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AN INVESTIGATION OF THE EFFECTS OF MEPROBAMATE ON
AUDITORY THRESHOLD AS MEASURED BY
CONVENTIONAL PURE TONE AND
GALVANIC SKIN RESPONSE AUDIOMETRY

by

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B.A., Montana State University, 1958

Presented in partial fulfillment of the requirements for the

degree of Master of Arts

MONTANA STATE UNIVERSITY

1960

Approved by:


Chairman, Board of Examiners


Dean, Graduate School

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TABLE OF CONTENTS

	Page
ACKNOWLEDGEMENT	ii
LIST OF TABLES	iv
CHAPTER	
I. INTRODUCTION	1
II. PROCEDURE	11
III. RESULTS	17
IV. DISCUSSION	21
V. SUMMARY AND CONCLUSIONS	28
BIBLIOGRAPHY	30
APPENDIX A	32

LIST OF TABLES

Table	Page
1. Analysis of Variance of Four Factors: Medication, Test, Frequency, and Order	19
2. Cell Mean Values for Medication, Test, and Frequency Factors	20

CHAPTER I

INTRODUCTION

Statement of Purpose

The purpose of this study is to determine the effects of meprobamate, (Miltown, Equanil), on auditory thresholds of a group of normal adults as determined by pure tone audiometry and by galvanic skin response audiometry.

Rationale

As the role of hearing and its loss becomes more apparent in the effectiveness with which we lead our lives, it also becomes more important that reliable methods of evaluating hearing ability be made available. Pure tone audiometry is probably one of the most widely used of these methods, and with the continued improvement of the pure tone audiometer, it is becoming one of the more reliable methods. However, it is obvious from the literature in the field of hearing that there is as yet no single procedure for the testing of auditory function in adults which is universally accepted. And a reliable method of testing hearing in small children is even less available. This is unfortunate, because it is in this age group that proper evaluation of hearing is especially important.

Myklebust has commented on the consequences of incorrect diagnosis of a child with a hearing loss who is treated as mentally deficient, aphasic or emotionally disturbed.¹ It is also pointed out that as a result of early diagnosis, proper disposition of the problem can be made at the most opportune time. But it is in this crucial age group that pure tone audiometry has its most serious inadequacies. These include the reliance on subjective responses and cooperation of the child, the presumption of an ability to understand verbal instructions, and the frequently observed incompatibility between the length of the test and the patience and cooperation of the child.

This situation, together with the difficulties of reliably testing individuals with language problems, functional deafness and various motor involvements, has prompted an effort to produce a more objective kind of hearing test.² One such test which has promise is a pure tone analysis utilizing the galvanic skin response.

Background

The basis for this kind of audiometry is the determination by Fere³ in 1888 that skin resistance to a weak electric

¹ Myklebust, H.R., Auditory Disorders in Children, Green & Stratton, New York, 1954, p. 1.

² Stewart, K.G., "Some Basic Considerations in Applying the GSR Technique to the Measure of Auditory Sensitivity", *JSHD*, 19, 1954, (2), p. 174.

current changed as a result of external stimuli.³ Later, in 1909, Veraguth⁴ showed, by interposing a galvanic element into the circuit, that when a direct current flowed through the body, stimulation of sense organs or psychic stimuli caused an increase in the intensity of the exosomatic current. This he called the "psychogalvanic reflex", but the term has been objected to by some because the same reflex impulse can be elicited after decortication.⁵ The names "galvanic skin response" or "electro-dermal skin response" have been suggested instead.⁶ However, Rothman⁷ points out that there are two galvanic skin responses, one of which depends upon eccrine gland activity (the psychogalvanic reflex) and the other independent of glandular function (the local galvanic reaction of Ebbecke). For the purposes of this paper, the term galvanic skin response will be adopted to refer to the former, with which we are concerned here.

³Fere¹, C., "Note sur des modifications de la resistance electrique sous l'influences des excitations sensorielles et des emotions." Compt. rend. Soc. de Biol. 5:217-219, 1888.

⁴Veraguth, O., Das Psychogalvanische Reflex Phaenomen, Karger, Berlin, 1909.

⁵Richter, C.P., "Galvanic Skin Reflex from Animals with Complete Transection of Spinal Cord", Am. J. Phys. 93, 1930, p. 418.

