Cognition Effects of Low-Grade Hypoxia

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INTRODUCTION: The effects of low-grade hypoxia on cognitive function are reported in this paper. The study compared cognitive function during short exposures at four different altitudes.

METHODS: Ninety-one subjects were exposed to simulated altitudes of ground level, 1524, 2438, and 3658 m (5000, 8000, and 12,000 ft) in the Brooks City-Base altitude pressure chamber in a balanced design. Oxygen saturation, heart rate, and cognitive performance on seven different cognitive tasks were measured. In addition, subjects indicated their symptoms from a 33-item subjective symptom survey.

RESULTS: As designed, oxygen saturation decreased and heart rate increased with higher altitudes. Very small degradations in performance were found at the two highest altitudes for only two of the cognitive tasks (continuous performance and grammatical reasoning). In the subjective symptom survey, 18 of the 33 possible symptoms were more common at 3658 m (12,000 ft) than at ground level.

CONCLUSIONS: The findings indicated a minimal influence of low-grade hypoxia on cognitive performance in contrast to some existing classic symptoms of hypoxia.

KEYWORDS: cognition, performance, hypoxia.

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Ascent in altitude is accompanied by a progressive hypoxic hypoxia. It is generally accepted that unpressurized flight above 3048 m (10,000 ft) mean sea level (MSL) requires supplemental oxygen as a countermeasure for the hypoxia.[4] The assumption is that, above that altitude, breathing air will result in a significant reduction in performance. However, Ernsting recommended 2438 m (8000 ft) as maximum altitude for operations without oxygen.[6,7] This was based on the consideration that a decrement in the learning phase of a complex task is just detectable at 1524 m (5000 ft) and is considerable at 2438 m (8000 ft). Significant impairment of task learning, reaction time, and reasoning abilities has been reported at altitudes as low as 1524–1829 m (5000–6000 ft).[5] Ernsting also reported that short-term and long-term memory tasks are affected when breathing air at 2438–3048 m (8000–10,000 ft). This would be important to aircrew if they were forced to perform a novel task. On the other hand, Pearson and Neal showed that hypoxia associated with breathing air at altitudes of 2438–3048 m (8000–10,000 ft) has no detectable effect on performance if the task was well learned first at ground level (GL).[15] Using manikin tasks up to 3658 m (12,000 ft), Denison found a significant effect on rate of learning, suggesting that hypoxia affected learning and memory at lower altitudes such as 2438 m (8000 ft).[5] Green and Morgan then attempted to reproduce the previous work, but were unable to support Denison's findings.[9]

Kelman and Crow, in a series of studies, reported memory and learning were not affected by hypoxia at any altitude below 3658 m (12,000 ft).[2,3,10,11] Fowler et al. also came to the conclusion that the minimum altitude at which hypoxic performance decrements can be detected is greater than 2438 m (8000 ft).[8] Fowler had doubts about the "task novelty" hypothesis as well. He found too many confounding variables in Denison's early work. He believed that reaction time decrements seen at an altitude of 2438 m (8000 ft) could be attributed to "task novelty" because the effect could not be seen anywhere but at the beginning of testing. Nesthus also attempted to clear up the debate by using flight-relevant tasks with simulated altitude.[13] The task

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battery incorporated time-shared performance on several subtasks under experimenter-manipulated workload conditions such as monitoring of dials and displays with dynamic tracking tasks and multiple resource management testing. Compared in measures of simulated flight performance and flight-following procedures during a 3-d, 2-h/d cross-country scenario were 10 pilots in a mild hypoxia group and a control group. Significantly more procedural errors were committed by the hypoxia group during simulated cruise flight at 3048 m (10,000 ft), both during the descent and approach phases from 3048 m (10,000 ft) and during descent from 3658 m (12,500 ft). This suggests that there may be a significant effect on pilot performance from hypoxia at altitudes lower than 3048 m (10,000 ft). Angerer and Nowak also report one study in which subjects were exposed to 3048 m (10,000 ft) for 6.5 h and found performance decreased by 10–20% at one or more time points for arithmetic, reasoning, long- and short-term memory, perceptual speed, and visual reaction time.[1] Except for short-term memory, no relationship was found with the duration of an exposure and some tests revealed large individual differences. Pavlicek et al. assessed the effects of hypoxia on subjects exposed to altitudes of 2999 or 4499 m (9840 or 14,760 ft) for 2 h and found no significant change in higher cognitive and emotional function tests, suggesting short-term adaptation mechanisms may lead to preservation of these functions.[14] Getting an accurate picture of the effects of low altitude on cognitive performance is complicated by the slightly different cognitive tests, altitudes, and durations of exposure. For a more in-depth review of hypoxic hypoxia at "moderate altitudes" [2438 to 4572 m (8000 to 15,000 ft)], the reader is directed to a recent article by Petrassi et al.[16]

