Motion-Sickness Medications for Aircrew: Impact on Psychomotor Performance

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Introduction: Motion sickness remains a significant problem for aircrew both in the flying environment (airsickness) and for aircrew deployed at sea (seasickness). While some anti-motion-sickness medications provide reasonable efficacy, adverse neurocognitive effects limit their use in military personnel engaged in safety-sensitive operational roles such as flying. The purpose of this study was to assess the impact on psychomotor performance of promethazine, meclizine, and dimenhydrinate and to determine if the addition of pseudoephedrine or d-amphetamine to promethazine would ameliorate its adverse effects. ***Methods:*** There were 21 subjects (11 men, 10 women), aged 22–59, who were assessed for psychomotor performance on 4 tasks as well as with sleepiness and drug side-effects questionnaires. Psychomotor testing was conducted prior to, and for 7 h after, ingestion of a single dose of each of placebo, promethazine 25 mg, meclizine 50 mg, dimenhydrinate 50 mg, promethazine 25 mg plus pseudoephedrine 60 mg, and promethazine 25 mg plus d-amphetamine 10 mg. ***Results:*** Relative to placebo, promethazine, meclizine, and promethazine plus pseudoephedrine impaired performance on all four tasks [serial reaction time (SRT), logical reasoning (LRT), serial subraction (SST), and multitask (MT)]. Dimenhydrinate impaired performance on the SRT only. Promethazine plus d-amphetamine did not impair performance on any task nor did it result in increased sleepiness. The times to recovery of normal performance for SRT with promethazine, meclizine, dimenhydrinate, and promethazine plus pseudoephedrine were > 7.25, 7.25, 4.25, and 7.25 h, respectively; for LRT were > 7.25, > 7.25, ns, and 7.25 h; for SST were > 7.25, > 7.25, ns, and 7.25 h; for MT were 7.25, 7.25, ns, and 7.25 h. Recovery times to baseline sleepiness levels for promethazine, meclizine, dimenhydrinate, and promethazine plus pseudoephedrine were 7.25, > 7.25, 6.25, and > 7.25 h. ***Conclusion:*** Only promethazine plus d-amphetamine was free from impact on psychomotor performance and did not increase sleepiness.

Keywords: meclizine, dimenhydrinate, promethazine, motion-sickness prevention, psychomotor performance, military aircrew.

MOTION SICKNESS can be debilitating whether it occurs in a car, on a ship, in an aircraft, or aboard a space vehicle (15). Various antihistamines, many of which are available over the counter, are commonly used to ameliorate motion sickness (12). Many antihistamines cause depressant actions on the central nervous system that limit their use in safety-sensitive activities where accurate performance is needed (25). The Canadian Forces medical service is looking for a drug that is effective for prevention of motion sickness in aircrew and which is relatively free of side effects.

Scopolamine, an anticholinergic, has been shown to be effective in prevention of motion sickness, but it too causes performance decrements (15). For short-term protection, scopolamine is effective, acting within 30 min to 1 h and providing protection for about 4 h. Development of transdermal drug transport techniques allowed a loading dose of 200 μg, followed in turn by controlled release of 10 $\mu g \cdot h^{-1}$ for up to 60 h via a patch placed behind the ear. The transdermal patch is reported to be as effective as oral scopolamine but appears to cause more variability between subjects in both the effectiveness and incidence of side effects than is found with repeated oral administration. When scopolamine is administered transdermally, peak blood levels are not reached until 8 to 12 h after application of the patch, making it necessary to anticipate the need for prophylaxis by at least 6 h (2). The side effects and the anticipation of prophylactic need make scopolamine unattractive for use in aircrew.

The antihistamines promethazine (Histantil®, Pharmascience Inc., Montreal, Quebec, Canada), meclizine (Bonamine®, Pfizer Inc., Kirkland, Quebec, Canada) and dimenhydrinate (Gravol®, Carter-Horne, Inc., Mississauga, Ontario, Canada), when taken orally are not effective until about 2 h after administration but provide prophylaxis against motion sickness for 8 to 12 h (3). Dimenhydrinate has been an effective anti-motion-sickness drug since the 1950s (6), while meclizine and promethazine have been used for motion sickness since at least the 1960s (14,24). All three of these drugs are antihistamine-H1 receptor antagonists that cause sedation as the most common subjective side effect (4). They also impact on various measures of psychomotor performance such as hand-eye coordination or tracking tasks (11,12,14,25), reaction time (5,20), spatial orientation (5,20), digit symbol substitution (13), and critical flicker fusion threshold (8,9,20). Maximum impact on performance typically occurs several hours after ingestion and approaches normal performance 8 to 12 h after ingestion (9,13).

