Original articles

The effects on performance of cyclizine and pseudoephedrine during dry chamber dives breathing air to 30 metres' depth

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Performance, nitrogen narcosis, medications, nasal decongestants, motion sickness, hyperbaric research

Abstract

(McGeoch G, Davis FM, Fletcher L. The effects on performance of cyclizine and pseudoephedrine during dry chamber dives breathing air to 30 metres' depth. *SPUMS J*. 2005; 35: 178-82.)
Twenty-four subjects ingested pseudoephedrine (60 mg), cyclizine (50 mg) or placebo approximately two hours before a dry chamber dive breathing air to five or 30 metres' seawater depth (msw; 151 or 404 kPa). Each subject did six dives, the sequence of drug ingestion and dive-depth order assigned according to a counterbalanced design. Tests of grammatical reasoning, manual dexterity and simple arithmetic were performed. A small decrease in performance occurred at 30 msw in grammatical reasoning ($P = 0.02$) and manual dexterity ($P = 0.02$) irrespective of the drug taken. The type of drug affected grammatical reasoning performance ($P = 0.002$) such that performance impairment at depth for cyclizine was more than for pseudoephedrine ($P = 0.007$) or placebo ($P = 0.002$). The effect of drug on manual dexterity was not significant ($P = 0.23$). There were no depth or drug effects on the simple arithmetic test. There were no significant effects of drug order for either manual dexterity ($P = 0.93$) or grammatical reasoning ($P = 0.10$), but performance improved for both manual dexterity ($P < 0.001$) and grammatical reasoning ($P < 0.001$) over the dive series despite pre-dive practice. Pseudoephedrine showed little or no effect on performance under these conditions, but the minor impairment with cyclizine suggests that it should be used with caution prior to air diving in open water conditions.

Introduction

Self-medication for various ailments including motion sickness and nasal congestion is common amongst sport divers.[1] There remains uncertainty about how this practice might affect performance at depth or diving safety.[2,3] This study investigated the effects on diver performance during simulated air dives in a dry decompression chamber of two drugs, an anti-emetic, cyclizine, and a nasal decongestant, pseudoephedrine, both widely used by divers. The aim of this study was to determine if either cyclizine or pseudoephedrine affected diver performance at depth. In the process, any interaction between the effects of the drugs and of depth and whether there was a drug-order effect in the experimental model used were also assessed. Although the present study was performed back in 1982, given the limited information in the literature on drugs and diving and the widespread use of the study drugs by divers, the results are highly relevant today.

Subjects and methods

Twenty-four experienced, male recreational divers aged between 21 and 50 years (average age 31.1 years; 95% CI 26.6, 35.5) with an average of 281 dives (95% CI 152, 411) were recruited from local recreational diving clubs. The only exclusion criterion was known allergy to either drug. The project was approved by the Christchurch Hospitals Ethical Committee, but at the time of the study, 1982, written informed consent was not required of such participants in New Zealand and consent was verbal. All participants were made fully aware of the potential risks of barotrauma and decompression sickness. Neither food nor drink was taken for four hours prior to each dive. Two hours before each dive the subjects ingested with water a capsule of pseudoephedrine (60 mg; Sudafed), cyclizine (50 mg) or placebo. Subjects were asked to report any unusual feelings that occurred after drug ingestion or during the dives. The identity of the drug and the depth of each dive were blinded for both subjects and in-chamber observers. Each subject took the same drug on two consecutive dives, six dives being completed in all. There was an interval of at least one week between dives for each subject. To minimise practice effects, the performance tests were practised twice before the dive series, once outside the chamber and once during a simulated dive in the chamber at ambient pressure. In addition, the order of presentation of the drugs and depths of dive was varied according to a counterbalanced experimental design over the six dives. With twenty-four subjects this utilised half of the forty-eight possible random sequences for drug/depth order.

