ORIGINAL RESEARCH

Association of Cognitive Performance with Time at Altitude, Sleep Quality, and Acute Mountain Sickness Symptoms

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Objective.—It is well documented that cognitive performance may be altered with ascent to altitude, but the association of various cognitive performance tests with symptoms of acute mountain sickness (AMS) is not well understood. Our objective was to assess and compare cognitive performance during a high-altitude expedition using several tests and to report the association of each test with AMS, headache, and quality of sleep.

Methods.—During an expedition to Mount Everest, 3 cognitive tests (Stroop, Trail Making, and the real-time cognitive assessment tool, an in-house developed motor accuracy test) were used along with a questionnaire to assess health and AMS. Eight team members were assessed pre-expedition, postexpedition, and at several time points during the expedition.

Results.—There were no significant differences ($P > .05$) found among scores taken at 3 time points at base camp and the postexpedition scores for all 3 tests. Changes in the Stroop test scores were significantly associated with the odds of AMS ($P < .05$). The logistic regression results show that the percent change from baseline for Stroop score ($\beta = -5.637$; $P = .032$) and Stroop attempts ($\beta = -5.269$; $P = .049$) are significantly associated with the odds of meeting the criteria for AMS.

Conclusions.—No significant changes were found in overall cognitive performance at altitude, but a significant relationship was found between symptoms of AMS and performance in certain cognitive tests. This research shows the need for more investigation of objective physiologic assessments to associate with self-perceived metrics of AMS to gauge effect on cognitive performance.

Key words: cognitive performance, hypoxia, altitude, AMS, cognition, expedition

Introduction

Moderate hypoxia has been shown to induce changes in visual, motor, somatosensory, and mental function. Performance in intelligence tests, reaction time, speech comprehension, hand steadiness, and visual contrast discrimination are some of the mental functions that have been shown to be negatively affected.^{1–3} Hypoxia affects individuals' ability to perform word association tests along with causing abnormal test responses.⁴ The effects of hypoxia go as far as inducing auditory and visual hallucinations⁵ and have even been documented to

induce feelings of depersonalization and out of body experiences.⁶ Visual function changes with hypoxia include narrowing of the visual field and vision blurring, with worsening levels of hypoxia causing failure of the entire retina and total loss of vision.^{7–9}

Over the years, stories of climbers not being able to perform simple mental tasks have become part of the literature documenting cognitive changes at altitude. Although it is well known that cognitive performance is impaired with altitude ascent, the exact nature and timing of these changes are not clear. Each year altitude-related hypoxia affects thousands of aviators, both military and civilian, and causes complications in rapid high-altitude troop deployments.¹⁰ In addition, many workers at extreme altitudes, and even recreational climbers and tourists, experience acute mountain sickness (AMS). Assessing possible cognitive degradation with altitude ascent is

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complex due to the multitude of factors that accompany altitude ascent. Lack of sleep, headache, and AMS with accompanying symptoms can all affect cognition, and isolating their effect from actual hypoxia can be difficult.¹¹

In the literature, a variety of different tests have been used to detect cognitive function changes with hypoxia and/or altitude. These tests focus on observing changes in motor and executive function, memory, response time, and hand–eye coordination. The sheer variety of tests available to researchers, along with the inherent variability within tests, may be a reason why there is debate in the literature on whether cognitive degradation occurs at certain elevations.^{11–15} Additional complications are added when taking into account variation in individual physiology. The difficult nature of field expeditions and the possible differences with controlled environmental chamber studies also does not help with the consistency of results. Hence, the focus of this research expedition was to assess degradation in cognitive performance by using multiple tests and to examine the relationship to the physiologic consequences of high altitude, specifically AMS, headache, and quality of sleep.

Several tests, such as the Stroop Color-Word and the Trail Making test, have been “grandfathered in” as standards for testing cognitive function. We decided to take a fresh approach and design a real-time cognitive assessment tool (RCAT) to examine changes in motor executive function, specifically speed, hand–eye coordination, and response time. The objective was to use the test in tandem with other tests normally used for altitude performance and to determine which tests were possibly better suited for detection of the specific symptoms accompanying altitude exposure. The test is designed to take advantage of progress in mobile technology with the intention of future deployment and use in the field (See online [Supplementary Appendix](#) for more information).