⁶Goldstein, R., Polito-Castro, S.B., Daniels, J.T., "Difficulty in Conditioning of Electrodermal Response to Tone in Normally Hearing Children", JSHD 20, 1955, (1), pp. 26-34.

⁷Rothman, S., Physiology and Biochemistry of the Skin, U. of Chicago Press, 1953, p. 17, 18.

Rothman further notes that from a review of the literature on the galvanic skin response that the functional state of the eccrine glands on the palmar areas is the predominant factor in the total galvanic resistance. From this it might be concluded that the filling of ducts with sweat (an electrolytic solution) is essential to the demonstration of the galvanic skin response. However, it was rather nicely shown by Darrow⁸ that "the psychogalvanic skin response does not depend on the actual moisture found in or on the skin . . . but that electrical changes precede the secretion of sweat by about one second".

The galvanic skin response was first used as an experimental method for the testing of hearing by Bordley, et.al.⁹ This procedure is based on the principles underlying classical Pavlovian conditioning and utilized the Tarchanow effect in its measurement. It should be noted that there are two methods of demonstrating the galvanic skin response. The first, which is the one typically used in GSR audiometry is the Tarchanow effect which is a measure of change in electrical potential between points on the skin surface. The second, the Feré¹ effect, is a change in the electrical resistance to the flow of current between two points on the skin.

⁸Darrow, C.W., "The Relation of the Galvanic Skin Reflex Recovery Curve to Reactivity Resistance Level and Perspiration", J. Gen. Psych. 7, 1932, pp. 261-273.

⁹Bordley, J.E., Hardy, W.G., Richter, C.P., "Audiometry

Conditioning for galvanic skin response audiometry consists simply of presenting the subject with an unconditioned stimulus (UCS), in this case, a mild faradic shock, which is associated in time with a conditioned stimulus (CS), the tone. If the UCS (shock) is presented supraliminally, it will produce an unconditioned response (UCR), the psychogalvanic skin response. Conditioning is said to have occurred when the GSR appears after the tone (CS) is presented alone, in which case it is referred to as the conditioned response (CR).

In this manner, a kind of audiometry was developed which did not rely on the conscious cooperation of the subject. Its primary application is in the verification of other test results in the detection of functional hearing loss and malingering. Also it has obvious promise in numerous other areas. However, as is the case with many a good thing, its popularity has occasionally carried it beyond its limitations. As Statten and Wishart¹⁰ have rather emphatically stated it:

"PGSR testing is difficult and may be an unpleasant experience for a child . . . Therefore, we condemn, with all our might, the indiscriminate distribution of this complex equipment under the assumption that it is a practical method of testing the hearing of any child by any operator."

with the Use of Galvanic Skin-resistance Response: A Preliminary Report", Bull. Johns Hopkins Hospital, 82:569 (May) 1948.

¹⁰Statten, P. and Wishart, D.E.S., "Pure Tone Audiometry in Young Children with Psychogalvanic Skin Response and Peep Show", Annals OLR, LXV, 1956, (2), p. 533.

Aside from the skill in subjective interpretation of the responses which must be developed, there is the unfortunate fact that changes in skin resistance can occur as a result of several other extraneous variables, among them, cortical activity and excessive motor movement, which tend to make GSR audiometry somewhat difficult and even suspect by some writers.¹¹ These variables become even more of a problem when this method is applied to small children. Their normal states of activity, or abnormal activity of a neurological nature cause difficulty in interpretation of results. In addition, Goldstein, et. al.¹² and Statten and Wishart¹³ indicate that children are frequently difficult to condition.

Clearly then, some means of controlling these variables is called for, if GSR audiometry is to be of more than limited use as a clinical tool. Recent intensive research in the field of pharmacology indicates that the "tranquilizers" may have some application to this situation. Strauss¹⁴ has studied the effects of one such drug (mephenesin carbamate) on normal hearing thresholds of adults and has found no

¹¹Stewart, op. cit., 174

¹²Goldstein, et. al., op. cit., p. 26

¹³Statten and Wishart, op. cit., p. 525

¹⁴Strauss, R.B., "An Investigation of the Effects of Mephenesin Carbamate (Tolseram) on Normal Hearing Thresholds as Determined by the Conditioned Psychogalvanic Skin Response and Conventional Pure Tone Audiometry", (unpublished Ph.D. dissertation), Univ. of Fla., Aug, 1956, p. 25.

