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Six Percent Oxygen Enrichment of Room Air at Simulated 5000 m Altitude Improves Neuropsychological Function

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ABSTRACT

Cognitive and motor function are known to deteriorate with the hypoxia accompanying high altitude, posing a substantial challenge to the efficient operation of high altitude industrial and scientific projects. To evaluate the effectiveness of enriching room air oxygen by 6% at 5000 m altitude in ameliorating such deficits, 24 unacclimatized subjects (16 males, 8 females; mean age 37.8, range 20 to 47) underwent neuropsychological testing in a specially designed facility at 3800 m that can simulate an ambient 5000 m atmosphere and 6% enrichment at 5000 m. Each subject was tested in both conditions in a randomized, double-blinded fashion. The 2-h test battery of 16 tasks assessed various aspects of motor and cognitive performance. Compared with simulated breathing air at 5000 m, oxygen enrichment resulted in higher arterial oxygen saturations (93.0 vs. 81.6%), quicker reaction times, improved hand–eye coordination, and more positive sense of well-being (on 6 of 16 scales), each significant at the $p < 0.05$ level. Other aspects of neuropsychological function were not significantly improved by 6% additional oxygen.

Key Words: cognitive function; motor function; high altitude; reaction times; hand–eye coordination; mood

INTRODUCTION

Although communities have existed for many generations in such regions as the Andean heights of South America, additional recent migrations to high altitude have occurred with the development of industrial and scientific interests. In Chile, for instance, mining operations have been estimated to employ 20,000 workers above 3000 m (Jimenez, 1995). Mountain summits and highlands are often favorable locations for telescope facilities, for example, the Mauna Kea Observatory, Hawaii, elevation 4200 m, and the proposed Atacama Large Millimeter Array, Chile, elevation 5000 m.

The physical consequences of initial high altitude exposure are familiar and predictable. Forster (1986) found an acute mountain sickness incidence of 80% among telescope workers after 1 day at 4200 m. Cognitive and motor function also deteriorate with the hypoxemia of high altitude. McFarland (1937a; 1937b; 1938) found significant impairments in arith-

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metical performance, word recognition, attention level, and short-term memory among high altitude expeditioners. High altitude workers often perceive a poor ability to concentrate (Forster, 1986), and learning complex mental tasks can take longer above 2400 m than at sea level (Denison et al., 1966). Kobrick (1975) found visual alertness to be impaired at 4000 m and higher. Jimenez has reported (1995) that to achieve equivalent productivity in mining operations at 4000 m, the man/hour ratio must be increased to 150–180% of what would be required at sea level.

One possible solution to the problem of high altitude hypoxemia, that of supplementing room air with oxygen to mimic the higher partial pressures of lower altitudes, has been shown to be theoretically promising (West, 1995) and technically feasible and beneficial for sleep (Luks et al., 1998). The long-term benefits of oxygen therapy on cognitive performance have been established in the treatment of sea level patients with chronic obstructive pulmonary disease (Heaton et al., 1983), but few studies have focused directly on the effects of oxygen enrichment upon altitude-induced neuropsychological deficits.

The goal of the present study was to evaluate the effectiveness of room air oxygen enrichment in reducing or reversing the immediate neuropsychological impairment experienced by poorly acclimatized individuals attempting to perform optimally at high altitudes. We chose 5000 m (16,400 ft) because this is now being increasingly used for state-of-the-art telescope facilities. The level of oxygen enrichment scenario was set at 6% because this is easily attainable in work areas of modest size and at 5000 m results in a reduction of equivalent altitude to 3200 m, which is known to be well tolerated.

METHODS

Subjects

Twenty-four subjects who live at sea level near the San Diego, California, area participated in this study. Informed consent was obtained with a protocol approved by the UCSD Human Subjects Committee. This group consisted of 16 males and 8 females with a median age of 25.5 years (mean 27.8, range 20 to 47). Seven of the participants were either undergraduate students or held a bachelors degree, while the remainder were either pursuing or held advanced degrees. All subjects were fluent in English, but six had spoken only a non-English language prior to grade school.

