Effects of Normobaric Hypoxia on Oculomotor Dynamics of Aviator Students During a Simulated Flight Task

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Table of Contents

1. INTRODUCTION

In 1862, James Glaisher and Henry Coxwell were the first humans to ascend above 29,000 ft (8839 m). This flight documented one of the first reports of aviation hypoxia and almost contributed to the death of both aeronauts (Deussing, Artino, & Folga, 2011; Doherty, 2003). Hypoxia has remained one of the most dangerous risks in aviation since the pioneering days of flight and is the primary environmental factor (Cable, 2003).

Hypoxia occurs when the body's tissues are unable to obtain adequate oxygen (Hackett & Roach, 2004). As altitude increases, barometric pressure decreases exponentially, resulting in a decreased pressure of oxygen or ambient partial pressure of oxygen (PO_2). Reduced PO_2 decreases the partial pressure of oxygen in the alveoli (PaO_2) and the percentage of binding sites carrying oxygen in the blood, known as oxyhemoglobin saturation (SpO_2); ultimately, reducing the slope of the oxygen transport cascade in what is known as hypobaric hypoxia (HH) (Coppel, Hennis, Gilbert-Kawai, & Grocott, 2015; Deussing et al., 2011; Richard & Koehle, 2012). Stimulation of the carotid bodies activates an autonomic compensatory response through the release of neurotransmitters, which leads to increased alveolar respiration, producing alkalosis, through increased heart rate (HR) and cardiac output (Marconi & Cerretelli, 2008; Shukitt-Hale, Banderet, & Lieberman, 1998). Also, redistribution of blood flow into the intracellular fluid compartment and the respiratory system from other regions of the body, such as the brain, leads to decreased blood plasma volume (McMorris, Hale, Barwood, Costello, & Corbett, 2017).

Above 7,600ft (2316 m), where atmospheric pressure is 560 mmHg, and PaO_2 falls to 60 mmHg, sympathetic response-driven increased cerebral blood flow cannot fully overcome the lack of O_2 (McMorris et al., 2017). Normobaric hypoxia serves as a practical laboratory

alternative utilizing air with a lower percentage of oxygen (FiO_2), which produces a comparable physiological response and approximate HH experience (Conkin, 2011). Proper brain function and cognition, which require oxygen activation at every stage (Virués-Ortega, Buela-Casal, Garrido, & Alcázar, 2004), are needed to operate an aircraft and is negatively affected in low oxygen environments (Lutz, Nilsson, & Prentice, 2003). Hypoxia leads to impaired vision, cognition, and motor control functions, which can negatively affect performance and become deadly if the pilot becomes incapacitated (Petrassi, Hodkinson, Walters, & Gaydos, 2012; Temme, Still, & Acromite, 2010).

Cabel et al. 's (2003) review of hypoxia incidents in military aircraft reported 656 hypoxia-related physiological episodes (PE) from 1967 to 1990 in the U.S. Air Force and 40 aircraft PEs with 67 fatalities reported by the U.S. National Transportation Safety Board. In more recent years, after temporarily grounding multiple aircraft fleets, a military report to Congress (2017) revealed an increase in PEs involving oxygen deficiency, cognitive impairment, and loss of consciousness. The Air Force recorded hypoxia-related PEs in the F-35A strike fighter (5 from one base and 10 others from 2011 to 2017), the F-22 (12 incidents between 2008 and 2011), the F/A-18 (297 events from May 2010 to October 2015), and the T-45 trainer (10 episodes in one month) (Cable, 2003). In response, pilots began appearing on news and media outlets expressing their safety concerns, boycotting training duties, and refusing to fly until the onboard oxygen generation systems were corrected. Although hypoxia-related incidents in military aircraft are more common at altitudes above 12,500 ft (3810 m), they have occurred at lower than 10,000 ft (Cable, 2003; Gertler, 2017; Ostrander, 2005).

