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16. Abstract

Fourteen men were studied to determine the combined effects of two altitudes {ground level (1,274 ft) and 12,500 ft}, and three preparations {lactose placebo, Compound A (Actifed ®), and Compound B (Dristan ®)}.

Physiological data show that A was a stimulant and B a depressant. Subjects reported least subjective attentiveness with A and greatest with lactose. Significant time effects were evident in subjective ratings (increasing fatigue and decreasing energy, interest, and attentiveness). The Multiple Task Performance Battery (MTPB) showed no effects of altitude, drugs, or time on overall performance; however, performance declined from the first to the second hour in several tasks, while problem solving improved. The data are compatible with reported decreasing interest and attentiveness; subjects enjoyed the problem-solving tasks and may have given those tasks preference as their levels of interest declined.

Though performance on the MTPB, with the drug doses evaluated, did not produce any changes in the overall composite scores earned by these healthy subjects, the results from physiological parameters and some subjective evaluations indicate that time after ingestion and type of compound ingested are important. Declines in energy and attentiveness 2 1/2 hr after ingestion could result in neglect of important although routine tasks. Hypoxia might enhance this effect and consequences might be worse in subjects whose medical conditions require these drugs.

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THE EFFECTS OF ALTITUDE AND TWO DECONGESTANT-ANTIHISTAMINE PREPARATIONS ON PHYSIOLOGICAL FUNCTIONS AND PERFORMANCE

I. Introduction.

A number of decongestant-antihistamine preparations are available for symptomatic treatment of common colds, hay fever, and allergies. Many of these can be obtained without prescription. Some of the decongestants and antihistamines found in such preparations are known to have effects on both physiological function and performance (1,2,3). In an earlier study (5), we found that the combination of a simulated high altitude and a drug containing the antihistamine chlorpheniramine produced a synergistic detrimental effect on a psychomotor task.

To provide data useful for aeromedical standards development and medical certification, this study was designed to measure the combined effect of altitude and each of two decongestant-antihistamine preparations on complex performance and physiological functions. The drugs evaluated were: Compound A (Actifed®), one of the most frequently prescribed medications of this type (9), containing 60 mg pseudoephedrine hydrochloride and 2.5 mg triprolidine hydrochloride; and Compound B (Dristan®), a common over-the-counter medication, containing 10 mg phenylephrine hydrochloride, 20 mg phenindamine tartrate, aspirin, caffeine, and aluminum hydroxide/magnesium carbonate co-dried gel.

II. Methods.

Fourteen healthy male paid subjects (aged 18 to 33 years) were tested in random sequence under six experimental conditions, with combinations of two altitudes (ground level {1,274 ft} and 12,500 ft) with the two drugs and a placebo of lactose. All subjects were interviewed and given physical examinations prior to selection. During the interviews subjects received a thorough explanation of the test procedures and purposes of the study. After selection, subjects were trained for 10 h on the Civil Aeromedical Institute (CAMI) Multiple Task Performance Battery (MTPB). After training, subjects reported individually to the laboratory twice a week (either Monday and Thursday or Tuesday and Friday) for 3 consecutive weeks for the experimental sessions described in Table 1.

TABLE 1. Experiment Schedule

Morning Time	Afternoon Time	Scheduled Activity
0900	1230	Report to laboratory Void urine, record time Execute subjective forms Insert rectal probe Place electrodes for heart rate recording
0930	1300	Take capsules
0950- 1000	1320- 1330	Begin ascent to preselected altitude Complete ascent
1000- 1200	1330- 1530	Experiment period in altitude chamber
1200- 1210	1530- 1540	Begin descent to ground level, Execute subjective forms Complete descent
1210	1540	Return to laboratory Collect urine, record time Remove probe and electrodes Release subjects from experiment

The preexperiment and postexperiment subjective forms completed by the subjects were the Subjective Fatigue Index (8) and a subjective nine-point rating scale for attention, energy, strain, interest, and irritability. During the experiments heart rate (HR) was recorded continuously via chest electrodes connected to an electromagnetic tape recorder. Measurements of internal body temperature (T_{re}) and blood pressure (BP) were obtained at the beginning of the experiment and during the last minute of each 15-min segment of the experimental period. Complex performance was measured throughout the 2-h experiment by using the CAMI one-man MTPB (4). The three monitoring tasks of the