In the present expedition to Mount Everest Base Camp (5500 m/17,300 ft), cognitive function was examined alongside changes in physiology that occur with altitude. The first objective was to use Stroop, Trail Making, and the RCAT to examine any changes in cognitive function that occur with graded exposure to altitude. The second objective was to use continuous monitoring to examine AMS, headache, and quality of sleep. The third objective was to report the association of each cognitive performance test with AMS, headache, and quality of sleep.

Methods

SUBJECTS

During the course of the expedition 8 subjects were monitored and tested. The experimental procedures were approved by the Mayo Clinic Institutional Review Board,

and each subject provided written informed consent prior to participation. Subject demographics were as follows (mean $\pm$ SD): age 35 ± 10 years, height 181 ± 5 cm, weight 86 ± 8 kg, body mass index 26 ± 2 kg/m². Before this expedition, 4 of the 8 subjects had experienced high altitude of 2500–3500 m or greater.

STUDY DESIGN

Figure 1 shows the ascent timeline to Everest Base Camp as well as the other altitudes along the trek at which expedition testing was performed. All members were tested before the climb, at 3 time points at base camp, and upon return. To minimize the effect of learning, subjects were asked to perform each test for approximately 20 minutes before collecting the baseline data.

COGNITIVE TESTING

Three tests were used to evaluate cognitive performance. In each session, all tests were administered in a randomized sequence with a maximum of a 1-minute break in between tests. Subjects were asked to take 3 of each test type and were isolated during gameplay to minimize the effect of distractions.

Stroop Color-Word test

In this test, subjects are asked to identify the color of the text and associate it with the proper text that spells the answer. Colors and text often contradict each other to increase confusion and demand more focus from the subject. The version we programmed for use on Android tablets lasted for 1 minute and awarded 1 point for a correct response and subtracted 1 point for an incorrect response. The data we tracked documented each choice and reported patterns in the errors made (eg, incorrect

Figure 1. Ascent timeline for the expedition from Kathmandu to base camp and back. Testing days are marked by large squares and trek days by small diamonds. The posttesting was done in the United States after the expedition.

text selection vs incorrect color identification). Metrics recorded were final score, number of choices made, correct choices made, incorrect choice made, time for each choice, and type of error (color mismatch vs word mismatch).

Trail Making test

This test is divided into Trail A and Trail B. In Trail A, subjects are asked to connect numbers 1 to 20 in sequence using a tablet pen. In Trail B, letters are factored in so the order is 1A, 2B, 3C, and so on. The programmed version times subjects and reports duration to complete each sequence as well as dwell time of each transition.

Rapid Cognitive Assessment Tool

The RCAT was designed to test speed, accuracy, and response time. The basic premise is to click spawning squares according to prompts based on color. The game lasts 1 minute and reports metrics every 10th of a second. The overall score is determined by speed, accuracy, and response time. For a detailed description of the development and design, please see [Appendix](#).

AMS, headache, and sleep quality assessment

In addition to regular physiologic and cognitive monitoring, subjects were weighed every morning and asked to take a modified Lake Louise survey for AMS along with other factors. The AMS survey was given using a programmed Android tablet questionnaire with each question weighed on a 4-point scale. When subjects highlighted a choice, a small description appeared to assist them in understanding the scale. Other questions asked about food intake, headache, and quality of sleep. All categories were tracked over the course of the expedition and analyzed for correlation with cognitive scores.

DATA ANALYSIS

Data gathered from cognitive tests of 8 subjects were analyzed with R (R Foundation for Statistical Computing, Vienna, Austria). Data were analyzed with several objectives. The first objective was to determine whether testing was repeatable within a testing session. The second objective was to determine whether cognitive function changes could be detected over the course of the expedition; cognitive scores for each test were analyzed and compared across different expedition time points (see [Figure 1](#)): pre-expedition, multiple base camp time points, and postexpedition. The second objective was to determine whether there was any association between

cognitive function and AMS, quality of sleep, or presence of headache.