In general aviation (GA) populations, there is a misconception that pilots are not at risk of experiencing hypoxia since most GA aircraft are incapable of reaching higher altitudes where

supplemental oxygen is required. However, hypoxia has been shown to affect pilot performance below simulated laboratory exposures of 12,500 ft (3810 m) (Nesthus, Rush, & Wreggit, 1997). Moreover, there is evidence to suggest that many common real-world cases of hypoxia may go unreported in both military and general aviation (Deussing et al., 2011; Holt et al., 2019).

Despite advancements in aviation technology through the implementation of oxygen breathing systems, pressurized cabins, physiology training, aircrew procedures, and warning systems; hypoxia continues to be a significant hazard in military and commercial aviation (Cable, 2003; Deussing et al., 2011; Temme et al., 2010; Thropp & Buza, 2018). When onboard oxygen systems fail, early-onset hypoxia identification is critical to alert the pilot and allow sufficient time of useful consciousness before incapacitation occurs (Kowoll, Welsch, Joscht, & Gunga, 2006). Eye-tracking (ET), linked to pilot tasks, could serve as a reliable, sensitive, objective, and non-verbal solution for pilot monitoring (Collewijn, Van der Mark, & Jansen, 1975; Stepanek et al., 2014).

In military and civilian aviation, it is well known that visual performance is negatively affected by hypoxia, and the visual system has been shown to serve as a means of monitoring the central nervous system and detecting brain states (Di Stasi & Diaz-Piedra, 2019; Di Stasi et al., 2013; Kowoll et al., 2006; McIntire, McKinley, McIntire, Goodyear, & Nelson, 2013; Stepanek et al., 2014; Thropp & Buza, 2018). Compact, portable ET systems can measure changes in oculomotor dynamics, which serve as a tool for detecting hypoxia-related brain activity (Stepanek et al., 2014; Thropp & Buza, 2018). Eye-movement consists of fixations and saccades. A fixation is a relatively stationary pause in eye-movement over an area of interest, while a saccade is a rapid eye movement that guides the fovea between two fixations (Findlay, 2009; Salvucci & Goldberg, 2000).

There are few studies on aviation-related hypoxia and ET (Peißl, Wickens, & Baruah, 2018). Of the few studies utilizing ET for hypoxia detection, there is disagreement and mixed results concerning specific eye metrics as a means to measure hypoxia (Kowalczuk et al., 2016; Stepanek et al., 2014). Previously used to detect substance use (Masson et al., 2000), cerebral activation, arousal (Di Stasi, Catena, Canas, Macknik, & Martinez-Conde, 2013), fatigue (Di Stasi et al., 2013; Diaz-Piedra et al., 2016), and sleep deprivation (Rowland et al., 2005), saccadic velocity measures aviator impaired states; however, recent studies show mixed results (Cymerman, Muza, Friedlander, Fulco, & Rock, 2005; Peißl, Wickens, & Baruah, 2018; Thropp & Buza, 2018).

During the slow ascent to high altitude, Cymerman et al. (2005) reported an increase in saccadic velocity, while Merz et al. (2013) did not observe any saccadic velocity changes. In acute hypoxia exposure studies, authors reported increased total saccadic time and increased intersaccadic drift velocity (Di Stasi et al., 2014), while other studies did not observe changes in saccadic movements (Kowalczuk et al., 2016; Stepanek et al., 2014). In a reduced oxygen breathing study, Van der Post et al. (2002) measured decreased peak velocity of large amplitude saccades when subjects experienced mild hypoxia. Thropp et al. (2018) noted variations in multiple eye metrics during slow decompression, observing a decrease in saccadic velocity.

Previous investigations have employed several different means of inducing hypoxia exposures under various settings and tasks; however, due to the complexity of ET, many of these studies have not been able to test eye metrics in an aviation applied task. The development of infrared camera-based ET systems has provided a technology that is more accessible, unobtrusive, less expensive, and more suitable for monitoring pilots during tasks (Di Stasi et al., 2014; Stern, Boyer, & Schroeder, 1994). Continuous ET to detect pilot's brain states could

potentially serve as an opportunity to improve pilot safety (Peißl et al., 2018) Therefore, the purpose of this study was to investigate saccadic velocity changes driven by acute normobaric hypoxia, measured with a lower resolution, infrared-based ET, during a simulated flying task; which does not appear to have been previously investigated.