Wood and Graybiel (24) demonstrated that d-amphetamine improves tolerance to Coriolis stimulation of the vestibular system. They found that d-amphetamine added to hyoscine and the antihistamines produced an

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increase in treatment effectiveness and reduced sedation. Benson stated that "Ephedrine is almost as effective as amphetamine in enhancing the effectiveness of the anti-motion sickness drugs and should be used in preference to amphetamine when prescription of these potentially addictive drugs is contraindicated" (3). Shaskov et al. confirmed the efficacy (effectiveness) of combining promethazine with ephedrine for prevention of motion sickness (21). Until recently, the combination of promethazine and ephedrine was the preferred motion-sickness prevention/treatment in the Canadian Air Force. Unfortunately ephedrine has recently been banned in Canada, due to adverse side effects. These side effects have not been noted with pseudoephedrine. While many drugs have been tested for efficacy of prevention of motion sickness, few have proven to be effective and none can completely prevent motion-sickness symptoms in everyone across the spectrum of provocative motion environments (3).

The purpose of this study was to compare three anti-motion-sickness medications (promethazine, meclizine, and dimenhydrinate) for depth and duration of impact on psychomotor performance. A secondary goal of the study was to determine to what extent the addition of pseudoephedrine to promethazine might improve the side-effect profile of promethazine relative to d-amphetamine.

METHODS

The design was a randomized, double-blind repeated-measures protocol to assess the impact of the following medications: promethazine 25 mg; promethazine 25 mg plus pseudoephedrine 60 mg; promethazine 25 mg plus d-amphetamine 10 mg; meclizine 50 mg (Bonamine®); dimenhydrinate 50 mg (Gravol®); and placebo on psychomotor performance. These are all standard clinical doses. Subjective levels of side effects for each of these medications were monitored via questionnaire. All subjects were run on their six medication conditions over 6 wk (one condition per week with 1 wk washout between adjacent conditions) on the same test day each week in counterbalanced treatment order.

There were 21 subjects (11 men and 10 women) ranging from 22 to 59 yr of age. Their average age was 34.2 ± 10.7. All subjects provided written informed consent in compliance with the declaration of Helsinki. Before being accepted into the study, all volunteers first passed a screening medical. Because any of these medications could be potentially harmful to a fetus, any woman who wished to participate was first required to undergo medical screening to preclude pregnancy. Subjects taking any prescription or over-the-counter medications at the time of the study were instructed to bring this to the attention of the principal investigator and the duty medical officer. Subjects were also instructed to refrain from the use of alcohol for 24 h before participation in any data collection session. Subjects were instructed to be well rested each time they came to the laboratory for an experimental session, and were asked to maintain a 3-d sleep log (provided by the experimental team) prior to each experimental session. The completed sleep log was presented to the run director on arrival to the laboratory for each of the six sessions.

Prior to commencement of the study, all subjects were trained to asymptote performance (i.e., fully trained to best performance) on both psychomotor test batteries: 1) a subset of the DRDC-Toronto sustained operations (SUSOPS) battery to measure serial reaction time (SRT) (23), logical reasoning (LRT) (1), and serial subtraction task (SST) (7); and 2) a multitask (MT) (16–19,22) designed to simulate the information processing characteristics of flight performance. All psychomotor tasks were administered from laptop computers. The three SUSOPS tasks took 10 min to complete—1 min for a subjective sleepiness/side effect questionnaire (to solicit subjective assessments of sleepiness, psychomotor impairment, agitation/nervousness, tremors/shakiness, irregular heat action, pounding heart, dizziness, dry mouth, nausea, and blurred vision) followed by 3 min of SRT, then 3 min of LRT, and finally 3 min of SST (which has an imbedded short-term memory component). The SUSOPS task battery was followed by the MT, which took 15 min to complete and which involved tracking toward various targets (waypoints) while attending to a flight director, monitoring attitude indicators for discrepancies, remaining vigilant for altitude command changes, and operating a tracking task analogous to the operation of the power quadrant of a large multi-engine transport aircraft. One trial of both task batteries (all four tasks) took 25 min to complete. The order of medication conditions was counterbalanced across subjects. On the test days, each subject performed a baseline psychomotor test session before ingestion of a single dose of medication at 09:00. Thereafter the subjects were tested for psychomotor performance once every hour for 7 h at the 'top of the hour.' All training on the psychomotor tasks and all experimental sessions were conducted at DRDC-Toronto. Each subject had at least 1 wk between test doses to allow for drug washout. The test doses were standard clinical doses as described above. In order to maintain the double-blind nature of this work, all medications (placebo, each of the three promethazine conditions, meclizine, and dimenhydrinate) were prepared in identical capsule format by the contract pharmacy (Central Medical Pharmacy, Toronto, ON, Canada). All medications were administered by the principal investigator or his designate in accordance with the dosing protocol established by the contract pharmacy. Because all subjects were in our care and control from 08:00 to 17:00, noon meals were provided.

