Cognitive and Perceptual Deficits of Normobaric Hypoxia and the Time Course to Performance Recovery

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BACKGROUND: Many in-flight hypoxia-like incidents involve exposure to normobaric hypoxia following an oxygen delivery equipment failure. Studies have documented the effect of hypoxia on specific aspects of human performance. The goal of the present study was to establish the effects of acute hypoxia on cognitive, psychomotor, and perceptual abilities and to chronicle the time required for these capabilities to fully recover to pre-exposure levels.

METHODS: Subjects were presented with a battery of tests designed to assess visual acuity, contrast sensitivity, color vision, executive control, and reaction time (simple reaction time, SRT, and choice reaction time, CRT) before, during, immediately following, 60 min, 120 min, and 24 h after hypoxic exposure. Oxygen saturation was continuously measured throughout the duration of the study using near-infrared spectroscopy measured on the forehead and finger pulse oximetry.

RESULTS: During the course of six assessment periods, contrast sensitivity, color vision, and subjective workload were affected to varying degrees during hypoxic exposure, but returned to baseline levels soon after a return to normoxia. Conversely, reaction time values and regional cerebral oxygen saturation (M_{rSO_2}), while also affected during hypoxic exposure (M_{SRT} = 362.17 ms, M_{CRT} = 389.55 ms, M_{rSO_2} = 79.36%), did not return to baseline levels (M_{SRT} = 337.35 ms, M_{CRT} = 372.75 ms, M_{rSO_2} = 99.75%) until the assessment period 24 h following exposure (M_{SRT} = 324.35 ms, M_{CRT} = 366.22 ms, M_{rSO_2} = 99.10%).

DISCUSSION: Evidence from this study suggests an impairment of specific performance characteristics following hypoxic exposure – some for a considerable period of time. Mitigation efforts should focus more on the prevention of hypoxia exposure rather than relying exclusively on training operators to recognize and react earlier to hypoxic symptomology.

KEYWORDS: hypoxia, normobaric hypoxia, human performance, performance recovery.

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Current military aircraft are not equipped with a failsafe warning system to detect conditions that cause or exacerbate hypoxia. Instead, operators must learn to recognize a broad range of hypoxia symptoms such as tingling in extremities, light-headedness, difficulty concentrating, and slowed reaction times before they become incapacitated.[1] However, in some cases, cognition and perception are significantly compromised before symptoms of hypoxia are expressed, thereby requiring an already impaired operator to initiate the necessary emergency procedures. Hypoxic symptomology has been reported to include the experiences of euphoria and a strong sense of well-being, dulling the perceived urgency of the problem and hindering any initiative to solve it.[14] In addition to these subjective symptoms, exposure to reduced levels of breathable oxygen has been documented to affect an operator's ability to maintain a constant airspeed, altitude, and directional heading during simulated flights.[5,15] Hence, a more complete understanding of the specific impairments caused by hypoxia and the degree to which the underlying functions are affected is a critical concern for the aviation community.

Historically, aviation hypoxia research and training have focused on hypobaric hypoxia, conducted through the use of

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hypobaric altitude chambers. However, most modern tactical aviation platforms deliver high concentrations of oxygen to the operator via an aviation mask, and therefore, if oxygen production is compromised, hypoxia can be experienced at any altitude. A review of Naval hypoxia hazard reports revealed that 35% of the hypoxia-like events experienced in the F/A-18 were at cabin altitudes at or below 10,000 ft (3048 m).[24] Thus, many hypoxia-related incidents that occur in modern military operations involve exposure to nearly normobaric hypoxia following an oxygen delivery equipment failure, that is, hypoxia experienced at a cabin altitude at or below 10,000 ft, where O_2 supplementation is not required. Normobaric hypoxia is difficult to recognize because there are no overt environmental cues to alert the operator, as is often the case with hypobaric hypoxia. For example, explosive or rapid cabin depressurization scenarios are marked by a characteristic loud noise, a rush of air as it exits the cabin, and a decrease in temperature, all accompanied by a reduction in oxygen density. A normobaric hypoxic event generally will not be attended by these warning signs before the low levels of oxygen lead to cognitive deficits and the potential for total incapacitation.

Numerous studies have documented the effects of hypoxia on human cognitive and perceptual capabilities, with its effect on visual perception being the most commonly reported. For example, considerable evidence is available to indicate that moderate hypoxic exposure significantly increases pupillary response latency.[13] Other studies have documented hypoxia's effect on human perception of stimulus intensity[10] and color vision.[7] Hypoxia's effect on reaction time is also well known, though it is difficult to determine whether this occurs at a perceptual level, a cognitive level, or a combination therein. A program of research conducted by Fowler and his associates compiled strong evidence to suggest that increases in reaction time associated with hypoxia occur at a perceptual level as opposed to a higher-order or cognitive level,[10–12] yet further research is required to completely explicate this issue.