2. HYPOTHESIS

The authors hypothesized that mean saccadic velocity will increase in conjunction with the sympathetic response when pilots are subjected to normobaric hypoxia during the simulated flight. Further, this study helped determine (1) if saccadic velocity was a valid biomarker to detect hypoxia, (2) if ET was feasible to implement during a simulated flight protocol, and (3) to attain a better understanding of the capabilities of oculomotor measures, coupled with other physiological measures.

3. METHODS

Ethical Approval

Before data collection, this study was approved by the Liberty University IRB (IRB# 4074 - approved: December 16th, 2019). Written informed consent was obtained from each participant before participating in this study.

Experimental Design

Participants performed one familiarization trial and three experimental trials within a single test day. Exposure to three levels of simulated (normobaric) altitudes served as the three environmental conditions (EC). The three EC's were single-blinded and served as the within-subjects' factors and included sea level (LA) at 0 ft (20.9% FiO_2), moderate altitude (MA) at 12,500 ft (12.9 % FiO_2), and high altitude (HA) at 19,000 ft (10.1% FiO_2). The first and third

trials were conducted at LA, and the second and fourth trials were counterbalanced between MA and HA. Saccade average peak velocity (SAPV) was collected at the beginning of Legs 1, 3, and 7 of the flight protocol.

Participants

Participants were all active Liberty University School of Aeronautics students with a minimum of a private pilot rating with an instrument add on. The descriptive data characteristics of the participants (11 males, 2 females) were height (cm) (176.85 ± 8.27), total body mass (kg) (80.49 ± 15.54), body fat (%) (22.54 ± 8.85), and age (y) (21.38 ± 3.5). Their mean total logged flight hours were 189.02 (range: 99.5 - 300).

Procedures

All Participants had a valid FAA medical certificate and were screened for disqualifying medical issues such as respiratory, cardiovascular, and digestive concerns. Participants completed a health history questionnaire and a physical activity readiness questionnaire before the study. Participants were nonsmokers, and dietary restrictions before trials were not imposed. Participants were tested individually. Participants were excluded, or data collection was postponed if symptoms of cold, flu, sinus congestion, nausea, upset stomach, or heartburn were reported. To preclude possible diurnal effects, all participants were tested between 1400- and 1800-hours local time. Participants were informed that they would be experiencing hypoxia-like symptoms during the simulated flight but were not kept aware of their current SpO_2 levels during the tests.

All familiarization, paperwork, data collection, and testing procedures were conducted on Liberty University's campus at the Human Performance Lab in the Center for Natural Sciences, and at the School of Aeronautics in Demoss Hall (Elevation: 282 m / 925 ft; Barometric

Pressure: 98KPa). Forms filled out by the participants communicated the risks, benefits, and confidentiality protocols of the study. The researchers informed the participants they were free to drop out of the study, ask any questions, and voice any concerns at any time. After completing the paperwork, participant's anthropometric measurements, including body fat percentage, height (cm), and weight (kg), were collected via a Seca medical scale (SECA, Chino, USA) with measurement rod attached and an Inbody 770 (Inbody, Cerritos, CA). Once the paperwork and anthropometric measurements were completed, a date was scheduled for the participant to complete the four trials at the School of Aeronautics in Demoss Hall.

Participants were tested individually. Before each trial participants donned a Sentec Transcutaneous CO_2 and pulse oximeter (carbon/dioxide and oxygen blood saturation, Sentec Inc., Therwil Switzerland) and a Zephyr BioModule chest strap (Bioharness, Zephyr Technology Corp., Annapolis, MD), which collected the participant's HR and respiration rate (RR). After donning the equipment, participants completed a 24-Hour History Form and were briefed on flight simulation tasks, safety protocols, and expectations. The participant then sat down and familiarized his/her-self with the certified Advanced Aviation Training Device (AATD) flight simulator (Piper Arrow PA-28; Frasca Simulations International, USA) equipped with a GNS 430 GPS, HSI, Single VOR, ADF, Transponder, and an S-Tec autopilot. The aircraft simulated conditions were 15°C and standard pressure.