The primary objective of this study was to determine the effects of short-term low-grade hypoxia on cognitive function using a larger number of subjects than in the earlier studies cited above. The study compared cognitive function during 1-h exposures to four different altitudes [GL, 1524, 2438, and 3658 m (5000, 8000, and 12,000 ft)]. The null hypothesis was that there would be no differences in cognitive performance among the four altitude conditions. The alternative was that cognitive degradation would occur at the 1524- through 3658-m (5000- through 12,000-ft) conditions (compared to GL).

METHODS

The hypobaric exposures were conducted in a hypobaric chamber used during many years of human decompression studies at Brooks City-Base (formerly Brooks Air Force Base), TX. These facilities had the necessary altitude chambers, safety monitoring equipment, and pass-through ports for communications, physiological, and cognitive function monitoring. The Brooks City-Base Institutional Review Board approved the protocol. There were 93 fully informed, nonsmoking personnel who volunteered and gave informed consent for this protocol, which included GL training and testing. All subjects were in the age range of active military personnel, passed the appropriate test subject physical examinations (U.S. Air Force class III flight physical), were human immunodeficiency virus negative, and were screened for evidence of conditions that might abnormally impair their tolerance to altitude. Female subjects had a negative urine pregnancy test within 36 h prior to each altitude exposure. Each subject was trained as stipulated in the Informed Consent Document, including an orientation exposure and instruction on use of oxygen equipment. The experiment involved 2 d (or parts of days) to medically qualify, become trained, and complete paperwork plus 1 d of data acquisition and altitude exposure.

The subjects were briefed that no scuba diving or other hyperbaric exposures would be permitted for 48 h prior to the hypobaric exposures. The subjects were reminded of the presentations of hypoxia and acute mountain sickness and of the need to report any symptoms promptly. Subjects were advised to eat breakfast that was low in protein, gas-producing foods, and fat on the morning of each exposure. On the day of the altitude exposures, the subjects initially entered the chamber and accomplished an ear and sinus check while the altitude chamber was taken to a pressure altitude of 1524 m (5000 ft) at a rate of 1524 $m \cdot min^{-1}$ (5000 $ft \cdot min^{-1}$) and returned to GL at the same rate. Time spent at 1524 m (5000 ft) was less than 5 s. During ascent and return to GL, subjects ensured they were able to equalize the pressure across their eardrums and to the sinuses. If subjects were unable to equalize ear and sinus pressure during altitude changes, they were rescheduled.

Subjects were then exposed, in series, to the four altitude conditions [GL, 1524, 2438, and 3658 m (5000, 8000, and 12,000 ft)]. The subjects were at rest during all exposures to altitude. For each altitude condition, ascent and descent were at 1524 $m \cdot min^{-1}$ (5000 $ft \cdot min^{-1}$). The subjects were allowed 20 mins to equilibrate at each altitude. To balance for potential confounding effects (e.g., learning, adaptation, fatigue), half of the subjects was exposed to the four altitudes in ascending order and the other half was exposed in descending order. The breathing gas for all exposures was air and the maximum stay at each altitude was 105 min. As much as possible, the subjects were blinded with respect to the various altitude exposures. The Brooks altitude chamber was located at 183 m (600 ft) above MSL, but the chamber GL pressure in these experiments was kept at approximately 457 m (1500 ft) MSL to avoid air leakage through the door of the pressure chamber, and the resultant air flow noise to reach GL both during ascent and descent helped in the blinding of the subjects.

The data collection tools were selected to assess the major facets of human performance that would impact military operations. Reaction time, memory, spatial processing, problem solving, and motor coordination were evaluated. Prior to the start of data collection, two 4-h orientation and training sessions were conducted to introduce the subjects to the purpose of the study and the data collection procedures. During the orientation, participants were trained to asymptotic performance on each of the cognitive tests [with the exception of the manikin test (see below)]. Cognitive testing was accomplished on a computer using seven tests from the Automated Neuropsychological Assessment Metrics (ANAM) battery.[17] The ANAM cognitive tests used in this study were selected after consultation with Air Force, Army, and Navy researchers experienced in cognitive testing and are universally used in many labs. Lowe et al. reviewed the results of ANAM use in the testing of a variety of stressors and found that the battery worked well across the board, including for altitude exposure.[12] The test battery required approximately 30 min to complete and was administered to each participant during each of the four altitude exposures. Outcome measures recorded from these tests were mean reaction time and accuracy of response. The cognitive testing comprised the following:

1. Choice Reaction Time Test: On each trial one of two unique icons was presented. As each randomly appeared on the screen, the subject was required to press the key specific to that icon.
2. Tower Test: This was a timed test requiring the subject to efficiently restack a set of four horizontal bars into a specific configuration while following a prescribed set of rules.
3. Continuous Performance Test: The subject determined whether a currently presented single-digit number was the same as the immediately previous number and memorized the current number for comparison to the next value.
4. Grammatical Reasoning Test: The subject answered whether two logic statements both accurately described the relational order of three symbols.
5. Mathematical Processing Test: On each trial an addition/subtraction problem was presented, each involving three single digits and two operands. The subject had to determine whether each answer was greater or less than 5.
6. Match to Sample Test: For each trial, the subject was presented with a 4 × 4 checkerboard block pattern to memorize. Subsequently, two block patterns were shown and the subject was required to choose the block matching the memorized pattern.
7. Spatial Processing Test: The subject had to determine whether two 4-bar histograms presented simultaneously (one rotated 90° or 270°) were the same or different.
8. Manikin Test: This is a spatial orientation test in which the subjects are presented with a human outline image in one of 16 orientations and are tasked to indicate the correct position. One of the goals of this study was to determine the effects of low-grade hypoxia on learning. To accomplish this goal, the participants were divided into four groups, with each group performing a manikin test at only one altitude [i.e., one group performed at GL, one at 1524 m (5000 ft), etc.]. The participants did not receive training on this task prior to the start of the study and were thus naive to the test when it was presented to them. Completing this task required each participant to read the task instructions and perform four example problems before each of four 3-min trials. Feedback was provided during the example problems by means of a smiling face for correct responses and a frowning face for incorrect responses. Participants were instructed to try their best and were informed that test proctors would not be able to provide any input during this portion of the study.

Each subject's blood oxygen saturation and heart rate were measured periodically with finger oximetry, and averages, per subject, were calculated at each altitude exposure for data analysis (Propaq Vital Signs Monitor Model 242, Protocol Systems, Inc., Beaverton, OR). During the last 15 min at each altitude, the participant completed a survey covering 65 symptoms. For each symptom, the participant gave a score ranging from 0 (not present) to 5 (severe). The survey was originally designed for general multipurpose use and, after studying the list of symptoms, we deemed that only 33 were pertinent to our study of the effects of low-grade hypoxia and will be included in this report.

For each cognitive test outcome measure (with the exception of the manikin test) and for the two physiological measures, a repeated measures analysis of variance (ANOVA) with one within-subjects factor (altitude) was performed to test for mean differences among the four altitude exposures. A Huynh-Feldt adjustment was made to the ANOVA degrees of freedom when assumptions of sphericity were not met. When significant ANOVA results were found, post hoc comparisons (Student's paired *t*-tests) were performed to compare each altitude mean with the GL mean. For the manikin test, a repeated measures ANOVA with one between-subjects factor (altitude) and one within-subjects factor (trial) was performed. The test of importance in this analysis is the test for an altitude by trial interaction. That is, is the learning curve different among the four altitude exposures? For the symptom survey, data frequency tables were first constructed to study the distribution and severity of the symptoms experienced. Nonparametric tests (Friedman's followed up with Wilcoxon signed rank when appropriate) were then performed for each symptom to determine if the rate of occurrence at the three altitudes differed from that at GL. To determine sample size for this study, the power analysis was based on the post hoc tests, and we determined that a sample of 100 subjects would provide an 83% chance (power) of detecting a relatively small difference (i.e., a difference of about 0.3 standard deviations of the difference in magnitude) when testing at the two-tailed 0.05 alpha level.

RESULTS

Data collection was completed on 93 subjects in 33 altitude chamber exposures. One subject was excluded from all of the data analyses due to post hoc admission of disqualifying medication, and one subject was excluded from the cognitive data analyses because inspection of the data showed that he clearly was not trained to asymptote on several of the cognitive tests. There were 45 subjects who were exposed to the altitudes in ascending order and 47 who were exposed in descending order.