Subjects were recruited largely from among the academic community. All were sea-level residents who had not visited high altitude in the 3 weeks prior to the study. Pregnant women, regular smokers, or people who had a history of pulmonary, cardiovascular, hematologic, renal, or hepatic disease were excluded. Female subjects were required to have regular menstrual cycles (or birth control medication cycles) and to start and the end the study within 14 days of the start of the cycle. This was to minimize the possibility that changing levels of progesterone, a respiratory stimulant, would affect their responses to altitude during the course of the study.

Experimental facility and adjustment of oxygen concentration

Testing was conducted at the Barcroft facility (elevation 3800 m) of the University of California's White Mountain Research Station, in a room specially designed for control of atmospheric oxygen. This room measures 3.5 × 3.0 × 2.4 m and includes a window across which the subject can communicate with and be observed by the investigator during testing. Both the subject and investigator were seated at small desks. Adequate ventilation of the room was achieved by means of a small fan mounted in a single inflow duct high on one wall; outflow occurred via random leaks.

Oxygen levels in the experimental room were adjusted by attaching a portable chamber containing 3 AirSep oxygen concentrators (AirSep, Buffalo, NY) to the ventilation circuit. By leaving the chamber door open to the outside environment and simply directing the 92.5% O_2 effluent from the concentrators into the room's ventilation duct, the room oxygen could be enriched by several percent in less than 90 min. Alternatively, by channeling the

O_2 effluent from the concentrators out of the closed chamber, thereby effectively directing N_2-enriched air into the ventilation duct, the room oxygen level was easily reduced by a few percent. Tuning the oxygen concentrators' output in coordination with fan speed allows fine control of room air oxygen levels. Oxygen and carbon dioxide levels in the room were continuously monitored using Beckman (Fullerton, CA) OM1 and LB2 gas analyzers. For a more complete discussion of the technical specifications of the experimental room for oxygen enrichment, see Luks et al. (1998).

Experimental design

The desired equivalent altitude and conditions were created by altering the oxygen concentration of the experimental room at the Barcroft facility. The partial pressure of oxygen in moist inspired gas is a function of the fractional concentration of oxygen and barometric pressure, as given by the equation $P_{IO_2} = F_{IO_2} (P_B - 47)$. At an altitude of 5000 m (P_B 420 mmHg), the inspired P_{O_2} during air breathing is 0.21 (420-47) = 78 mmHg. The same inspired P_{O_2} can be obtained at the 3800 m Barcroft facility (P_B 483 mmHg) by reducing the oxygen concentration to 18%, thus giving an inspired P_{O_2} of 0.18 (483-47) = 78 mmHg. At 5000-m altitude, enriching the oxygen concentration by 6% gives an inspired P_{O_2} of 0.27 (420-47) = 101 mmHg. This can be simulated at the Barcroft facility by raising the concentration to 23% because 0.23 (483-47) = 100 mmHg. Thus, for this study, 18% oxygen in the test room was called the "ambient air 5000-m treatment," and 23% oxygen was designated the "6% oxygen-enriched 5000 m treatment."

Subjects drove from sea level to the laboratory in about 8 h and arrived in the mid-afternoon. The 2-h battery of neuropsychological tests described below was administered to each subject on three occasions, beginning the morning after arrival. This first "practice" session was conducted to minimize later practice effects by familiarizing the subject with the testing procedures. No atmospheric alterations were made; the doors to the experimental room were left open and the oxygen concentrators turned off. Subjects were always tested individually although their test schedules were coordinated as pairs.

On the third afternoon, approximately 44 h after arrival, subjects repeated the neuropsychological battery. This time the room air was maintained at either 18 or 23% oxygen, and each subject spent a quiet 50-min "acclimatization" period in the room before testing commenced. Arterial oxygen saturations were measured by pulse-oximeter (as 2.5-min averages) just prior to and upon completion of the battery, while the subject was still in the room. By allowing the subjects to reside 2 days at 3800 m before exposing them to the atmosphere of 5000 m, the severity of a direct ascent from sea level was avoided.

Counterbalancing was achieved by testing each subject in the same fashion during the fourth afternoon with the oxygen conditions reversed, the order being randomized and double-blinded for each pair. Thus, each subject served as his or her own control for comparing neuropsychological performance under the two treatments. The randomized treatment orders were determined beforehand by collaborators not involved in evaluating subjects' performances, and were not revealed to the test administrator until completion of the study. These collaborators also set up and operated the ventilation/oxygenation apparatus for each test session. Blinding of the test administrator was further accomplished by placing a drape across the area containing the apparatus.