A facemask covering the nose and mouth was fitted onto the participant and checked for an airtight seal, and then the ET system (Tobii Wireless II; Tobii Technology, Stockholm, Sweden) was donned and calibrated. The ET system consisted of a head-mounted glasses unit and a wire attached recording unit. Four cameras captured gaze data at a sampling frequency of 100 Hz while one full HD wide-angle scene camera captured participants' forward field of view.

The device used corneal reflection, binocular, and dark pupil measurement techniques. One-point calibration validation, parallax compensation, automatic slippage compensation, and 3D eye model tracking technique allowed accurate ET data collection during the flight simulation task. The pre-determined altitude exposure of either LA, MA, or HA was delivered with an oxygen extracting apparatus (MAG-10 Altitude Generator, Higher Peak, USA) via a face mask, expansion buffer bag, breathing bag, and O_2 analyzer at the beginning of each trial. 6 participants were exposed to EC's in the order of MA, LA, then HA, while 7 participants were exposed to EC's in the order of HA, LA, and then MA.

Participants then completed the four 10-minute flight trials with at least 8 minutes of recovery between trials to allow time for the oxygen extracting apparatus to produce the subsequent simulated altitude exposure and to allow the participant to recover fully. The participant was deemed recovered when SpO_2 levels reached baseline. Participants were instructed to take flight controls ten seconds before the start of the test. Participants followed a modified pattern B protocol, which was displayed on a piece of paper to communicate the specific headings and flight protocols, both graphically and with text. The flight simulator operator counted down before each flight maneuver to ensure each participant kept on pace with the tracking software to eliminate as many extraneous variables as possible.

For each trial, physiological biomarkers were collected at the beginning of Legs 1, 3, and 7. ET gaze data was collected during the first 30 seconds of Legs 1, 3, and 7. These time points occurred during identical task conditions where the pilot was directed to fly straight (holding a constant airspeed, heading, and altitude). Changes of eye position were extracted by the Tobii system and used to calculate the angular velocity of the eye. Fast eye movements with an angular

velocity above the 30° · s−1 threshold were classified as saccades (Zee, 1999). SAPV was calculated by averaging all saccades that exceeded this threshold within the 30-second window.

During the flight trial, participant's SpO_2 and HR were monitored, and the test was stopped if: (1) SpO_2 reached 75% or lower, (2) SpO_2 fell below 80% for longer than 2 minutes, (3) SpO_2 fell below 85% for longer than 5 minutes, or (4) the participant reached a max HR (220-age).

After the participant completed the 10-minute flight task, the test was ended, and the simulator data card information was retrieved. A flight performance score was calculated based on the participant's ability to control the aircraft inside of the designated altitude, heading, rate of turn, and airspeed parameters using Frasca's nationally utilized NIFA scoring module (National Intercollegiate Flying Association). Deviation outside of these parameters negatively impacted flight performance scores. After completion of each flight simulation task, a researcher detached the air tube, and the participant completed post-trial questionnaires during recovery.

Statistical Analyses

Data were analyzed using SPSS version 25 (IBM, New York, USA). A 3 (EC) x 3 (Legs 1, 3, 7) repeated-measures Analysis of Variance (ANOVA), with two within-subjects factors (altitude and Leg), was used to analyzes the effects of normobaric hypoxia on the dependent variables (e.g., SAPV, SpO_2, HR, RR). A Greenhouse Geiser adjustment was made to the ANOVA degrees of freedom when the assumption of sphericity was not satisfied.

