Pradhan, G. N., Ottestad, W., Meland, A., Kåsin, J. I., Høiseth, L. Ø., Cevette, M. J., Stepanek, J. (2021). Oculometric Feature Changes During Acute Hypoxia in a Simulated High-Altitude Airdrop Scenario. *Aerospace Medicine and Human Performance, 92*(12), 928-936. http://dx.doi.org/10.3357/AMHP.5930.2021

Oculometric feature changes during acute hypoxia in a simulated high-altitude airdrop scenario

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Abstract:

Background: Severe acute hypoxia results in a rapid deterioration of cognitive functioning and thus poses a risk for human operations in high altitude environments. This study aimed at investigating the effects of oxygen system failure during a high-altitude high opening (HAHO) parachute jump scenario from 30'000 ft on human physiology and cognitive performance using a non-contact eye-tracking task.

Methods: Nine healthy male volunteers (ages 27–48) were recruited from the Norwegian Special Operations Commando. Eye-tracking data were collected to derive information on cognitive performance in the context of rapid dynamic changes in pressure altitude while performing a modified King Devick test. The baseline data was collected at 8000 ft while breathing 100% oxygen during decompression. For every test, the corresponding arterial blood gas analysis was performed.

Results: The study subjects endured severe hypoxia, which resulted in significant prolongations of fixation time (range:284.1-245.6 ms) till 23397 ft and fixation size (range:34.6–32.4 mm) till 25389 ft as compared to the baseline (217.6±17.8 ms, and 27.2±4.5 mm, respectively). The increase in the saccadic movement and decrease in the saccadic velocity was observed till 28998 ft and 27360 ft, respectively.

Discussion: This is the first study to investigate cognitive performance from the measured oculometric variables during severe hypobaric hypoxia in a simulated high-altitude airdrop mission scenario. The measurement of altered oculometric variables under hypoxic conditions represents a potential avenue to study altered cognitive performance using non-contact sensors that can derive information and serve to provide the individual with a warning from impending incapacitation.

Keywords: oculometric; acute hypoxia; cognitive performance; high-altitude high opening

Main Text:

Introduction:

Hypobaric hypoxia can be assessed by methods reflecting oxygenation either globally (e.g. arterial blood gases, blood oxygen saturation) or regionally (e.g. cerebral oxygenation using near-infrared spectroscopy[16]). While these measurements are associated with cerebral functioning they do not adequately assess the complexities of cognitive performance. The intriguing aspect of using a dynamic task and utilizing non-contact eye-tracking tools is the possibility to quantify alterations in oculometrics. These alterations occur in the multiple neural pathways that control eye movements (motor cortex, visual cortex, numerous ocular nuclei, autonomic nervous system, and cranial nerves). Furthermore, a visual task is frequently an important component of human cognition especially in the aerospace environment, be that a pilot scanning instruments, or a parachutist checking for malfunctions in their equipment, the altitude and direction of flight, making it a potentially valuable target of further study. The unobtrusive nature of eye tracking and the presence of computers and screens demanding visual scanning tasks of operators in many environments potentially further adds to the value of pursuing investigations in this domain.

Changes in several oculometric variables have been reported to correlate with cognitive performance[8,23,25]. Our objective was to assess oculomotor paradigms related to fixation and saccadic eye movements as descriptors for cognitive performance. Fixation and saccadic behavior play vital roles in the cognitive tasks that involve reading or scanning which is common in military flight operations. Fixation relates to the cognitive processing required to maintain a gaze and visually process and construe the target of interest[9]. Increased fixation times have been associated with neurologic impairments and a state of impaired cognitive functioning during alcohol intoxication[14]. Saccadic eye movements are related to attention and can be

affected by injury to the underlying oculomotor reflex[5]. Thus, the present study aimed to evaluate cognitive performance from the measured oculometric variables during severe hypobaric hypoxia in a simulated high-altitude airdrop mission scenario.