Mean oxygen saturations and heart rates are shown in **Fig. 1**. ANOVA indicated significant differences among altitude conditions for both oxygen saturation and heart rate [mean squared error (MSE) = 3.83, $F_{(2,174)} = 875.1$, $P < 0.001$; and MSE = 24.3, $F_{(3,235)} = 55.4$, $P < 0.001$, respectively].

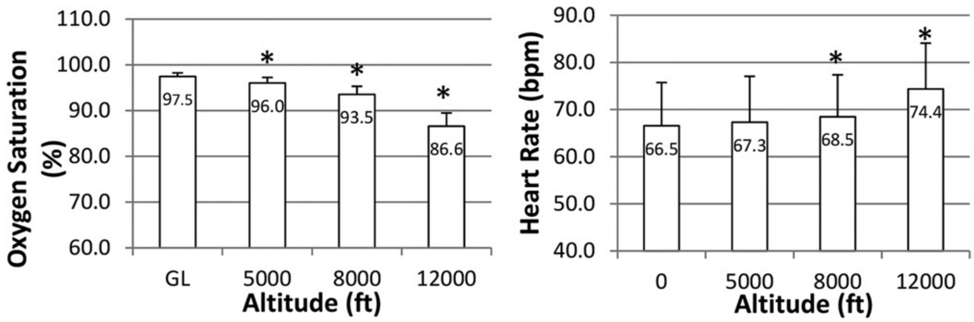

Fig. 1. Oxygen saturation (in %) and heart rate at the four simulated altitudes. The bars represent standard deviation. *Indicates statistically significant difference from ground level (Student's paired *t*-test, $P < 0.05$).

Oxygen saturation monotonically decreased from 97.5% (± 0.8) at GL to 86.6% (± 2.9) at 3658 m (12,000 ft), with the difference from GL being statistically significant at all three altitudes. Note that the variability in oxygen saturation was most pronounced at the higher altitudes, as reflected by the increased standard deviation. Heart rate monotonically increased from 66.5 bpm (± 9.2) at GL to 74.4 bpm (± 9.7) at 3658 m (12,000 ft) and was significantly higher than GL heart rate at 2438 m (8000 ft) and 3658 m (12,000 ft).

Descriptive statistics and statistical test results are summarized in **Table I** for each outcome measure of the cognitive tests (except for the manikin test). To aid with interpretation, figures of the results will be shown for all cognitive measures where significant effects were detected.

For the Continuous Performance Task, significant altitude main effects were observed for both accuracy and mean response time (MRT). Specific post hoc testing revealed accuracy was significantly decreased at both 2438 and 3658 m (8000 and 12,000 ft) relative to GL. Mean response time demonstrated a significant, and approximately equivalent, increase at 1524, 2438, and 3658 m (5000, 8000, and 12,000 ft) relative to GL (**Fig. 2**). It should be noted that, even though significant differences were detected, they are relatively small. Mean accuracy at 3658 m (12,000 ft) represents a mere 1.5% reduction from GL accuracy and MRT at 3658 m (12,000 ft) represents an increase of only 2.4% from GL.

For the Grammatical Reasoning Task, a significant altitude main effect was observed for the accuracy measure. Post hoc testing indicated that accuracy significantly decreased at the 3658-m (12,000-ft) exposure relative to GL. However, the change was relatively small, amounting to about a 2.5% change from GL (**Fig. 3**).

For the Math Processing Task, no significant differences were observed. Accuracy remained at about 95% across all altitudes, and the observed MRT was slightly lower (although not statistically) at all altitudes compared to GL.

For the Spatial Processing Task, no significant differences were observed. Accuracy was 91–92% across all conditions, and MRT remained relatively flat, with the largest difference from GL being only 19 ms at 3658 m (12,000 ft).

For the Tower Task, no significant differences were observed. The largest observed difference from GL occurred at 2438 m (8000 ft) and represented about a 3% increase relative to GL.

For the Two Choice Response Time Task, no significant differences were observed. Accuracy dropped by only 0.8 percentage points from GL to 3658 m (12,000 ft), and the largest MRT difference from GL was only 7 ms, occurring at 1524 m (5000 ft).

Recall that the purpose of the Manikin Task was to compare learning rates under the four altitude conditions. The ANOVA detected significant trial main effect differences, with accuracy increasing from trial 1 to 4 and MRT decreasing from trial 1 to 4. These results were expected, as per design. However, the trial by altitude interaction test was not significant for either accuracy or MRT. Thus, there was no evidence that the rate of learning differed among the four altitude conditions. Because of the interest generated in the literature concerning the potential negative effect of altitude on learning, we are including graphs of the mean data (**Fig. 4**) to provide a visual impression of the results. An inspection

Table I. Cognitive Performance Measures, Means, and SDs for Each Altitude and Results of ANOVAs and Post Hoc Tests.

