2 g reliably reduces the pronounced nature of the vestibulo-sensory and vestibular-somatic reactions.
2. The conducted studies make it possible to recommend meprobamate as a means of increasing the organism's resistance to vestibular effects.

References

1. Ageyeva-Maykova, O. G.; and Zhukovich, A. V. Osnovy otorinolaringonevrologii ["Fundamentals of Otorhinolaryngoneurology"], Moscow, Medgiz, 1960, 299 p.
2. Aleksandrovskiy, Yu. A. Sostoyaniya psikhicheskoy dezadaptatsii i ikh kompensatsiye (pogranichnyye nervno-psikhicheskiye rasstroystva) ["States of Mental Dysadaptation and Their Compensation (Boundary Neural-Psychic Disorders)"], Moscow, Nauka, 1976, 272 p.
3. Bazarov, V. G. "Stato-Kinetic Stability During Vestibular Disorders," Vestn. otorinolar. No 1, 1976, p 14-19.
4. Berezhnoy, V. P. "Use of Trioxasine to Reduce Emotional Stress in Young Soldiers," Voyenno-med. zhurn., No 1, 1974, p 84.
5. Bokhov, B. B.; Frolova, N. N.; and Komissarova, I. V. "Certain Results of Use of the Vertical Writing Test and Visual Successive Shape in Vestibular Stimulation," in Mater. nauch. konf. molodykh spets. posv. pamyati prof. A. V. Lebedinskogo ["Materials of Scientific Conference of Young Specialists Dedicated to the Memory of Professor A. V. Lebedinskiy"], Moscow, Meditsina, 1965, p 10-11.
6. Budnikas, V. A. "Effect of Meprobamate on Mental Performance Capacity, State of Health and Psychic Human State," in Voprosy farmakologii neurotropnykh sredstv ["Questions of Pharmacology of Neurotropic Resources"], Riga, 1974, p 18-21.
7. Glod, G. D.; Belay, V. Ye.; Vasil'yev, P. V.; and Orlova, T. A. "Joint Effect of Stimulants and Tranquilizers on Performance Capacity of Human Operator," Kosmich. biol. No 4, 1972, pp 77-83.
8. Gukovich, V. A.; and Trasevich, E. P. "Fukuda Writing Test in Evaluating Vestibular Reactions During Stapedioplasty and in the First Days After It," Zh. ushn., nos. i gorl. bol. No 5, 1975, p 23-28.
9. Yerenkov, V. A. "Objective Technique for Studying Coordination of Arm Movements," Zh. Nevropat. i psikiatr. 66, No 1, 1966, p 51-54.
10. Ioseliani, K. K. "Certain Features of Higher Cortical Functions in the Flight Staff Under Stress Conditions," in Aviatsionnaya i kosmicheskaya meditsina ["Aviation and Space Medicine"], Moscow, vol 1, 1969, p 264-267.
11. Kamenskiy, Yu. N.; Sokolova, Ye. A. "Effect of Vibration and Noise on Certain Indices of Performance Capacity of MI-4 Helicopter Crews," Kosmich. biol. No 5, 1978, p 56-59.
12. Kopanev, V. I. "Problem of Stato-Kinetic Human Stability in Aviation and Space Medicine," Izv. AN SSSR (ser. biol.), No 4, 1974, p 476-498.
13. Kurashvili, A. Ye.; Babiyak, V. I. Fiziologicheskiye funktsii vestibulyarnoy sistemy ["Physiological Functions of Vestibular System"], Leningrad, Meditsina, 1975, 279 p.

14. Lapayev, E. V.; Voinova, I. I.; Vorob'yev, O. A.; Barmicheva, N. M. "Aminalon as a Means of Preventing Motion Sickness," Zh. ushn, nos. i gorl. bol., No 5, 1978, p 35-39.
15. Lobastov, O. S.; Spivak, L. I.; Panov, B. P. "Prevention of Excessive Emotional Stress by Psychotropic Resources," Voyenno-med. zhurn, No 5, 1968, p 26-28.
16. Lukomskaya, N. Ya.; and Nikol'skaya, M. I. Izyskaniye lekarstvennykh sredstv protiv ukachivaniya ["Search for Medicines Against Motion Sickness"], Leningrad Nauka, 1971, 227 p.
17. Mashkovskiy, M. D. Lekarstvennyye sredstva (posobiye po farmakoterapii dlya vrachey) ["Medicines (Manual on Pharmacological Therapy for Physicians)"], Moscow, Meditsina, part 1, 1977, p 79.
18. Olisov, V. S. Labirintopatii ["Labyrinthopathy"], Leningrad, Meditsina, 1973, 294 p.
19. Frolov, N. I. "Evaluation of Performance Capacity of Pilot During Flight Shift," Voyenno-med. zhurn. No 7, 1976, p 65-68.
20. Furman, Yu. N. "Effect of Elenium and Derivatives of Benzodiazepine Close to it on Certain Functions of the Nervous System," Vrachebnoye delo, No 2, 1974, p 9-11.
21. Khilov, K. L. Funktsiya organa ravnovesiya i bolezni peredvizheniya ["Function of Organ of Equilibrium and Motion Sickness"], Leningrad, Meditsina, 1969, 279 p.
22. Fukuda, T. "Vertical Writing With Eyes Covered. A New Test of Vestibulo-Spinal Reaction," Acta oto-laryngol., 1959, 50, No 1, pp 26-36.
23. Hartman, B. O., Hale, H. B., Harris, D. A., Sandord, L. F. "Psychobiologic Aspect of Double Crew Long Duration Missions in C-5 Aircraft," Aerospace Med., 1974, 45, No 10, pp 1149-1154.
24. Hurst, P. M., Radlow, R., Bagley, S. K. "Drug Effects Upon Data Processing as Functions of Storage and Retrieval Parameters," Ergonomics, 1970, 13, pp 435-444.
25. Johnson, W. H., Fenton, R. S., Evans, A. "Effects of Droperidol in Management of Vestibular Disorders," Laryngoscope (St. Louis), 1976, 86, No 7, pp 946-954.
26. Kielholz, P., Goldberg, L., Obersteg, In. Strassenverkehr, Tranquilizer and Alcohol, Dtsch. med. Wschr., 1967, 92, No 35, pp 1525-1531.
27. Molnar, G., Lipak, J., Kleininger, O. "Die Veranderung pathologischer psychischer Funktionen bei Angstzustanden unter Behandlung mit Librium," Ther. Umschau, 1967, 24, No 2, p 68-73.

28. Seth, S. M., Sinha, A., Kacker, S. K. "Vestibular Disturbances After Stapedectomy" Ann. Otolaryng. (Paris), 1968, 77, pp 256-295.
29. Iamkov, Iv. and Kirov, K. Klinicheskaya psikhofarmakologiya ["Clinical Cycle Pharmacology"], translated from Bulgarian by L. M. Rozet/ed by G. Ya. Avrutskiy, Moscow, Meditsina, 1971, 356 p.
30. Veyt, R. De Luchchi M. "Labyrinth and Proprioceptive Aspects of Aviation and Space Medicine," Aviatsionno-kosmicheskaya meditsina (Problemy bezopasnosti poleta) ["Aviation-Space Medicine (Problems of Flight Safety)"], collection of articles translated from English by V. Gorshkova and A. Novobytova/ed by A. Gyurdzhian, Moscow, Voenizbat, 1975, p 15-35.

COPYRIGHT: Fiziologicheskiy zhurnal, 1979.