EFFECTS OF SOME MOTION SICKNESS SUPPRESSANTS ON TRACKING PERFORMANCE DURING ANGULAR ACCELERATIONS

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**Abstract**

Student pilots sometimes experience motion sickness early in their flight training and drug remedies may be prescribed for dual flights. Moreover, prescriptions are not required for some motion sickness preventives. In addition, business associates or spouses often accompany private pilots on flying trips; some of these passengers, who may be required to pilot the aircraft in an emergency, use antimotion sickness drugs. While the basic efficacy of such drugs is rooted in the reduction of motion sickness symptoms, adverse side effects are important practical considerations of their usage in aviation. The two studies reported here examined the influence of three established antimotion sickness drugs on tracking performance in static (stationary) and dynamic (angular acceleration) conditions and on visual fixation ability during motion. In Study I, 40 young men were randomly assigned in equal numbers to either a control (lactose placebo), dimenhydrinate (50 mg), promethazine hydrochloride (25 mg), or mixture (25 mg promethazine plus 10 mg d-amphetamine) group. Study II used 30 new subjects equally divided into control, dimenhydrinate (100 mg), and promethazine (50 mg) groups. Following practice, tests were conducted prior to 1, 2, and 4 hours after drug ingestion. The depressant drugs had little effect on static tracking, but impaired dynamic tracking performance and reduced ability to maintain visual fixation on a localizer/glide slope instrument due to increased ocular nystagmus. The mixture of promethazine and d-amphetamine produced none of these deleterious effects.

**Keywords**

Performance
Motion Sickness
Drugs
Visual-Vestibular Interactions
Medical Certification Policy

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EFFECTS OF SOME MOTION SICKNESS SUPPRESSANTS ON TRACKING PERFORMANCE DURING ANGULAR ACCELERATIONS

Introduction.

Student pilots sometimes experience motion sickness to varying degrees early in their training and the use of drug remedies is not prohibited when prescribed for dual flights. Moreover, prescriptions are not required for some motion sickness preventives. In addition, spouses or business executives often accompany private pilots on flying trips; some of these passengers, who may be required to pilot the aircraft in an emergency, use antimotion sickness drugs.

The recommended use of drugs to suppress motion sickness involves a prior assessment of undesirable side effects. In most cases, the side effects that are considered are those such as drowsiness, dry mouth, blurred vision, irritability, talkativeness, etc. (8). In some cases, performance data under drug conditions are available, but almost invariably such data are based on performance in static (stationary) environments. There are data, however, that indicate that moderate doses of two types of depressant drugs, alcohol and secobarbital sodium, may have no demonstrable effect on the performance of a tracking task in a static environment but may produce significant impairment of both performance and visual fixation ability in a dynamic (angular acceleration) environment (1,4,9,10). Since motion sickness suppressants are specifically used in dynamic environments, the possible deleterious effects of such prescriptions on performance and visual acuity during motion are important considerations in a variety of applications for transportation systems. Thus, the present study was designed to compare the effects of several drugs used as motion sickness preventives on performance at an eye-hand coordination task (tracking) under both stationary conditions and conditions involving whole-body angular motion and concomitant nystagmic eye movements.

Method.

Subjects. In the first of two experiments, 40 male college students served as subjects; none had any previous laboratory experience involving vestibular stimulation. These students were assigned to one of four groups of 10 subjects each: (i) control (lactose placebo), (ii) 50 mg dimenhydrinate, (iii) 25 mg promethazine hydrochloride, and (iv) a mixture group (25 mg promethazine hydrochloride plus 10 mg d-amphetamine). The latter combination of drugs was included because it has been cited as one of the most effective antimotion sickness drugs in laboratory studies (13). A second experimental series involved higher drug dosages administered to 30 new subjects who were placed in three groups of 10 each: (1) control (lactose placebo), (ii) 100 mg dimenhydrinate, and (iii) 50 mg promethazine hydrochloride.
Apparatus. A modified Stille-Werner RS-3 rotation device provided the angular stimulation, viz, a triangular waveform stimulus with a 48-s period and a peak turning velocity of 120°/s in both the clockwise and counterclockwise directions. Subjects were seated in the device with their heads secured in a headrest positioned so as to place the lateral pair of semicircular canals approximately in the plane of stimulation.

