Effects of transcutaneous scopolamine and depth on diver performance

T. H. WILLIAMS, A. R. WILKINSON, F. M. DAVIS, and C. M. A. FRAMPTON

Hyperbaric Unit, The Princess Margaret Hospital, Christchurch, New Zealand

Williams TH, Wilkinson AR, Davis FM, Frampton CMA. Effects of transcutaneous scopolamine and depth on diver performance. Undersea Biomed Res 1988; 15(2):89–98.—Transdermal scopolamine is an effective anti-motion-sickness medication that has less CNS side effects at normal ambient pressure than orally ingested agents. To see whether it has an effect on performance at depth, 24 healthy sport divers were exposed to depths equivalent to 5 m (1.5 ATA) and 36 m (4.8 ATA) in a dry recompression chamber, breathing air and wearing a skin patch containing either scopolamine or inactive placebo. Patches and dive depths were presented in a counterbalanced, double-blind experimental design. Tests of sentence comprehension, simple arithmetic, and manual dexterity were used to evaluate psychometric and cognitive performance. Drug side effects were recorded. The Bennett Hand Tool Dexterity Test was evaluated for its suitability for repeated measures testing, and found to be robust. Manual dexterity and sentence comprehension were significantly impaired at depth whereas arithmetic skills were not. No significant effects on diver performance from transdermal scopolamine were seen. Certain side effects such as blurred vision were more common with scopolamine than with placebo. The use of transdermal scopolamine as an antiemetic during diving operations deserves field evaluation.

diving scopolamine antiemetics psychomotor

INTRODUCTION

Sea sickness is a common ailment of sport divers and one for which they probably frequently self-medicate. Orally ingested anti-motion-sickness agents are potent CNS depressants with marked psychotropic side effects, such as impaired cognitive and manual skills and somnolence. Therefore, from the safety point of view they are not advocated for use during scuba diving.

A detailed review of the limited research on drug-depth interactions (1) concluded that the behavioral and physiologic effects of these interactions were unpredictable. Some drug actions seemed to be potentiated by depth and some antagonized, whereas others were seemingly unaffected. These responses could be quite independent of predicted effects from normal ambient pressure studies. Various oral antiemetics
have been evaluated under pressure (1, 2) and so far all have been found to produce some performance impairment at depth.

Recently, a transdermal mode of delivery of scopolamine (Transderm-Scop) has been reported to be an effective anti-motion-sickness preparation (3–5). It is thought to provide sustained, low therapeutic drug levels that have little effect on performance at normal atmospheric pressures (3, 6), although tasks requiring memory storage and those requiring continuous concentration have recently been reported to be impaired (7). Since transdermal scopolamine seems to have theoretical advantages over oral agents, it may be safe for use as an anti-motion-sickness drug during diving. We have compared it with placebo on the performance impairment of divers during dry air diving in a recompression chamber.

Subjects

Twenty-four volunteer sport divers, 18 male and 6 female, with 2 to 17 yr diving experience were studied. Ages ranged from 19 to 43 (average age 29.8 yr). None of the divers was “chamber sophisticated.”

METHODS

Subjects followed their normal routines for the 24 h preceding the trial. They agreed not to consume alcohol within 18 h of the dive. On the evening before each test dive the subject applied a drug patch on the skin over the mastoid process behind one ear. This patch contained either scopolamine in the form of Transderm-Scop or was an inert placebo. Subjects, observers, and chamber operators were double-blinded to patch type. Subjects were asked to report any unusual feelings such as tiredness, visual disturbances, difficulty concentrating, or a dry mouth while wearing a patch, including during the dive. Diving in pairs, each subject did a total of 4 dives breathing air, 2 at each of 2 test depths (5 and 36 msw depth equivalent) wearing either a Transderm-Scop or placebo patch on each dive. Time for descent was 3 min and testing commenced at 5 min. All ascents included a decompression stop at 3 m depth. Subjects and observers were kept blind to the depth of any one dive by the operator disguising in a number of ways the different rates of compression and decompression.