significant change in threshold as measured either by GSR or pure tone audiometry. He then suggests that further study might reasonably be done with this drug on infants and young children. There are, however, a number of reasons for not using mephenesin carbamate with children. Among these are:

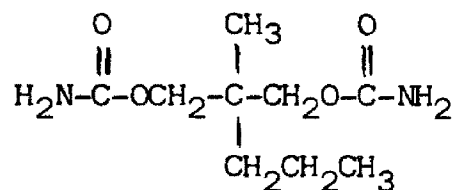
- a. It is not as well documented as other such drugs.
- b. There is some disagreement in the literature over function and result.
- c. Mephenesin carbamate is primarily a muscle relaxant, whereas meprobamate has both muscle relaxing and tranquilizing properties.

Krantz and Carr¹⁵ state that "it appears that the activity of the drug (mephenesin carbamate) is confined to a depressant effect mainly on the spinal cord". In this discussion, there appears to be disagreement among investigators over its utility in a variety of situations. There is little else in the available literature to indicate the specific action or effect of mephenesin carbamate on the various systems of the body.

¹⁵Krantz, Jr., J.C., and Carr, C.J., The Pharmacologic Principles of Medical Practice, Williams & Wilkins Co., 1958, pp. 706-710.

The Drug of Choice

Meprobamate ("Miltown", Wallace) is a simple aliphatic compound (2-methyl-2-n-propyl-1,3-propanediol dicarbamate) and has the following structural formula:



It is a white crystalline powder of characteristic bitter taste, which is stable in dilute acid and alkali, and is not broken down at hydrogen ion concentrations occurring in gastric or intestinal fluids.

Meprobamate has three distinct behavioral and physiological properties; a muscle relaxant action, an anticonvulsant action and a pronounced ataraxic effect. The muscle relaxant action is similar to that of mephenesin but of greater potency and longer duration. Only voluntary muscles are significantly affected. The diaphragm is relatively insensitive to the action of meprobamate and for this reason respiration remains unimpaired even after administration of extremely large doses.¹⁶

¹⁶Berger, F.M., "The Pharmacological Properties of (meprobamate)(Miltown), a New Interneuronal Blocking Agent", J. Pharm. & Exper. Therapy, 112, 1954, pp. 413-423.

The drug is reported to produce certain behavioral changes which can best be observed in monkeys. "After a suitable dose of meprobamate, the animals lose their fear, hostility and aggressiveness and become friendly and tame. Appetite remains unimpaired, and full interest in the environment is retained".¹⁷ Unlike chlorpromazine and reserpine, meprobamate does not interfere with conditioned responses.¹⁸ However, the most striking property of meprobamate is its selective action on the thalamus. Hendley, et. al.,¹⁹ report:

"The increased amplitude and decreased frequency seen in this area are similar to the changes found in the cerebral cortex in association with decreased functional activity. Presumably, therefore, the thalamus is more or less specifically depressed by meprobamate. However, sensory relays through the thalamus are probably not greatly affected by meprobamate since no sensory impairment is apparent in animals or reported by humans at normal dosage, and since auditory responses in our cat preparations are not affected except at very high dosage levels".

The only serious side effect reported after meprobamate medication is the rare occurrence of allergic reactions. In a review of studies involving more than 8000 cases,²⁰ there

¹⁷Berger, F.M., *ibid.*

¹⁸Pfeiffer, C.C., et. al, "Comparative Study of the Effect of Meprobamate on the Conditioned Response . . . ", Ann. New York Acad. Sc. 67, 1957, pp. 734-745.

¹⁹Hendley, C.D., et. al., "Effect of Meprobamate on Electrical Activity of Thalamus and Other Subcortical Areas", Tranquilizing Drugs, ed. Himwich, H.E., AAAS, Washington, D.C., March 1957, pp. 35-46.

²⁰Wallace Laboratories, Miltown, Physicians' Reference Manual, 4th edition, 1958.

was less than one quarter of one percent of allergic reactions. It was noteworthy however, so far as audiometric premedication is concerned, that this review reports these allergic responses develop, as a rule, in patients who have had only one to four doses of meprobamate and have not had previous contact with this drug.