Subjects were asked to complete a short questionnaire each morning regarding how long and how well they felt they had slept the night before.

Neuropsychological tests

The battery of 16 tests used in this study included verbal, paper-and-pencil, and computerized tasks designed to assess (among other things) concentration, cognitive processing speed, short-term and working memory, pattern analysis, reaction time, and eye–hand coordination. Subjective assessments of sleepiness, perceived effort, and mood were also included.

Testing sessions began with the following investigator-administered tests: (1) Story Memory (Heaton et al., 1991), (2) Trail Making A and B (Army Individual Test Battery, 1944; Reitan and Davison, 1974), (3) Digit Symbol (Wechsler, 1981), (4) Finger Tapping (Halstead, 1947), (5) Digit Vigilance (Lewis and Rennick, 1979), (6) Grooved Pegboard (Reitan and Davison, 1974), (7) Paced Auditory Serial Addition (Gronwall, 1977), and (8) Matrix Reasoning (Wechsler, 1997).

Next was a 25-min computer-administered test package developed for the NASA Neurolab that consists of: (1) Karolinska Sleepiness Scale (Akerstedt and Gillberg, 1990), (2) Probed Recall Memory (Dinges et al., 1993), (3) Psychomotor Vigilance Task (Dinges and Kribbs, 1991; Dinges, 1992; Dinges et al., 1994, 1997), (4) Calculation Performance Task, (5) Compensatory Tracking Task (Aerospace Medical Panel Working Group 12, 1989), (6) Performance Effort and Rating Scales (Dinges et al., 1992), and (7) Visual Analog (mood) Scales (Dinges et al., 1997). Last, the computerized Rapid Visual Information Processing task (Robbins et al., 1994) was given each session in two forms: numbers and shapes.

The following tests are available in more than one version and were presented to subjects using a different version each session to avoid the learning of specific sets of answers for subsequent test sessions: Story Memory, Trail Making, Digit Symbol, Digit Vigilance, Probed Recall Memory, Calculation Performance Task, and Rapid Visual Information Processing.

The same investigator administered all test sessions including the observation of computerized tests.

Statistical analysis

For all neuropsychologic tests scores, self-assessments, and Sao_2 measurements, paired t-tests were used to compare the enriched oxygen treatment with simulated room air at 5000 m.

Post-hoc investigation of confounding practice effects was done by stratification by treatment-order group (i.e., ambient-then-enriched vs. enriched-then-ambient) and subsequent repeated measures analysis of variance. There were two within-subjects factors (ambient, enriched) and one between-subjects factor (order).

Efforts to rule out possible confounding inherent differences in the two treatment groups due to unfavorable random assignment of subjects were accomplished by paired t-test. Subjects' age, education level, gender, native language, participation in a concurrent sleep study, and subjective ratings of sleep duration and quality the night before testing were considered.

RESULTS

Participation

Twenty-three subjects completed their entire test sequences and reported experiencing relatively minor if any discomfort (usually headache) during the experimental sessions. One subject felt too ill to complete her first session in the simulated 5000-m environment. Although she did return to her testing schedule the next day, her data are reported only for those tasks and measurements which she was able to complete at all three sessions.

Due to an electronic malfunction, complete data from Rapid Visual Information Processing (RVIP) was not acquired for 6 of the subjects. Analysis of RVIP data was applied only to those 17 subjects from whom valid data was obtained at all 3 sessions.

Arterial oxygen saturation

Altering room air oxygen levels reliably altered the subjects' arterial oxygen saturations (Sao_2). When in simulated 5000-m ambient conditions, subjects had a mean Sao_2 of 81.6 ± 2.7%, while their mean Sao_2 was 93.0 ± 1.4% with oxygen enrichment. This difference is significant at the $p < 0.0001$ level.

Computer-administered tests

Table 1 summarizes subjects' performances on computer-administered tests conducted under simulated 5000-m ambient air and oxygen-enriched conditions.