Methods:

Subjects:

The study protocol was approved by the Regional Committees for Medical and Health Research Ethics (REC South East, reference 2014/469). (https://rekportalen.no/#hjem/home) Each subject provided written informed consent before participating. Nine healthy men were recruited among personnel qualified for performing HAHO-procedures in the Norwegian Special Operations Commando. All were healthy nonsmokers, age 31 (27– 48) years [mean (range)]. Subjects abstained from solid foods for 4 hours, clear liquids for 2 hours, and physical exercise and any analgesics for 24 hours before the hypobaric exposure and none were acclimatized to altitude.

Equipment and/or materials:

Hypobaric chamber and flight profile: The experiment was conducted in a hypobaric chamber (Aeroform Poole, Dorset, UK) at the Institute of Aviation Medicine, Oslo, Norway. To facilitate denitrogenation and to decrease the risk of decompression sickness, a 60-min oxygen pre-breathe started at ground level (1,017 hPa [763 mmHg]). The 60-min pre-breathe complies with both standard operation procedures during hypoxia training in the Norwegian army and in NATO. The subjects breathed 100% oxygen using an oxygen mask (Gentex MBU 20, Gentex, Carbondale, PA) on a pressure demand regulator (CRU-73, Cobham Life Support, Davenport, IA). Approximately 40 min into the denitrogenation, pressure was reduced to 753 hPa (565 mmHg, 8000 ft), simulating standard cabin pressure during flight. All baseline measurements were completed, and a safety brief performed. When the 60-min pre-breathe was completed,

the chamber was decompressed from 753 hPa (565 mmHg) to 301 hPa (226mmHg, 30,000 ft) at 4,000 ft/min. At 301 hPa (226 mmHg) while breathing oxygen, each subject was instructed to do 30 deep squats, and then to sit down, to simulate the workload associated with exiting the airplane. To simulate parachute drop and flight, the chamber was re-pressurized from 30,000 ft to 28,998 ft in 15 s at 4000 ft/min to simulate the free fall phase, followed by a descent from 28,998 ft to ground level at 1000 ft/min to simulate descent under a canopy. Supplemental oxygen was removed at the start of chamber recompression and subjects breathed ambient air throughout the descent profile. Ottestad et. al.[15] presents the same flight profile methodology to discuss physiological responses, while this study specifically aims at the cognitive performance and altered oculometric variables during acute severe hypoxia in greater detail. The overall aim of the study was to explore the risks associated with a loss of supplemental oxygen during HAHO operations. The broader purpose of the study was thus to reduce the risk of such training/ operations.

Eye Tracking Setup: During the experiment, the subjects were seated in a chamber facing a 19" computer screen (resolution of 1440 x 900 pixels) and positioned to maintain a viewing distance of approximately 65-70cm, a distance within the recommended reading range. A noninvasive eye-tracking device (Tobii X1 Light, Tobii Technology, Stockholm, Sweden) was affixed to the bottom of the computer screen. The Tobii X1 tracker consists of infrared cameras, which capture eye movements by tracking the corneal reflections of infrared reference lights. The eye tracking data was collected at a sampling rate of 40 Hz with an accuracy of 0.5º. The lighting in the chamber was consistently maintained at the same level (240 lux) throughout the experiment for all subjects. To warrant accurate tracking of eye movements, equipment calibration was performed for each subject prior to the data collection.

Fig 1. here

Mental workload task: A mental workload task was created by modifying the King-Devick (K-D) test[4] due to its proven efficacy in describing altered cognitive performance in the concussion[3,20] and hypoxia domains [21,22]. The original K-D test requires reading numbers aloud arranged from left to right on sequential lines shown on three different test cards or screens (40 numbers per card/screen). Based on our previous studies [21,22], the entire K-D test completion time during normoxia was 46.3 ± 10.4s and in a hypoxic exposure (i.e., 8% oxygen with balance nitrogen gas mixture - equivalent altitude of 23,300 ft for 3 minutes) it was 54.5 ± 12.4 s. However, the current flight profile was dynamic with rapid recompression and the goal was to measure cognitive performance during changes in ambient pressure every 2 minutes throughout the profile (corresponding to approximately every 2000 ft descent). To perform the entire K-D test with all three cards that consisted of reading out loud 120 numbers every 2 minutes for more than 10 times continuously would have been an extremely tiring process for the subjects. This would have potentially led to difficulty in quantifying cognitive performance and oculometric measurements purely due to hypoxia. In addition, in a recent study[17], we have established the normative values of oculometrics separately for all three K-D cards. We discovered that the "baseline" oculometrics and reading times were significantly different across all three cards because they offered varying cognitive load by presenting the numbers to read in different formats. Hence, presenting three cards with different cognitive loads would have been another potential confounding factor. As a result, we had to modify the K-D test by reducing the test to only one card with 20 numbers from the center four rows of the middle card (as shown in Figure 1a). The described flight profile provided an ideal platform to keep mental workload consistent while measuring raw eye movements during acute and severe hypoxia.