Obviously, extreme hypoxia will cause the total incapacitation of all cognitive abilities. Identifying the subtle effects of mild to moderate hypoxia on higher-order processing has proven to be difficult. Investigators quickly realized that hypoxic effects on more complex tasks could be easily masked through extra effort or the adoption of new strategies by subjects during exposure.[22,23] Furthermore, individual variability in hypoxic ventilation response also leads to highly variable hypoxia effects on performance.[19] Due to these issues, studies that document hypoxia's effect on higher-order cognitive abilities are not easy to interpret. Evidence of impaired higher-order processing brought about by hypoxia is matched in number with studies showing little or no effect during mild or moderate hypoxia.[19]

A recent study exposed subjects to a simulated altitude of 17,500 ft (5334 m) while testing them on three popular measures of higher-order cognitive function: the word-color Stroop test, a forward and backward digit-span test, and a trail making test. Following 30 min of exposure, no effects were found on the Stroop test or the forward digit-span test. Conversely, effects were found on the trail making test and on backward digit span.[2] These trends may suggest a differential effect on specific aspects of higher-order cognition. Thus, more scrutiny of the issue is needed to further elucidate mild to moderate hypoxia's effect on higher-order cognition.

Researchers have often assumed that performance effects stemming from hypoxia disappear when blood oxygen saturation has returned to baseline levels. However, more recent studies have shown that there appear to be residual performance deficits that persist following the restoration of oxygen saturation (S_pO_2) to normal levels.[20,21] Phillips et al. also observed that hypoxia exposure resulted in a residual negative effect on regional frontal cerebral O_2 saturation (rSO_2) for up to 10 min after exposure, as measured through near infrared spectroscopy (NIRS).[20,21] The measured residual performance deficits and physiological depression in rSO_2 suggested that hypoxia, or the body's reaction to it, may affect cerebral function significantly longer than previously thought. If the restoration of pre-hypoxic performance capabilities is in fact delayed, flight crews may continue to be impaired for the remainder of a sortie following a hypoxic in-flight emergency.

Few studies have documented the effects of hypoxia on the subjective perception of mental workload. One study employed the NASA Task Load Index (NASA-TLX) to measure a global workload rating of the task performed, in this instance, a working memory task.[8] The global workload rating of the NASA-TLX is calculated through a combination of six subscales relating to the workload demands imposed by the task (Mental Demand, Physical Demand, and Temporal Demand) and the assessment of one's interaction with the task itself (Performance, Effort, and Frustration).[16] It was reported that at altitudes of up to 15,000 ft (4572 m), there were no significant effects of increased subjective workload associated with a working memory task. It is noted that Dahiya and Tripathi did not expose their subjects to simulated altitudes above 15,000 ft.[8] Given that the effects of a higher altitude exposure on subjective mental workload have not been documented with the NASA-TLX, it is desirable to record these outcomes such that the effect of an exposure above 15,000 ft can be established.

The goals for the present study were to establish the effects of acute hypoxia on performance for a specific set of cognitive, psychomotor, and perceptual abilities, and to chronicle the time required for these abilities to fully recover to pre-exposure levels. Based on previous literature, it was anticipated that reaction time, executive function, visual acuity, and color vision would be significantly affected by hypoxia. It was also anticipated that performance on these tasks would remain depressed for a significant period of time after S_pO_2, as measured by a pulse oximeter, returned to baseline levels. The regional saturation of oxygen (rSO_2) measured within the frontal lobes of the brain, as indexed by NIRS, was expected to remain slightly depressed, on average, for an extended period of time following hypoxia exposure as observed by Phillips et al.[20] Additionally, it was expected that cognitive workload, as measured by the NASA-TLX, would show that the overall level of workload experienced by subjects would be greater when exposed to hypoxic stress.

METHODS

Subjects

The study protocol and informed consent document were approved in advance by the Naval Aeromedical Research Laboratory Institutional Review Board. Each subject provided written informed consent before participating. Data were collected at the Naval Aeromedical Research Laboratory in Pensacola, FL, which is approximately 8 ft (2.4 m) above sea level. A total of 19 subjects completed all stages of the experimental protocol. All subjects were active duty military personnel with a current flight physical on record. Subjects with pre-existing medical conditions, including a previous or current diagnosis of anemia, asthma, cardiovascular disease, epilepsy (or other seizure disorders), emphysema, or hypertension, were excluded from the study.

Additionally, subjects were disqualified if they reported being diagnosed with pneumonia during the previous year, were habitual tobacco smokers, reported having lived at altitudes above 5000 ft (1524 m) within 3 mo prior to being enrolled, or reported being claustrophobic. Further, potential subjects were not included in the study if they reported consuming more than three alcoholic beverages in the last 48 h or that they were using over-the-counter or prescription medications or nutritional supplements. Prior to reporting, subjects were asked to consume their normal amount of caffeine on testing day.

As rSo_2 readings are very sensitive to individual differences in cranial shape and density, subjects were tested using the NIRS device during their second visit in order to ensure that accurate measurements could be obtained. In the event that a subject did not show an rSo_2 value greater than 50, it was unlikely that the measurement represented blood O_2 concentration in the cerebral cortex. In cases such as these, subjects were excused from the remainder of the study. A total of four potential subjects were excluded from the study for this reason.

