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## The physiological effects of acute and ramp hypoxic exposure during simulated flight tasks

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THE PHYSIOLOGICAL EFFECTS OF ACUTE AND RAMP HYPOXIC EXPOSURE  
DURING SIMULATED FLIGHT TASKS

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Dean of the Graduate School

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2023

THE PHYSIOLOGICAL EFFECTS OF ACUTE AND RAMP HYPOXIC EXPOSURE  
DURING SIMULATED FLIGHT TASKS

by

JASMIN RENEE JENKINS, BS, MS

DISSERTATION

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The University of Texas at El Paso  
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for the Degree of

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## Abstract

The purpose of the present study was to examine the effects of hypoxia at simulated altitudes of  $\text{FiO}_2$  15.4% (8000' equivalent),  $\text{FiO}_2$  13.2% (12,000' equivalent), and a Ramp Hypoxic exposure on perceived workload, cardiovascular activity, electrodermal activity, oximetry, and flight simulator performance. A total of 17 participants (10 female & 7 males; mean  $\pm$  SEM, age  $24.82 \pm 1.6$  yrs, BMI  $25.87 \pm 1.0$ ) who were apparently healthy, asymptomatic, and physically active performed 3 flight tasks using a video game head-mounted display (HMD) flight simulator while exposed to simulated altitudes of Normoxia,  $\text{FiO}_2$  15.4%,  $\text{FiO}_2$  13.2% and a Ramp Hypoxic Exposure (breathing at 8,000 ft altitude for 5 minutes before being exposed to 12,000 ft altitude during the flight simulation) in randomized single-blinded order. Physiological measures and questionnaires were collected to monitor vagal state throughout each simulated altitude condition. The results indicated that acute hypoxic exposure decreased ( $p \leq 0.05$ ) in time- and frequency-domain measures of heart rate variability (HRV). Acute hypoxic exposure decreased ( $p \leq 0.05$ ) Peripheral Oxygen Saturation ( $\text{SpO}_2$ ), which indicated a significant ( $p \leq 0.05$ ) decrease in oxygen availability during each hypoxic exposure. Simulated flight tasks showed a decrease in Electrodermal Activity (EDA) skin conductance which indicated reduced hand sweat during the Course and Landing Tasks compared to the Math Task. Analysis of neuromuscular activity using electromyographic (EMG) techniques showed an increase ( $p \leq 0.05$ ) in motor unit activation (EMG RMS) and an increase ( $p \leq 0.05$ ) in motor unit action potential conduction velocity (EMG MPF) during the Course Task. These results raised the possibility of increased neck strain during particular flying activities, which may occur regardless of exposure to hypoxia. Although, flight performance was not altered during hypoxic exposures, the scores of the symptom questionnaires indicated a greater incidence of hypoxic and simulator sickness during the Math Task. When

compared to the other simulated Flight Tasks, the Math Task was found to have the highest workload, with subscores of mental and temporal demand having the lowest performance ratings. This study demonstrates the complex interplay among simulated altitude exposures, physiological responses, and cognitive performance during flight tasks. The stability observed in flight performance at mild hypoxic exposures suggested that potential performance impairments may manifest more prominently under severe hypoxic conditions. The cardiovascular stability noted in this study may be attributed to an effective baroreflex reset in response to hypoxia, underscoring the adaptive nature of the autonomic nervous system. If true, this may represent the adaptive nature of the autonomic nervous system. Moreover, the study highlights the ergonomic implications of using technologies HMD's in flight simulators, as prolonged use has been associated with neck pain and fatigue. In summary, simulated altitude exposures and their impact on the physiological responses, cognitive performance, and pilot well-being provides valuable insights into the effects of low-level hypoxic exposure on these variables. This study contributes new information on the effects of hypoxia's influence on human performance in aviation, paving the way for more targeted and comprehensive investigations in the future to enhance safety and optimize pilot well-being.



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## Chapter I - Introduction

Aerospace medicine practitioners specialize in enhancing human performance and integrating human systems, focusing on mitigating unique hazards in the aviation environment. Often regarded as the "Father of Aviation Medicine," Dr. Theodore Lyster revolutionized aviation medicine by introducing flight surgeons and establishing research laboratories.<sup>1</sup> Today, flight surgeons play a crucial role in providing primary care for pilots and military aviation personnel on special duty status within squadrons.