An aircraft localizer-glide slope indicator located directly in front of the subject provided the visual stimulus for the one-degree-of-freedom tracking task. While the room was in total darkness during the trial, the indicator was illuminated at a level comparable to that recommended for aircraft instruments during night flight, viz, one fL. The vertical needle of the indicator was driven to the left and right of center by a sinusoidal forcing function with a 14-s period. Movements of the needle were thus in the same approximate plane as the eye movements arising from the rotary stimulation. The subject was instructed to make compensatory movements of a joystick in order to maintain the needle in the center or null position. Deviations from the null position were considered as errors and a voltage proportional to these deviations was electronically integrated over 1-s intervals and recorded. Further details concerning the operation of the tracking task are presented elsewhere (3).

To monitor and record eye movements during vestibular stimulation, electrodes were taped beside the outer canthus of each eye. An electrode placed on the forehead served as a ground. The eye movement signals passed through a series of slip rings located at the base of the rotation device and were then recorded on a Beckman Type T electroencephalograph located in an adjoining room. Calibration of these ocular movements was accomplished by having the subject sweep his eyes between two small flashing lights on the front of the rotator.

Procedure. The basic experimental paradigm was nearly identical to that used in previous studies concerning the effects of alcohol and of secobarbital on performance (1,10). The subjects were tested on five separate occasions during a single day. A practice session was used to acquaint the subject with the task and with the sensations arising from the stimulation. This was followed by a predrug session and three postdrug sessions conducted 1, 2, and 4 hours after the subjects ingested their respective capsules. The capsules were administered using a double-blind procedure. Subjects were not allowed to smoke or to drink beverages containing caffeine, except during a 2-h lunch period which preceded the final session. Each experimental testing session consisted of (i) 1 1/2 min of static tracking (30-s warmup; 1-min scored) prior to the start of motion, and (ii) dynamic tracking during five periods of angular accelerations (first period for warmup). Prior to each session, subjects rated 15 adjectives (active, drowsy, dull, sluggish, tired, sleepy, bored, lazy, leisurely, nonchalant, energetic, vigorous, fatigued, happy, and annoyed) from the 80-item Composite Mood Adjective Check List (CMACL) developed by Malstrom (7). Each rating was on a 9-point scale ranging from...
"not at all" descriptive through "moderately" to "definitely" descriptive of the subject's current feelings. Three mood scores were calculated, viz, fatigue, vigor, and sleepy (7).

Scoring. Tracking error was measured in 1-s intervals for both the static and dynamic conditions. Error scores were accumulated and averaged across groups for the last min of static tracking and for the first min (following warmup) of dynamic tracking. For the same period of dynamic tracking, the amount of slow-phase eye displacement was measured and the frequency of nystagmic eye movements was calculated; mean values were then determined and used as measures of nystagmic output. Scores on each of the two measures of nystagmus were used in separate statistical analyses. Additional scoring of tracking error and nystagmus included the three dynamic periods following warmup to assess other effects of time on task. All these data were treated by analysis of variance techniques followed by Tukey's Honestly Significant Difference (HSD) tests.

For some graphic presentations, "change" scores were computed. For each group and each measure, the mean score for the predrug session was plotted as "zero" and the percentage of increase or decrease in scores during subsequent sessions was plotted as "percent increase" or "percent decrease" from the predrug level.

Results.

TRACKING

Within Groups Comparisons. Although error scores for the placebo and mixture groups (see Figure 1) generally declined across sessions, the decline during static tracking in Study I was significant only for the placebo group; all three postingestion sessions were lower (better performance) than the preingestion session (p < .01 - .001). For the same duration of dynamic tracking (1 min), the placebo group scored significantly better (p < .05) during the 2-h postingestion session than during the preingestion level while the mixture group had significantly (p < .05) less error during the 1-h and 2-h postingestion session in comparison with predrug performance. For both static and dynamic tracking, the dimenhydrinate and promethazine groups showed no significant change across sessions.