To compensate for first order interaction between treatment and practice effects, the 4 depth-and-drug combinations, counterbalanced in 24, 4-dive sequences, were randomly allocated, 1 to each diver. A series of training sessions was held before the experimental dives so as to reduce the carry-over effect of learning in the performance tests used, thereby improving the sensitivity of the experiment. Practice and trial sessions were spaced 3 or 4 d apart, the entire sequence being compiled over a 3-wk period for any 1 subject. Tests were presented in the same order and in a standardized manner on each trial dive.

Psychometric tests

The 3 tests employed were chosen either because of their past repeated use for diver performance testing (8–10) and/or for their known reliability in repeated mea-
asures testing (11–13). This stability adds statistical power to the assessment of the impact of environmental changes on performance.

**Manual dexterity**

A modification of the Bennett Hand Tool Dexterity Test (14) was used. A full description of this test as used for previous diver performance studies appears elsewhere (8). In essence, the time taken to transfer, using spanners, two sets of nuts, bolts, and washers, in a predetermined sequence from one vertical brass plate to another was recorded.

Since this test had not previously been evaluated for equality of variance over repeated measures, consistency of intertest correlations, and rapid achievement of a linear learning curve (15), these variables were specifically studied before the experiment. A group of 12 healthy, young male soldiers were asked to carry out the test twice a day for 5 d. Like the divers they were tested in pairs, and the motor task trials were separated by a random number generation task. This intervening task took approximately 7 min. Results of these 10 (2 × 5) trials were then examined statistically to see whether this test met the criteria proposed (15).

**Grammatical reasoning**

This test is described in detail elsewhere (8, 16). In summary, it comprises a series of 64 sentences claiming to describe the order of the two letters A and B, which follow the sentence as a letter pair AB or BA. The description of the letter pair corresponding to that sentence is identified by a tick in a “true” or “false” column. Three minutes were allowed to complete as many as possible. At each testing the subject was given a different test form. The number of sentences completed and the number of errors made were recorded.

**Simple arithmetic**

Subjects were asked to complete as many simple arithmetic problems as possible in a 4-min period. The numbers of correct and incorrect answers were recorded. At each session, the subjects were given a different set of problems, these being presented in a specific order so that equivalent numbers of addition, subtraction, multiplication, and division problems were attempted at each session. This was a modification of the test analyzed by Seales et al. (13), the complexity of the sums being simplified and the test period being shortened to fit into the planned dive profile at 36 m.

**Statistical analysis**

This was performed using the computer statistical package BMDP (17). The design of the experiment encompassing all 24 possible sequences of the four depth-drug combinations, one per subject, meant that unless there were large diver-learning interactions, any effects of depth or drug would be detectable using analysis of variance with repeated measures in a $24 \times 2 \times 2$ design. This design, compensating
for any linear time effect by equal replication over the four conditions, allowed the
effects of depth and drug to be analyzed as within-subject variations.

For the Bennett Hand Tool Dexterity Test, the statistical criteria of Bittner et al.
(15) relating to intratrial consistency, homogeneity of variance, and to intertrial
correlations were tested using linear regression, the $F_{\text{max}}$ test, and the Lawley test,
respectively. The Lawley test (18) tests the hypothesis of a single principal axis within
a sample correlation matrix, which in essence is testing the equality of the $p(p - 1)/2$
correlations. The calculated test statistic is asymptotically distributed as $\chi^2$ with
$(p + 1)(p + 2)/2$ degrees of freedom (df).

RESULTS

Manual dexterity test

The mean times taken over 10 test exposures in the Army volunteers are shown in
Fig. 1. Time to completion decreased consistently each day. On the 5 successive
days of testing, the second attempt was faster than the first in 87% of cases. The
learning curve demonstrated equality of variance and consistency of intertest corre-
lations after only one test, $\chi^2 = 26.76$ (55 df), $F_{\text{max}} = 5.15$ (9, 11 df). A stable linear trend
was seen after 3 tests ($R = -0.479$, 82 df, $P < 0.001$; Fig. 1).

The mean times to completion of the manual dexterity test in the 4 study conditions
are shown in Table 1. There was a small but statistically significant difference between

![Manual Dexterity](image)

**Fig. 1.** The learning curve for the manual dexterity test over 10 trials ($n = 12$). Bars indicate SEM for each trial. *See* text for statistical analysis.