		MEAN ± SD				ANOVA TEST FOR ALTITUDE EFFECTS			
TEST	VARIABLE	GL	1524 m (5000 ft)	2438 m (8000 ft)	3658 m (12,000 ft)	MSE	Df	*F*	*P*
Continuous Performance	Accuracy (%)	97.4 ± 2.5	97.2 ± 2.9	96.4* ± 3.6	95.9* ± 4.2	6.56	3245†	7.89	<0.001
	MRT (ms)	462 ± 84	473* ± 82	472* ± 86	473* ± 92	1064.84	3240†	2.79	0.048
Grammatical Reasoning	Accuracy (%)	91.8 ± 7.8	90.5 ± 11.1	91.0 ± 9.8	89.5* ± 10.3	30.84	3242†	3.02	0.036
	MRT (ms)	5206 ± 1306	5095 ± 1473	5129 ± 1450	5281 ± 1610	435,698	2208†	1.72	0.164
Math Processing	Accuracy (%)	95.9 ± 5.1	95.8 ± 5.8	95.8 ± 4.3	94.9 ± 6.0	16.12	3270	1.27	0.286
	MRT (ms)	1738 ± 397	1724 ± 433	1711 ± 389	1716 ± 430	23,966	3261†	0.532	0.654
Spatial Processing	Accuracy (%)	91.5 ± 8.0	91.7 ± 7.1	90.6 ± 7.7	90.9 ± 7.3	45.553	3270	0.444	0.722
	MRT (ms)	1117 ± 341	1124 ± 375	1113 ± 334	1136 ± 366	24,820	3251†	0.415	0.743
Tower Task	MRT (ms)	1430 ± 441	1464 ± 509	1477 ± 601	1445 ± 416	89,760	2209†	0.541	0.654
Two Choice	Accuracy (%)	99.1 ± 1.8	98.8 ± 2.7	98.7 ± 2.2	98.3 ± 2.7	5.434	3243†	2.17	0.098
	MRT (ms)	440 ± 68	433 ± 60	440 ± 72	437 ± 72	1700.0	3250†	0.572	0.623

Numbers in each cell of the table represent the mean ± standard deviation.
* Indicates mean is significantly different from the GL mean (paired *t*-test, $P < 0.05$).
† Huynh-Feldt adjustment was made to the ANOVA degrees of freedom.

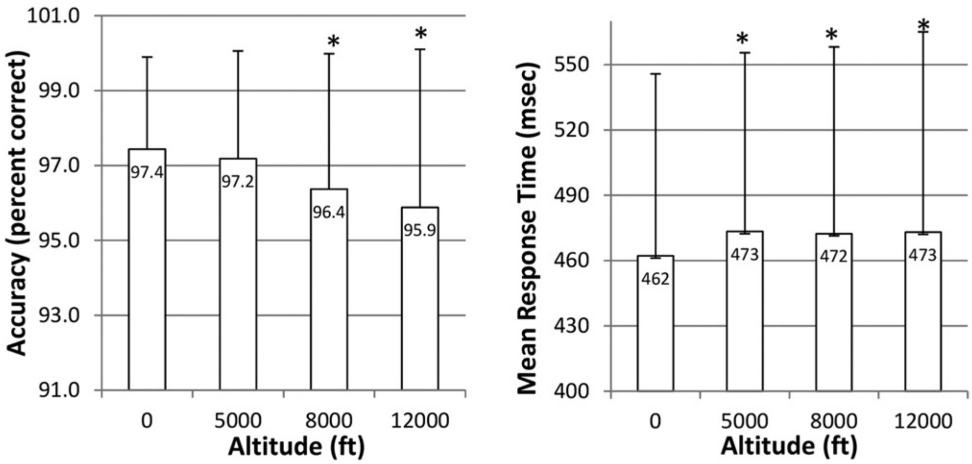

Fig. 2. Continuous performance task (accuracy and MRT) at the four simulated altitudes. The bars represent standard deviation. *Indicates statistically significant difference from ground level (Student's paired *t*-test, $P < 0.05$).

of the accuracy figure subjectively suggests that learning might have been slightly reduced at the two higher altitudes, although statistically this could not be confirmed even with our large sample. For MRT, on the other hand, the learning curves are quite parallel with the exception of the curve for 2438 m (8000 ft), which appears to have slightly less slope than the other curves.