In the Psychomotor Vigilance test the subject pushed a button as quickly as possible after

TABLE 1. COMPUTER-ADMINISTERED TESTS—COMPARISON OF SUBJECTS' PERFORMANCES UNDER AIR-BREATHING AND OXYGEN-ENRICHED CONDITIONS AT SIMULATED 5000-m ALTITUDE

	Air		*O_2-Enriched*		*Air vs. O_2-Enriched*	
Task	*Mean*	*(SD)*	*Mean*	*(SD)*	t	p
Probed Recall Memory[a]						
words correct	3.87	(1.49)	3.96	(1.43)	−0.318	0.754
time (sec)	48.4	(14.4)	50.0	(14.9)	−0.482	0.634
Calculation Performance[a]						
attempted	55.6	(13.9)	55.0	(14.2)	0.548	0.590
correct	50.9	(11.8)	51.9	(13.6)	−0.686	0.500
accuracy (%)	92.4	(0.1)	94.6	(0.1)	−1.637	0.116
Psychomotor Vigilance[a]						
mean reaction time (msec)	273.6	(48.9)	257.8	(41.1)	3.326	0.003
lapses[c]	2.3	(3.0)	1.1	(2.5)	2.598	0.016
anticipations[d]	2.6	(6.0)	3.9	(11.2)	−1.128	0.272
slope ($sec^{-1}min^{-1}$)[e]	−0.011	(0.045)	−0.020	(0.044)	0.711	0.484
1/intercept (msec)[e]	258.3	(39.8)	241.8	(32.7)	3. 949	<0.001
Compensatory Tracking[a]						
control losses	8.8	(8.9)	7.0	(8.5)	1.453	0.160
cursor deviation (rms)	0.620	(0.160)	0.566	(0.167)	2.595	0.016
Rapid Visual Information Processing[b]						
Numbers						
correctness (A')[f]	0.929	(0.034)	0.928	(0.044)	0.204	0.841
bias (B")[g]	0.972	(0.027)	0.974	(0.030)	−0.285	0.779
mean reaction time (msec)	525.3	(69.5)	523.8	(77.8)	0.107	0.916
Shapes						
correctness (A')[f]	0.937	(0.082)	0.944	(0.063)	−0.457	0.654
bias (B")[g]	0.881	(0.254)	0.672	(0.450)	1.524	0.147
mean reaction time (msec)	660.0	(189.4)	607.7	(142.3)	1.568	0.136

[a] $n = 23$
[b] $n = 17$
[c] Defined as reaction times ≥500 msec
[d] Defined as responses made either prior to or <100 msec after the stimulus (considered too early to be physiologically possible).
[e] Of the plot of 1/reaction time versus time on task.
[f] From signal detection theory, A' estimates the correctness of a subject's set of responses.
[g] From signal detection theory, B" estimates a subject's bias toward responding one way or the other.

(but not before) a small counter appeared on the computer screen at random variable short time intervals over a 10-min period. Subjects were quicker to respond to these stimuli when in an oxygen-enriched environment. Both mean reaction times and instantaneous initial reaction times (1/intercept on the plot of 1/reaction time vs. time on task) were about 16 msec faster with enrichment ($p = 0.003$ and $p < 0.001$, respectively). Subjects in oxygen-enriched conditions also suffered half as many attention lapses, as defined by a reaction time ≥ 500 msec for any given appearance of the counter stimulus.

The slope of the inverse reaction time curve can be used to determine the extent to which a subject's attention level wanes over the course of this monotonous 10-min task. No difference was found between treatments in this aspect.

Compensatory Tracking assessed the subject's eye–hand coordination by measuring his or her ability to use a computer mouse to keep an inherently unstable cursor within a fixed target in the center of the screen. Subjects were more successful in maintaining the cursor's position when tested in oxygen enrichment, as indicated by a significantly lower average deviation from center (root mean square 0.566 with enrichment, 0.620 with ambient air; $p = 0.016$).

The three neuropsychological tests in this group that focus on cognitive function did not reveal significant differences between treatments.

Investigator-administered tests

Table 2 summarizes subjects' performances on investigator-administered tests conducted under simulated 5000-m ambient air and oxygen-enriched conditions. This group of neuropsychological tests generally did not detect significant differences between treatments.

The Grooved Pegboard test evaluated the manipulative dexterity of each hand separately. With the dominant hand, subjects showed a trend toward faster completion of the task in enriched air, but were significantly faster in ambient air when the nondominant hand was used. The reason for this is unclear. However, for either hand the actual time differences were small.