Procedure:

The baseline eye-tracking data during the modified K-D test was collected at 8000 ft while breathing 100% oxygen. It should be noted that the hyperoxic baseline measurements were

performed from HAHO operating conditions perspective and may not represent normoxic performance at sea level equivalent since hyperoxia will result alterations in central nervous system blood flow (vasoconstriction) and altered carbon dioxide metabolism. 10 minutes prior to the baseline test, 10 practice trials reading the modified K-D card were performed to familiarize the subject with the test procedure and desensitize potential learning effects. During the flight profile, eleven K-D tests and simultaneous eye movements were collected at every 2000 ft descent (i.e., every 2 mins) from 30,000 ft to ~9000 ft. The first K-D test during the flight profile was performed at 28998 ft. At the end of the experiment, a post-baseline test was performed at ground level. For every K-D test, the corresponding arterial blood gas analysis was performed using Radiometer 133 ABL 90 FLEX (Radiometer. Brønshøj, Denmark).

The raw eye movement captured by the eye-tracking device is represented as the scan-path plotted on the modified K-D test card (Figure 1b) that was presented as a mental workload. The eye-tracking device transformed the relative position of the corneal reflection and the pupil center in each frame to pixel coordinates (x, y) on the presented computer screen. All saccadic movements were calculated based on the euclidean distance between eye positions on two consecutive frames. To identify fixations (maintenance of visual gaze within a specific area of the screen or region of interest) and saccades (rapid eye movements between fixations), we used an algorithm[17] that required two input parameters: 1. "*saccadic threshold*", defined as the threshold for the length (or size) of the saccade represented on the screen, and 2. "*minimum sample for fixations*", defined as the threshold for the number of eye-tracking data points sampled in the fixation, which is the amount of time spent within a specific area of the screen. The input values for *saccadic threshold* and *minimum sample for fixations* were set to 14 mm (i.e., less than 1-degree amplitude) and four eye-tracking data points, respectively, for classifying fixations and saccades during the reading of all three test cards. The saccadic movements above the saccadic threshold (i.e., greater than 1 deg) were classified as saccades.

Further, a cluster of at least four consecutive micro-saccades (i.e., less than 1 deg) between two consecutive saccades were classified as fixations. The classified saccades were converted later into degrees based on the visual angle between screen and eye.

Statistical Analysis:

The measures related to fixations were fixation time (ms) (time looking at a target), and fixation size (mm) (total eye movement i.e. micro-saccadic small eye movements within a fixation). The measures related to saccades were total saccadic amplitude (deg), average horizontal saccadic velocity (deg/s) i.e. transitioning between numbers on a line and average oblique saccadic velocity (deg/s) i.e. transitioning between lines. The arterial blood gas partial pressures of oxygen and carbon dioxide (PaO_2 and $PaCO_2$) and all oculometric data related to fixations and saccades at baseline and different altitudes during the flight profile were tested for normality using Shapiro-Wilk's test to find no significant departure from the normal distribution. Hence, we analyzed the changes in the individual oculometrics related to fixations and saccades between baseline and different altitudes during the flight profile using the parametric, one-way repeated measures ANOVA test for statistical significance. Statistical analysis was performed using MATLAB software. The values are presented as mean ± standard deviation. Statistical significance was set at $p <= 0.05$. Due to the small number of subjects, Cohen's d was computed to evaluate the effect size. We also presented these changes against the major environmental stressor of hypoxia as measured by arterial blood gas (PaO_2 and $PaCO_2$) at the tested altitudes.