The psychomotor test results (dependent variables or # of correct responses for the SUSOPS tasks and 'total score' for the multitask) were plotted over time (independent variable) for each of the six drug conditions in order to establish the manner in which performance changed over time for each of the drug conditions. The dependent variables from the questionnaires were also compared across drug conditions. All dependent variables (from all data sets) were submitted to repeated-measures analysis of variance. The least significance difference test was used for post hoc assessment of any main effects or interactions. The significance level was set at 0.05.

RESULTS

Psychomotor Data

The data from all four psychomotor tasks (SRT, LRT, SST, and MT) are plotted across drugs and trials and are illustrated in **Fig. 1.** The four psychomotor data sets were submitted to two-way repeated-measures ANOVA where each of the experimental drugs was compared with placebo [2 levels of drug (placebo and the each of the drugs in turn) × 9 levels of trial (one pre-ingestion trial and 8 post-ingestion trials)]. The results of post hoc testing of the drug × trial interactions for all psychomotor tasks are illustrated in Table A*, which can be viewed in the online version of this article.

SRT: The drug × trial interactions indicate that all three drugs caused a significant impairment of SRT [dimenhydrinate $F(8,160) = 2.30$, $p < 0.023$; promethazine $F(8,160) = 9.13$, $p < 0.000001$; meclizine $F(8,160) = 5.23$, $p < 0.00001$]. The addition of d-amphetamine to promethazine completely abolished the impact on SRT [$F(8,160) = 0.49$, $p < 0.90$], but pseudoephedrine did not [$F(8,160) = 5.37$, $p < 0.00001$].

The time course of the effects of SRT was different for each medication. Dimenhydrinate decreased SRT only from 1.25 h to 3.25 h post-ingestion. The effect of meclizine began later, at 4.25 h with return to baseline on the last test session at 7.25 h. Promethazine had the most prolonged impact, evident by 2.25 h and still present at the end of the last psychomotor test session. The addition of pseudoephedrine diminished the duration of the promethazine effect by 1 h, limiting it to 6.25 h. As mentioned, with d-amphetamine promethazine did not effect SRT.

LRT: The drug × trial interactions indicate LRT was not affected by dimenhydrinate [$F(8,160) = 0.90$, $p < 0.516$], but promethazine [$F(8,160) = 5.44$, $p < 0.000001$] and meclizine [$F(8,160) = 4.63$, $p < 0.00004$] impaired logical reasoning. Again, d-amphetamine [$F(8,160) = 0.61$, $p < 0.77$] prevented the negative impact of promethazine on logical reasoning, but pseudoephedrine [$F(8,160) = 2.75$, $p < 0.007$] did not. Meclizine's effect on logical reasoning began at 4.25 h and persisted through the remaining test sessions. The effect of promethazine on LRT was apparent by 3.25 h and also persisted through 7.25 h. Pseudoephedrine shortened the impact from 4.25 h to 6.25 h only.

SST: The drug × trial interactions indicate SST was not affected by dimenhydrinate [$F(6,160) = 0.72$, $p < 0.68$] but was affected by meclizine [$F(8,160) = 4.24$, $p < 0.0001$] and by promethazine [$F(8,160) = 2.84$, $p < 0.006$]. D-amphetamine [$F(8,160) = 0.18$, $p < 0.99$], but not pseudoephedrine [$F(8,160) = 2.85$, $p < 0.006$] prevented the negative impact of promethazine on SRT. Meclizine impacted SST from 4.25 h through to 7.25 h. Promethazine, alone or in combination with pseudoephedrine, decreased SST beginning at 2.25 h. Alone, the effect lasted through to 7.25 h of testing, but with pseudoephedrine SST returned to placebo level by 6.25 h.