An analysis of variance (ANOVA) was used to look for repeatability of performance within subjects for each test. A repeated measures ANOVA and Student's *t* test was used to examine difference between performances pre-expedition, at multiple base camp time points, and postexpedition. Data for each testing session were then compared with AMS symptom data (total AMS score, headache, and sleep disturbance) using a univariate logistic regression, specifically examining the association of cognitive performance with the odds of symptom presence at multiple expedition time points. *P* values < .05 were considered significant.

Results

Eight subjects were analyzed for cognitive performance pre-expedition, at base camp, and postexpedition. Better performances on the Stroop and RCAT register as higher scores, while the Trials A and B register as lower times due to the shorter time it takes to complete the test (time to completion is the outcome variable). Descriptive statistics for all the raw scores are shown for each test in [Table 1](#). To normalize the large differences in individual performance and skill, scores were assessed as percent change from baseline for all tests.

A repeated measures ANOVA showed that there was no significant difference in the variation between repeated attempts in a given RCAT testing session ($.19 < P < .87$), confirming that the developed test was reproducible. For more information on work showing test reproducibility, see [Appendix](#), Section IV.

[Figures 2](#) and [3](#) show a series of boxplots comparing performance of Stroop, RCAT, and Trials A and B performance at baseline, three base camp time points, and postexpedition. Both raw scores ([Figure 2](#)) and percent change in score ([Figure 3](#)) are represented. There were no significant differences ($P > .05$) found between scores taken during the 3 time points at base camp and the postexpedition scores for all 3 tests. However, there was substantial individual variation in performance on a day-to-day basis. The RCAT, Stroop, Trial A, and Trial B showed a standard deviation of 13%, 19%, 13%, and 17%, respectively, across all time points during the expedition.

To investigate this individual variation, we examined the relationship between individual performance and specific symptoms (AMS, headache, sleep disturbance). The logistic regression results ([Table 2](#)) show that the percent change from baseline for Stroop score ($\beta = -5.637$; $P = .032$) and Stroop attempts ($\beta = -5.269$; $P = .049$) are significantly associated with the odds of

Table 1. Test scores for each testing session shown in mean (standard deviation) format

<i>Time point</i>	<i>Stroop</i>		<i>RCAT</i>	<i>Trail A</i>	<i>Trail B</i>
	<i>Attempts</i>	<i>Score</i>	<i>Score</i>	<i>Time</i>	<i>Time</i>
Baseline	33.52 (7.31)	31.81 (7.99)	3127.78 (948.89)	25.47 (5.05)	73.64 (41.37)
T1	44.54 (10.20)	39.21 (10.72)	3356.50 (584.08)	20.01 (3.31)	46.72 (12.68)
T2	43.17 (8.08)	40.83 (8.38)	3995.52 (443.73)	18.42 (4.46)	44.74 (20.66)
T3	43.87 (9.49)	41.63 (9.41)	3444.38 (794.51)	17.87 (2.96)	39.89 (11.14)
Post	47.05 (8.28)	45.10 (7.69)	3950.15 (625.67)	17.13 (4.82)	51.11 (24.91)

RCAT and Stroop are represented as raw scores, with Stroop also showing total number of attempts per game. Trial A and Trial B are shown in time taken in seconds.

meeting the criteria for AMS. A 50% increase in score is associated with odds of AMS reduced by 93% and 94%, respectively.

Discussion

In the present study, 8 members of a research expedition to Everest Base Camp were monitored and assessed for

cognitive function, AMS, sleep quality, and headache. Cognitive function was tracked using three different tests: Stroop, Trail Making, and the RCAT, designed in house. There was no significant difference between base camp time point scores and those acquired post-expedition. However, some test scores were associated with changes in subject-perceived presence of headache, AMS, or lack of sleep. The Stroop test performances

Figure 2. Series of boxplots comparing performance of Stroop, RCAT, and Trials A and B performance at baseline, 3 base camp time points, and postexpedition. The unit of measurement here is the raw score (or time in seconds in the case of the Trials) of each test.