**TABLE 1**
**Manual Dexterity Test**

<table>
<thead>
<tr>
<th>Depth, m</th>
<th>Placebo</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Scopoderm</td>
</tr>
<tr>
<td>5</td>
<td>181.5 ± 35.5</td>
<td>187.6 ± 41.3</td>
</tr>
<tr>
<td>36</td>
<td>191.5 ± 39</td>
<td>189.2 ± 40.8</td>
</tr>
</tbody>
</table>

*Mean ± SD time taken (s) to complete the Bennett Hand Tool Dexterity Test in the 4 diving conditions. 95% confidence limits for difference between drug groups = 1.9 ± 7.8. See text for statistical analysis.*
the 2 depths, with the completion time being longer at 36 m than at 5-m depth ($P < 0.05$). There was no evidence of a main drug effect or of any drug-depth interaction.

**Grammatical reasoning test**

The total number done at 36 m was significantly less than at 5-m depth ($P < 0.05$; Table 2). There was no deterioration with Transderm-Scop compared with placebo and no evidence of an adverse drug-depth interaction. Indeed, the reverse was the case, performance tending to be slightly better with the active drug patch than placebo at the 5-m depth ($P < 0.05$). The number of correctly completed sentences also showed a significant reduction at depth ($P < 0.01$) but no drug effect nor dive depth-drug interaction (Table 2). The total number of errors did not change significantly with different depths or between placebo and drug conditions.

**Arithmetic test**

No significant differences were observed in the total number done with diving depth or drug (Table 3). Nor did the error counts show significant changes with dive depth or drug. Of the other three ways of analyzing the error scores (percent correct, number correct, correct minus wrong), only the percentage correct score reached a $P$ value of less than 5% when comparing active drug with placebo. However, this was insufficient to achieve statistical significance (Bonferroni correction; $\alpha = 0.0125$ for significance in this case).

**Drug side effects**

The incidence of reported side effects is shown in Table 4. Fatigue was reported on 9 placebo-patch days and 11 Transderm-Scop-patch days (not significant). Central nervous system symptoms occurred on 2 and 11 d, respectively ($\chi^2$ test, $P < 0.01$). In total, symptoms of one form or another were reported on approximately 25% of

### Table 2

**Grammatical Reasoning Test**

<table>
<thead>
<tr>
<th>Depth, m</th>
<th>Placebo</th>
<th>Drug</th>
<th>Scopoderm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number Done</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>37.6 ± 11.2</td>
<td>39.2 ± 10.9</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>34.7 ± 11.3</td>
<td>37.6 ± 10.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Number Correct</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>30.7 ± 14.1</td>
<td>32.0 ± 14.3</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>27.7 ± 13.7</td>
<td>29.2 ± 12.7</td>
<td></td>
</tr>
</tbody>
</table>

Mean ± sd number of completed sentences and mean ± sd number of correct sentences in the grammatical reasoning test; 95% confidence limits in numbers completed for difference between drug groups = 2.25 ± 2.8. See text for statistical analysis.
TABLE 3
ARITHMETIC TEST

<table>
<thead>
<tr>
<th>Depth, m</th>
<th>Placebo</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number Done</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>28.2 ± 9.9</td>
<td>28.9 ± 10.2</td>
</tr>
<tr>
<td>36</td>
<td>28.1 ± 8.8</td>
<td>27.9 ± 11.2</td>
</tr>
<tr>
<td></td>
<td>Number Correct</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>24.7 ± 10.3</td>
<td>24.7 ± 11.5</td>
</tr>
<tr>
<td>36</td>
<td>24.2 ± 9.2</td>
<td>23.6 ± 11.9</td>
</tr>
</tbody>
</table>

Mean ± SD number of problems completed and mean ± SD number of numbers correct in the arithmetic test; 95% confidence limits for difference between drug groups in number done = 0.25 ± 1.927. See text for statistical analysis.

TABLE 4
SIDE EFFECTS

<table>
<thead>
<tr>
<th>Side Effects</th>
<th>Placebo</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tiredness</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>CNS symptoms</td>
<td>2</td>
<td>11**</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>All symptoms</td>
<td>13</td>
<td>21</td>
</tr>
</tbody>
</table>

Side effects reported by subjects during the period for which each patch was worn.

***(χ² = 7.21, P < 0.01).

placebo-patch days and 40% of Transderm-Scop days (not significant), some subjects experiencing more than one symptom.