The divers were compressed singly or in pairs with an observer in a multiplace recompression chamber on air to the equivalent of five or 30 metres' seawater depth (msw; 151 or 404 kPa). The depth of the dives was disguised from the subjects by masking gauges, by having a standard descent time and by keeping noise levels constant (achieved by having the air intake and exhaust open simultaneously). Five minutes after starting the dive, performance testing was commenced. Three tests were presented, always in the same sequence. Instructions were repeated to the diver by the observer in a prescribed manner before each test on each dive.

The three tests employed were chosen for their known validity in repeated measures testing and/or because of their past repeated use and known sensitivity for diver performance testing.[4–8]

GRAMMATICAL REASONING

This test is described in detail elsewhere.[7] 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 (e.g., A follows B – AB; B does not precede A – AB, etc). The subject has to decide whether the sentence gives a correct description of the letter pair corresponding to that sentence and put a tick in a 'true' or 'false' column. Three minutes are allowed to complete as many items as possible. At each testing, the subject is given a different set of sentences. The number of sentences completed and the number of errors made are the performance measures in this test.

MANUAL DEXTERITY

A modification of the Bennett Hand Tool Dexterity Test was used.[5,8] A full description of this test as used for previous diver performance studies appears elsewhere.[5] In essence, the time taken to transfer two sets of nuts, bolts and washers using spanners in a set sequence from one vertical brass plate to another is the measure of performance.

SIMPLE ARITHMETIC

A series of 20 five-digit additions is presented and the subject completes as many as possible during a three-minute period. The time taken (if less than three minutes) and the number of correct and incorrect answers are recorded. At each testing the subject is given a different set of additions.

STATISTICAL ANALYSIS

Analysis was performed using SPSS (SPSS (1999) version 10 <www.spss.com/spss10>). Pair-wise comparison of groups was effected using paired comparison t-tests. In order to investigate any order effect, an analysis of variance with repeated measures was carried out by dive number. Over each dive the design was counterbalanced with respect to drug, depth of dive and number of subjects so the effect of these should be eliminated. The data were then analysed by drug order (pseudoephedrine–cyclizine–placebo, placebo–pseudoephedrine–cyclizine, etc), drug type and dive depth using repeated measures analysis of variance.

Results

Abnormal symptoms such as undue tiredness, nausea or feeling drunk were reported by nine divers following 13 dives; seven at five msw and six at 30 msw; four with placebo, two with pseudoephedrine and seven with

Table 1
Average results for grammatical reasoning, manual dexterity and simple arithmetic tests by dive depth and drug (placebo, pseudoephedrine 60 mg and cyclizine 50 mg)

Depth		**5 metres**			**30 metres**	
Drug	**Placebo**	**Pseudoephedrine**	**Cyclizine**	**Placebo**	**Pseudoephedrine**	**Cyclizine**
Grammatical reasoning						
Mean number done	36.4	36.0	33.4	35.0	33.4	32.4
(95% CI)	(32.1, 40.7)	(32.2, 39.9)	(30.3, 36.5)	(30.4, 39.7)	(30.3, 38.6)	(28.6, 36.1)
Mean number of errors	5.3	5.3	4.6	6.6	6.1	5.4
(SD)	(5.7)	(6.5)	(5.2)	(5.9)	(6.0)	(5.2)
Manual dexterity						
Mean time (sec)	199.0	197.7	188.9	204.3	201.7	201.5
(95% CI)	(182.3, 215.7)	(175.6, 219.9)	(171.1, 206.7)	(184.4, 224.1)	(183.1, 220.3)	(176.5, 226.4)
Simple arithmetic						
Mean time	109	102	103	109	119	112
(95% CI)	(89.4, 129.0)	(83.8, 119.6)	(81.6, 123.4)	(85.2, 133.7)	(92.8, 145.0)	(86.4, 137.7)
Mean number of errors	1.4	1.6	1.7	1.5	1.9	2.1
(SD)	(1.8)	(1.9)	(1.7)	(2.2)	(1.8)	(1.8)

cyclizine. The study code was broken once when a subject had a minor road accident after a five msw placebo dive. He was told only that the dive had not contributed to his accident. There were no missing data for any of the three performance tests for any of the drug/depth combinations. A summary of the data is presented in Table 1.