Results:

Eight subjects completed the entire flight profile and they performed a mental workload at pre-determined tested altitudes throughout the entire exposure. One subject experienced loss of consciousness at 25,400 ft and was excluded from the analyses due to lack of data. However,

early and striking prolongations of fixation time, well beyond the other subjects, were recorded in the subject that lost consciousness.

Fig 2. here

Figure 2a and 2b shows the PaO_2 and $PaCO_2$, values, respectively, across 8 subjects during baseline at 8000 ft (breathing 100% oxygen before recompression) and then descent, breathing ambient air, from 30,000 ft to ~9000 ft at every ~2000 ft descent and one at ground level. In descent, PaO_2 dropped instantly from baseline (18.5 ± 0.36 kPa [95% CI: 18.2-18.9 kPa]) at 28,998 ft (4.8 ± 0.35 kPa [95% CI: 4.3-5.3 kPa]) and further worsened at 27360ft (3.5 ± 0.28 kPa [95% CI: 3.2-3.7 kPa]). . PaO_2 gradually increased for the remaining part of the descent from 25,389ft and finally reached 11.9 ± 1.4 kPa [95% CI: 10.7-13.1 kPa]) at ground level, still statistically lower than the baseline because baseline PaO_2 was markedly hyperoxic, while ground level PaO_2 during descent was approaching normoxic. Similarly, due to hyperoxia during baseline, $PaCO_2$ baseline values (3.9 ± 0.33 kPa [95% CI: 3.6-4.1 kPa]) were lower than normal levels (5.3 kPa). In descent, $PaCO_2$ slightly increased at 28998 ft (4.1 ± 0.35 kPa [95% CI: 3.8-4.4 kPa]) because subjects performed 30 deep squats before hypoxic exposure that might have resulted in production of CO_2 due to the metabolic needs of the muscle tissue. However, $PaCO_2$ levels at 27360 ft (3.3 ± 0.34 kPa [95% CI: 3-3.6 kPa]) decreased soon due to severe hypoxia and maybe also due to hypocapnia in attempted compensation by increased ventilation.

Fig 3. here

Fixation Time: The fixation time indicates the average amount of time required for the subject to fixate on the number to read it. During the severe hypoxic exposure endured in this flight profile, we recorded significant alterations in fixation times from baseline to 28,998 ft ($F(1, 7) = 16.2$, $p = 0.005$), 27,360ft ($F(1, 7) = 13.9$, $p = 0.007$), 25,389 ft ($F(1, 7) = 8.9$, $p = 0.02$), and 23,397 ft ($F(1, 7) = 6.7$, $p = 0.036$). (Figure 3a and Table 1). These findings suggest a decline in cognitive

performance during severe hypoxia at altitudes of 28,998 ft, 27360 ft, 25,389 ft and 23,397 ft followed by subsequent values approaching baseline levels with further descent, as seen in Figure 3a. From 19,429 ft to ground level, the fixation times were numerically almost identical to baseline with no significant differences.

Table I here

Fixation Size: The fixation size indicates the total eye movement within the fixation, i.e. small saccadic movement that represents spatial characteristic of the fixation. The fixation sizes during severe hypoxia at high altitudes 28,998 ft (34.6 ± 10.7 mm), 27,360 ft (34.3 ± 9.4 mm) and 25,389 ft (32.4 ± 9.3 mm) were significantly larger than the baseline fixation size (27.2 ± 4.4 mm) (Figure 3b and Table 1). The alterations in fixation sizes at altitudes from 23,397 ft to the ground level were not statistically different from baseline. However, significantly higher inter-subject variability in fixation size was observed throughout the flight as compared to the baseline (Figure 3b).