DISCUSSION

In this study we examined the interaction between transdermally administered scopolamine and pressure effects while breathing air at depth. Data were collected in two areas; objective measurements of performance on psychometric tests and subjective side effects.

Psychometric testing

The U.S. Navy Performance Evaluation Testing for Environmental Research (PETER) program outlined the factors required for efficient, reliable performance tasks for repeated measures testing (15). In designing our study we took into account these and other criticisms that have been made of performance evaluation in hyperbaric environments in the past (19). Subjects were exposed to the test conditions in
a counterbalanced, double-blind design. Close attention was paid to equating environmental conditions during each trial, practice effects were accounted for, and psychometric measures were carefully selected.

Of the 3 tests used, the Bennett Hand Tool Dexterity Test (14) was not evaluated in the PETER program, although it has been used in a number of diver performance studies (9, 10, 20). In ambient pressure trials with a separate group of subjects, this test was found to perform satisfactorily to all the criteria set out by Bittner et al. (15). Also, this particular manual task seems to be sufficiently sensitive to exhibit state-dependent effects readily.

Statistical analysis of the psychometric tests gave us objective information about effects from three main sources: the depth of the dive, the effect of the drug, and any depth-drug interactions. Performance on the manual dexterity test and on the grammatical reasoning test was clearly impaired at the 36-m depth compared with the shallow, 5-m dive to a degree consistent with previous observations on dry air diving (21–23). It is currently hypothesized that these changes are a consequence of a general slowing of information processing (22, 23).

The arithmetic test, however, did not show a decrease with depth. A shortened and simplified version of the test examined by Seales et al. (13) was used in the present study. This was necessary to keep the bottom time at 36 m to within 20 min. A similar shortened form of the arithmetic test used in a previous open water study (9) did show a decrease with depth. It is presumed that shortening the test reduces its sensitivity, and that the effect found in open water diving (9) was a result of an interaction between depth effects and the added stress of the underwater environment, producing sufficient performance impairment to be detected by the shortened test.

No significant effect from transdermal scopolamine was seen in any of the tests, in keeping with the previously cited studies comparing Transderm-Scop with placebo at ambient pressure (3, 4, 6, 24). All three measures also failed to detect any change in performance attributable to a depth-drug interaction. Discounting the arithmetic test because of its apparent insensitivity here to any depth effect, this lends support to the hypothesis that Transderm-Scop has minimal effects on psychomotor aspects of performance.

A wide range of tests has been used previously to compare Transderm-Scop with placebo at ambient pressures (7, 6, 24), and most measures have shown no performance decrements with Transderm-Scop. However, in a study comparing various oral doses of scopolamine with Transderm-Scop, Parrott (7) found that two out of a wide range of tasks that he tested did show a performance decrement. These two tasks required either sustained narrow attention or memory storage of information. Parrott suggested that the impairment due to scopolamine is probably selective to tasks requiring those types of performance, hence the limited detection of impairment by other researchers. One of the measures that showed such a decrement, the reaction time on a four-choice reaction test was found to be very sensitive and reliable in the PETER evaluation (25). These results imply an aspect of test selection that would be an important consideration in the design of further research.

The dry hyperbaric chamber does not replicate the open water diving environment. It lacks the extra effort and visual effects of a liquid medium as well as the cold, motion effects and the complex stresses usual at sea. Research on factors affecting performance, such as anxiety (9, 26), cold (10), and narcosis (27), and their interaction
with depth, has shown much greater performance impairment in an open water environment than in the recompression chamber. Biersner (19), in summarizing this research, comments on the importance of these interactions and on the relative paucity of open water research in this area.

Side effects

Commonly reported side effects from oral scopolamine have included feelings of drowsiness or fatigue, transient blurring of vision, and dryness of the mouth. Previous studies of transdermally administered scopolamine have generally found the side effects, although present, to be significantly less than with oral doses (3, 6, 24, 28), although Parrott (7) disagreed with this. Subjects in the present experiment were asked to comment on their subjective state after completing each trial. There was a statistically insignificant trend toward more frequent reporting of fatigue or drowsiness with Transderm-Scop than placebo. There was a significant trend to experience more CNS symptoms, such as difficulty concentrating on tasks during the day or blurred vision, with Transderm-Scop than with placebo. Parrott reported that such side effects were not noted when subjects were exposed to motion such as being at sea, and concluded that motion may in some way counteract these effects.