4. RESULTS

HR: A repeated measures ANOVA revealed a statistically significant difference in the main effect of Altitude on HR among LA, MA, and HA (93.152 ± 5.349, 98.515 ± 5.402, and 104.424 ± 4.131 /min) $p<0.001$. There was also a statistically significant difference in the main

effect of Leg on HR among L1, L3, and L7 (92.818 ± 5.197, 99.939 ± 4.945, and 103.333 ± 4.766 /min) $p<0.001$. There was a statistically significant interaction between Altitude x Leg for HR among LAL1 and LAL3 (91.182 ± 5.150, 92.818 ± 5.842 /min) at $p=.050$, MAL1 and MAL3 (93.909 ± 6.094, 98.636 ± 5.348 /min) at $p=0.022$, MAL1 and MAL7 (93.909 ± 6.094, 103.000 ±5.034 /min) at $p<0.001$, HAL1 and HAL3 (93.364 ± 4.611, 105.727 ± 4.376 /min) at $p<0.001$, HAL1 and HAL7 (93.364 ± 4.611, 103.000 ± 5.034 /min) at $p<0.001$, and HAL3 and HAL7 (105.727 ± 4.376, 114.182 ± 4.015 /min) $p=0.002$.

RR: A repeated measures ANOVA revealed there was a statistically significant difference in the main effect of Leg on RR between L1 and L3 (15.455 ± .771, 17.636 ± .989 /min) $p=0.027$ and L1 compared to L7 (15.455 ± .771, 19.152 ± 1.410 /min) $p=0.025$.

SpO_2: A repeated measures ANOVA revealed a statistically significant difference in the main effect of Altitude on SpO_2 among LA, MA, and HA (96.394 ± .324, 91.909 ± .392, and 87.091 ± .511) $p<0.001$. There was a statistically significant difference in the main effect of Leg on SpO_2 among L1, L3, and L7 (96.758 ± 0.331, 91.394 ± 0.356, and 87.242 ± 0.505) $p<0.001$. There was a statistically significant interaction between Altitude x Leg for SpO_2 among LAL1 and LAL3 (96.727 ± 0.359, 96.273 ± 0.384) at $p=0.025$, MAL1 and MAL3 (96.909 ± 5.150, 92.818 ± 5.842) at $p<0.001$, MAL1 and MAL7 (96.909 ± 5.150, 87.455 ± 0.608) at $p<0.001$, MAL3 and MAL7 (91.182 ± 5.150, 87.455 ± 0.608) at $p<0.001$, HAL1 and HAL3 (96.636 ± 0.364, 86.545 ± 0.824) at $p<0.001$, HAL1 and HAL7 (96.636 ± 0.364, 78.091 ± 0.868) at $p<0.001$, and HAL3 and HAL7 (86.545 ± 0.824, 78.091 ± 0.868) at $p<0.001$.

SAPV: A repeated measures ANOVA revealed a statistically significant difference in the main effect of Leg on SAPV between L1 and L7 (187.724 ±11.023, 173.349 ± 11.002, p=.046 deg/sec).

5. DISCUSSION

The present study was conducted to investigate saccadic velocity changes driven by acute normobaric hypoxia during a simulated flying task. The results of this study did not support our hypothesis as statistically significant changes to SAPV were not observed during normobaric hypoxia exposure. However, our research did demonstrate accurate detection of saccadic velocity during an instrument guided simulated flying task while using an oxygen mask to induce normobaric hypoxia is feasible.

The aviation community's national focus on the current state of hypoxia-related PE's, sparked by the uptick in fatalities, fleet grounding, and incidents, indicates that hypoxia remains a significant threat to pilots, aircrews, and national defense. Additionally, ET metrics and continuous pilot monitoring have shown promise as an indicator of operator cognitive states during flight tasks.