Fig 4. here

Saccadic Amplitudes and Velocities: The saccadic amplitude signifies the sum of total saccadic eye movement transitioning between all the numbers on the modified K-D card (i.e. horizontal saccades) and total saccadic eye movement transitioning between all the lines on the card (return sweep i.e. oblique saccades). The saccadic amplitude was increased immediately from 58.6 ± 9.1 deg at baseline to 74.8 ± 18.9 deg ($F(1,7) = 6.8$, $p = 0.035$) at 28,998 ft (Table 1). During remaining descent, there was no significant difference in saccadic amplitudes due to high inter-subject variability during hypoxic exposure. However, as it can be noticed in Figure 4a, variabilities in saccadic amplitudes across subjects are more stable in altitudes closer to the ground and at ground level as compared to high altitudes (i.e. hypoxic environment). Similar to saccadic amplitudes, the horizontal saccadic velocities ($F(1,7) = 24.53$, $p = 0.0017$) and oblique

(F(1,7) = 9.3, p = 0.01) were instantaneously reduced at 28,898 ft from baseline (Figure 4b & 4c, and Table 1).

Discussion

Visual performance measures represent a direct physiological sign of cognitive activity[10], therefore oculometric measures are recently being studied as indicators to detect hypoxia-induced cognitive performance decrements[22,28,30]. All studies to date have tested the changes in oculometric measures in a steady state hypoxic environment, meaning, at a particular altitude or by simulating low oxygen levels with hypoxic gas mixtures. This study is the first to systematically examine the continuous changes in oculometric measures during severe hypoxia and rapidly changing ambient pressure.

Across all tested individuals, the completion time of the modified K-D test until ~25,000 ft was significantly longer than the overall baseline (5.6 ± 0.8 s), which was performed before jumping while breathing 100% oxygen (as seen in Table 1). Severe hypoxia will result in compensatory increased ventilation, which results in cerebral vasoconstriction and a left shift of the oxy-hemoglobin dissociation curve. These mechanisms will create further decreases in tissue oxygen delivery and independently decrease human performance and functioning, which may have an impact on cerebral perfusion of oculomotor centers. This suggest the relevant importance of exploring the alterations of oculometric measures during the cognitive workload task (i.e., reading numbers) to detect an early decline in cognitive performance.

A previous study using a similar methodology has related fixation time to cognitive performance[18], suggesting the increase in fixation time was associated with a decline in cognitive performance. Consistent with this finding, we observed a significant increase in fixation time until ~23,000 ft, where PaO_2 levels were lowest during that period of the flight

profile, and PaCO$_2$ levels were around 3.3 kPa (Figure 2), which is a departure from normal levels of 5.3kPa corresponding to a potential vasoconstriction effect of up to 30-40%, suggesting a decline in cognitive performance. Given the K-D structure, the duration of fixation on each number plays a crucial role in assessing cognitive function since it involves the integration of information to read, verbalize, plan the motor movement, and direct attention to the next number[7,20]. Such types of cognitive tasks involve brain regions that are responsible for executive functions and attention, which have been reported to be affected also in mild traumatic brain injury[24]. In line with this, prolonged fixation time has also been reported in concussed versus healthy adults[20]. This suggests that monitoring increases in fixation time during cognitive workload has the potential to provide signs of cognitive decline during military operations like our tested flight profile.

Fixation size is the total length of the small-amplitude involuntary eye movements i.e., micro-saccades within the fixation[17]. The increase in fixation size indicates a reduction in fixation stability. These micro-saccadic eye movements provide information on brain function and related oculomotor circuits concerning cognition and attention[6,11]. We found a significant increase in the fixation size until ~25000 ft. There have been no studies that analyze micro-saccadic eye movements within the fixation in terms of total length, except one study that documented fixation size as an indicator of fixation stability and perceptual learning that indicated the maturation process in healthy youth athletes[18]. We believe that the fixation size represents a good reflection of cognitive processes associated with mental attention i.e., performance during a cognitive workload task such as reading[19]. This supports the importance of monitoring the changes in the fixation size during the cognitive or attentional task to assess focus in military operations to detect acute cognitive impairment. In this study, as seen in the bar plot of Figure 3b, the range of deviation of fixation size across tested individuals is much larger during the entire test profile as compared to baseline while breathing oxygen before jump flight.

The differences are not statistically significant because of the observed high inter-subject variability as well as high intra-subject variability at different altitudes (Table 1). This indicates that acute severe hypoxia has caused fixation instability due to the involuntary nature of micro-saccadic eye movements. Our finding is aligned with the work that observed an increment in inter-saccadic drift velocity due to hypoxia that caused diminishing eye stability[2].