In Study II, no significant change across sessions occurred for any group in static tracking (see Figure 2). Dynamic tracking scores showed significant effects only for the dimenhydrinate group, viz, the 2-h postingestion session had significantly more error than either of the two preceding sessions (p < .05 in both cases). Higher error scores for the promethazine group during the last two sessions approached but did not reach significance due primarily to increased variance.
STATIC TRACKING

DYNAMIC TRACKING

FIGURE 1. Changes in tracking performance in Study I under static (stationary) and dynamic (angular acceleration) conditions. Drug dosages were 50 mg dimenhydrinate, 25 mg promethazine hydrochloride, and a mixture of 25 mg promethazine hydrochloride plus 10 mg dextroamphetamine.

Between Groups Comparisons. Analyses of variance yielded no overall differences for static tracking in Study I but simple effects tests showed significantly (p < .05) less error for the placebo vs. the promethazine group 2-h postdrug, while the placebo vs. dimenhydrinate difference for the same session fell just short of significance. The analyses for dynamic tracking yielded several significant effects. Scores for the mixture group were (i) better (p < .01) than those for dimenhydrinate subjects during the 1-h postingestion session, (ii) better (p < .001) than both the dimenhydrinate and promethazine groups during the 2-h session, and (iii)-better (p < .05) than promethazine scores during the final session. In addition, placebo scores were better (p < .001) than both dimenhydrinate and promethazine during the 2-h session and were better (p < .05) than promethazine during the final session.

In Study II, differences between groups in static tracking scores were relatively slight and no statistically reliable differences were found. Dynamic tracking scores for the placebo group were better (p < .05) than those for the two drug groups during the 2-h postingestion session.
FIGURE 2. Changes in tracking performance in Study II under static (stationary) and dynamic (angular acceleration) conditions. Drug dosages were 100 mg dimenhydrinate and 50 mg promethazine hydrochloride. Plotting procedures were as in Figure 1.

NYSTAGMUS WHILE TRACKING

Within Groups Comparisons. In Study I, all postdrug sessions for both measures of nystagmus showed less output for the placebo and mixture groups, and (with one minor exception) increased output for the dimenhydrinate and promethazine groups when compared to predrug levels (see Figure 3). However, analysis of variance for repeated measures yielded significant sessions effects for measures of both slow-phase (p < .001) and frequency of eye movements (p < .01) only for the mixture group. Simple effects tests indicated significantly less slow-phase output for mixture subjects during all three postdrug sessions (p < .05 - .001) in comparison with the predrug session, and a lower frequency of nystagmus (p < .01) during the 2-h postdrug trial.