DEPTH EFFECT

There was a small but significant effect for depth in grammatical reasoning, such that subjects completed more items at five msw than at 30 msw (main effect of depth: $F(1,18) = 6.436$; $P = 0.021$) and there was a small but consistent trend ($P = 0.01$) shown for one more error at 30 msw than at five msw. For the manual dexterity measure, subjects performed more slowly (about 3% prolongation) at 30 msw than at five msw (main effect of depth: $F(1,18) = 7.22$; $P = 0.02$). No effect of depth on the arithmetic task was observed (main effect of depth: $F(1,18) = 0.91$; $P = 0.35$).

DRUG EFFECT

For the number of items completed in the grammatical reasoning test, there was a significant effect for drug (main effect of drug: $F(2,36) = 7.68$; $P = 0.002$). *Post hoc* tests revealed a significant difference in numbers completed between placebo and cyclizine (placebo mean 35.7, cyclizine mean 32.9; $P = 0.002$) but not between placebo and pseudoephedrine (placebo mean 35.7, pseudoephedrine mean 35.2; $P = 0.51$). There was also a significant difference between the two active drugs (cyclizine mean 32.9; pseudoephedrine mean 35.2; $P = 0.01$). However, error rates were not significantly different between the two drugs and placebo.

There was no significant effect of either drug compared with placebo on the time taken to complete the manual dexterity task at either five or 30 msw (main effect of drug: $F(2,36) = 1.54$; $P = 0.23$). Fewer arithmetic errors occurred with placebo than with pseudoephedrine and fewer with pseudoephedrine than with cyclizine, but this trend did not reach statistical significance (main effect of drug: $F(2,36) = 2.83$; $P = 0.07$. Mean errors: placebo = 1.44; pseudoephedrine = 1.73; cyclizine = 1.90).

ORDER EFFECT

For grammatical reasoning, the drug effect was influenced by the order in which the drugs were presented ($F(10,36) = 4.50$; $P = 0.001$), but this is difficult to interpret because there was also a dive-order effect, with performance improving significantly ($P < 0.001$) over the dive series. Unlike speed of performance, the percentage of errors did not change with dive number.

For manual dexterity, there was no significant interaction effect of depth and drug order ($F(5,18) = 0.26$; $P = 0.93$). The speed of performance increased significantly ($P < 0.001$) during the series of dives although this did not appear to be linear over all dives, most improvement being between the first and second dives. There was a significant interaction ($P = 0.001$) between each drug and the order in which the drugs were presented implying that the effect of a drug was influenced by that order. Overall, there was no effect of drug order (main effect of drug order: $F(1,5) = 0.26$; $P = 0.93$). However, as for grammatical reasoning, no clear pattern could be identified.

In the simple arithmetic test, there was no dive number (main effect of dive order: $F(5,115) = 0.77$; $P = 0.57$) or drug order (main effect of drug order: $F(1,5) = 1.65$; $P = 0.20$) effect.

Discussion

Self-medication for various ailments including motion sickness and nasal congestion is common amongst sport divers. A postal survey of experienced Australian and USA divers reported that 11.5% used anti-emetics before most or all dives and a quarter used them occasionally.[1] Ten per cent used pseudoephedrine before most or all dives and 36% occasionally. It is important to test individual drugs, as there is evidence that behavioural effects of any particular drug may change under pressure in ways not predictable from their characteristics at ambient pressure or likely class behaviour.[9]

Cyclizine is an antihistamine popular in the treatment of motion sickness. Other drugs in this group, including dimenhydrinate, an antihistamine which is also frequently used by divers, have been shown to decrease performance under hyperbaric air conditions.[2,10] Dimenhydrinate adversely affects mental flexibility at depth and this effect, when added to the adverse effect of depth on memory, may contribute to the dangers of diving.[2] Transdermal scopolamine has become popular with divers in some countries in the last 20 years and has not been shown to significantly affect diver performance although it has a number of other side effects.[3] No studies on cyclizine in divers have been located in the literature. An increase in error rates and prolongation in learning time were observed in the present study following cyclizine ingestion, and this effect was additional to the narcotic effect of depth at 30 msw.