Figure 3. Series of boxplots comparing performance of Stroop, RCAT, and Trials A and B performance at baseline, 3 base camp time points, and postexpedition. The unit of measurement here is the percent change from baseline for each test.

decreased significantly with self-reported AMS symptoms and with headache trending. The RCAT scores trended toward poorer performance with headache. Trial A performance also trended toward poorer performance self-reported AMS.

Published studies examining cognitive performance with hypoxia and at altitude have used widely

heterogeneous methods and techniques to reach the conclusions on which this research is based. Articles documenting cognitive deficiencies in early aviation and altitude research show a gradual degradation of cognitive prowess starting at 2500 m with a sharp drop off in performance at approximately 5000 m.^{16,17} However, more recent literature points toward no significant cognitive impairments in simulated gradual exposures to altitudes below 7000 m.^{13,18,19} Field studies show more conflicted results, with some groups showing a change in cognitive function and others showing little or no change.^{13–15,20,21} For example, Harris et al¹³ used CogState to evaluate cognitive performance at 5100 m and showed no impairments in individuals or the group as a whole, but at base camp of Kangchenjunga (5350 m) Pagani et al¹⁵ showed decrement in a memory task they had developed. Moreover, differences between chamber and expedition testing are apparent even when using the same cognitive test. Evans and Witt²⁰ reported decreased performance in the Digit Symbol Substitution Test at 4300 m, but Kennedy et al¹⁸ used the same test and saw no changes with gradual decompression up to

Table 2. Univariate logistic regression: association (β) of various cognitive metrics with the odds of reported AMS symptom (quality of sleep, headache, and AMS score).

	Stroop		RCAT	Trail A	Trail B
	Attempts	Score	Score	Time	Time
AMS score	–5.637 ^a	–5.269 ^a	–1.281	3.075	1.090
Headache	–3.289	–3.702	–3.062	1.589	–.527
Sleep	.712	–.572	–.504	1.461	–1.136

The numbers are the regression coefficients, and they describe the strength of the relationship between the scores and the log-odds of the outcome.

^a Indicates a significant relationship ($P < .05$).

8845 m. Many complications arise when comparing findings from different expeditions with their own unique conditions and techniques of varying complexity (even individual cognitive tests like the Stroop have different versions). In addition, there is an added layer of complexity when taking into account the wide variation in individual physiologic responses to altitude. Thus, isolating the effects of altitude and hypoxia on cognition is even more difficult given the multitude of factors that can influence cognitive performance.

In a review for the 1967 USARIUM symposium “Biomedicine of High Terrestrial Elevations,” McFarland¹⁶ nicely outlines the difficulties of interpreting cognitive performance during expeditions: “The subtle influence of hypoxia may often be masked by changes in the learning process or by ‘trying harder’.” In interpreting the results he notes that “motivation is an extremely difficult variable to control.” He goes on to list numerous other hard-to-control factors that demand caution when interpreting expedition results: smoking, alcohol, drugs, diet, temperature extremes, and clothing. Attention, fatigue, nausea, mood, headache, and lack of sleep are a few critical factors that are amplified in a field expedition in which subjects are likely facing many challenges. In such situations, rather than just altitude and hypoxia causing the decline in cognitive function, it is likely that an amalgam of conditions can cause a disturbance in cognitive performance.

In an attempt to dissect the specific causes of cognitive degradation during this expedition, AMS, headache, and quality of sleep were assessed along with cognitive function. Our analysis found that drops in Stroop test performance were associated with subjects reporting symptoms of AMS. Although it is simple to conclude that people who believe they have such symptoms would be inclined have their concentration and cognitive performance affected, the effects of AMS and symptoms on cognitive function is controversial. de Aquino Lemos et al²² correlated multiple cognitive performance tests, including the Stroop, to rapid eye movement sleep patterns to show the effects of decreased sleep quality on cognitive performance. Virues-Ortega et al²³ believe that AMS is a “sufficient but not necessary condition for altitude neurophysiological impairment.” Some studies revealed no significant correlation between AMS symptoms and cognitive functions²⁴, while others reported that participants who developed AMS showed more cognitive impairment.^{14,25} In the absence of such AMS symptoms, it could be concluded that gradual acclimation to high altitude may not induce cognitive degradation, similar to what was seen in simulated gradual exposures to altitudes below 7000 m.^{18,19}

It is important to note that assessing AMS and symptoms relies on individual reporting, so any association between cognitive performance and symptoms is in fact dependent on subjects’ perceived mental state. Clearly there is a need for more objective metrics that can be gauged in tandem with cognition. In a good first step, de Aquino Lemos et al²² observed rapid eye movement sleep patterns to get a more objective assessment of sleep quality. In a similar manner, pairing objective physiologic metrics such as heart rate variability and electroencephalogram with AMS and symptoms may help elucidate the mechanisms driving cognitive degradation at altitude.