In Study II, analyses of variance within each group yielded significant sessions effects (p < .01 - .001) for both measures of nystagmus for the
FIGURE 3. Slow-phase displacement and the frequency of nystagmus obtained in Study I while subjects were tracking in the dynamic condition. Drug dosages were 50 mg dimenhydrinate, 25 mg promethazine hydrochloride, and a mixture of 25 mg promethazine hydrochloride plus 10 mg dextroamphetamine. Measures for the pretrial (before ingestion of the drug or placebo capsule) were set at 0. Measures for the post-ingestion sessions were converted to percentages of increase or decrease from the pre-ingestion baseline.
FIGURE 4. Slow-phase displacement and the frequency of nystagmus obtained in Study II while subjects were tracking in the dynamic condition. Drug dosages were 100 mg dimenhydrinate and 50 mg promethazine hydrochloride. Plotting procedures were as in Figure 3.
FIGURE 5. Tracking error, slow-phase nystagmus displacement, and fast-phase frequency of nystagmus, across the 48-s stimulus periods in each session of Study I. Scores for each measure for the first 48-s stimulus of the first session (preingestion) were set at 0; all subsequent scores across stimulus periods and sessions for each measure were plotted as percentages of increase or decrease from that 0 baseline.
FIGURE 6. Tracking error, slow-phase nystagmus displacement, and fast-phase frequency of nystagmus across the three 48-s stimulus periods in each session of Study II. Plotting procedures were as in Figure 5.
placebo and the promethazine groups (see Figure 4). The direction of the effects were opposite, however, in that the placebo group showed a steady decline across postdrug sessions while the promethazine group had higher scores for all but one of the postdrug sessions. Dimenhydrinate resulted in no significant effects, although increased nystagmus characterized the 1-h and 2-h postdrug sessions for both measures. For slow-phase measures, simple effects tests showed that the outputs for both the 2-h and the 4-h postdrug sessions for placebo were less than the predrug session ($p < .01$), and the 4-h postdrug session for promethazine had higher scores than both the predrug and first postdrug session ($p < .05$). For the frequency of eye movements, (i) both the 2-h and 4-h postdrug sessions had less output than the predrug session ($p < .001$) for placebo, (ii) the 4-h session output was greater than the predrug ($p < .01$) and the 1-h ($p < .001$) sessions for promethazine, and (iii) the 2-h postdrug output was greater ($p < .05$) than the 4-h postdrug output for dimenhydrinate.

**Between Groups Comparisons.** Overall analyses of variance for the two eye movement measures yielded three significant F-ratios in Study I; one for slow-phase scores ($p < .001$ between groups) and two for the ocular frequency ($p < .01$ between groups and $p < .05$ for the groups x sessions interactions). HSD tests for slow-phase scores yielded significantly less nystagmus for the mixture group than for the dimenhydrinate and the promethazine conditions during all three postdrug sessions ($p < .05 - .001$). HSD tests for the frequency of eye movements yielded effects only for the 1-h and 2-h postdrug sessions, viz, less eye movement for the mixture group than for dimenhydrinate ($p < .05$) in the former session, and again less nystagmus for the mixture condition than for each of the other three conditions ($p < .05 - .001$) during the second postdrug hour.

Overall analyses of variance in Study II yielded significant F-ratios for groups and for the groups x sessions interactions for both the slow-phase ($p < .01$ in both cases) and frequency ($p < .001$ in both cases) measures. HSD tests showed, for both measures of nystagmus, more eye movement for promethazine ($p < .01$ in all cases) than for the placebo condition during both the 2-h and 4-h postdrug sessions. The 4-h postdrug sessions also yielded significantly more eye movement for promethazine than for dimenhydrinate ($p < .05$ for slow-phase; $p < .01$ for frequency). In addition, the frequency of eye movements was greater for dimenhydrinate than for the placebo ($p < .01$) during the second postdrug session.

**Effects of Longer Durations of Angular Stimulation.** Tracking error and nystagmus measures were also tabulated for each of the three scored 48-s periods of angular acceleration following warmup. "Change" scores were computed on a percentage basis using the mean score for the first period of the first session as 100 percent; each subsequent 48-s period for a given condition was plotted in terms of "Percent Change" from the base (Figures 5 and 6).
In both studies, postingestion tracking scores tended to increase across each block of three 48-s periods regardless of drug or placebo, with the two depressant drugs, dimenhydrinate and promethazine, showing the largest average increases in tracking error. Nystagmus measures yielded similar but less consistent results. There was invariably less nystagmus (both slow and fast phases) during the third 48-s period of each session for the placebo and mixture groups in Study I, but the third period uniformly had more nystagmus than the first period for the placebo group in Study II. Promethazine tended to produce increased nystagmus during third-period stimulation, with the effects more pronounced in Study II (Figure 6). Results for dimenhydrinate were less consistent; both Study II measures for the third period showed more nystagmus than the first period but the opposite effect was evident for the frequency measures in Study I.