Equipment

Reduced Oxygen Breathing Device (ROBD): The ROBD (Environics®, Tolland, CT) is a computerized gas-blending instrument that alters blood oxygenation levels by simulating transitions to altitude in a normobaric environment. The system uses thermal mass flow controllers to combine breathing air and nitrogen to produce the sea level equivalent of atmospheric oxygen contents for altitudes up to 34,000 ft (10363 m), breathed by subjects through a standard aviation mask. The ROBD was intended for deployment to operators in the field for training purposes, and was therefore designed to require as little maintenance and calibration as possible. The ROBD runs self-tests during an initial power up phase and then guides the user via a simple interface through a series of additional self-tests prior to operation. These tests include flow and O_2 checks for several simulated altitudes in the range 0 - 34,000 ft. If the ROBD fails any self-tests, altitude profiles cannot be run. If O_2 concentration falls outside tolerances for a target altitude during operation, the ROBD automatically interrupts the exposure and administers 100% O_2. For the 18,000 ft (5486 m) exposure employed in this study, target fraction of inspired oxygen was 9.96% with tolerance limits of 9.80–10.10% O_2 concentrations. The stated accuracy of the ROBD O_2 sensor is $< 1\%$ with a resolution of 0.1%.[25]

Near-Infrared Spectroscopy (NIRS): Regional saturation of oxygen and changes in the blood volume index (BVI) were measured bilaterally from the frontal lobe by means of an INVOS Cerebral/Somatic System (INVOS 5100C®, Somanetics, Troy, MI). Care was taken to ensure consistent sensor placement throughout study participation by recording the lateral distance of the sensors to the midline, superior to the brow on each side, and inferior to the hairline. The two sensors were positioned on the left and right sides of the subjects' foreheads to avoid sinus cavities and hair that might interfere with the signal recordings. Cerebral oxygenation measures were averaged and automatically recorded by the oximeter at a rate of 0.2 Hz. It has been noted that rSo_2, as measured with NIRS, and central venous oxygen saturation are highly correlated values, but are not necessarily interchangeable indices of saturation.[9] Rather than examining absolute values of oxygen saturation, fluctuations in rSo_2 trends were monitored and recorded as deviations from an individual's baseline.

Pulse oximetry: Blood oxygen saturation was measured with a finger oximeter (Model 3900 P, Datex Ohmeda Corporation, Helsinki, Finland) placed on the index finger on the subjects' nondominant hand.

Blood pressure and heart rate: Subjects were fitted with a standard blood pressure cuff connected to a Propaq Encore Medical Monitor® (Welch-Allyn, Inc., Skaneateles Falls, NY) to continuously collect blood pressure and heart rate throughout the task.

Inspired and expired O_2 and CO_2 (F_IO_2; F_ICO_2): A Powerlab Gas Analyzer® (Colorado Springs, CO) sampled O_2 and CO_2 concentrations in subjects' inspired and expired breath to determine if the observed simulated altitudes were representative of expected gas concentrations.

Cognitive/perceptual test battery: The cognitive/perceptual test battery consisted of the following five subtests which were administered to subjects in a random order for each iteration of the test battery during the study.

Freiburg Visual Acuity and Contrast Test (FrACT): The FrACT is a relatively rapid computer-based battery of tests that measures visual acuity (VA) and contrast sensitivity (CS). For both components, a Landolt C optotype (a ring with a missing segment) was selected. (Dark "C" on a white background option was selected for the VA test.) In the VA portion of the test, the "C" is randomly oriented with the gap in eight possible positions (i.e., up, down, left, right, up-left, up-right, down-left, and down-right) and subjects are required to identify the position of the gap by pressing the corresponding key on a keypad. The size of the "C" is altered according to an adaptive staircase procedure, referred to as the Best-PEST algorithm,[3] which rapidly converges to the steepest point on the detection rate versus optotype size curve. This psychometric curve has been found to

be well-fit by a logistic curve with the top asymptote at 100% (perfect detection) and the bottom asymptote at 12.5% (pure chance for eight gap positions). The steepest slope of the logistic curve occurs at 56.25%, the inflection, or "halfway," point of the curve. VA is defined around this point, since any changes in detection rate are accompanied by the smallest possible changes in the acuity values; thereby an individual's VA can be "zeroed in" on. In practice, the staircase procedure has been found to lead to a higher threshold than an ascending strategy, and the Best PEST algorithm also assumes a lower threshold criterion (56.25%) than the standard in EN ISO 8596 (60%);[6] both effects were corrected by multiplying results by 0.892. Because guessing accuracy rate at the inflection point is roughly 50%, subjects will often experience a fair amount of psychological discomfort at this point, since they are least sure of the correctness of answers. (Consider that when guessing at 12.5% correct, one knows that his/her responses are arbitrary.) Hence, verbal prompts, such as assuring subjects that it is normal to be unsure of responses, were occasionally used in order to assure timely completion of trials and to prevent subject fatigue.