MTPB (red lights, green lights, and meters) were presented continuously during the testing session. The other MTPB tasks were presented in different combinations for each 15-min interval of the session. These tasks were: (i) tracking and arithmetic; (ii) problem solving and arithmetic; (iii) problem solving and pattern identification; (iv) tracking and pattern identification. The same schedule was repeated during the second hour of the testing. The postexperimental urine collections were preserved and later analyzed for their epinephrine (E), norepinephrine (NE), and 17-ketogenic steroid (17-KGS) content (7).

III. Results.

All data were subjected to analysis of variance techniques (6). The level considered to be statistically significant was $p \leq .05$.

A. Physiological Parameters.

Heart rate. Mean HR data are presented in Table 2. There were several statistically significant effects on HR: An altitude effect, with mean HR higher at 12,500 ft than at ground level; a drug effect, with mean HR greatest with Compound A and lowest with Compound B; and an altitude-drug interaction with the difference in HR between Compound A sessions and Compound B sessions being greater at 12,500 ft (about 8 beats per min) than at ground level (about 4 beats per min). There was also a time effect; HR decreased over the 2-h experimental period.

Internal body temperature. The mean T_{re} data are presented in Table 3. The mean T_{re} was significantly higher at ground level than at 12,500 ft. There was also a drug effect with subjects having the highest mean T_{re} during Compound A sessions and the lowest mean T_{re} during the Compound B sessions.

Blood pressure. Blood pressure data are presented in Table 4. The anticipated altitude effects were evident with systolic blood pressure (SBP) and diastolic blood pressure (DBP) significantly greater at ground level than

TABLE 2. Mean Heart Rate Data

(N = 14) (beats per minute)

	Time Interval (minutes)							
	0–15	15–30	30–45	45–60	60–75	75–90	90–105	105–120
Ground Level								
Compound A	80	79	79	78	77	77	76	76
Compound B	76	74	73	72	72	72	72	72
Placebo	78	77	76	76	74	73	72	71
Mean	78	77	76	76	75	74	73	73
12,500 Feet								
Compound A	87	86	86	86	88	87	86	87
Compound B	80	78	78	78	78	78	78	80
Placebo	83	81	81	79	79	78	78	78
Mean	83	82	82	81	82	81	81	82
Compound A Mean	83	83	82	82	82	82	81	82
Compound B Mean	78	76	75	75	75	75	75	76
Placebo Mean	81	79	78	78	79	76	75	75
Mean Through Time	81	80	79	78	79	77	77	77

at 12,500 ft and pulse pressure (PP) greater at 12,500 ft. There was a drug effect for SBP only, with Compound B sessions exhibiting the highest mean value. Both SBP and PP declined through time. The mean DBP exhibited a significant time-altitude interaction, with mean values declining slightly at 12,500 ft and increasing at ground level.

TABLE 3. Internal Body Temperature (in ^{o}C)

	Altitude		
	Ground Level	12,500 Feet	Mean
Compound A	37.29	37.22	37.26
Compound B	37.08	37.06	37.07
Placebo	37.22	37.07	37.15
Mean	37.20	37.12	37.16

Urinary hormone excretion. There were no significant findings for the urinary excretion of E. The 17-KGS and NE data are presented in Tables 5 and 6. The only drug effect was for 17-KGS with the highest mean values occurring when subjects took Compound A and the lowest mean values occurring when subjects took Compound B.

B. Complex Performance.

Performance on the MTPB was assessed by computing two composite scores, one representing all tasks and one representing only the monitoring tasks. These scores were calculated so that each measure from the individual tasks made an equal contribution to the variance of the composite score. Reciprocals of the response time and tracking scores were used. The composite scores were then analyzed in a treatment-by-subjects analysis of variance; altitude, drugs, and hours (first and second) within sessions were

TABLE 4. Blood Pressure
(in mm Hg)