At any rate, the incidence of untoward reaction would not seem to preclude the medically supervised use of the drug in audiometric premedication, if it can be determined that it has no significant effect on hearing thresholds, as measured by pure tone audiometry for a direct comparison with tests in an untreated condition, and as measured by GSR audiometry as a check on the galvanic skin response and conditioning with the drug. The latter factor is particularly important in evaluating this drug for eventual use in the GSR clinical test situation, where its effect might conceivably be of value. If it is the case then, that meprobamate has no statistically significant effect on either auditory threshold or conditioning and GSR, and since it is a drug which has been effectively used with children, then a way might be opened to further investigation of such a population with both normal and abnormal hearing thresholds.

CHAPTER II

PROCEDURE

Statement of the Problem

This investigation was intended to determine if there is a statistically significant effect on the hearing thresholds of a group of essentially normal adults following the use of meprobamate, a muscle relaxing drug with tranquilizing properties, as measured by pure tone audiometry and by galvanic skin response audiometry. In the event no such effect is demonstrated, it might then be pertinent to ask if this drug could be used with small children and those with neuromotor involvements in a clinically practical way to obtain more valid estimates of their hearing thresholds.

The hypothesis to be tested was that: There is no statistically significant effect on auditory threshold following the use of meprobamate as determined by pure tone or galvanic skin response audiometry.

Subjects

The subject group consisted of 28 male volunteers between the ages of 18 and 26, with a mean age of 21.25 years. They were all students at Montana State University who gave

no history of tranquilizer medication or abnormal auditory involvement, and reportedly were in essentially normal health at the time of testing. Each subject was given a complete pure tone threshold test prior to the commencement of the study as a screening measure to exclude those whose hearing was not within normal limits at the frequencies used in this study.

He was then instructed that his hearing would be tested by two methods and each test situation would be preceded by the administration of either a meproamate tablet or a placebo. The administration of the placebo was intended to reduce functional reactions to a minimum. Both the medication and the placebo were supplied in similar form and administered under the medical supervision of Robert W. Hanson, M.D., Director of the University Health Center. Neither the experimenter nor the subject was to be aware of the contents of the tablets at the time of testing.

Instrumentation

These subjects were then tested in the research laboratories of the Montana State University Speech and Hearing Clinic. The testing was done in an Industrial Acoustics Corporation Sound Treated Audiometric Testing Room, Model 1 AC 403 S, located in the Montana State University Health

Center. This room was adjacent to a control room from which the experimenter could manipulate his audiometric testing equipment while viewing the subject through a unidirectional double plate glass window.

A factory-calibrated Beltone F-1 audiometer was used for the audiometric testing and this was coupled to a Grason-Stadler PG/R, Model E664, and Sanborn heat stylus recorder for the assessment of GSR responses. These instruments were located in the adjacent control room.

Experimental Design

The experimental design used in this study is an analysis of variance, specifically a Treatment (medication) by Treatment (test) by Treatment (frequency) by Subject, with the following four combinations of medication by test treatments counter-balanced for order using a Latin Square.

- a. pure tone test with meprobamate medication
- b. pure tone test with placebo medication
- c. galvanic skin response with meprobamate medication
- d. galvanic skin response with placebo medication

The design involved four dimensions, (medication, test, frequency, order) with the order dimension resulting from a counterbalancing of the four treatment combinations of medication and tests noted above.

The 28 Subjects were randomly divided into four groups, with each group taking the treatment combinations in a dif-

ferent order but in the same sequence. Where possible, each test was scheduled for the same time of day one week apart which well exceeds the minimum of 48 hours required to eliminate the drug from the body.²¹

Test Procedure

Each test was initiated by the presentation of an envelope marked with the subject's identification number, and containing either a meprobamate (400 mg) tablet or a placebo tablet. This dosage was selected after consultation with medical and pharmacological staff members of Montana State University, and upon recommendation of the manufacturer.²² The nature of the contents of the envelope was not to be known to either the subject or the experimenter at the time of the test. The medication was administered a minimum of one hour prior to the scheduled time of the subject's test.