The FrACT has a number of format options for VA output. In this study, VA values were output in terms of decimal VA, which is the Snellen fraction expressed as a decimal. The minimum angle of resolution (MAR) was calculated by taking the reciprocal of decimal VA and then converting to logMAR (logarithm of MAR). Since this measure has an inherently logarithmic progression it can be legitimately averaged without using the geometric mean. Multiplying logMAR by -1 results in logVA, which has the advantage of intuitive directionality, i.e., higher logVA values mean higher VA. We chose logVA as our acuity measure, which we calculated by ignoring the steps just mentioned and simply taking the log of decimal VA in the first place. A further advantage of logVA is that it has been found to have an approximately normal distribution.[4] LogMAR has the further advantage of having an approximately normal distribution;[4] it is theoretically continuous, but, in practice, only approximately continuous due to the inherent limitations of pixel resolution of the visual display – for modern LCD displays such as employed in this study, however, continuity is a reasonable assumption.

For the contrast sensitivity portion of the FrACT, the contrast (defined by the Michelson contrast ratio: $luminance_{max} - luminance_{min} / luminance_{max} + luminance_{min}$) between the circle and the background was reduced as the trials progressed, in order to identify the point at which the subject could no longer distinguish the circle from the background, as indicated by reduced accuracy in naming the direction of the segment. For additional information regarding the Freiburg Visual Acuity Test, see Bach.[4]

To ensure measurement accuracy among all assessments of visual perception, ambient luminance in the laboratory was controlled by blacking out all windows and keeping lighting consistent within and between trials. Ambient luminance was checked by a trained optometrist using a LX1330B Digital Luminance Meter (HisTest, Union City, CA). LCD display luminance was calibrated by applying gamma correction using a Spyder4Pro (Datacolor, Lawrenceville, NJ); this ensured the monitor gamma matched the FrACT gamma of 1.0, which is necessary for accurate identification of the CS threshold. Distance to the display monitor was set to 62.5" and controlled by instructing subjects to maintain contact with a pad situated behind the head (hypoxia symptoms permitting). An acceptable distance to the monitor was determined by entering display resolution into the FrACT settings interface to ensure a sufficient range of VA could be measured.

Ishihara plates: Ishihara color plates were designed as a test to detect deficiencies in visual color perception, and were utilized in this study due to hypoxia's known effect on color vision. The plates consist of colored dots, with a number formed by different colored dots embedded in the surrounding array. Color deficiency is indicated by an inability to identify the number. Traditionally, this test does not include an assessment of tritan (yellow-blue) deficiency; however, the set of Ishihara plates used in this study did incorporate one into the examination.

The presentation order of Ishihara Plates was randomized for each administration to prevent learning effects. Ishihara plates were utilized in this study due to hypoxia's known effect on color vision. Although more sensitive measures are available they require a significantly longer assessment period that did not facilitate repeated measurement of effects within one 20- to 30-min hypoxia exposure.

To ensure measurement accuracy among all assessments of visual perception, ambient luminance in the laboratory was controlled by blacking out all windows and keeping lighting consistent within and between trials. Display luminance was checked and controlled by a trained optometrist using a LX1330B Digital Luminance Meter.

The Number Stroop Task: The Number Stroop Task was employed as a measure of executive control. Subjects were presented with stimuli where an automated or overlearned response would normally conflict with the required response, and would be required to exercise a form of executive control to inhibit the automated, overlearned response and give the required response.

The Number Stroop Task is a variation of a Stroop task where numbers and number names are used rather than colors and color names. This task was chosen as opposed to the Color Stroop Task due to concerns that hypoxia's negative effect on color vision would interfere with performance and complicate interpretation of the Stroop effect. This task was divided by the manner in which the stimuli were presented, as words, or as digits. During the worded portion of the task, subjects were presented with a series of one to four words at random on a computer monitor and were asked to respond as quickly as possible either to the number of words presented, regardless of their numeric connotation, or their numerical value, regardless of the number of items presented. Throughout the task, the number and connotation of the words presented could be considered congruent, such as a presentation of the words four, four, four, four, or incongruent, such as a presentation of the words three, three, three, three, which in both cases required a

response of "four", indicative of the number of words presented. During the digit portion of the task, similar response instructions were given, but alphanumeric digits were presented rather than words. For example, a presentation of 2, 2, 2, 2, still required a response of four from the subject.

Each iteration of the Number Stroop Task consisted of 24 stimuli presentations: 12 worded presentations – 6 congruent with the number of words presented, and 6 incongruent with the number of words presented – and 12 digit presentations, 6 congruent, and 6 incongruent.

Reaction time: This task was designed to measure subjects' response speed to visual targets where the presented stimuli and associated responses were static throughout the length of the task. Simple and choice reaction time tasks were included in the performance battery due to the relatively large number of studies that have identified hypoxia's significant effect on response latency.[11,12]

In the simple reaction time trials, subjects were required to depress and hold the "5" key on a computer keyboard's numeric pad until an "up" arrow appeared on the computer screen (the interstimulus interval varied at random between 2000 and 10,000 ms), after which the subject released the 5 key and depressed the 8 key with the same finger. The time from the target being presented to the subject releasing the 5 key was calculated as reaction time, whereas the time from the 5 key being released to when the 8 key was depressed was calculated as movement time.