There were 33 symptoms selected from the general purpose symptom survey as relevant for this study which are listed in **Table II**. Initially, we generated frequency tables to study the rate and severity of occurrence of each of these symptoms and found that the occurrence of severe symptoms (arbitrarily defined as a score of 4 or 5 for this study) was rare. For example, under the most extreme condition [3658 m (12,000 ft)], only 10 cases of a severe symptom were reported. One subject accounted for four of these, scoring 4 for cold hands, cold feet, sleepy, and tired. Two other subjects gave high scores to sleepy and one reported a high score for tired. Two subjects scored 4 for short of breath. Finally, one subject scored 4 for heart pounding (but gave the same score at the other two altitudes and a score of 3 even at GL). Table II contains the percentage of subjects experiencing each of the 33 symptoms at each altitude and shows the results of the nonparametric tests used to compare the percentages.

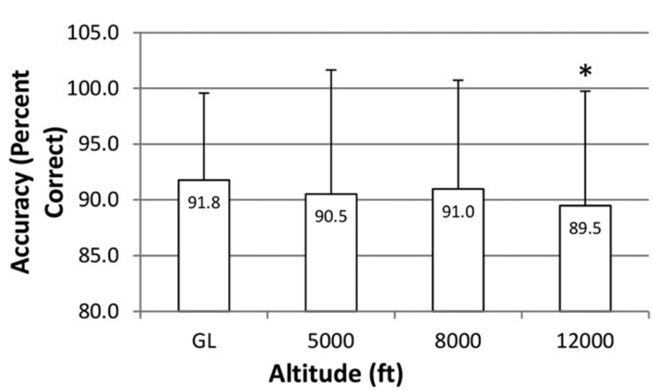

Fig. 3. Grammatical reasoning task (accuracy) at the four simulated altitudes. The bars represent standard deviation. *Indicates statistically significant difference from ground level (Student's paired *t*-test, $P < 0.05$).

DISCUSSION

The oxygen saturation data (Fig. 1) were representative of values usually seen during such hypobaric exposures.[7] Heart rate, measured at the same time as oxygen saturation, also increased at the higher altitudes in accordance with earlier established information from hypobaric exposures.[7] These results validate the goal of the experimental design to create an appropriate hypoxic environment.

Through exploration of the cognitive task array it seems there is a small but consistent decrement only in the higher order/higher workload tasks. Statistically significant decrements in performance were seen for continuous performance and grammatical reasoning. However, the decrements, on average, appeared to be relatively small. The presence of these significant findings may be a function of high statistical power rather than effect size (i.e., the large sample size of 91 subjects allowed the tests to detect very small differences, even though these differences may not be meaningful in an operational environment). On the other hand, one must consider that the observed differences (about 2%) may be enough of a decrement in a complex environment, such as a flight deck, to cause concern in terms of cognitive workload. In addition, it should be noted that increased physical activity, high acceleration forces, and other high stress physiological factors may significantly increase the cognitive dysfunction in the operational setting.

To arrive at a clearer picture of the results, we generated frequency distributions for the two most extreme cases [changes

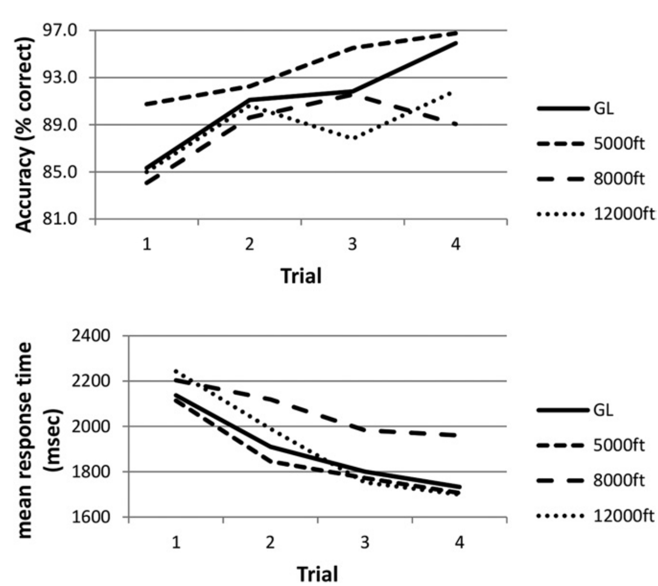

Fig. 4. Manikin test (accuracy and MRT). Means across the four trials for each of the altitude conditions.

Table II. Percent of Subjects Reporting the Occurrence of Each Symptom at Each Altitude Condition.