	Time (minutes) 0	15	30	45	60	75	90	105	120
Ground Level	115/ 70 (45)	112/ 72 (40)	112/ 72 (40)	111/ 73 (38)	109/ 72 (37)	110/ 72 (38)	111/ 73 (38)	110/ 72 (38)	110/ 73 (37)
12,500 Feet	116/ 72 (44)	112/ 69 (43)	110/ 70 (40)	110/ 69 (41)	109/ 69 (40)	108/ 68 (40)	107/ 69 (38)	107/ 67 (40)	107/ 69 (38)
Compound A	115/ 72 (43)	113/ 70 (43)	112/ 72 (40)	112/ 72 (40)	109/ 70 (39)	108/ 70 (38)	109/ 72 (37)	108/ 69 (39)	108/ 70 (38)
Compound B	114/ 70 (44)	112/ 71 (41)	112/ 72 (40)	111/ 70 (41)	109/ 70 (39)	110/ 72 (38)	111/ 71 (40)	110/ 70 (40)	109/ 71 (38)
Placebo	117/ 71 (46)	112/ 71 (41)	110/ 70 (40)	109/ 70 (39)	109/ 71 (38)	108/ 70 (38)	107/ 70 (37)	108/ 70 (38)	107/ 72 (35)
Mean	115/ 71 (44)	112/ 71 (41)	111/ 71 (40)	111/ 71 (40)	109/ 70 (39)	109/ 71 (38)	109/ 71 (38)	109/ 70 (39)	108/ 71 (37)

Legend: Systolic/
Diastolic
(pulse pressure)

the three sources of variance. The mean scores associated with these analyses are reported in Table 7. No significant differences were found in the overall composite scores. The analysis of the monitoring composite showed no significant effects of altitude or drugs, but there was a significant ($p \leq .05$) effect of hours, with the second hour of performance being poorer than the first.

TABLE 5. 17-Ketogenic Steroid Excretion (in Micrograms per hour)

	Altitude Ground Level	12,500 Feet	Mean
Compound A	622	718	670
Compound B	436	569	503
Placebo	546	688	617
Mean	535	659	597

TABLE 6. Norepinephrine Excretion (in Nanograms per hour)

	Altitude Ground Level	12,500 Feet	Mean
Compound A	2,100	2,005	2,053
Compound B	2,262	1,984	2,123
Placebo	2,684	1,944	2,314
Mean	2,349	1,978	2,163

Similar analyses performed on the individual performance measures revealed only a significant effect of hours

TABLE 7. Mean MTPB Scores*

	ALTITUDE		DRUGS			HOURS	
	GL	12,500 Ft	Compound A	Compound B	Placebo	First	Second
Composite, All measures	503	497	495	508	498	501	500
Composite, Monitoring	503	497	496	507	497	514	486**
Green Lights	512	487	495	511	493	506	494
Red Lights	510	490	492	504	503	507	492**
Meters	500	500	484	489	525	502	497
Arithmetic, time	493	507	496	498	507	489	511
Arithmetic, percent	493	507	483	512	506	509	491
Pattern Id., time	521	491	513	502	504	497	516
Pattern Id., percent	480	497	485	500	479	490	487
Problem Solving, time	493	482	482	490	489	474	501**
Problem Solving, percent	508	508	505	515	505	502	514
Problem Solving (confirmation, time)	493	483	484	503	476	469	507**
Problem Solving (confirmation, percent)	512	509	504	522	506	517	505
Tracking	521	480	504	498	500	528	472**

* Transformed to standard format (mean = 500, S.D. = 100). High scores represent better performance.

** Statistically significant at $p \leq .05$

within sessions. Red lights, meter monitoring, and tracking were significantly poorer in the second hour; problem-solving solution time and problem-solving confirmation time were significantly better during the second hour.

C. Subjective Evaluations.

Fatigue. The only statistically significant finding for the Subjective Fatigue Index was a time effect with all subjects reporting greater fatigue at the end of the experiment than at the beginning ($p \leq .01$) (Table 8).

TABLE 8. Subjective Fatigue*

	Pretest Score	Posttest Score
Ground Level		
Compound A	7.5	9.8
Compound B	8.1	9.3
Placebo	7.6	9.7
12,500 Feet		
Compound A	8.6	10.9
Compound B	7.6	9.4
Placebo	7.2	10.4
Mean	7.7	9.9

* On a 20-point scale, 0 = fully refreshed, 20 = completely exhausted.