Statistical analyses yielded significant period effects during tracking (increased error) for both doses of promethazine (p < .05) and for the double dose of dimenhydrinate (p < .05). In Study I, the placebo and mixture groups showed significant period effects (p < .05 - .01) for both measures of nystagmus (less output) and dimenhydrinate yielded a significant (p < .05) fast phase effect (less output). There were significant period effects for all three groups in Study II for both measures of nystagmus (p < .05 - .01).

MOOD SCORES

**Within Groups Comparisons.** The three mood factors in Study I showed no significant differences across sessions for placebo or dimenhydrinate subjects (see Table I). For the promethazine group, scores for the last session were higher (p < .01) than the predrug session for both the fatigue and sleepy mood factors. For the mixture group, (i) the high sleepy score on the final session differed (p < .05) from the low score for the 2-h session, and (ii) the fatigue factor was higher for the final session than for each of the preceding sessions (p < .05 - p < .01).

In Study II, analyses for each of the three mood factors yielded no sessional differences for the placebo group. Two hours after taking the drug, dimenhydrinate subjects had higher (p < .05) sleepy scores than they did during the 1-h postdrug session and reported more fatigue (p < .05) and less vigor (p < .01) than during the predrug session; their vigor scores remained significantly depressed (p < .01) during the final session. Promethazine subjects also showed mood changes but they were shifted toward the final session. Specifically, for promethazine subjects (i) fatigue scores were significantly higher than the predrug level, 2-h (p < .05) and 4-h (p < .001) postingestion; scores for the 4-h session were also higher (p < .01) than the first postdrug session; (ii) vigor scores were lower (p < .05) during the final session than they were prior to drug-taking; (iii) sleepy scores peaked during the final session and were higher than both the predrug (p < .001) and the first postdrug (p < .01) sessions.
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<td></td>
<td></td>
<td>SD</td>
<td>6.2</td>
<td>8.0</td>
<td>8.8</td>
<td>4.7</td>
<td>6.4</td>
<td>9.6</td>
<td>5.5</td>
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Between Groups Comparisons. Statistical comparisons of Study I scores between groups for each mood factor led to no significant differences for the fatigue ratings. The mean sleepy score during the final sessions for the promethazine group was the highest obtained for that factor and differed significantly (p < .05) from that of the placebo group. Only one other difference was significant between groups, viz, the higher vigor score for the mixture group vs. the reduced score for the dimenhydrinate groups (p < .05) during the 2-h postingestion session.

In Study II, comparisons of difference scores showed the dimenhydrinate group to be significantly lower in vigor than the placebo group (p < .05) during each of the last two sessions; the mean vigor score for the final session was also lower (p < .05) than that of placebo. Scores for the fatigue and sleepy factors yielded an identical pattern of significant effects; for both mood factors, promethazine scores were significantly higher (p < .05 in all cases) than both placebo and dimenhydrinate during the final session.

Discussion.

Tracking and Nystagmus. The patterns of results obtained in this study both for tracking and for nystagmus during dynamic tracking are highly similar to those obtained in previous reports dealing with effects of alcohol (1,4,9), and of secobarbital and d-amphetamine (2,10), on the same measures. Specifically, subjects given placebos show, over several test sessions, (i) some decrease or no change in static tracking error, (ii) some improvement in dynamic tracking scores, and (iii) some reduction in the amount of nystagmus during dynamic tracking.

On the other hand, with due consideration given for the action times of the various drugs, subjects given substances that are primarily depressants (alcohol, secobarbital, dramamine, and phenergan) show (i) no improvement in static tracking performance or less improvement than placebo subjects, (ii) impairment of dynamic tracking, and (iii) increases in the amount of nystagmus (less control of eye movements) during dynamic tracking. Conversely, d-amphetamine (either alone (10) or as it was administered in the present study with promethazine) produced opposite effects in subjects, viz, (i) improved static tracking scores, (ii) improved dynamic tracking performance, and (iii) marked reductions in nystagmus (better ocular control) during dynamic tracking.