Choice reaction time: The choice reaction time trials were similar to the simple reaction time trials, but the stimulus arrow corresponded to one of the four directional keys on the numeric key pad (i.e., up, down, left, or right). Subjects were given the same response instruction as with the simple reaction time trials, but following the release of the 5 key, they were required to depress the key on the numeric key pad that corresponded to the direction of the arrow (up – 8, down – 2, left – 4, right – 6). Subjects were instructed to use the index finger on their dominant hand to press and hold the 5 key, and to use the same finger to press the reciprocal response key. During every iteration of the task, subjects completed up to 20 response time trials, alternating between simple and choice tasks, and although the speed of their responses was emphasized, they were given an unlimited amount of time during this portion of the experimental trials. Subjects were monitored via closed circuit video to ensure that they were responding as instructed.

NASA Task Load Index (NASA-TLX): In order to assess the subjective workload of task activity before and after hypoxic exposure, subjects were required to complete the NASA-TLX after the conclusion of the baseline experimental block, the conclusion of the first period of recovery following the hypoxic episode, and after each ensuing recovery block. This instrument is considered to be one of the most effective measures of perceived mental workload currently available.[16] It provides a reliable measure of global workload on a scale from 0 to 100, and also identifies the relative contributions of six sources of workload. Mental, Temporal, and Physical Demand reflect the demands placed on the subject by the task, while the remainder, Performance, Effort, and Frustration, characterize the interaction between the subject and the task at hand. It is important to emphasize, however, that the NASA-TLX is a subjective scale, and there is always some question as to whether any form of self-report accurately reflects a respondent's true perceptual experiences.

Methodologically speaking, workload was not assessed as part of the hypoxic episode due to an expected inability to accurately report subjective workload. As an alternative, subjects were asked to reflect on and recall the workload experienced during the hypoxic episode and to report these values at the conclusion of the ensuing neuropsychological test battery rather than reporting the values normally associated with that testing period. As such, five assessments of the TLX were included in the analysis.

Procedure

Subjects reported to the Naval Aerospace Medical Research Laboratory on three separate occasions prior to the scheduled hypoxia exposure. Subjects gave consent during the first visit and had the opportunity to ask questions of the researchers pertaining to study involvement.

During both the second and third visits, each subject was administered the cognitive/perceptual test battery. The second visit served to provide subjects additional familiarization with the test battery. On the third visit, the test battery was administered three times, averaged together in what will be known throughout the remainder of this manuscript as the baseline. Additionally, physiological measures of overall blood oxygen saturation, rSo_2, blood pressure, and heart rate were recorded during these intervals and averaged together to provide a baseline point for each subject from which ensuing deviations could be assessed. After completion of this series of trials, subjects completed the NASA-TLX measure of cognitive workload.

Subjects then reported for a fourth day where they completed the cognitive/perceptual battery under hypoxic conditions while physiological measures were also collected. At the commencement of testing, subjects were immediately exposed to a reduced oxygen gas mixture equivalent to conditions found at 18,000 ft using the ROBD for a period of 30 min or until their finger S_pO_2 saturation levels dropped below 50%. Over the course of the 30-min hypoxic exposure, subjects were administered three iterations of the cognitive/perceptual test battery, averaged together for analysis purposes in what will be known as the Hypoxia Exposure time period. Following exposure, subjects were provided a 21% O_2 gas mixture (sea-level equivalent) and immediately began a 30-min cognitive/perceptual test session, including three additional administrations of the test battery, averaged together, and referred to as the Recovery 0 time point. At the conclusion of the 30 min, subjects completed the NASA-TLX, and were then excused for a break.

Subjects returned for three 30-min follow-up assessments beginning approximately 60 min, 120 min, and 24 h after the end of exposure to hypoxia, each consisting of three iterations of the cognitive/perceptual test battery and averaged together as Recovery 60, Recovery 120, and Recovery 24, respectively.

Following each of these time periods, subjects again completed the NASA-TLX. In sum, during the course of investigation, those able to complete the entire 30-min hypoxia exposure were administered 18 iterations of the cognitive/perceptual test battery and completed 5 assessments of subjective workload using the NASA-TLX. All physiological monitoring including rSo_2 and BP was collected continuously throughout the experimental sessions.

Statistical Analysis

In the following figures and tables, all data are presented as mean ± SE. All data were examined using a series of repeated-measures analyses of variance (ANOVAs), and statistical significance was set at an alpha level of $P < 0.05$. Where appropriate, Box's Epsilon was used to correct for violations of the sphericity assumption. If significance was found within a main effect or interaction, the Bonferroni-Holm correction was applied to post hoc tests to account for inflated family-wise error rates.

RESULTS

Visual acuity and contrast sensitivity: Visual acuity was reported in terms of the Snellen fraction and converted to LogMAR units of vision loss for analysis purposes. A repeated measures analysis of variance (ANOVA) did not reveal a main effect for time. The main effect for time period in this analysis was not statistically significant, $F(5, 90) = 2.09$, $P > 0.05$, but was indicative of a tendency toward declining visual acuity during the hypoxic episode.

As can be seen in the right panel of **Fig. 1**, subjects' contrast sensitivity values were similar during the Baseline testing phase and all subsequent recovery time periods, but declined during the hypoxic episode. These trends were substantiated by a single factor repeated measures ANOVA of subjects' Log (contrast sensitivity) values during each time period, $F(3.04, 54.70) = 9.92$, $P < 0.05$, $\eta_p^2 = 0.36$. Post hoc Bonferroni-Holm corrected *t*-tests confirmed the only significant source of variance was that of hypoxia exposure. In this and all subsequent ANOVAs, Box's epsilon was used when necessary to correct for violations of the sphericity assumption.[17]

Color vision acquisition: The effect of hypoxia on correct responses to the presentation of the Ishihara Color Plates was not significant via a single factor repeated measures ANOVA, $P > 0.05$, as the proportion of correct responses remained high throughout the experimental portions of the study.