The audiometric evaluation was then begun and threshold values for the frequencies of 500 cps and 2000 cps were obtained by whichever procedure had been assigned for that subject during that testing session. A descending technique was used to establish thresholds, since with normal ears, values of tone

²¹Wallace Laboratories, Miltown, Physicians' Reference Manual, 4th edition, 1958.

²²Davis, W.A., M.D., Wallace Laboratories, Inc. personal communication, 6 January 1960.

first missed on a descending series presentation seldom differ enough from values first responded to on an ascending series, when the audiometer is attenuated in 5 db steps as is the case here, to make a mean value meaningful or necessary.²³

If the subject was scheduled for testing by GSR, the following test procedure was used: He was seated in a chair equipped with arm rests and in view of the control room window. The instructions were given that he was to relax and sit as quietly as possible and that no overt response would be required of him. The unconditioned stimulus (shock) electrodes were attached to the palmar surfaces of the first and third fingertips of the left hand and the isolation electrode to the wrist of the same hand. The pick-up electrodes were attached in the same locations on the right hand. Earphones were put in place and the test begun.

The galvanometer was calibrated to the subject's basal skin resistance and the conditioned stimulus (tone) was presented initially to determine the existing state of conditioning. Conditioning was then undertaken with the conditioned stimulus presented for 2 sec. followed by a .5 sec. delay from onset of the CS, and the unconditioned stimulus (shock) for .5 sec. Shock intensity was increased until responses were

²³Carhart, R., and Jerger, J.F., "Preferred Method for Clinical Determination of Pure Tone Thresholds", JSND, 24, 1959, pp. 330-345.

obtained, and this shock randomly accompanied the CS 60% of the time.²⁴ The CS for conditioning was a tone of 2000 cps at 40 db above normal threshold (Odb). Conditioning was considered successful after three consecutive responses to the CS alone. The CS intensity was then reduced and the following criterion, suggested by Doerfler and McClure²⁵ was used to determine threshold.

"The lowest intensity level of presentation at which the subject responded with three galvanic skin responses which met the criteria was accepted as the threshold for hearing."

In view of the fact that the equipment used in this study differed from that used by Doerfler and McClure in that there is continuous and unscaled adjustment of the sensitivity of the recorder itself, thus permitting infinite manipulation of the dimensions of the response, there is no way of equating responses with respect to height and slope dimensions such as theirs. Therefore, a time restriction of 1. to 4. sec. was used as the criterion for judging a response.

²⁴Meritser, C.L., and Doerfler, L.G., "The Conditioned Galvanic Skin Response Under Two Modes of Reinforcement", JSHD, 19, 1954, pp. 350-359.

²⁵Doerfler, L.G., and McClure, C.T., "The Measurement of Hearing Loss in Adults by Measurement of the Galvanic Skin Response", JSHD, 19, 1954, p. 187.

CHAPTER III

RESULTS

Organization of the Data

The results obtained in this investigation were evaluated by means of an analysis of variance technique. The analysis involved a consideration of four factors. These are as follows:

1. The type of medication used (drug, placebo) which is symbolized by (M).
2. The kind of audiometric technique used (conventional, GSR), symbolized by (T).
3. The frequencies tested (500 cps, 2000 cps) symbolized by (F).
4. The order resulting from counterbalancing the treatment combinations of medication and tests (1, 2, 3, 4) symbolized by (O).

The analysis of variance of this data is given in Table 1. Table 2 indicates the mean threshold values for the three variables of experimental interest (medication, test, frequency). These values were obtained from the data presented in Appendix A. The results of the analysis of variance indicate that there are no statistically significant differences

between either the main effects, or their interactions, at the 10% level of significance.

There is then, no evidence for rejecting the hypothesis of no difference on auditory threshold as measured by pure tone and galvanic skin response audiometry from the use of meprobamate as a clinical premedication, to be derived from the data presented.

However, because it is impossible to reject the null hypothesis, it seemed desirable to determine whether it would be possible to reject the additional hypothesis that the true difference between medication means is as great as plus or minus 2.5 db. The following "t" test was used:

$$t = \frac{\sqrt{112} [2.5 \text{ db} - (\bar{D} - \bar{P})]}{\sqrt{\frac{2 \text{ MS}_{\text{error}} (W)}{\text{df error } (W)}}}$$

df for "t" =
df_{error} (W)

On the basis of the above-listed "t" test, this hypothesis can be rejected at the 1% level of significance.

