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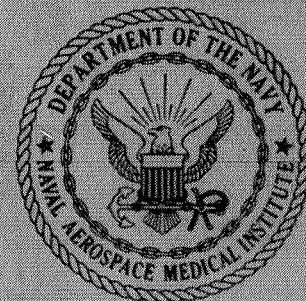
EVALUATION OF ANTIMOTION SICKNESS DRUGS: A NEW
EFFECTIVE REMEDY REVEALED

Charles D. Wood and Ashton Graybiel

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NAVAL AEROSPACE MEDICAL INSTITUTE

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

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EVALUATION OF ANTIMOTION SICKNESS DRUGS: A NEW

EFFECTIVE REMEDY REVEALED*

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SUMMARY PAGE

THE PROBLEM

Three single drugs (one used in three dosage levels) and three drug combinations were compared in their effectiveness to prevent motion sickness under standardized stress conditions in a slow rotation room.

FINDINGS

An unexpected finding was that a combination of promethazine 25 mg with d-amphetamine 10 mg had the same range of effectiveness as that found in earlier studies (and confirmed here) for scopolamine 0.6 mg plus d-amphetamine 10 mg. When scopolamine was tested alone, halving the "usual" dose (0.6 mg) reduced its effectiveness about one-fifth and doubling the usual dose increased effectiveness by 29 per cent; thus, the optimum dose of scopolamine appeared to be approximately 0.5 mg. Betahistine hydrochloride (4 mg) was ineffective and cinnarizine (50 mg) was of small benefit.

ACKNOWLEDGMENTS

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INTRODUCTION

In previous investigations (1, 5-8) dealing with antimotion sickness drugs it was found that only those with parasympatholytic or sympathomimetic action and some of the antihistamines were notably effective. This report consists of an extension of those studies and presents the evaluation of one new drug and either new combinations or different dosage levels of drugs previously tested.

PROCEDURE

The subjects in the present study were ten healthy men, 18 to 23 years of age, who demonstrated normal responses to functional tests of the sensory organs of the inner ear. Baseline susceptibility to motion sickness was determined by rotating each subject in the slow rotation room at increasing speeds until he reached the predetermined endpoint of severe malaise (M III) (2) in less than fifty head movements during performance of the Dial Test (3). This speed of rotation was then maintained for that subject during the drug trials. Severe malaise, although a mild level of motion sickness, is of demonstrably high reliability as an endpoint under the circumstance of the present experiment. The Dial Test consists of setting the pointer on each of five dials arranged around the subject in such a manner as to require him to make five different head-body movements out of the plane of the room's rotation. The head movements are paced by a tape recording that gives numbers to be set on the dials in randomized order at a rate of one every 6 seconds.

The eight "drugs" (three in different combinations) administered along with two placebos according to a ten-unit Latin square design were as follows:

betahistine hydrochloride	4.0 mg
l-benzhydryl-4-cinnamylpiperazine (cinnarizine)	50.0
l-scopolamine hydrobromide	0.3
	0.6
	1.2
promethazine hydrochloride	25.0
plus	
ephedrine sulfate	50.0
promethazine hydrochloride	25.0
plus	
dextroamphetamine sulfate	10.0
l-scopolamine hydrobromide	0.6
plus	
dextroamphetamine sulfate	10.0

The drugs and placebos were placed in identical opaque gelatin capsules, and the double blind technique of administration was used. The percentage increase in the number of head movements with an active drug, or combination of drugs, over the baseline trial (placebo) was taken as the effectiveness of that drug.

RESULTS AND DISCUSSION

The results are summarized in Figure 1. The outstanding finding was the effectiveness against motion sickness of the drug combination promethazine and amphetamine that ranked just below scopolamine and amphetamine, which had been tested also on previous occasions. Ephedrine combined with promethazine was still highly effective although significantly less than the aforementioned combinations. Scopolamine in a "usual" dose (0.6 mg) was more effective (19%) than half the dose but less effective (29%) than double the dose. Betahistine was ineffective and cinnarizine in the dosage used was of small benefit.

Although in previous experiments both promethazine and amphetamine were shown to be highly effective in preventing motion sickness, it was not expected that these effects would sum when given together inasmuch as the combination of an antihistamine (meclizine) with amphetamine afforded less protection (+20 head movements) than either meclizine (+23 head movements) or amphetamine (+50 head movements) taken singly. The demonstration that the new combination is about equal in effectiveness to the combination of scopolamine and amphetamine increases the scope of preventative therapy, partly on the basis of individual differences in response to drugs and partly on the basis of differences between promethazine and scopolamine in their side effects. Among antimotion sickness drugs scopolamine ranks high in side effects (4) and its use may be contraindicated, e.g., in patients with severe glaucoma or urinary retention. Promethazine ranks low both in side effects and contraindications.

Promethazine combined with ephedrine, although much less effective than with amphetamine, nevertheless ranked among the best four preventative drugs. The differences in side effects between ephedrine and amphetamine may make the former the more desirable drug under certain circumstances or in certain cases.