Previous findings[1,12,22] have revealed either no significant changes in saccadic velocities due to acute hypoxia, while few other studies[26,28] have observed a decrease in saccadic velocity due to hypobaric hypoxia, mainly in larger amplitude saccadic[28] and finer gaze movements during free-viewing[26]. In this study, we observed a significant increase in total saccadic movement (Figure 4a) and significant decrease in saccadic velocities (Figures 4b and 4c) in finer horizontal saccades (between numbers) as well as larger oblique saccades (between lines) during the first K-D test in the flight profile at ~29,000 ft (i.e., immediately after sudden hypoxic exposure). Also, throughout the entire flight profile, significant variance in both the horizontal and oblique saccadic velocities was observed (Table 1). These findings in saccadic movements during the performance of a cognitive workload task in hypoxic flight profile may indicate visual instability[26] and serve to detect early signs of acute cognitive impairment.

There are several limitations to this study, first the small number of highly selected subjects may limit the external validity of our data. The eye-tracking hardware used in this study utilizes a 40 Hz sampling rate, which may lead to difficulty in adequately describing saccadic performance. We anticipate improved detection of subtle changes in oculometric performance with improved sampling rates in the future. The repetitive nature of the K-D test may have introduced fatigue and boredom effects, confounding our results, however since all oculometric variables normalized within ~23,000 ft these effects should be marginal. As far as learning effect[29] as a confounding factor is concerned, the task was not to remember the digits, and subjects would have no real benefit by learning the task by heart. Also, the raw eye-tracking scan path data

(e.g., Figure 1b) disproves such effects as the gaze data shows that all subjects moved their eyes to every digit throughout the experiment. Furthermore, humans are limited to holding up to seven digits in working memory under normoxic conditions[13], whilst hypoxia impairs short-term memory and may introduce learning effects during cognitive testing[27]. Even though the K-D test is widely used in sideline concussion testing in contact sports to identify severe cognitive impairment in athletes, it is yet to be clinically proven to be effective in detecting mild cognitive impairment. Oculometric performance during the K-D test may have limited value as a proxy for cognitive performance in more complex real-life scenarios, especially during less severe hypoxia.

In this study, the flight profile set up in a controlled hypobaric chamber was designed to collect oculometric measures to assess cognitive performance in a dynamic extremely hypoxic emergency situation (oxygen system failure). It should be noted that the ability to perform such standardized testing in a laboratory setting may not predict the ability to perform a correct action in an emergency in a real setting. During flights or operations such as HAHO, the operator continuously receives sensory and cognitive inputs in the form of cognitive mental workload tasks. This requires attention, extensive information processing, and a level of executive functioning. During the performance of real-life emergency situations (e.g., HAHO and oxygen system failure), the eye movements can represent early signs of cognitive impairment. Hence, such studies may reveal the oculometric patterns that need to be monitored or detected to deliver early warning signs to the operator. In addition, it gives important insights for the operators on what to expect in such emergency situations, which could inform training regimes and improve mental readiness.

Severe hypoxia during the HAHO simulated scenario resulted in consistent prolongations of fixation time, fixation size, and increased saccadic movement, whereas saccadic velocity decreased. These unobtrusively measured oculometrics warrant further large-scale trials to

investigate the detection of cognitive performance decline due to influence of acute hypoxia. We also found that these oculometrics measures were significantly different from baseline in severe hypoxic high altitudes, but not in moderate or mild hypoxic lower altitudes. These findings may encourage further investigation of the use of oculometric measures in advancing field testing capability to detect mild cognitive impairment as well as early changes in cognitive performance.

Acknowledgments:

Disclosures:

No conflicts of interest, financial or otherwise, are declared by the authors.