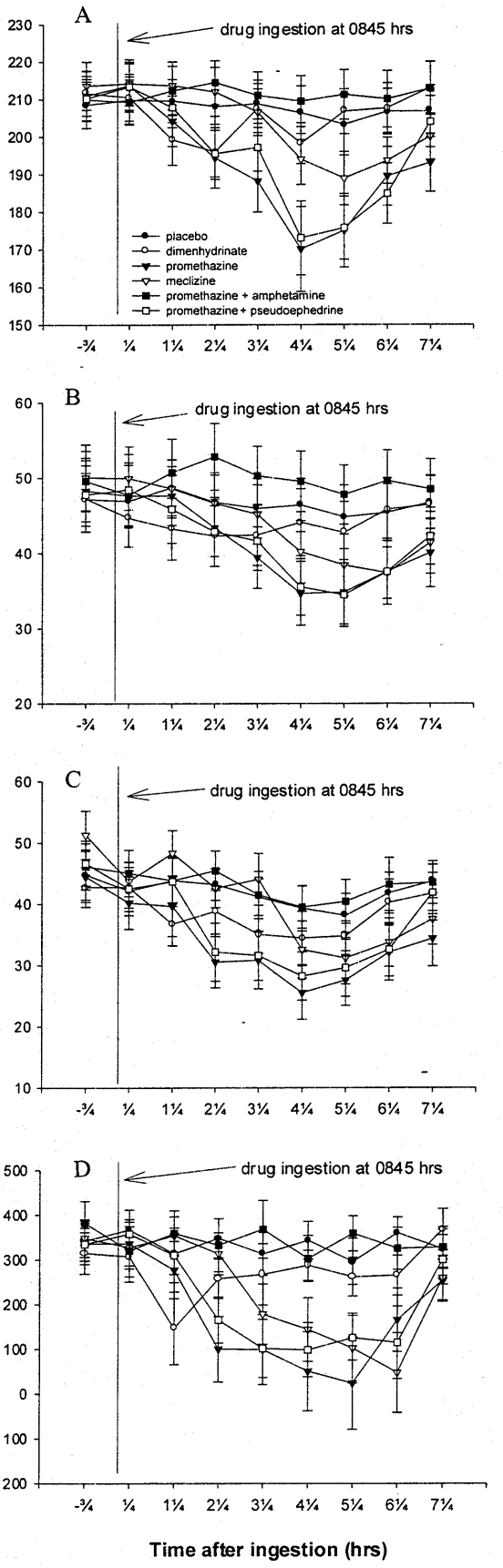

Fig. 1. Number of correct responses to the A) serial reaction time (SRT), B) logical reasoning (LRT), and C) serial subtraction task (SST), as well as D) the 'multitask score.' All values are mean ± SEM and are plotted over 'drugs' and 'hours post-ingestion.'

* For Table A, see http://www.asma.org and click on the link for the online journal.