Self-assessments

Table 3 summarizes subjects' self-assessments made under simulated ambient air and oxygen-enriched conditions. As part of the Neurolab test package, subjects were shown 16 different scales depicting pairs of mood opposites and asked to position the cursor where their own mood lay between the extremes of each scale. For example, placing the cursor two thirds of the distance from "interested" to "bored" would indicate that at that time the way the subject felt was better described as bored than as interested. Compared with how they felt under simulated 5000-m ambient conditions, with oxygen enrichment subjects felt significantly more alert, stronger, more clearheaded, better coordinated, more energetic, and more quick-witted (p values = 0.001, 0.010, 0.016, 0.004, 0.004, and 0.050, respectively). On

TABLE 2. INVESTIGATOR-ADMINISTERED TESTS—COMPARISON OF SUBJECTS' PERFORMANCES UNDER AIR-BREATHING AND OXYGEN-ENRICHED CONDITIONS AT SIMULATED 5000-m ALTITUDE

	Air		*O_2-Enriched*		*Air vs. O_2-Enriched*	
Task[a]	*Mean*	*(SD)*	*Mean*	*(SD)*	t	p
Trail making (sec)	40.9	(12.7)	35.3	(12.4)	1.441	0.164
Digit symbol (translations)	74.1	(8.4)	75.4	(9.6)	−1.545	0.137
Finger tapping[b]						
dominant hand	56.6	(5.6)	56.4	(5.8)	0.477	0.638
nondominant hand	53.1	(5.8)	52.6	(5.7)	1.360	0.187
Digit vigilance						
time (sec)	326.8	(61.9)	331.4	(55.6)	−1.096	0.285
omissions	4.0	(3.8)	3.6	(4.5)	0.383	0.706
Grooved pegboard time (sec)						
dominant hand	56.9	(7.4)	54.4	(7.5)	1.774	0.090
nondominant hand	59.2	(6.4)	61.8	(7.3)	2.159	0.042
Paced auditory serial addition						
attempted	182.2	(13.1)	181.2	(16.3)	0.531	0.601
correct	176.0	(15.4)	175.5	(19.0)	0.244	0.809
Matrix reasoning[c]						
correct	20.8	(2.5)	20.9	(2.3)	−0.162	0.873
time cues[d]	5.8	(2.4)	5.8	(3.2)	−0.056	0.956
Story memory						
learning rate (points)[b]	17.5	(4.2)	18.1	(3.8)	−0.821	0.420
recall (points)	18.9	(3.7)	17.6	(2.6)	1.627	0.118
loss (%)	8.9	(8.6)	8.4	(9.0)	0.208	0.837

[a]$n = 23$, except where noted.
[b]$n = 24$.
[c]This test was not given during the practice session due to the special concern that learned responses could be applied to later test administrations.
[d]Number of problems for which the subject took >20 sec to respond.

TABLE 3. SELF-ASSESSMENTS—COMPARISON OF SUBJECTS' SELF-RATINGS UNDER AIR-BREATHING AND OXYGEN-ENRICHED CONDITIONS AT SIMULATED 5000-m ALTITUDE