	ALTITUDE, m (ft)			
SYMPTOM	GROUND LEVEL	1524 (5000)	2438 (8000)	3658 (12,000)
Alert	83	83	80	78*
Blurred Vision	8	8	5	11
Reduced Coordination	4	5	7	14*
Cough	2	2	2	3
Dizziness	1	0	2	13*
Dry Mouth	3	5	3	10*
Eye Irritation	3	9*	10*	15*
Feeling Faint	0	0	0	8*
Feeling Good	90	91	88	88*
Cold Feet	19	22	23	30
Forgetfulness	2	2	7	8*
Abdominal Gas	12	16	19	28*
Cold Hands	17	20	23	22
Headache	13	13	10	12
Hard to Breathe	0	0	0	10*
Heart Pounding	2	2	2	7*
Hungover Feeling	2	0	0	3
Irritable	1	2	2	3
Light Headed	5	3	4	20*
Muscle Cramps	0	1	0	3
Nausea	0	0	0	2
Difficulty Concentrating	5	15*	15*	28*
Difficulty Hearing	1	2	1	5
Numbness	0	1	2	3
Restless	11	10	3*	7
Short of Breath	0	0	0	14*
Sinus Problems	0	1	1	8*
Sleepy	25	30	33*	46*
Tired	19	26	20	35*
Vision Difficulty	4	5	4	11
Weak	2	1	4	10*
Wide Awake	20	25	31*	23
Worried	0	1	0	2

Three of the entries (Alert, Feeling Good, and Wide Awake) were not "symptoms," but were included in the survey as a check for subject compliance.
* Indicates a significant difference at that altitude compared to ground level ($P \leq 0.05$, Wilcoxon signed rank test).

in accuracy and MRT for the continuous performance test when going from GL to 3658 m (12,000 ft)]. These distributions are shown in **Fig. 5**. Of 91 subjects, 58 (64%) showed decreases in accuracy. Note, however, that the majority of decreases were relatively small, with only 13 subjects experiencing decreases of more than 5 percentage points and, of those, only 3 had decreases of more than 10 percentage points. Of the 91 subjects, 54 (59%) experienced increases in MRT, but, again, the majority of these increases were small, with only 5 subjects experiencing increases exceeding 100 ms. The results shown in Fig. 5 suggest that, for the majority of personnel who might be exposed to altitudes as high as 3658 m (12,000 ft), there may be a slight effect on higher cognitive performance that may, or may not, be of practical/operational relevance and that there is likely a small subset of individuals who may be significantly impacted by such exposures. One must also keep in mind that some of the extreme results seen in this study may be due to distraction or inattention not related to hypoxia, but there is no way of verifying those possibilities.

The results seen for the continuous performance task seem to provide some insight to working memory capacity. This task essentially occupies the majority of working memory capacity through constant recall and memorization, which makes it a slightly different measure of working memory than the math processing and spatial processing tasks (which are not time intensive). Since neither the math processing nor spatial processing tasks showed any significant result, it seems likely that hypoxia affects working memory capacity by decreasing an individual's ability to quickly encode and recall information. In addition, the higher workload of the task, by nature, may be illuminating the finer working memory aspects of this task when compared to the simpler math processing and spatial processing tasks. Grammatical reasoning, a higher order (abstract reasoning) task, was only impacted by hypoxia in the accuracy measure. Across altitudes, response time was roughly equivalent. Perhaps the low-grade hypoxia, while not affecting basal response speed, was detrimental enough to affect higher order processing (i.e., the prefrontal cortex in some manner, while not affecting more basic level functions).

Contrary to previous research discussed in the introduction, rate of learning, as demonstrated with the manikin test, does not appear to be impacted by the degree of hypoxia encountered in this study. Even though visual inspection of Fig. 4 gave the subjective impression that learning might have been slightly reduced at the two higher altitudes, there was no statistical evidence of an effect even with our large sample.

Significant differences in symptoms between the two lower altitudes and GL were sparse, but at the 3658-m (12,000-ft) condition, occurrence rates were significantly higher than at GL for 18 of the 33 symptoms. Even so, the fact that only three cognitive measures showed a significant decrement in performance at 3658 m (12,000 ft) compared to GL (and those differences were small) suggests that the presence of symptoms does not imply that cognitive performance at the altitudes used in this study will be negatively affected. That is, subjects appear to be able to satisfactorily perform their tasks even when experiencing the symptoms associated with low-grade hypoxia.