One should be cautious in extrapolating from the dry chamber environment to the sea. Although the results of this study point toward the safety of using transdermal scopolamine during diving activities, confirmation regarding performance decrement in divers must await suitable sea trials that should include additional choice reaction tasks.

This project was funded with a grant from Ciba-Geigy (New Zealand) Ltd. The authors gratefully acknowledge the cooperation of all the subjects, including the volunteers from Addington Barracks, New Zealand Army. Thanks are also extended to the chamber operators, particularly Mr. Kevin Boyce. —Manuscript received March 1987; accepted November 1987.

Williams TH, Wilkinson AR, Davis FM, Frampton CMA. Effets de la scopolamine transcutanée et de la profondeur sur la performance du plongeur.—Undersea Biomed Res 1988; 15(2):89–98. La scopolamine transdermique est une médication efficace contre le mal du mouvement qui a moins d’effets secondaires sur le système nerveux central sous pression ambiante normale que les substances ingérées par voie buccale. Afin de vérifier si elle a un effet sur la performance en profondeur, 24 plongeurs sportifs en santé furent soumis à des profondeurs équivalentes à 5 m (1.5 ATA) et 36 m (4.8 ATA) dans une chambre de compression sèche, respirant de l’air et portant un disque cutané contenant soit de la scopolamine ou un placebo inactif. Les disques et les profondeurs de plongée furent présentés dans un schéma expérimental à double-insu. Des tests de compréhension de phrase, d’arithmétique simple, et de dextérité manuelle furent utilisés pour évaluer la performance psychométrique et cognitive. Les effets secondaires de la substance furent notés. Le test de dextérité de Bennett pour les outils manuels fut évalué pour sa convenance dans les essais avec mesures répétées et s’avéra être robuste. La dextérité manuelle et la compréhension de phrase furent significativement affectées en profondeur, tandis que les habiletés en arithmétique ne le furent pas. Aucuns effets significatifs sur la performance du plongeur ne furent observés avec la scopolamine transdermique. Certains effets secondaires, telle que la vision embrouillée, étaient plus communs avec la scopolamine que le placebo. L’emploi de la scopolamine transdermique comme agent anti-émétique durant les opérations de plongée mérite d’être évaluer sur les lieux.
SCOPODERM AND DIVING

Williams TH, Wilkinson AR, Davis FM, Frampton CMA. Efectos de la escopolamina administrada por vía transcutánea y de la profundidad en la actuación de buceadores.—Undersea Biomed Res 1988; 15(2):89–98. La escopolamina por vía transdérmica es un medicamento eficaz para el mareo, que posee menor cantidad de efectos colaterales para el sistema nervioso a presión ambiental normal, que los agentes administrados por vía oral. Para conocer si tiene efectos sobre la actuación de buceadores a profundidad, se expuso a 24 buceadores deportivos sanos a profundidades equivalentes a 5 m (1.5 ATA) y 36 m (4.8 ATA) en una cámara de recompresión seca. Respiraron aire y se les colocó un parche en la piel con escopolamina o placebo inactivo. El diseño experimental de los parches y las profundidades fue doble ciego. Se empleó pruebas de comprensión de oraciones, aritmética sencilla y destreza manual, para evaluar la actuación psicométrica y cognitiva. Se reportó los efectos colaterales de la droga. Se evaluó la prueba de destreza mano-herramienta de Bennett, debido a su conveniencia para mediciones repetitivas; demostró ser de gran solidez. Se observó que a profundidad, la destreza manual y la compresión se afectaron significativamente. La habilidad aritmética no sufrió cambios. No se observó efectos significativos de la escopolamina transdérmica en la actuación del buceador. Se encontró que algunos efectos colaterales, como la visión borrosa, tenían una frecuencia mayor con escopolamina transdérmica que con placebo. El empleo de la escopolamina transdérmica como antihemético en las actividades de buceo, merece ser valorado en el campo.

REFERENCES

7. Parrott AC. The effects of transdermal scopolamine and four dose levels of oral scopolamine (0.15, 0.3, 0.6, and 1.2 mg) upon psychological performance. Psychopharmacology 1986; 89:347–354.