Equally important to achieve an understanding of the mechanisms of cognitive degradation at altitude is teasing out the effect that disparate individual physiologic responses to hypoxia have on cognitive function. In an ongoing study investigating real-time cognitive function under the effects of normobaric hypoxia while monitoring forehead near-infrared spectroscopy, oxygen saturation, cerebral blood flow, and gas exchange, our findings suggest that forehead near-infrared spectroscopy is a crucial predictor of cognitive performance.²⁶ Further analysis of cerebral blood flow and other metrics may help uncover the physiologic underpinnings behind cognitive degradation during hypoxia.

LIMITATIONS

There are several limitations to this study that echo the sentiments expressed by McFarland and others conducting environmental altitude research. The first and key limitation is that a field study offers limited control over circumstances that are normally easily manipulated in a laboratory environment. Testing a subject who was sleeping in an extremely cold tent is very different from testing subjects who are well rested and used to their normal routine. Solar chargers and limited use of a hydrogenerator were available, but constant supply of power for electronic testing was also an issue that had to be planned around. Battery power is quickly depleted in the cold, and laptops and tablets had to be kept in researcher sleeping bags to ensure functionality the next day. The chaotic nature of the environment did not always lend itself to ideal conditions for subject cognitive testing. Compared with conducting a hypobaric chamber study, the lack of control in the field is a limitation, but it also is a more accurate reflection of the reality of the effects of altitude experienced by climbers, operators, and sojourners.

Although there were expected complications during the field testing, there were other limitations in aspects unrelated to field issues. We had limited control over the period of time postexpedition when subjects were tested. The majority of the group was tested approximately

1 week after return, but some members were in the 2-week time period. During the course of the expedition subjects occasionally played the cognitive tests when bored or being competitive. The total time each person spent outside of actual testing did not amount to over 20 minutes, but this could have contributed to an increased learning effect (an aspect of the RCAT we strived to minimize by design; see [Appendix](#)). This learning effect could account for a portion of the improved scores in the postexpedition reporting.

Of importance is the inherent variability in such cognitive tests (see [Appendix](#), Section IV), which, when combined with our small sample size of 8, can also account for some of the differences seen in cognitive performance. To combat this, we used the individualized scores represented as a percent of baseline to make comparisons. However, the combination of high testing variability and small sample size negatively affects the statistical power of this study.

Conclusions

This study has a couple of notable implications. In this small field study of travelers ascending to high altitude, we found no significant change in overall cognitive performance with altitude, but we did find a significant relationship between symptoms of AMS and performance in certain cognitive tests. Further investigation with larger sample sizes may reveal additional associations that did not meet our significance criteria in this analysis. Moreover, this research highlighted the need for more investigation into less subjective physiologic metrics that can be associated with perceived metrics of AMS. There is also a strong need for new robust tools that are, to quote Harris et al.,¹³ “portable, easy to interpret, rapid, and provide clinically relevant, individualized information.”

Combining metrics such as heart rate variability and oxygen saturation with cognitive performance and self-assessed AMS could help build a more robust field diagnosis tool for cognitive impairment. This goal is made more realistic by the advancements in mobile monitoring technology in recent years. Furthermore, cognitive tests can more easily be modified or designed for the integrative electronic environment in which we now exist.²⁷ Using the knowledge gained from research to improve the accuracy of tests while catering to the interface of mobile devices will be crucial for creating semiautomated in-field assessments of cognition useable by the nonresearch population.

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Appendix. Supplementary Materials

Supplementary material cited in this article is available online at <http://dx.doi.org/10.1016/j.wem.2016.04.008>.

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