An increase in participant's HR was observed in response to reduced FiO_2 exposure leading to decreased SpO_2 levels, which is consistent with previous research (Nesthus, Rush, & Wreggit, 1997; Richard & Koehle, 2012; Truszczynski, Wojtkowiak, Biernacki, & Kowalczuk, 2009). These trends continued as the duration of exposure increased. Acute altitude exposure has been demonstrated to induce an autonomic nervous system response, which causes an increase of HR and blood pressure to combat the reduced PO_2 and maintain adequate tissue oxygenation (Bernardi et al., 1998; Hainsworth et al., 2007). Independent of EC, there was a statistically significant difference in HR between Leg 1 and Leg 3, indicating the flight task stressed

participants. A decrease in SpO_2 varied between participants and between the two levels of hypoxic exposure. Consistent with previous findings, the rate at which SpO_2 drops depends on the degree of the hypoxic stress (Harding & Mills, 1983). With no statistically significant changes observed in RR between hypoxic and baseline levels of altitude exposure, it is evident that participants compensated for the decrease in oxygen availability by increasing cardiac output rather than ventilation.

There were no observed differences in SAPV for the two hypoxia EC's compared to the baseline condition. The observed SAPV measurements of the current study support previous findings, which also observed no statistically significant differences in SAPV during hypoxic exposure (Cymerman et al., 2005; Di Stasi et al., 2014; Kowalczuk et al., 2016; Merz et al., 2013). The current findings contradict previous studies reporting increases and decreases in SAPV (Thropp & Buza, 2018; Van der Post et al., 2002). Van der Post et al. (2002) and Cymerman et al. (2005) did not account for participant's fatigue levels, which may have led to the contradicting results (Di Stasi et al., 2014). Although there was no statistical difference in SAPV observed in the present study between hypoxia and baseline exposures, there was a statistical difference between Legs 1 and 7. Therefore, observed changes in the current study support the conclusion of Di Stasi et al. (2012) that time on task decreases SAPV independent from hypoxia exposure and serves as an indicator of mental fatigue. The differences in SAPV response could also be attributed to the differences in task demands. Studies utilizing fast-paced reading, tracking, and reaction time tasks could have influenced SAPV by demanding larger saccades than what is required for instrument scanning in the current study (Thropp & Buza, 2018). The decrease in SAPV observed by Thropp et al. (2018) could be attributed to the gradual hypoxic exposure, which differed from the current study's acute exposure protocols.

Additionally, there is evidence to suggest that the body responds differently to normobaric and hypobaric altitude equivalent exposures (Coppel et al., 2015; Richard & Koehle, 2012). Normobaric induced hypoxia in the present study may have produced a less severe hypoxic stress compared to a hypobaric altitude equivalent. For example, Coppel et al. (2015) observed differences in physiological biomarkers (minute ventilation and nitric oxide levels) between the two methods of altitude exposure.

Using NH, instead of HH, may have mitigated the magnitude of the sympathetic nervous response, which was hypothesized to induce increased SAPV. Due to the subject group's availability, another limitation arose with the testing of all three exposures on the same data collection day, as opposed to a longer multi-day recovery. Hypoxic stress during Trials 2, 3, and 4, may have produced a dampened response to the repeated exposures due to normalization. With some participants expressing confusion on the task scoring system and others having more experience with the flight task, differences in arousal and mental work-load may have produced another limitation. Although this study design allowed for adequate recovery between hypoxic exposures and while testing on the same day, this limitation may have affected the results of the metrics analyzed. One participant's biomarkers and ET data were not collected for Leg 7 of HA due to the implementation of stoppage protocols. One participant's biomarkers were not collected due to a change in protocols. One Participants HR during HA was not collected on Leg 1 due to researcher error.

6. CONCLUSION

In summary, we found SAPV to be affected by time on task independent of acute normobaric hypoxia exposure. This finding provides further understanding of specific eye movement metrics as they relate to cognitive function and physiological response of operators to

flying tasks. Efforts to understand objective eye movements as indicators of operator brain states have shown inconsistent results but still merit further study. Future studies should be conducted using participants with similar levels of experience and familiarity with the flight task and protocols. Although SAPV was not shown to detect early changes in pilot hypoxia exposure, other saccadic and fixational eye metrics should be tested in cockpit environments using visually guided flight tasks.

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