The Number Stroop Task: An analysis of response times and correct response records among subjects' Number Stroop Task data did not reveal a significant main effect for time period, Stroop Task type (congruent counting, incongruent counting, congruent digit recognition, and incongruent digit recognition), or an interaction between the two factors, $P > 0.05$ in all cases.

Simple and choice reaction time trials: Median response times from the simple and choice reaction time trials are plotted as a function of time period in **Fig. 2**.

It is evident in the figure that response times for each task type slowed consequent to the induction of the hypoxic episode and did not return to baseline levels until the Recovery 24 taken 24 h after exposure. This finding was confirmed with separate repeated measures ANOVAs, $F(5, 90) = 15.21$, $P < 0.05$, $\eta_p^2 = 0.46$, and $F(5, 90) = 16.54$, $P < 0.05$, $\eta_p^2 = 0.48$, for the simple reaction time task and the choice reaction time task, respectively. A priori planned pairwise comparisons with Bonferroni-Holm corrections ($\alpha = 0.05$) indicated that subjects' response times did indeed deviate from, and did not return to, baseline levels during Recovery 0, 60, or 120. Subjects' observed posthypoxia performance had returned to their pre-exposure baseline levels when the 24-h recovery assessment was taken.

Regional oxygen saturation: Mean rSo_2 values and their associated standard errors are presented in **Fig. 3**. A single factor repeated measures ANOVA revealed a significant effect for assessment period, $F(1.98, 35.71) = 184.43$, $P < 0.001$, $\eta_p^2 = 0.91$, while post hoc *t*-tests with Bonferroni-Holm corrections indicated that rSo_2 levels declined rapidly during hypoxic exposure and did not return, on average, to pre-exposure levels until the 24-h recovery assessment.

The NASA-TLX: Following a procedure recommended by Nygren,[18] subjects rated their workload on each of the six subscales of the TLX, each ranging from 0 to 100, which can be seen in **Table I**. A combination of the overall mean of each subject's subscale ratings provided a composite index of global workload,

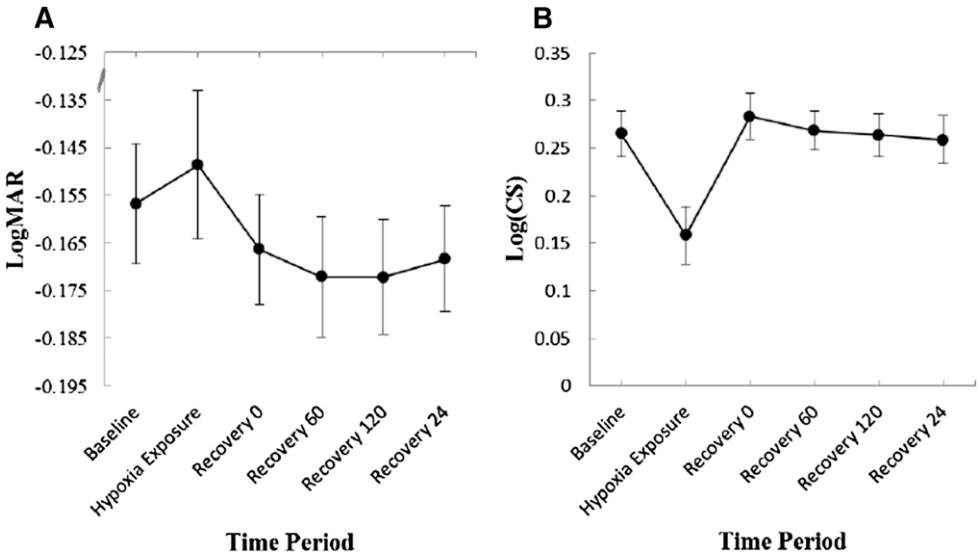

Fig. 1. Visual acuity (in LogMAR units) and contrast sensitivity (in Log CS units) values as a function of time period. Error bars depict standard errors.

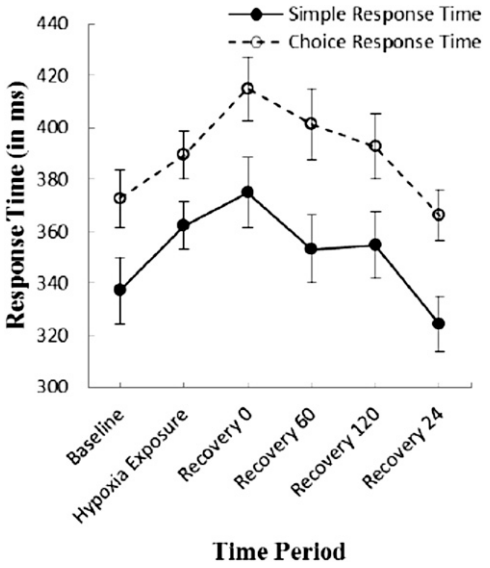

Fig. 2. Median response times in the simple and choice reaction time trials as a function of time period. Error bars depict standard errors.