Pseudoephedrine is a decongestant related to adrenaline with few cardiac or central nervous system side effects, which is used widely by divers. Anecdotally, some slowing of judgement and impaired coordination have been reported under normal ambient conditions, but no objective effects on visual performance were seen in one study.[11] Pseudoephedrine has not been shown to cause significant alterations in psychometric performance at 3 ATA (20 msw, 300 kPa) that might increase the risk of diving.[2] In the present study, pseudoephedrine had little or no effect on the performance measures used.

Nine divers in 13 dives reported mild non-specific symptoms, such as lethargy and poor concentration. These occurred in small numbers with both drugs and with placebo and at both depths, and were too few to analysis statistically. This was a reasonably experienced group of recreational divers, the majority being naive to dry recompression chamber diving and unable to consistently identify the depth of the 'dives'.

There are two broad approaches to the study of diver performance: either the analysis of a single complex task or the use of a battery of simpler tests of cognitive or mental performance that are sensitive to environmental stress.[12] Based on the work of the Navy Biodynamics Laboratory performance evaluation tests for environmental research (PETER), the three tests used were chosen as having limited learning effects and being sensitive to environmental effects. They had been used in previous diver performance studies by one of the authors,[4,6] or used extensively for other diver performance studies.[5,7,13,14]

Despite prior practice, a counterbalanced experimental design to minimise repeated-measures and drug-order effects and selection of tests regarded as having a limited learning effect,[4] any changes related to depth and drug ingestion were partially masked by a significant learning effect in two of the tests. There is some evidence from the analysis to suggest that the order of presentation of the drugs also altered the learning curves, but a much larger group of subjects would be required to test this hypothesis. A power analysis was carried out retrospectively which showed a power of 80% to detect a difference in means of 1.5 points at the 5% significance level if such a difference truly existed, confirming that the sample size was sufficient. Other aspects of the experimental design could have interfered with performance changes related to depth and drug ingestion. For instance, it was noted in the dives where subjects were paired that some degree of competition between them tended to develop in the manual task, where an individual's performance was visible and audible to the other. In addition, environmental factors such as noise levels, temperature and humidity, though similar, could not be rigidly controlled for every dive.

In this study, grammatical reasoning and manual dexterity were slightly impaired at 30 msw compared with five msw depth, which is in keeping with previous studies.[15,16] This was not so with the arithmetic test, which has been reported previously to be a sensitive and reproducible test.[17] The drug effect in the arithmetic test approached statistical significance ($P < 0.07$), but there was almost certainly a loss of sensitivity from the test being simplified and shortened to minimise the bottom time at 30 msw to remain within the no-stop limit on the US Navy air decompression tables. This finding is similar to that reported by Williams et al.[3]

In only the grammatical reasoning test did either cyclizine or pseudoephedrine significantly impair performance at depth and this was more marked with cyclizine. Even so, the drug effects observed were smaller than the effect produced by 30 msw depth alone, which in itself was small. Such impairment may not be sufficient to be of practical significance.[16] However, a relatively trivial decrement in performance in a dry pressure chamber may become a dramatic decrement when subjects are tested in the more stressful conditions of the open sea.[10,15]

Conclusions

The findings of this study are consistent with the limited literature on drug effects on diver performance. Pseudoephedrine exhibited a very minor effect on grammatical reasoning. We have demonstrated that cyclizine had a small adverse effect on grammatical reasoning, which is increased at depth, but had no effect on a manual task. This confirms the findings of other studies on sedative antihistamines. Although the changes in performance with both drugs were small, it would be unwise to make an unconditional extrapolation from the dry chamber to the open water condition because of the increased complexity of interaction of the various modifying stresses in open water diving.[12] Based on reviewed evidence and this study, pseudoephedrine should be reasonably safe to use before air diving, but cyclizine should be taken with caution before air dives as its detrimental effects on performance could well be enhanced in a stressful environment. There is still a need for further chamber and open water testing of the effects on diver performance of commonly used medications despite the passage of two decades since this study was conducted.

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Conflict of interest

The authors declare that there were no conflicts of interest in conducting this study.

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