Stress adversely affects flying skills, impacting psychomotor, working memory, and attentional cognitive components.<sup>2,3</sup> Monitoring physiological status, such as electrodermal activity (EDA), enables stress evaluation during aviation tasks, facilitating pre-exposure training for high-stress scenarios crucial for maintaining performance skills.<sup>4-6</sup> Incorporating chaos theory into physiological systems adds a layer of complexity to our understanding. Chaos theory, originally studied in mathematics and physics, is also used in biological systems research. Chaos theory uses non-linear dynamics to measure the sensitivity to initial conditions and the emergence of seemingly random behavior, with the aim of revealing the underlying order.<sup>7</sup> When applied to physiological systems, chaos theory provides insights into the dynamics of the Autonomic Nervous System (ANS), which includes the Sympathetic Nervous System (SNS) and Parasympathetic Nervous System (PNS).<sup>8</sup>

Key aspects of chaos theory, such as non-linear dynamics, sensitivity to initial conditions, and the emergence of complex patterns, resonate with the intricate interplay between the SNS and PNS in maintaining homeostasis.<sup>7</sup> Cardiovascular sympathetic efferents, including gluco-sensitive, thermo-sensitive, and baro-sensitive groups, play a crucial role in regulating heart rate, contractility, and blood vessel tone.<sup>7</sup>

The robustness of chaotic systems relies on stochasticity, or randomness, which underlies the intrinsic randomness in ANS dynamics.<sup>7</sup> Physiological stability integrates real random fluctuations, and perturbations may induce system oscillations, returning to the same endpoint.<sup>7</sup> The cardiac system, a part of the ANS, can be perturbed in many ways, changing the system dramatically.

In modern aviation, military pilots operate sophisticated technology in extreme environments, which necessitates the early detection of clinically relevant variations or abnormalities that may impair their performance. Acute hypoxic exposure poses a significant physiological threat due to the exponential decrease in barometric pressure at high altitude.<sup>9</sup> The concentration of oxygen in the atmosphere remains relatively constant at around 21% at sea level, irrespective of altitude. However, as one ascends from sea level to 100,000 feet, although the percentage of oxygen in the atmosphere remains constant, the overall reduction in atmospheric pressure leads to a decrease in the number of oxygen molecules available per unit volume. This results in a lower oxygen concentration, making it challenging for humans to breathe without supplemental oxygen. Dalton's law, which states that each gas mixture exerts a pressure based on its concentration independently of other gases, elucidates the specific mechanism behind this phenomenon. For instance, at sea level, the mole fraction (number of molecules) in dry atmospheric air comprises nitrogen (78.08%), oxygen (20.95%), argon (0.03%), carbon dioxide (0.04%), and trace amounts of other gases. While the concentration of these gases remains constant during altitude ascent, the concomitant decrease in barometric pressure diminishes oxygen availability in high-altitude environments.<sup>9</sup> This reduced oxygen availability directly influences arterial concentration, leading to what is termed hypoxic hypoxia.



Hypoxic physiology depends on onset rate and degree, both of which influence novel task performance and cognitive functions.<sup>9-11</sup> Altitudes of 5,000-10,000 ft induce rapid exposure, affecting heart rate and psychomotor skills.<sup>12</sup> At 10,000-15,000 ft, the hypoxic ventilatory response impacts mental alertness.<sup>10</sup> Above 15,000 ft, cognitive impairment may lead to euphoria, overconfidence, and loss of consciousness. Recognizing these stages is critical for initiating emergency procedures and avoiding the point of no return.

Advancements in computer-based technologies and virtual reality-based simulators enhance pilot training, offering realistic mission rehearsals.<sup>13, 14</sup> Pilot selection and training improvements, along with aircraft design enhancements, contribute to aviation safety.<sup>15, 16</sup> However, increasing operational demands, time constraints, and environmental factors highlight the need to understand how stressors influence physiological well-being in modern aviation.<sup>17, 18</sup>

Efforts to comprehensively characterize in-flight physiological performance using a real-time multi-sensor approach aim to detect and reduce unexplained physiological events in military pilots.<sup>19</sup> The present investigation focuses on early detection of low-grade hypoxia, with a specific emphasis on exposures occurring below 10,000 ft. The purpose of this research is to investigate the physiological and cognitive effects of a low-grade, rapid hypoxic exposure to simulate an immediate oxygen breathing device failure and an insidious Ramp Hypoxic exposure simulating a gradual oxygen leak. Furthermore, it is postulated that the Ramp exposure protocol is analogous to the acclimation process, wherein the physiological and cognitive deficits induced at higher altitudes are lessened by the immediate compensatory mechanisms' ability to maintain regular homeostatic function at low altitude levels. This research study will add to the current literature of investigating the physiological effects of hypoxia at simulated altitudes from mean seal level (MSL

) to 8000 ft and 12,000 ft. for 20 minute periods each, and during a rapid ramp exposure from MSL to 8,000 ft. for 5 minutes, immediately followed by an ascent to 12,000 ft. for 20 minutes.