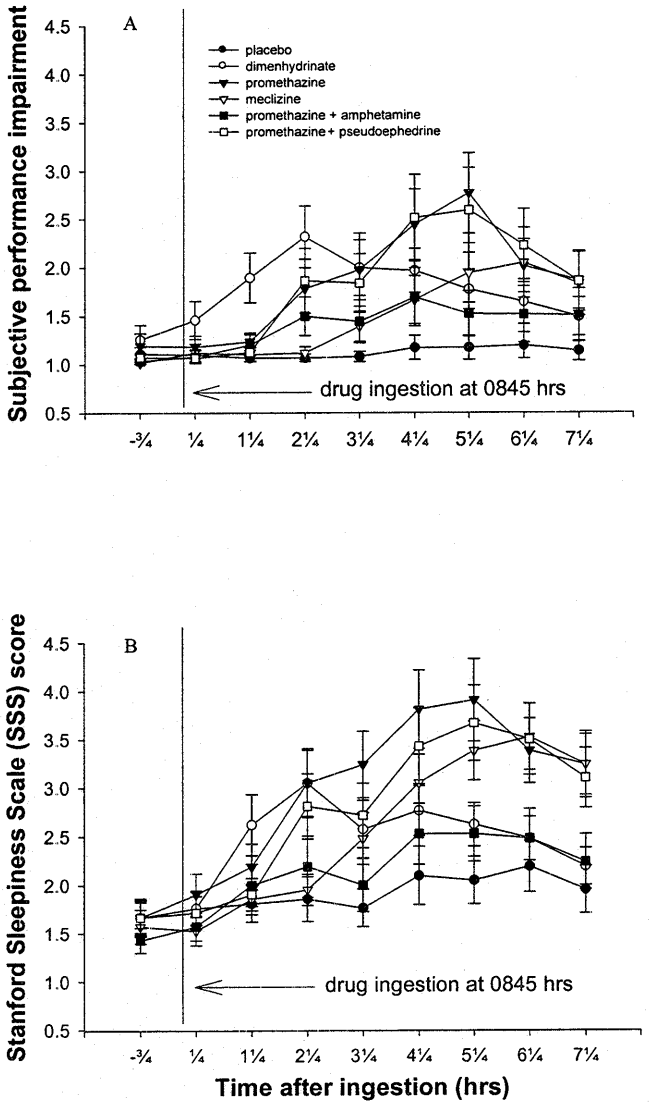

Fig. 2. A) Subjective performance impairment, and B) Stanford Sleepiness Scale scores (SSS). All values are mean ± SEM and are plotted over 'drugs' and 'hours post-ingestion.'

MT: The drug × trial interactions indicate that dimenhydrinate [F (8,160) = 1.39, $p < 0.20$] did not significantly affect MT, but both meclizine [F (8,160) = 4.85, $p < 0.00002$] and promethazine [F (8,160) = 3.59, $p < 0.001$] did impact MT performance. Again, d-amphetamine [F (8,160) = 1.29, $p < 0.25$], but not pseudoephedrine [F (8,160) = 3.97, $p < 0.0003$] counteracted the effect of promethazine on MT. The meclizine effect on MT became significant by 3.25 h post-ingestion, lasting through to 6.25 h. The promethazine effect was evident earlier at 2.25 h, lasting to 6.25 h, a time course not altered by the addition of pseudoephedrine, but abolished by d-amphetamine.

Subjective Data

The subjective impairment and sleepiness data are plotted across drugs and trials and are illustrated in **Fig. 2.** Both data sets were submitted to two-way repeated-measures ANOVA where each of the experimental drugs was compared with placebo [2 levels of drug (placebo and each of the drugs in turn) × 9 levels of trial (one pre-ingestion trial and 8 post ingestion trials)]. The results of post hoc testing of the drug × trial interactions for all of both subjective data sets are illustrated in Table B**, which can be viewed in the online version of this article.

Subjective Impairment

Subjects rated subjective impairment using a 7-point Likert scale ranging from 1 to 7, with 1 meaning 'no impairment' and 7 meaning 'extremely impaired.' The drug × trial interactions indicate that all three motion-sickness drugs caused subjects to report subjective impairment [dimenhydrinate F (8,160) = 3.22, $p < 0.002$, onset 1.25 h, resolved by 7.25 h; meclizine F (8,160) = 3.84, $p < 0.0004$, onset at 4.25 h persisting through 7.25 h; promethazine F (8,160) = 5.18, $p < 0.00001$, onset by 2.25 h persisting through 7.25 h]. The subjective impairment of promethazine was unchanged by the addition of pseudoephedrine [F (8,160) = 6.20, $p < 0.000001$], but was abolished by d-amphetamine [F (8,160) = 1.63, $p < 0.12$].

Subjective Sleepiness

The questionnaire also asked subjects to rate sleepiness (Stanford Sleepiness Scale). All three drugs produced subjective sleepiness [dimenhydrinate F (8,160) = 3.05, $p < 0.003$, onset at 1.24 h through 6.25 h; meclizine F (8,160) = 11.39, $p < 0.000001$, onset by 3.25 h lasting thought 7.25 h; promethazine F (8,160) = 9.78, $p < 0.000001$, onset by 2.25 h persisting through 7.25 h]. The effect of promethazine was unchanged by pseudoephedrine [F (8,160) = 7.81, $p < 0.000001$]. With the addition of d-amphetamine to promethazine, subjects did not report any subjective sleepiness compared with placebo [F (8,160) = 1.48, $p < 0.17$]. Besides impaired performance and sleepiness, no other questionnaire side effects were significant

DISCUSSION

Our a priori experimental design calculations indicated that 28 subjects were required to have a power of 80% to detect a difference of 4 responses · min^{-1} (about a 6% change in performance of our SUSOPS tasks). With only 21 subjects, this recruiting target was not achieved. However, the effect size was much higher than 6%. At 4.25 h after ingestion, relative to placebo, performance on promethazine (Histantil®) dropped by about 18% on SRT, by about 25% on LRT, by about 35% on SST, and by 85% on MT. Our existing number of subjects is easily adequate for such effect sizes.