TABLE 1. Analysis of Variance of Four Factors: Medication, Test, Frequency, and Order.

Source	Sum of Squares	Degrees of Freedom	Mean Squares	F Ratio*
<u>BETWEEN</u>	2689.89	27		
Interaction between	631.32	6	105.22	**
Error between	2058.57	21	98.03	NS
<u>WITHIN</u>	3690.22	192***		
Medication (M)	.01	1	.01	NS
Test (T)	4.96	1	4.96	NS
Frequency (F)	6.16	1	6.16	NS
Order (O)	2.80	3	.93	NS
M x T	.14	1	.14	NS
M x F	.11	1	.11	NS
T x F	1.03	1	1.03	NS
M x T x F	.70	1	.70	NS
O x F	2.33	3	.77	NS
O x M	21.81	1	21.81	NS
O x T	5.76	2	2.88	NS
O x M x T	13.41	1	13.41	NS
O x M & O X M X T	6.58	2	3.29	NS
O x M x F	1.39	1	1.39	NS
O x T x F	1.66	2	.83	NS
O x M x T x F	.30	1	.30	NS
O x M x F and O x M x T x F	12.82	2	6.41	NS
Error within	3116.43	167	18.66	
<u>TOTAL</u>	6380.11	223		

* Between MS / MS_{error} (B) and Within MS / MS_{error} (W)

** NS = Nonsignificant at the 10% level of significance

*** 4 degrees of freedom lost as result of assigning mean values for subject who failed to condition to GSR

TABLE 2. Cell Mean Values for Medication, Test and Frequency Factors.

Factor	Cell Mean Values	
Medication	Drug - .77	Placebo -.72
Test	Pure Tone -1.96	GSR .48
Frequency	500 cps -1.04	2000 cps -.31

CHAPTER IV

DISCUSSION

The basic question to which this investigation was addressed was to determine whether meprobamate, a tranquilizer with muscle relaxant action, has a significant effect on the auditory thresholds of normal adults. The results of a procedure designed to demonstrate such an effect, if present, are set forth in the previous chapter. The data accumulated during the experimental portion of this study indicate that, under the conditions described, meprobamate has no statistically significant effect on auditory threshold as measured by pure tone and GSR audiometry.

Subjects

Before the study was begun, each subject was given a complete pure tone threshold examination, primarily for the purpose of excluding any whose hearing was not within normal limits for the frequencies used in this investigation.

All of the subjects who participated in this study were successfully conditioned for GSR audiometry, with one exception, and thresholds were obtained according to the procedure

outlined in Chapter II. Attempts to condition one subject to the GSR task were unsuccessful and abandoned after approximately 45 minutes. This failure to condition was presumed to be due to the fact that the stimulus at maximum (2.5 milliamperes) was not sufficiently intense to effectively serve as the unconditioned stimulus in the conditioning process for this subject. In this case, mean values for the group were assigned. Conditioning to the pure tone task was successful in all cases, as would be expected with cooperative adult subjects.

Control

Each subject served as his own control through random assignment to groups which were counterbalanced with respect to order of testing. Pure tone thresholds were determined by galvanic skin response audiometry and by conventional audiometry. Both GSR and pure tone tests were conducted twice, once with the subject on meprobamate medication, and once under a condition of placebo medication in an attempt to control functional reactions to the meprobamate.

Medication

Statistical analysis of the data indicates that meprobamate in the amount given has no significant effect on auditory threshold as measured by techniques previously described.

However, the question arises as to the appropriateness of the dosage involved. The effects desired by the audiologist need be only of short duration as opposed to the long term effects desired in typical clinical regimes of meprobamate. Therefore, the dosages recommended by the manufacturer, (generally with the latter situation in mind), may not be appropriate to these specific needs of the audiologist. One might then reasonably contend that the dosage used in this study is not sufficient for quickly accruing, objectively measurable effects. This implies a need for further investigation of the drug, preferably in a variety of situations, but particularly utilizing various dosages. In the available literature relating to meprobamate, there is only a single mention of its use in the clinical situation of short duration, although its other uses are particularly well-documented.²⁶