## Chapter II – Literature Review

### HYPOXIC ALTITUDE EXPOSURE

#### McLellan et al., 1990

The purpose of this study<sup>20</sup> was to investigate the effect of hypoxia (mean  $\pm$  SD;  $10.8 \pm 0.6\%$  oxygen) on supramaximal dynamic exercise. Twelve men ( $27.9 \pm 3.4$  yrs,  $88.4 \pm 18$  kg,  $12.4 \pm 3.5\%$  body fat,  $52.2 \pm 6.8$  ml  $\cdot$  kg<sup>-1</sup>  $\cdot$  min<sup>-1</sup>,  $42.5 \pm 14.7\%$  vastus lateralis slow-twitch fibers) were randomly assigned to either a 30 s or 45 s Wingate test on a mechanically-braked cycle ergometer. The resistance was set to perform 4.4 J of work  $\cdot$  kg<sup>-1</sup> body weight. At the same time, power output (watts), peak power output (PPO), mean power output (MPO), and fatigue index (FI) were reported variables of interest. Participants were exposed to normobaric hypoxic concentration at  $10.8 \pm 0.6\%$  or normoxic conditions in a balanced order. Open circuit spirometry assessed total  $\text{VO}_2$ , carbon dioxide production ( $\text{VCO}_2$ ), and expired ventilation ( $\text{V}_E$ ). In addition, blood samples were taken before and after a 5-minute warm-up, before and after the Wingate test, and at 3, 5, 8, and 10 minutes after exercise for analysis of lactate, pH, and blood gases. The results indicated a reduced oxygen saturation in hypoxia (30s  $83.0 \pm 2.7\%$ ; 45s  $83.3 \pm 0.8\%$ ) compared to normoxia (30s  $98.7 \pm 0.5\%$ , 45s  $97.0 \pm 1.8\%$ ) in both Wingate durations. The  $\text{VO}_2$  was lower in hypoxia ( $1.71 \pm 0.21$  L) compared to normoxia ( $2.16 \pm 0.26$  L) only in participants performing the 45s Wingate. There was no difference between condition or Wingate duration for any power variable. Blood lactate concentrations were greater in the hypoxic conditions for after the 30s ( $67.5 \pm 7.9$  mmol  $\cdot$  kg<sup>-1</sup> dry weight) and 45s ( $66.6 \pm 42.0$  mmol  $\cdot$  kg<sup>-1</sup> dry weight) compared to after the 30s ( $27.1 \pm 16.9$  mmol  $\cdot$  kg<sup>-1</sup> dry weight) and 45s ( $34.6 \pm 19.1$  mmol  $\cdot$  kg<sup>-1</sup> dry weight) in the normoxic condition. The authors concluded that supramaximal exercise is not affected by hypoxia,

suggesting the respiratory alkalosis associated with breathing the hypoxic gas could account for the increased rate of muscle LA accumulation.