Each psychomotor task session took 25 min to complete (1 min for a questionnaire, 3 min for each of SRT, LRT, and SST, and 15 min for the multitask). The 25 min required for completion of each session allowed us to sample psychomotor performance once per hour, thus providing reasonably good temporal resolution of

** For Table B, see http://www.asma.org and click on the link for the online journal.

changes in psychomotor performance over time, and allowing approximately 30 min of rest between psychomotor test sessions. It is possible that had the tasks been set up for longer, more sustained periods, the results might have been somewhat different. However, we prefer our current approach that assesses psychomotor speed (SRT), higher order cognition (LRT), mental arithmetic and short-term memory (SST), and provides an appreciation of simulated flying performance (MT).

Dimenhydrinate (Gravol®) resulted in an early, transient increase in subjective sleepiness and impairment of performance, but apart from the transient (1 h) impairment of SRT, dimenhydrinate did not impair objective measures of performance (LRT, SST, or MT). This suggests that the sleepiness induced by dimenhydrinate is sufficient to transiently affect the psychomotor speed inherent in the SRT task, but not the higher order cognitive demands of the LRT, SST, or MT. In general, dimenhydrinate is not as effective as promethazine for preventing motion sickness (24), but for mildly provocative environments, dimenhydrinate may be effective, and although not tested in this protocol, the addition of d-amphetamine might be anticipated to prevent its mildly sedative adverse effects.

Of the three core study drugs, promethazine (Histantil®) caused the largest increases in subjective impairment and sleepiness as well as the most profound and longest lasting impact on psychomotor performance (5 h impact on SRT, 4 h on LRT, 5 h on SST, and 4 h on MT). Meclizine (Bonamine®) caused a subjective sensation of sleepiness and subjective performance impairment similar to promethazine (Histantil®), but with slightly later onset. The impact of meclizine on objective measures of performance also began somewhat later than with promethazine, but overall the magnitude of objective performance decrement with meclizine was similar to that of promethazine. Given that meclizine is less effective than promethazine as an anti-motion-sickness medication (24), it appears a less favorable alternative than promethazine combined with d-amphetamine.

While ephedrine has been demonstrated to successfully ameliorate the adverse effects of promethazine on performance (3,10), the results here indicated pseudoephedrine does not have the same protective effect. In this study, pseudoephedrine failed to prevent either the subjective adverse effects or the objective performance decrements caused by promethazine. However, the addition of d-amphetamine successfully mitigated both the adverse subjective and objective performance effects of promethazine. Because of the potential for adverse psychological and behavioral effects, the use of d-amphetamine in aircrew has fallen into some disfavor in recent times. A possible alternative for d-amphetamine as a countermeasure to the adverse effects of promethazine is modafinil, and further research into this alternative is planned. Further, while d-amphetamine prevented the adverse effects of promethazine on the relatively short tests used in this protocol, it is not certain that this effect would be sustained over longer test periods especially involving monotonous tasks.

CONCLUSIONS

All three active drugs cause increased sleepiness. Dimenhydrinate (Gravol®) causes a mild and short-acting impact on psychomotor speed but does not appear to affect higher order cognition. Promethazine (Histantil®) and meclizine (Bonamine®) both cause significant impact on psychomotor performance with the impact due to meclizine being somewhat less and appearing later post-ingestion than the impact due to promethazine. The addition of pseudoephedrine to promethazine is ineffective in reducing the negative effects of promethazine; however, the addition of d-amphetamine is remarkably effective in that role. The results of this study support the possibility for carefully supervised use of promethazine and d-amphetamine to prevent motion sickness in aircrew.