	Air		*O_2-Enriched*		*Air vs. O_2-Enriched*	
Measure[a]	*Mean*	*(SD)*	*Mean*	*(SD)*	t	p
Sleepiness scale (1–9)[b]	4.9	(1.5)	3.5	(1.3)	3.261	0.004
Performance Scales						
performance (1–7)[c]	3.4	(1.0)	2.9	(1.0)	1.775	0.090
effort expended (1–4)[d]	2.4	(0.6)	2.3	(0.7)	1.000	0.328
could do better? (1–3)[e]	1.6	(0.5)	1.6	(0.6)	0.000	1.000
Mood scales (0–100)[f]						
alert (vs. sleepy)	43.1	(21.5)	65.1	(23.3)	−3.661	0.001
calm (vs. excited)	64.4	(19.7)	59.9	(20.8)	0.934	0.360
strong (vs. weak)	50.6	(22.9)	66.9	(15.4)	−2.797	0.010
clear headed (vs. groggy)	45.0	(24.3)	62.6	(20.6)	−2.607	0.016
well-coordinated (vs. clumsy)	49.3	(19.4)	66.3	(19.9)	−3.238	0.004
energetic (vs. sluggish)	40.3	(21.6)	61.4	(24.0)	−3.208	0.004
contented (vs. discontented)	62.4	(24.9)	68.8	(21.3)	−0.989	0.333
tranquil (vs. troubled)	66.8	(21.4)	69.2	(20.5)	−0.456	0.653
quick witted (vs. mentally slow)	46.5	(25.9)	59.7	(22.5)	−2.069	0.050
relaxed (vs. tense)	57.0	(19.8)	59.8	(25.3)	−0.395	0.697
attentive (vs. dreamy)	52.7	(22.8)	62.6	(22.8)	−1.558	0.134
competent (vs. incompetent)	60.6	(23.0)	69.0	(24.1)	−1.391	0.178
sad (vs. happy)	30.1	(21.2)	31.4	(22.2)	−0.243	0.810
friendly (vs. hostile)	71.0	(22.6)	75.1	(23.6)	−0.776	0.446
interested (vs. bored)	49.2	(27.5)	55.0	(27.5)	−1.000	0.328
sociable (vs. withdrawn)	53.1	(26.5)	58.5	(23.3)	−0.914	0.371

[a] $n = 23$.

[b] 1 = "very alert"; 3 = "alert-normal level"; 5 = "neither alert nor sleepy"; 7 = "sleepy-but no effort to keep awake"; 9 = "very sleepy, great effort to keep awake, fighting sleep."

[c] "I felt my performance during this bout was: (1) extremely good, (2) very good, (3) good, (4) fair, (5) poor, (6) very poor, (7) extremely poor."

[d] "The effort I had to expend to achieve this level of performance was: (1) very little effort, (2) a moderate amount of effort, (3) quite a lot of effort, (4) an extreme effort."

[e] "Could you have performed even better during this bout? (1) No, I could not have done any better. (2) Yes, I could have done a little better if I had tried harder. (3) Yes, I could have done much better if I had tried harder."

[f] Subjects were shown 16 individual analog scales depicting pairs of mood opposites and asked to position the cursor where their own mood lay between the extremes of each scale. Each 0–100 scale was oriented with 100 corresponding to the word listed first in this table.

the other 10 scales subjects also tended to report more "positive" moods with oxygen enrichment, although the differences from ambient conditions were not statistically significant.

Subjects were asked to rate their sleepiness on a scale from 1 (" very alert") to 9 (" very sleepy, great effort to keep awake, fighting sleep"). Because subjects answered this twice per session—at the beginning and again at the end of the Neurolab sequence— and their responses rarely changed by more than 1 scale unit, the average of the two was taken to represent each subject's sleepiness during a given test session. Subjects generally felt "neither alert nor sleepy" when in the 18% O_2 environment. They felt significantly more alert in 23% O_2, with an average rating close to "alert—normal level" ($p = 0.004$).

After completing the Neurolab portion of a test session, subjects were asked to rate their performance. Subjects felt on average that they had performed in the range of "good" to "fair," had to expend a "moderate amount" to "quite a lot" of effort to achieve this level of performance, and could have done either "no better" or only "a little better" if they had tried harder. These responses were consistent regardless of oxygen conditions.

Post-hoc analyses

Although the counterbalanced design of this study allows direct comparison of the effects of the two oxygen treatments on each subject, an unavoidable risk of repeated neuropsychological testing is the potential for confounding effects of practice. To estimate the extent to which this occurred, the subject pool was stratified into two groups for comparison by treatment order—that is, according to whether they had been tested first in ambient oxygen conditions ("A–E") or first in enriched conditions ("E–A").

Of the 10 neuropsychological tests that did not reveal significant sensitivity to oxygen treatment as assessed by paired *t*-tests, 7 show some significant order effects and/or treatment-by-order interactions by repeated measures analysis of variance (Table 4). For instance, both the A–E and E–A groups became significantly faster at Trail Making between their first and second experimental sessions ($p = 0.031$). It should be noted that by definition the A–E group received the additional benefit of oxygen enrichment at its second session, whereas the E–A group did not. Thus the A–E group improved at Trail Making by about 16 sec, while the E–A group became faster by only about 6 sec. However, this pattern does not hold for all tests considered.