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[Altitudes (Feet), Time Elapsed (Minutes)]	Time and Oculometric Performance During modified K-D Test Mean ± Standard Deviation (95% CI) Cohen's d value, p-value (repeated-measure one-way ANOVA)					
	Time (s)	Fixation Time (ms)	Fixation Size (mm)	Total Saccadic Amplitude (deg)	Horizontal Saccadic Velocity (deg/s)	Oblique Saccadic Velocity (deg/s)
Baseline	5.7 ± 0.8 (5 – 6.3)	217.6 ± 17.8 (202.7 – 232.5)	27.2 ± 4.5 (23.5 – 31)	58.7 ± 9.1 (51.1 – 66.3)	47.3 ± 5 (43.1 – 51.5)	143.4 ± 11.8 (133.5 – 153.3)
28998, 0.33	**7.9 ± 1.2 *** (6.9 – 8.8) 2.2, 0.0009	**274.1 ± 49.1 *** (233 – 315.1) 1.7, 0.005	**34.6 ± 10.7 *** (25.7 – 43.5) 0.96, 0.037	**74.8 ± 18.9 *** (59 – 90.6) 1.15, 0.035	**40.8 ± 5.1 *** (36.5 – 45.1) 1.28, 0.0017	**123.8 ± 14.7 *** (111.5 – 136) 1.48, 0.01
27360, 2	**7.7 ± 1.8 *** (6.2 – 9.1) 1.6, 0.01	**284.1 ± 52 *** (240.6 – 327.6) 1.9, 0.007	**34.3 ± 9.4 *** (26.4 – 42.2) 1, 0.009	61.5 ± 8.5 (54.4 – 68.6) 0.32, 0.44	**44.3 ± 3.5 *** (41.4 – 47.2) 0.7, 0.05	132.8 ± 17.9 (117.8 – 147.8) 0.7, 0.25
25389, 4	**7.1 ± 1.4 *** (5.9 – 8.3) 1.3, 0.04	**275.2 ± 53.9 *** (230.2.5 – 320.2) 1.6, 0.02	**32.4 ± 9.3 *** (24.6 – 40.2) 0.75, 0.04	63 ± 9.4 (55.2 – 70.9) 0.47, 0.26	45.5 ± 5.4 (40.9 – 50) 0.35, 0.3	134.4 ± 18.1 (119.3 – 149.5) 0.6, 0.29
23397, 6	6.2 ± 1.2 (5.2 – 7.3) 0.6, 0.29	**245.6 ± 32.8 *** (218.1 – 273.1) 1.1, 0.036	30.9 ± 9.3 (23.1 – 38.6) 0.52, 0.13	62.2 ± 10.8 (53.1 – 71.2) 0.35, 0.41	46.2 ± 4.4 (42.5 – 49.9) 0.23, 0.49	131.4 ± 9.5 (123.5 – 139.3) 1.1, 0.06
21394, 8	5.6 ± 0.8 (4.9 – 6.3) 0.05, 0.8	228 ± 23.4 (208.4 – 247.6) 0.51, 0.2	30.7 ± 10.9 (21.7 – 39.9) 0.46, 0.22	63.8 ± 11.7 (54 – 73.6) 0.49, 0.26	46.6 ± 4.5 (42.9 – 50.4) 0.14, 0.49	138.4 ± 14.7 (126.1 – 150.7) 0.38, 0.34
19429, 10	5.8 ± 0.5 (5.4 – 6.2) 0.24, 0.52	218.4 ± 20.4 (201.4 – 235.5) 0.04, 0.85	30.2 ± 7.5 (23.9 – 36.5) 0.49, 0.095	65.3 ± 11.3 (55.8 – 74.7) 0.64, 0.17	44.1 ± 5.9 (39.2 – 49) 0.58, 0.1	**131.2 ± 16.9 *** (117 – 145.3) 0.85, 0.037
17436, 12	5.5 ± 0.7 (5 – 6.2) 0.12, 0.76	206.1 ± 26.9 (183.6 – 228.6) 0.5, 0.09	29.3 ± 7.6 (22.9 – 35.6) 0.34, 0.29	63.3 ± 8.6 (56.1 – 70.5) 0.52, 0.26	43.3 ± 5.2 (38.9 – 47.6) 0.78, 0.052	128.3 ± 29.1 (104 – 152.6) 0.74, 0.12
15452, 14	5.7 ± 0.8 (5 – 6.3) 0.02, 0.96	207.5 ± 18.4 (192.1 – 222.8) 0.56, 0.05	30.3 ± 8.9 (22.9 – 37.8) 0.45, 0.16	62.9 ± 10.7 (53.9 – 71.8) 0.42, 0.34	44.3 ± 6.7 (38.6 – 49.9) 0.51, 0.19	130.3 ± 29.5 (105.6 – 154.9) 0.64, 0.14
13486, 16	5.6 ± 0.8 (4.9 – 6.2) 0.14, 0.69	212.6 ± 27.5 (189.6 – 235.6) 0.2, 0.52	30.3 ± 8 (23.6 – 37) 0.48, 0.17	60.4 ± 7.6 (54.1 – 66.8) 0.21, 0.61	46.2 ± 7 (40.3 – 52) 0.18, 0.52	135.1 ± 16.2 (121.5 – 148.7) 0.6, 0.13
11512, 18	5.2 ± 0.8 (4.6 – 5.9) 0.52, 0.1	210.1 ± 19.3 (193.9 – 226.3) 0.4, 0.18	30.9 ± 7.7 (24.5 – 37.4) 0.6, 0.085	60.4 ± 6.6 (54.9 – 65.9) 0.22, 0.53	44.2 ± 6.4 (38.8 – 49.5) 0.54, 0.13	132 ± 22.2 (113.4 – 150.6) 0.67, 0.12
9535, 20	5.8 ± 0.9 (5 – 6.5) 0.09, 0.81	211.5 ± 15.1 (198.9 – 224.2) 0.37, 0.39	30.6 ± 9.4 (22.8 – 38.5) 0.49, 0.14	59.3 ± 7.1 (53.3 – 65.3) 0.08, 0.77	45.7 ± 6 (40.7 – 50.8) 0.29, 0.3	136.7 ± 17.4 (122.2 – 151.3) 0.46, 0.12
Ground, 30	5.8 ± 1.2 (4.8 – 6.8) 0.1, 0.81	210.2 ± 24.2 (189.9 – 230.4) 0.35, 0.43	31.4 ± 11 (22.2 – 40.6) 0.53, 0.22	61.8 ± 11.6 (52.2 – 71.5) 0.31, 0.27	46.1 ± 4.8 (42.1 – 50.1) 0.24, 0.68	130.2 ± 24.1 (110.1 – 150.3) 0.74, 0.16