Energy. Complementing the fatigue data, subjects reported having less energy ($p \leq .01$) at the end of the experiment than at the beginning. However, there was also a drug effect ($p \leq .01$) on reported energy levels (Table 9). Subjects reported highest energy levels after the placebo session and lowest levels after the session that involved Compound A.

Strain, irritation, and interest. Table 10 presents the data for strain, irritation, and interest. The only statistically significant findings were for time; subjects reported more strain, more irritation, and less interest from beginning to end of experiment ($p \leq .01$).

TABLE 9. Energy*

	Pretest Score	Posttest Score
Ground Level		
Compound A	4.2	3.1
Compound B	4.1	3.6
Placebo	4.8	4.1
12,500 Feet		
Compound A	4.0	2.5
Compound B	4.1	3.4
Placebo	4.8	3.4
Mean		
Compound A	4.1	2.8
Compound B	4.1	3.5
Placebo	4.8	3.8
Overall	4.3	3.4

* On a 9-point scale, 0 = lowest, 9 = highest

TABLE 10. Strain, Irritation, and Interest*

	Pretest Score	Posttest Score
Strain	2.7	3.3
Irritation	0.6	1.4
Interest	6.5	4.8

* On a 9-point scale, 0 = lowest, 9 = highest

Attentiveness. The subjects were less attentive ($p \leq .01$) after the experiment than before (Table 11). There was also a drug effect ($p \leq .05$) on attentiveness, reported attentiveness being least following Compound A sessions and greatest following the placebo sessions.

TABLE 11. Attentiveness*

	Pretest Score	Posttest Score
Compound A	4.6	3.4
Compound B	4.7	4.1
Placebo	5.2	4.2
Mean	4.8	3.9

* On a 9-point scale, 0 = lowest, 9 = highest

IV. Discussion.

The drugs used in this study caused statistically significant changes in several of the parameters measured. Altitude also produced an effect. In only one parameter, HR, was there a significant drug-altitude interaction. The HR increase when 12,500 ft and Compound A were combined was greater than the sum of the HR increases for the two factors independently.

The physiological and biochemical data, averaged over the 2-h period, indicate that Compound A acted as a stimulant and Compound B as a depressant. Heart rate, T_{re} and the 17-KGS were highest values when subjects were taking Compound A and lowest when they were taking Compound B. This time period covers from 1/2 to 2 1/2 h after ingestion.

The subjective evaluations were made before and after the test but cannot be interpreted as reflecting the average feelings of the subjects during the 2-h period. Subjects reported the least energy and attentiveness when taking Compound A and the greatest when taking the placebo. One of the reported effects of the antihistamine components of these compounds is "drowsiness"; this could account for the decline in feelings of energy and alertness.

The overall composite MTPB scores showed no effects of altitude, drugs, or time. However, the significant decline in performance from the first to the second hour in the monitoring composite, red light monitoring, and tracking scores and the improvement from the first to the second hour in problem-solving solution time and problem-solving confirmation time may both be directly compatible with the subjects' self-reports of increasing fatigue as well as decreasing energy, interest, and attentiveness. The subjects generally reported enjoying the problem-solving tasks more than the other MTPB tasks; they may therefore have devoted more attention to problem solving as their general levels of interest and attention declined, while allocating less attention to the more ambiguous and less enjoyable tracking and monitoring tasks. Thus, the decline in performance on the "less enjoyable" tasks was offset by improved performance on the "more enjoyable" tasks, resulting in no significant change in the composite score.

For performance on the MTPB, the drugs and dosages evaluated in this study did not produce any significant changes in the overall composite scores earned by otherwise healthy subjects, although with time there were changes in the levels of effort and attention devoted to different tasks. However, the results from some of the physiological parameters and some of the subjective evaluations indicate that the time after ingestion and the type of compound ingested are important considerations. The decline in self-reported energy and attentiveness reported 2 1/2 h after ingestion could result in the neglect of important although routine tasks that require some degree of concentration. This drug effect could be enhanced by hypoxia and consequences might be less favorable in subjects whose medical condition requires the use of these drugs.

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