Scopolamine (0.6 mg) alone has consistently been shown to be an effective preventative in our previous studies. Doubling the usual dose provided even more protection but resulted in side effects such as drowsiness. Since the smaller dose of 0.3 mg was only slightly less effective than the 0.6-mg dose, it would appear that approximately 0.5 mg would be a suitable amount of scopolamine when it is used alone.

The effective drugs all have strong central nervous system actions. Scopolamine is a strong anticholinergic and has a much greater central effect than does atropine. Promethazine has the strongest "atropine-like" effect of any of the antihistamines. On the other hand, amphetamine also has strong central effects that are entirely different from those two drugs. These results indicate that the action of the effective antimotion sickness drugs is on the central nervous system and that at least two separate areas are involved in motion sickness. Further research on this possible mechanism is now in progress.

The antimotion sickness drugs appear to act by raising the threshold of susceptibility to motion sickness. They can prevent the development of motion sickness in a given stress situation, but they do not confer immunity in situations of extreme stress due to motion.

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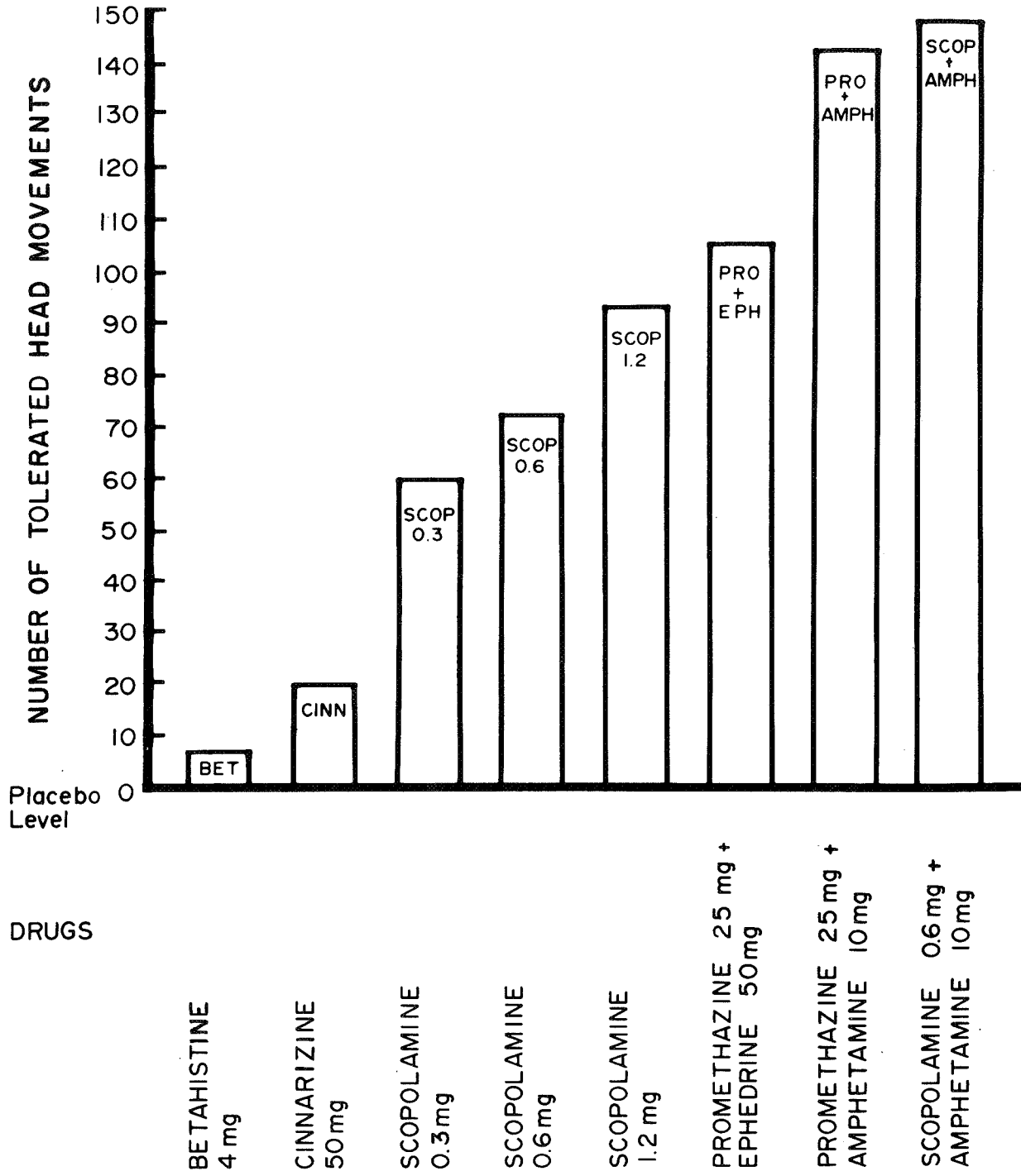


Figure 1

Drugs and Combinations of Drugs Ranked According to Effectiveness

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