Some of the previous low-grade hypoxia studies discussed above used very small numbers of subjects (e.g., Denison, $N = 8$; Fowler, $N = 12$; Nesthus, $N = 10$). Our current study was based

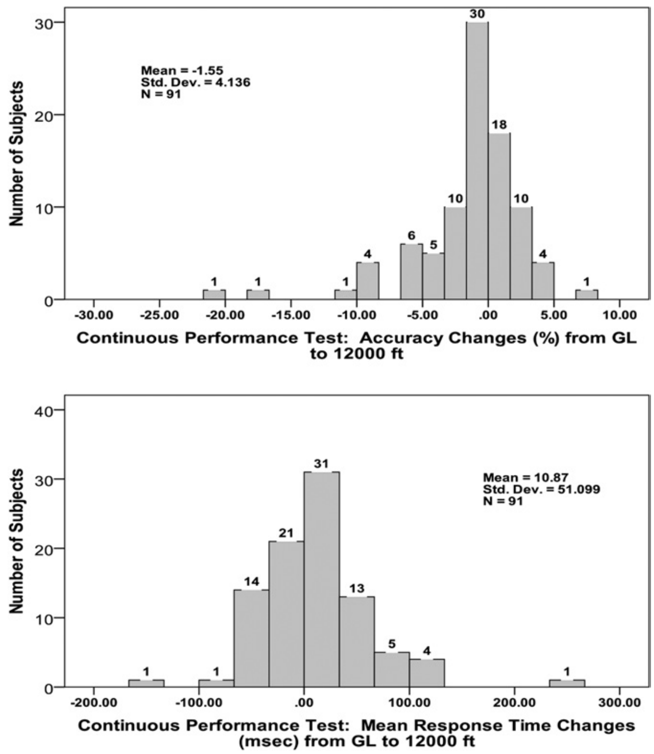

Fig. 5. Frequency distribution of the changes from GL to 3658 m (12,000 ft) for the accuracy and MRT measures of the continuous performance test.

on data from 91 subjects. Obviously, the statistical power of such a large subject pool is much greater than that of any previous work that we are aware of. As was noted in the results section, variation among the subjects' responses to the cognitive tests tended to be high. The subjective nature of the testing, individual variability, physiological compensatory responses, training times, and other variables are likely the reason for the disparity. The large amount of variations observed in this type of data points to the hazards of drawing conclusions from the previous low-grade hypoxia studies with very small numbers of subjects.

The large amount of variation seen in the subjects' responses to the cognitive tests may be the result of a number of extraneous factors. At the altitudes used in this study, hypoxia is accompanied by hyperventilation, resulting in hypocapnia and respiratory alkalosis. This can result in changes of cerebral oxygen delivery either through changes in blood oxygen content and/or cerebral blood flow. Hypocapnia shifts the oxygen dissociation curve to the left, resulting in an increase in blood oxygen level. On the other hand, hyperventilation also causes cerebral vasoconstriction, resulting in less cerebral oxygen availability. The balance between these two effects may contribute to the variability in oxygen saturation, as reflected by the increased standard deviation and the minimal performance decrement at the higher altitudes. The subjects' breathing patterns and end-tidal carbon dioxide levels were not measured. However, all the subjects had a 20-min adaptation period at each simulated altitude before the first pulse oximetry measurements were taken, and the second measurements were done at the end of each altitude exposure. Both measurements were also preceded by a 2-min rest period. These precautions were done to decrease the likelihood of hyperventilation having a major impact on the cognition results. However, despite these measures, individual variability may have contributed to the role of hyperventilation in the results.

A number of other factors may be involved in the variability in cognition found in these results. Subject distraction and state of mind may play a role. Insufficient training may have been a factor, but was addressed by the use of the crossover technique described in the methods section. Acute mountain sickness can decrease cognitive performance. However, there was no indication that this condition was a factor. The exposure times and altitudes appeared to be insufficient to develop acute mountain sickness.

In conclusion, the findings in this low-grade hypoxia study indicate none to very minor decreases in cognitive performance at 1524 and 2438 m (5000 and 8000 ft). Some significant differences were found between GL and 3658 m (12,000 ft); however, the decrements were relatively small and the operational relevance of those decrements will have to be determined by those making such decisions in their respective fields. There were significant differences between GL and 3658 m (12,000 ft) with respect to the number and frequency of symptoms reported, creating a contrast between objective cognitive measurements and subjective symptomatology. These combined results suggest that subjects were generally able to perform their assigned tasks even though they experienced some of the classic hypoxia symptoms.

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