while the scores for each subscale identified the contribution of the individual dimensions to the workload profile. A single factor repeated measures ANOVA of the composite workload index revealed that subjects rated their experience to be significantly more difficult during the hypoxic episode, $F(2.75, 41.28) = 18.82$, $P < 0.05$, $\eta_p^2 = 0.56$, when compared to the baseline and recovery ratings. Subsequent single factor repeated measures ANOVAs of each subscale for each assessment indicated that the hypoxic episode was the sole contributing factor to the reported increase in workload. As previously noted, it was expected that subjects would be unable to accurately report their workload ratings during the hypoxic episode, and thus were asked to recollect their experiences following the next administration of the neuropsychological test battery.

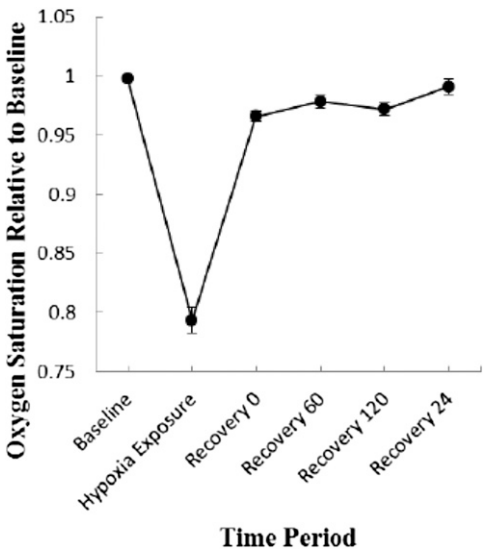

Fig. 3. Mean regional blood O_2 saturations as measured by near infrared spectroscopy as a function of time period. Error bars depict standard errors.

DISCUSSION

In-flight safety data have indicated that hypoxia remains a significant aeromedical risk factor, and as such, understanding the extent to which pilots and aircrews are affected during hypoxia exposure and cataloguing the time course of recovery should be of significant interest to the aviation community. The present study was designed to examine the role that hypoxia plays in terms of performance effects on specific cognitive, psychomotor, and perceptual processes, subjective workload, and the duration of these effects following a hypoxic episode.

The study returned divergent findings with regard to the visual-perceptual processes assessed by components of the FrACT and the Ishihara Color Plates. While hypoxia's effect on visual contrast sensitivity was apparent during exposure, results found with regard to visual acuity were not significant throughout the course of the trials. Subjects did not exhibit a reduction in the ability to discern color differences, as evidenced by the high proportion of correctly determined color plates. Thus, it can be ascertained that, under the parameters of the current study, the Ishihara Color Plates are not sensitive to the color vision deficiency often found in conjunction with hypoxia exposure. Observed performance effects on the contrast sensitivity portion of the FrACT disappeared within 30 min following the subjects' return to normoxia. These results indicate that some aspects of visual processing are negatively affected by a disruption of oxygen delivery, as proposed by Fowler and his associates.[10] Data from the current study suggest that differing aspects of visual perception are affected at different rates and to different degrees.

In the case of simple and choice reaction time, a slowing of response times became apparent during hypoxic exposure and did not appear to recover during the recovery 0, recovery 60, or the recovery 120 assessments. Performance on simple and choice reaction time returned to pre-exposure levels when assessed at the 24 h recovery session. The lingering effect of hypoxia on simple and choice reaction time supports the conclusion made by Phillips and his colleagues that some aspects of performance may not recover immediately after subjects are returned to a normoxic environment.[20,21]

Analysis of near infrared spectroscopy data appeared to be consistent with those observations made on the SRT and CRT tasks. Regional oxygen saturation readings dropped significantly throughout hypoxia exposure and did not return to pre-exposure levels, on average, until the assessment taken approximately 24 h following hypoxia exposure. This suggests some disruption in cerebral blood O_2 concentration for a prolonged time after exposure to hypoxic stress. This pattern is similar to that observed in a previous hypoxia study conducted using NIRS where Phillips et al. also observed that following hypoxia exposure, rSo_2 readings failed to return to their prebaseline levels over a 10-min recovery period.[20] The underlying mechanisms between depressed rSo_2 values following hypoxia exposure and the diminished performance on reaction time tasks remains unknown. While these findings may be indicative of an error based on sensor location or slippage from their original placement, attempts were made to

Table I. Mean NASA-TLX Subscale Scores (SE) by Time Period.