REFERENCES

1. Baddley AD. A 3 min reasoning test based on grammatical transformation. Psychonomic Science 1968; 10:341–2.
2. Benson AJ. Transdermal hyoscine: a review. Drug Ther Bull 1989; 27: 91–2.
3. Benson AJ. Medication for motion sickness. In: Medication for military aircrew: current use, issues, and strategies for expanded options. Neuilly-sur-Seine, FRANCE: NATO Research and Technology Organization; 2001:73–6.
4. Carruthers SG, Shoeman DW, Hignite CE, et al. Correlation between plasma diphenhydramine level and sedative antihistamine effects. Clin Pharmacol Ther 1978; 23:375–82.
5. Cowings PS, Toscano WB, DeRoshia C, et al. Promethazine as a motion sickness treatment: impact on human performance and mood states. Aviat Space Environ Med 2000; 71:1013–22.
6. Hardman JG, Limbird LE, Molinoff PB, et al. Goodman and Gilman's the pharmacological basis of therapeutics, 9th ed. New York: McGraw-Hill; 1996.
7. Heslegrave RJ, Angus RG. The effects of task duration and work-session location on performance degradation induced by sleep loss and sustained cognitive work. Behav Res Methods Inst Comp 1985; 17:592–603.
8. Hindmarch I, Shamsi Z, Kimber S. An evaluation of the effects of high-dose fexofenadine on the central nervous system: a double-blind, placebo-controlled study in healthy volunteers. Clin Exp All 2002; 32:133–9.
9. Hindmarch I, Shamsi Z, Stanley N, et al. A double-blind, placebo-controlled investigation of the effects of fexofenadine, loratadine and promethazine on cognitive and psychomotor performance. Br J Clin Pharmacol 1999; 48:200–6.
10. Homick JL. Space motion sickness. Acta Astronautica 1979; 6:1259–72.
11. Kotzan JA, Honigberg IL, Francisco GE, et al. Rotary pursuit, a measure of human performance, and plasma concentrations of promethazine. Biopharm Drug Dispos 1986; 7:293–300.
12. Large ATW, Wayte G, Turner P. Promethazine on hand-eye coordination and visual function. J Pharm Pharmacol 1971; 23: 134–5.
13. Manning C, Scandale L, Manning EJ, et al. Central nervous system effects of meclizine and dimenhydrinate: evidence of acute tolerance to antihistamines. J Clin Pharmacol 1992; 32:996–1002.
14. Molson GR, Mackay JA, Smart JV, et al. Effect of promethazine hydrochloride on hand-eye coordination. Nature 1966; 209:516.
15. Parrott AC. Transdermal scopalamine: a review of its effects upon motion sickness, psychological performance, and physiological functioning. Aviat Space Environ Med 1989; 60:1–9.
16. Paul MA, Brown G, Buguet A, et al. Melatonin and zopiclone as pharmacologic aids to facilitate crew rest. Aviat Space Environ Med 2001; 72:974–84.
17. Paul MA, Gray G, Lange M. The impact of sertraline on psychomotor performance. Aviat Space Environ Med 2000; 73: 964–70.
18. Paul MA, Pigeau RA, Weinberg H. Human factors of CC-130 operations. Volume 6: fatigue in long-haul re-supply missions.

Toronto, Canada: Defence and Civil Institute of Environmental Medicine; 1998. DCIEM Report No. 98-R-19.
19. Paul MA, Pigeau RA, Weinberg H. CC130 pilot fatigue during re-supply missions to former Yugoslavia. Aviat Space Environ Med 2001; 72:965–73.
20. Shamsi Z, Kimber S, Hindmarch I. An investigation into the effects of cetirizine on cognitive function and psychomotor performance in healthy volunteers. Eur J Clin Pharmacol 2001; 56:865–71.
21. Shashkov VS, Kotovskaia AR, Orlov OI, et al. An experimental validation of pharmacological agents to arrest the vestibulo-autonomic syndrome (motion sickness). Eksp Klin Farmakol 1999; 62(6):11–5.
22. Weinberg H, Jantzen KJ, Cheyne D, et al. Jetlag, gamma activity and managing pilot fatigue. In: Transport Canada Conference Proceedings TP 13375. Fatigue in Transportation Workshop: Multimodal Issues and Solutions; Oct. 15-16, 1998; Ottawa, Canada. Ottawa: Transport Canada; 1998.
23. Wilkinson RT, Houghton D. Portable four-choice reaction time test with magnetic tape memory. Behav Res Methods Inst Comp 1975; 7:441–6.
24. Wood CD, Graybiel A. Evaluation of sixteen anti-motion sickness drugs under controlled laboratory conditions. Aerosp Med 1968; 39:1341–4.
25. Wood CD, Manno JE, Manno BR, et al. Side effects of anti-motion sickness drugs. Aviat Space Environ Med 1984; 55:113–6.