An attempt was made by the experimenter to determine subjectively the type of medication taken by each subject at the time of each test on the basis of overt behavior and of his recorded responses on the GSR tests. This attempt was not an actual part of the experimental design, but rather was made simply to determine if there were readily apparent

²⁶Pronko, N.H., and Kenyon, G.Y., "Meprobamate and Laboratory-induced Anxiety", Psychological Reports, Mono. Supp. 2, 1959, pp. 217-238.

behavioral effects deriving from the use of the drug. The attempt was largely unsuccessful in the observation of overt behavior but in a few cases, there was a marked reduction in extraneous fluctuation on the GSR recordings of individuals in the meprobamate condition. There is no implication to be drawn from this except to raise the question of whether these individuals might have been hypersensitive to the effects of meprobamate and thus demonstrated behavior which would have been the case more frequently if the dosage were increased.

One further comment on the drug seems germane. The medication, both meprobamate and placebo, was provided in uncoated tablet form, which could be distinguished both by taste and appearance, a situation obviously not in keeping with the assumptions underlying the use of placebo medication. Therefore, it is suggested that in other investigations in which meprobamate is used that the supply be triturated and encapsulated, or obtained from the manufacturer with some sort of uniform coating.

Equipment

The auditory thresholds of the subjects as a group were consistently lower than audiometric zero on the initial screening threshold tests. This might be expected in view of recent investigations of the applicability of the American standard for

this measure.²⁷ However, a slight line loss in the equipment used in this study precluded the need for introducing an attenuation factor into the circuitry.

While not of direct consequence to this investigation, it seems noteworthy from an evaluational standpoint that the equipment used for the GSR portion of the study had some minor inadequacies, which, if modified might provide a useful tool in the evaluation of meprobamate and similar drugs. One important deterrent to a practical evaluation of the effects of such drugs, is the lack of a sufficiently refined technique for demonstrating them. The nature of the GSR equipment is such that it is quite sensitive to subtle changes in the physical and mental states of the subject. This being the case, it seems conceivable that GSR equipment might be the instrument of choice for demonstrating effects of these drugs on those aspects of the organism which the equipment is designed to measure. These include changes in basal skin resistance, tolerance for shock, and the sensitivity of the galvanic skin response itself. Unfortunately, it is in just these aspects that standard GSR equipment does not provide sufficiently precise quantification of what can be observed in a qualitative way. It is interesting to speculate on the uses to which this equipment might be put if it were to be refined

²⁷Davis, H., "For an International Audiometric Zero", Asha, 1, 1959, pp. 47-49.

in these aspects. For example, would tolerance for shock be increased as a result of reduced apprehension and motor tension? Would basal skin resistance be changed consistently and what would be the implications of such changes? Would the ratio of response amplitude to the amplitude of extraneous fluctuation be increased as a result of reducing this fluctuation by inhibition of excess motor activity, and thus make the responses easier to identify and interpret? It would seem that a few relatively minor modifications in GSR equipment would make it possible to investigate these questions. It is suggested that these modifications might consist mainly of adding a calibrated template to the sensitivity control and making more precise the measurement afforded by the basal skin resistance and shock intensity controls.

Recommendations

This study has dealt with the problem of determining the effect of meprobamate on the auditory thresholds of essentially normal adults. It was intended to be a preliminary investigation in a more comprehensive study of the effect and practicality of "tranquilizing" premedication in clinical audiometry. This includes both adults with whom relaxation is an important factor, as in GSR audiometry, and other cases who, by reason of comparative youth or neuromotor disorders, cannot be tested under typical clinical conditions.

It is recognized that many questions remain to be answered about the nature and function of ataraxic drugs such as meprobamate, particularly as utilized in short term situations, but its widespread acceptance by the medical profession and the amount of information which has been accumulated relating to it, in comparison to other drugs of similar nature, appear to establish it in the position of the drug of choice at this time for the purposes previously described. Before this drug is used as an objective clinical aid in audiometry then, it is recommended that at least the following factors be considered:

1. The assessment of the effects deriving from varied dosage of meprobamate within the limits of safety on the auditory acuity of normal-hearing adults.
2. The determination of an objectively quantifiable method of assessing subtle effects of meprobamate.
3. An inquiry into the effects of meprobamate in very young children and individuals with a variety of neuromotor disorders.
4. An investigation into the value of such medication in testing the auditory acuity of these individuals.