	SUBSCALE						
ASSESSMENT	**MD**	**PD**	**TD**	**P**	**E**	**F**	**COMPOSITE**
Baseline	18.53	9.84	18.59	27.63	25.97	16.69	19.54
	(4.25)	(2.36)	(4.18)	(5.04)	(5.35)	(3.02)	(3.32)
Hypoxia	25.75	26.69	24.31	36.56	38.25	23.75	29.22
	(3.74)	(4.84)	(4.55)	(4.77)	(5.39)	(5.19)	(1.83)
Recovery 60	14.75	10.50	16.19	23.38	23.13	12.06	16.67
	(4.60)	(3.88)	(5.00)	(5.51)	(5.84)	(3.86)	(1.04)
Recovery 120	12.69	11.25	14.25	27.25	21.75	12.63	16.64
	(3.13)	(3.57)	(3.54)	(5.80)	(5.34)	(2.58)	(1.04)
Recovery 24	10.81	7.63	11.88	24.19	18.56	9.50	13.76
	(2.54)	(2.40)	(3.73)	(5.36)	(4.93)	(2.76)	(0.86)
Mean	16.51	13.18	17.04	27.80	25.53	14.93	
	(2.54)	(2.40)	(3.73)	(5.36)	(4.93)	(2.76)	

Subscales are abbreviated as follows: Mental Demand, MD; Physical Demand, PD; Temporal Demand, TD; Performance, P; Effort, E; Frustration, F.

minimize potential confounds by only removing the sensors following the final test of each day and maintaining consistent placement through careful measurement. Additionally, day to day variability within each subject, such as changes in cerebral perfusion or hypocapnia, cannot be discounted from producing erroneous results. However, given the consistent directionality of these results, it would seem that a confound of this sort is at least reasonably unlikely to be the case.

Similar to the findings showing the disruption to visual contrast sensitivity, hypoxia also significantly increased subjects' subjective workload ratings on the NASA-TLX, which subsequently reverted to baseline levels in the ensuing assessment. Along with the composite scores increasing, each subscale score was elevated during the hypoxia-associated assessment relative to pre- and postexposure assessments. Thus, a single or even a subset of factors cannot be identified as the primary factor or factors contributing to an increased experience of workload during hypoxia. It must be acknowledged that retrospective ratings were used to evaluate workload during hypoxia exposure due to inability of participants to provide meaningful ratings immediately following hypoxia exposure. Therefore, NASA-TLX ratings conducted while under hypoxia exposure may have been negatively affected by short-term memory loss and impaired judgment.

No significant hypoxia-related effects were apparent in the tests of executive function as measured by the Stroop Task, which suggests that this test may not have been sensitive enough to variations in performance brought about by hypoxia exposure. Though many aspects of performance have been shown to be affected by hypoxia exposure at higher O_2 concentrations than employed in the present study, the Number Stroop Task does not appear to be susceptible to this type of physiological insult, and thus, likely should not be included in future hypoxia research as an indicator of hypoxia's effect on executive function.

The pattern of results exhibited by the subjects taking part in this study seems to indicate that hypoxia may variably affect different cognitive and perceptual abilities. Effects on visual perception become apparent soon after the onset of hypoxic stress and rebound immediately following return to normoxic conditions. Tests of simple and choice response time also appear to be affected soon after the onset of hypoxia, but may continue to show effects for up to 24 h following return to normoxia.

When taken together, these results indicate that hypoxia detrimentally affects some cognitive and perceptual processes and that some effects may persist beyond an individual's return to normal oxygen saturation. This finding should warrant further attention given that, under normal conditions, aviators must maintain a high level of sustained attention and execute physically and mentally demanding maneuvers to operate an aircraft effectively. Under hypoxic conditions, even when a pilot recognizes the onset of symptoms early, it is possible that cognitive and perceptual abilities are degraded to the extent that performance is compromised throughout the duration of the sortie. However, further research must establish the effects of shorter duration hypoxic exposures at various altitudes.

A balanced placebo condition with a "dummy" hypoxia exposure and the same number of recovery blocks was not used in this experiment. Therefore, performance decrements observed on SRT/CRT during the recovery assessments may have been associated with time-on-task cognitive fatigue. However, it is noteworthy to point out that no such residual hypoxia performance effects were observed on other tasks. In fact, all other observed hypoxia effects disappeared immediately after subjects returned to normoxic air. Additionally, trends in rSo_2 data match observations made on SRT/CRT, suggesting that some residual disruption of O_2 saturation in cerebral tissues may linger for a significant period of time following hypoxia exposure. Nevertheless, future studies addressing the recovery of performance should balance the exposure condition with a randomized and blinded placebo condition to rule out the possibilities that time-on-task cumulative cognitive fatigue or a depressed psychological arousal following hypoxia exposure, or a combination of the two, negatively affect performance during recovery assessments.

The delayed recovery of rSo_2 and RT following hypoxia, and their possible association, must be regarded as preliminary findings pending more extensive study with appropriately-balanced control exposures. Future research should also address the severity and duration of hypoxia's effects on cognitive and

perceptual processes using a broader range of altitude exposure profiles in both normobaric and hypobaric environments. Intervening recovery strategies such as breathing 100% O_2 following hypoxic exposure should also be explored both in terms of alleviating immediate performance deficits and shortening the protracted recovery period evidenced in this study.

Evidence from this study suggested an impairment of specific performance characteristics following hypoxic exposure, some for a considerable period of time. If these results are replicated, mitigation efforts should focus more on the prevention of hypoxia exposure rather than training operators to recognize and react quickly to hypoxic symptomology. This line of research may also provide guidance regarding the time course of performance recovery from exposure to hypoxic stress so that flight duties can be delayed until operators are fully recovered.

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