The improvement across sessions in tracking scores and in (reduced) nystagmus for control subjects appears to reflect positive effects of practice. The introduction of d-amphetamine (alone or in the combination used in this study) appears not to interfere with this learning process. However, each of the depressant drugs tested so far has produced an opposite pattern of results, viz, during the period of peak effectiveness of the drugs (and depending upon the dosage), clear impairment both of dynamic tracking performance and of visual fixation ability has occurred.
Performance during static tracking may be misleading regarding the deleterious influence of those drugs since improvement has occurred following alcohol ingestion (4) and since control subjects sometimes do not show improvement (as in Study II of this report). Parenthetically, in addition to data on motion sickness prevention, Wood and Graybiel (14) reported the absence of any significant changes in (static) visual acuity, balance, reaction time, and decision-making behavior following administration of either dimenhydrinate or promethazine. But the negative performance effects of the depressants have been consistent in the motion environment and suggest strongly that, for many practical situations, knowledge regarding the influence of drugs on various types of performance requires an assessment of motion effects.

The deleterious effects on dynamic tracking performance, which have been consistently obtained with depressant drugs, have been accompanied by a loss of ability to maintain adequate visual fixation during vestibular stimulation. The impairment of visual acuity arising from the inability to suppress vestibular nystagmus by visual means seems to be a primary proximal cause of the increased tracking errors (3,6,10).

The addition of d-amphetamine to promethazine obviated the undesirable ocular and performance consequences of the depressant. This positive effect is of particular significance since the combination of these substances is so highly effective as a motion sickness preventive. In fact, the addition of d-amphetamine (or ephedrin) to depressants such as promethazine hydrochloride or scopolamine, two drugs which are themselves reasonably effective in preventing motion sickness, tends to improve their effectiveness in this regard (5,12,13). Thus, these combined drug treatments have the advantages of greater protection against motion sickness and (at least with the d-amphetamine plus promethazine mixture, and probably with the other analeptic/depressant combinations noted above) abolition of ordinary undesirable side effects such as drowsiness, plus protection against some practical but less well-known consequences associated with performance and visual fixation during motion.

Effects of Longer Durations of Angular Stimulation. Over the three consecutive 48-s periods of angular stimulation, it is clear that tracking error tended to increase with time on task (even though overall performance might have generally improved from session to session, as with the placebo and mixture groups). The between-period increases in error occurred irrespective of drug or placebo conditions, but were more pronounced for dimenhydrinate and promethazine. It is difficult to assess the effects on nystagmus of prolonging the angular stimulation since the pattern of significant findings was not necessarily in the same direction (even for the placebo conditions) across the two studies. Thus, while it may be reasonable to conclude that tracking error increases with time-on-task (within the limits of this study) and probably increases more under a depressant drug, effects on nystagmus are less clear.
Mood Ratings. The presence or absence of the various drugs and dosages was reflected to some degree by the mood scores. Effects were particularly evident in Study II where decreased vigor and increased fatigue and sleepiness were associated with the times of action for dimenhydrinate and promethazine. At the lower dosages (Study I) the fatigue and sleepy scores showed significant effects associated with the final session and, interestingly, they involved more fatigue and sleepiness for the promethazine and the mixture groups. The latter group may have been demonstrating a wearing-off of the d-amphetamine while the promethazine was still active, a rebound depressive effect of the d-amphetamine, or both. While the mood scores showed some drug effects consistent with known symptoms, (i) they did not appear to relate meaningfully to static tracking scores in either Study I or Study II, and (ii) they generally showed inconsistent relationships in both studies (particularly for the final session) with respect to dynamic tracking scores and measures of nystagmus; an exception was the nystagmus measures for promethazine in Study II. The latter result suggests that the mood-altering effects of the drugs may have properties and a time course that differ somewhat from the effects on tracking skill and the ability to use the visual fixation mechanism to inhibit vestibular nystagmus or, that at these dosage levels, the direction of attention to a task can override some of the depressant subjective characteristics of those drugs.
REFERENCES