Additionally, in virtually every case the A–E group performed better than the E–A group at any point in time despite randomization of group assignments. This suggested the possibility of inherent differences between the groups themselves, and prompted an effort to rule out other confounding factors. Subjects' age, education level, gender, native language, participation in a concurrent sleep study, and subjective ratings of sleep duration and quality the night before testing were considered. The A–E group was significantly younger (24.8 ± 5.0 vs. 31.2 ± 8.7 years; $t = -2.229$, $p = 0.0364$), but also, accordingly, had completed

TABLE 4. ORDER EFFECTS—COMPARISON OF TREATMENT ORDER GROUPS BY REPEATED MEASURES ANALYSIS OF VARIANCE; ONLY THOSE NEUROPSYCHOLOGICAL TESTS THAT REVEAL SIGNIFICANT DIFFERENCES BETWEEN GROUPS ARE INCLUDED HERE

	Means				*RMANOVA*			
	A–E[a]		*E–A*[b]		*Order*		*Treatment × Order*	
Task	A	E	E	A	F	p	F	p
Trail making B (sec)	42.6	26.5	44.8	39.0	5.38	0.031	11.77	0.003
Digit symbol (translations)	77.5	80.5	69.9	70.4	7.62	0.012	4.54	0.045
PASAT[c]								
attempted	186.1	189.7	171.9	177.9	5.96	0.024	8.72	0.008
correct	180.1	186.1	163.9	171.6	6.15	0.022	13.93	0.001
Matrix reasoning								
correct	21.2	22.1	19.6	20.3	4.96	0.037	2.23	0.151
time cues[d]	7.0	4.2	7.6	4.4	0.18	0.678	36.34	<0.001
Probed recall memory								
words correct	4.50	4.58	3.27	3.18	7.60	0.012	0.00	0.989
Calculation performance								
attempted	54.3	56.6	53.2	57.1	0.00	0.957	7.63	0.012
correct	50.1	54.1	49.6	51.8	0.07	0.791	5.58	0.028
RVIP[e] numbers								
correctness (A′)	0.945	0.956	0.887	0.907	22.36	<0.001	3.60	0.077
mean reaction time (msec)	529.4	497.5	561.2	519.5	0.64	0.435	9.04	0.009
RVIP[e] shapes								
correctness (A′)	0.933	0.970	0.906	0.943	0.67	0.427	10.63	0.005
Bias (B″)	0.922	0.481	0.944	0.821	2.82	0.114	5.17	0.038

[a]This group breathed air first and oxygen-enrichment second; $n = 13$.
[b]This group received oxygen enrichment first and air second; $n = 11$.
[c]Paced auditory serial addition.
[d]Number of problems for which the subject took >20 sec to respond.
[e]Rapid visual information processing.

fewer years of advanced education (as approximated by degrees held and/or pursuing, 16.3 ± 1.9 vs. 18.5 ± 2.3 years total; $t = -2.502$, $p = 0.0203$). These two factors might ordinarily be expected to have opposing effects on performance. However, the spectrum represented in this study's subjects (undergraduate through doctorate) is largely irrelevant directly to the abilities targeted by this study. There were no other significant differences between the two groups.

DISCUSSION

The most important conclusion from this study is that some aspects of the subjects' neuropsychological performances were improved by 6% O_2 enrichment at a simulated altitude of 5000 m. The two tests that showed the greatest sensitivity to treatment were Psychomotor Vigilance and C ompensatory Tracking, from the computerized Neurolab package. Subjective measures of mood and sleepiness were also responsive to supplemental oxygen.

The Psychomotor Vigilance task challenges the subject to respond as quickly as possible to an inconspicuous stimulus repeated often but at random variable intervals over a 10-min period. Both the average reaction time and the instantaneous initial reaction time were 16 msec faster in simulated 5000 m air than in 6% oxygen enrichment, a modest but statistically significant improvement. Subjects also displayed half as many attention lapses when tested under oxygen enrichment.