Table I. Comparing the changes in the oculometric and cognitive performance throughout the flight profile at pre-determined altitudes. Note: * indicates p <= 0.05 in comparison with baseline.

Captions for figures:

Figure 1: (a) The mental workload task in the form of modified King-Devick (K-D) test card (only middle 4 rows of Card #2 consisting of 20 numbers). (b) The raw eye-tracking scan-paths with saccades (in blue) and fixations (in red).

Figure 2: (a) PaO_2 and (b) $PaCO_2$ levels through the simulated flight profile (n=8) from 30000 ft to ground level (recompression) in 30 minutes. The data points indicate mean, and error bars indicate one standard deviation.

Figure 3: The relationship between fixation-related features (left Y-axis) and PaO_2 (right Y-axis) during the simulated flight profile from 30000 ft to ground level (recompression) in 30 minutes. (a) Fixation Time and (b) Fixation Size. (Note: * indicates $p <= 0.05$; ** indicates $p < 0.01$. On each box, the central mark indicates the median, and the bottom and top edges of the box indicate the 25th and 75th percentiles, respectively. The whiskers extend to the most extreme data points.)

Figure 4: The relationship between saccade-related features (left Y-axis) and PaO_2 (right Y-axis) during the simulated flight profile from 30000 ft to ground level (recompression) in 30 minutes. (a) Total saccadic movement, (b) Horizontal saccadic velocity (in-between numbers), and (c) Oblique saccadic velocity (in-between lines) (Note: * indicates $p <= 0.05$; ** indicates $p < 0.01$. On each box, the central mark indicates the median, and the bottom and top edges of the box indicate the 25th and 75th percentiles, respectively. The whiskers extend to the most extreme data points.)