McLellan et al., 1993

The purpose of this study<sup>21</sup> was to investigate respiratory alkalosis while hypoxic and the effect on a 45s supramaximal dynamic exercise test. The first experiment, 12 men (mean  $\pm$  SD, 26.3  $\pm$  4.7 yrs, 79.9  $\pm$  8.1, 1.77  $\pm$  0.05 m, 49.4  $\pm$  8.3 ml  $\cdot$  kg<sup>-1</sup>  $\cdot$  min<sup>-1</sup>) performed a 45s supramaximal Wingate test breathing normoxic (20.9% oxygen), hypoxic (11.3% oxygen), and normocapnic hypoxic (H+CO<sub>2</sub>; 11.5% oxygen and 2.25% carbon dioxide) gas mixture for 20-min before to performing the Wingate Test. Open circuit spirometry was used to measure total ventilation volume, CO<sub>2</sub> production, and VO<sub>2</sub>, along with blood samples for analysis of lactate, pH, and blood gases. The second experiment included 9 of the previous participants (23.3  $\pm$  3.7 yrs, 74.7  $\pm$  9.5 kg, 1.81  $\pm$  0.08 m, 48.5  $\pm$  6.0 ml  $\cdot$  kg<sup>-1</sup>  $\cdot$  min<sup>-1</sup>) where prior to the Wingate they breathed normoxic gas for 20-minutes or the hypoxic gas for 10, 20, or 30-minutes. The same variables were collected as in the first experiment. The results of the first experiment indicated that VO<sub>2</sub> in the hypoxic (1.22  $\pm$  0.23 L) and normocapnic hypoxic (1.12  $\pm$  0.18 L) conditions were different from the normoxic (1.78  $\pm$  0.18 L) condition, and that the hypoxic differed from the normocapnic condition. The mean power output was reduced in both the hypoxic (6.8  $\pm$  0.6 W  $\cdot$  kg<sup>-1</sup>) and normocapnic hypoxic conditions (6.8  $\pm$  0.6 W  $\cdot$  kg<sup>-1</sup>) compared to the normoxic condition (7.0  $\pm$  0.6 W  $\cdot$  kg<sup>-1</sup>). Blood pH was greater immediately before (7.46  $\pm$  0.02) and after (7.39  $\pm$  0.05) the Wingate compared to other time points within the hypoxic condition and was lower immediately after (7.35  $\pm$  0.03) the Wingate compared to before but was greater compared to other periods during recovery in the normocapnic hypoxic condition. The results of the second experiment indicated a decrease in peripheral oxygen saturation, VO<sub>2</sub>, and mean power output while breathing the hypoxic gas

mixture 10, 20, and 30 minutes before the Wingate compared to normoxic condition. Blood gas analysis also revealed lower PCO<sub>2</sub> and pH before and after the Wingate test in all hypoxic conditions compared to the normoxic condition. There was no difference between prior hypoxic breathing length (10, 20, or 30 minutes) for any variable. The authors concluded that breathing 11% oxygen reduced mean power output during a 45s supramaximal exercise and that there was no effect of duration of breathing the hypoxic gas before the Wingate test.

#### Nishi, 2011

The purpose of this study<sup>22</sup> was to investigate in-flight oxyhemoglobin saturation (SpO<sub>2</sub>) in aircrews operating Mitsubishi UH-60J helicopters without a pressurized cabin at altitudes of up to 13,000 ft. Ten healthy male aircrew members (4 pilots and 6 nonpilots, mean 33 yrs) underwent measurements of SpO<sub>2</sub> and heart rate using finger pulse oximeters at preflight, ground level (18 ft), 5,000 ft, 8,000 ft, and 10,000 ft in a UH-60J helicopter ascending at 500-1,000 ft/min. The preflight SpO<sub>2</sub> was  $97.4 \pm 0.31\%$  and fell to  $89.2 \pm 0.63\%$  during flight at 10,000 ft, where SpO<sub>2</sub> was less at all altitudes compared to preflight. Heart rate increased from  $69.3 \pm 4.4$  bpm preflight to ground level, 5,000 ft, and 10,000 ft ( $83.3 \pm 4.0$  bpm). The author concluded SpO<sub>2</sub> decreases at altitudes over 5,000 ft in an unpressurized cabin.

#### Park et al., 2022

The purpose of this study<sup>23</sup> was to compare the effects of acute moderate hypoxia (3000 m or ~10,000 ft) and normoxia on metabolic function (skeletal muscle oxygenation), and cardiac function during endurance exercise at the same heart rate level. Twelve men (mean  $\pm$  SD,  $25.1 \pm 2.3$  yrs,  $179.9 \pm 4.4$  cm,  $83.6 \pm 13.3$  kg) performed 30 minutes of cycling exercise at 70% of maximal heart rate in randomized order during normoxia or hypoxia. Exercise load, rating of perceived exertion (RPE), metabolic function (peripheral oxygen saturation; SpO<sub>2</sub>, minute