The Psychomotor Vigilance test is considered to measure "physiological" (as opposed to "cognitive") attention because of its simple stimulus and uncomplicated response. In addition to reaction time and attention lapses, this test assesses maintenance of attention level over time. The more negative the slope of the inverse reaction time versus time on task curve, the more a subject's attentiveness is considered to be dropping off through the 10-min task. It is interesting to note that despite significantly decreasing mean reaction time, initial instantaneous reaction time, and number of lapses, oxygen enrichment caused no discernible improvement in subjects' ability to maintain their attention level over time. Ten minutes may not be long enough to fatigue these subjects' attentiveness under either treatment condition.

Supplemental oxygen also helped subjects with their eye–hand coordination as measured by Compensatory Tracking. Because this test is programmed such that the abruptness of a subject's response exacerbates the spatial instability of the cursor on the computer screen, successful tracking requires the ability to correct the cursor's position not only early and accurately but also smoothly. With oxygen enrichment subjects maintained the cursor more consistently near the center of the screen than when air breathing at simulated 5000 m. Thus, supplemental oxygen may help reverse some of the altitude-induced impairments in higher motor processing as well.

It is possible that the subjects' motor-related resources were more sensitive to alterations in oxygen levels than were other domains of testable neuropsychological function. The highly motivated character of the subjects, however, may have been a significant contributor to the finding of few differences in test performance despite differing oxygen conditions. These competitive and highly achieving people in general scored very well on the entire neuropsychological battery, perhaps even reaching a "ceiling" in such tests as Rapid Visual Information Processing and Paced Auditory Serial Addition.

As others who have worked at high altitude have noted, short-term concentration may temporarily overcome real underlying deficits. About 75 years ago Barcroft et al., who carried out studies at Cerro de Pasco, altitude 4330 m, observed such a compensatory effort at mental concentration:

> Judged by the ordinary standards of efficiency in laboratory work, we were in an obviously lower category at Cerro than at the sea-level. By a curious paradox this was most apparent when it was being least tested, for perhaps what we suffered from chiefly was the difficulty of maintaining concentration. When we knew we were undergoing a test, our concentration could by an effort be maintained over the length of time taken for the test, but under ordinary circumstances it would lapse. It is, perhaps, characteristic that, whilst each indi-

vidual mental test was done as rapidly at Cerro as at the sea-level, the performance of the series took nearly twice as long for its accomplishment. Time was wasted there in trivialities and "bungling," which would not take place at sea-level. (Barcroft et al., 1923)

It appears that regardless of actual test performance, participants in this study tended to feel substantially better about themselves when room oxygen levels were higher (Table 3). Not only did they report a better physical state of being (e.g., stronger and less sleepy), but they also rated their abilities more positively (e.g., more clear-headed and well-coordinated). This is a consistent pattern, as 13 of 16 mood scales go in the direction of more positive self-assessment, 6 of which were significant at the $p < 0.05$ level. Interestingly, oxygen conditions did not affect whether subjects felt they could have performed any better, even though they showed a trend toward rating their oxygen-enriched performances more highly.

The counterbalanced design of this study derives its power by making comparisons between each subject's own performances under the two different treatments. The ability of neuropsychological testing to detect differences, especially when dealing with cognitive skills, requires that a standardized balance exist between the subject's competence to perform within a test's sensitive range and his or her overfamiliarity with its "tricks" and "shortcuts." A particular challenge of this study, therefore, was to maintain the statistical advantages of repeated testing despite the risk of confounding practice effects. With this in mind, this neuropsychological battery was compiled as a set of relatively challenging tasks in a reasonably broad range of neuropsychological domains. Every effort was made to take advantage of tests that could be administered with a different stimulus set for each of a subject's three sessions.

Nevertheless, practice effects did appear and in general scores were consistently high (see Post-Hoc Analyses above). Both of these facts make interpretation of subtle patterns difficult. It might be suggested that recruiting subjects of more average aptitude and motivation would have increased the sensitivity of this study. However, it was felt that the purpose in investigating oxygen enrichment and neuropsychologic performance at high altitude would be most relevant to those who have been chosen specifically for their ability to face demanding tasks (e.g., high altitude telescope workers). Indeed, graduate students were targeted as appropriate surrogates.

In summary, this study of oxygen enrichment at simulated 5000-m altitude showed that oxygen enrichment reduced simple reaction time, improved eye–hand coordination, and enhanced the subject's sense of effectiveness and well-being. Other aspects of neuropsychological function in these subjects were not significantly improved by adding 6% O_2 to room air.

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