CHAPTER V
SUMMARY AND CONCLUSIONS

An investigation was made to determine if meprobamate (Miltown) in a single dosage of 400 mg would produce statistically significant changes in the auditory thresholds of a group of essentially normally hearing adults, as measured by conventional pure tone and galvanic skin response audiometry.

Thresholds for each of a group of 28 male volunteers were determined twice with each of these audiometric techniques; once under a condition of drug medication and once with placebo medication, using the test frequencies of 500 cps and 2000 cps.

The results obtained were evaluated by means of an analysis of variance technique. This analysis involved a consideration of the following four factors:

1. Medication (M), (Drug - Placebo)
2. Test (T), (Conventional pure tone - GSR)
3. Frequency (F), (500 cps - 2000 cps)
4. Order (O), (1, 2, 3, 4)

The last factor (order) resulted from the counterbalancing the four combinations of the medication and test factors

for order with the use of a Latin Square.

The analysis indicates that there are no statistically significant differences between either the main effects or their interactions at the 10% level of significance. The additional hypothesis that a difference of plus or minus 2.5 db is significant can be rejected at the 1% level of significance.

Limitations of the study were discussed and recommendations for further study were proposed.

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APPENDIX A

Auditory Threshold Values for Subjects by Groups
with reference to 0 db

Code

A - Medication
1 - meprobamate
2 - placebo

B - Order
1
2
3
4

C - Frequency
1 - 500 cps
2 - 2000 cps

D - Test
1 - pure tone
2 - GSR

Group 1

Subj.	A ₁				A ₂			
	D ₁ (B ₁)		D ₂ (B ₂)		D ₁ (B ₃)		D ₂ (B ₄)	
	C ₁	C ₂	C ₁	C ₂	C ₁	C ₂	C ₁	C ₂
101	-5	0	0	-5	-5	0	-5	-10
104	0	-5	0	0	0	0	5	5
111	-5	-5	0	0	-5	-5	0	-5
117	0	0	5	5	0	0	0	5
119	0	5	5	5	0	5	0	5
122	10	5	10	5	10	10	10	10
114	-5	0	-5	0	-5	-5	-5	-5

Group 2

Subj.	A ₁				A ₂			
	D ₁ (B ₄)		D ₂ (B ₁)		D ₁ (B ₂)		D ₂ (B ₃)	
	C ₁	C ₂	C ₁	C ₂	C ₁	C ₂	C ₁	C ₂
103	-10	-10	-5	0	-5	-10	-10	-10
107	-5	0	-5	-10	-5	0	5	5
109	-10	5	0	-5	-10	0	0	0
116	-5	0	-5	-5	-5	0	-5	-5
118	-5	0	0	10	0	10	0	10
120	0	10	-5	5	0	5	0	5
123	0	-5	0	0	0	-5	5	5

Group 3

Subj.	A ₁				A ₂			
	D ₁ (B ₃)		D ₂ (B ₄)		D ₁ (B ₁)		D ₂ (B ₂)	
	C ₁	C ₂	C ₁	C ₂	C ₁	C ₂	C ₁	C ₂
102	-5	0	5	5	-5	0	-5	5
110	0	-5	5	10	0	-5	-5	0
112	0	-10	0	-5	0	-10	0	-10
113	-5	-5	.83	3.33	0	0	-3.33	-2.5
124	0	5	5	5	0	0	0	0
126	-10	0	-5	0	-5	-5	-5	-5
128	-5	-10	-5	5	-5	-5	-5	-5

Group 4

Subj.	A ₁				A ₂			
	D ₁ (B ₂)		D ₂ (B ₃)		D ₁ (B ₄)		D ₂ (B ₁)	
	C ₁	C ₂	C ₁	C ₂	C ₁	C ₂	C ₁	C ₂
105	5	-5	0	0	0	-5	10	10
106	0	-10	-5	-5	-5	-10	-10	-10
108	-5	10	-5	0	0	5	-5	5
115	0	-5	5	-5	0	-5	10	15
121	0	-5	0	5	-5	-5	5	5
125	0	-10	5	0	0	-10	0	0
127	0	0	0	5	-5	5	5	10