ventilation;  $V_E$ , oxygen consumption;  $VO_2$ , carbon dioxide excretion;  $VCO_2$ , respiratory exchange ratio; RER, and oxygen pulse), skeletal muscle oxygen profiles (oxyhemoglobin; oxhb, deoxygenated hemoglobin; dxhb, total hemoglobin; tohb, and tissue oxygen saturation;  $StO_2$ ), and cardiac function (heart rate; HR, stroke volume; SV, cardiac output; CO, end-diastolic volume; EDV, end-systolic volume; ESV, and ejection fraction; EF) were assessed during the endurance exercise. The results indicated that participants exercised at a lower exercise load in the hypoxic condition to achieve the same target heart rate in normoxia. Endurance exercise in a hypoxic environment showed lower  $SpO_2$ ,  $VO_2$ , and oxygen pulse but a higher RER at the same heart rate level compared to normoxia. In addition, there was a lower  $O_2hb$  and  $thb$ , but higher  $Hhb$  during endurance exercise in the hypoxic condition. There was no difference in cardiac function between normoxic and hypoxic endurance exercise at the same heart rate level. The authors concluded that endurance exercise under simulated 3000 m resulted in a decreased exercise load, a greater metabolic function, greater muscle oxygenation response, but no change in cardiac function when compared to endurance exercise at the same heart rate level. The main finding of this study was that hypoxia increased RER and decreased  $SpO_2$ , despite a lower  $VO_2$  from a reduced exercise load at an equivalent relative intensity during endurance exercise.

Jenkins et al., 2023

The purpose of this article<sup>24</sup> was to examine the effects of a normobaric hypoxic exposure of fraction of inspired oxygen ( $FiO_2$ ) 16% and 14.3% on the 3-repetition deadlift (MDL), hand-release push-ups (HRP), and leg tuck (LTK) events of the U.S. Army Combat Fitness Test (ACFT). Fourteen participants (mean  $\pm$  SEM; 27.36  $\pm$  1.12 yrs, 1.71  $\pm$  2.79 m, 80.60  $\pm$  4.24 kg, 1 repetition maximum: 1RM 135.27  $\pm$  8.16 kg) performed the MDL, HRP, and LTK events while exposed to normoxia,  $FiO_2$  16%, and  $FiO_2$  14.3%, while measures of heart rate and total body. Peripheral

oxygen saturation (SpO<sub>2</sub>) was recorded from finger pulse oximeter after each event. Fitness tests were scored based on ACFT manual standards for each event. The results indicated SpO<sub>2</sub> was reduced at FiO<sub>2</sub> 16% and 14.3% compared to normoxia, where SpO<sub>2</sub> after the MDL and HRP events were lower in FiO<sub>2</sub> 14.3% compared to FiO<sub>2</sub> 16%. Heart rate was increased after exercise compared to rest but did not differ between conditions or events. There was no change in Scores or the number of achieved repetitions due to hypoxic exposure. The authors concluded that FiO<sub>2</sub> 16% and 14.3% did not alter performance of the three events but did decrease SpO<sub>2</sub>. Heart rate increased only after exercise but was not affected by acute normobaric hypoxic exposure.

### **Hypoxic Flight Performance**

#### Gold & Kulak, 1972

The purpose of this study<sup>25</sup> was to investigate pilot flight performance during hypoxic exposure to 12,000 ft to 15,000 ft. altitude. The study utilized seven male Federal Aviation Administration instrument-rated pilots and one rated Air Force pilot (age range 23-33 yrs) with flight experience ranging from 500 to 2,000 hours of total time and 75 to 400 hours of instrument time. A Link GAT 1 single-engine general aviation trainer was used for the participants to perform an instrument landing system (ILS) approach while exposed to  $13.0 \pm 0.25\%$  oxygen (~12,300 ft) and again at  $11.4 \pm 0.03\%$  (~15,000 ft). Participants made two consecutive runs after being exposed to hypoxia for 55 minutes for the first run and 59 minutes for the second run. Data were collected on five of 13 recorded inputs during the flight simulation: 1) air speed, 2) heading, 3) vertical velocity, 4) ILS localizer, and 5) ILS glide slope. The condition at FiO<sub>2</sub> of 13% showed an increase in "glide slope" absolute average error (8.47% of full scale) compared to sea level control (7.65% of full scale). At FiO<sub>2</sub> of 11.4% there was an increase in absolute average error for air speed (1.75 to 1.94 mph), heading (2.04 to 2.64 degrees), vertical velocity (65.37 to 74.10 ft

per minute), localizer (3.64 to 4.50% of full scale), and glide slope (7.18 to 8.48% of full scale). The authors concluded that there is a need for supplemental oxygen at or above 12,000 ft for flight crew members.

Nesthus et al., 1997

The purpose<sup>11</sup> of this study was to evaluate complex pilot performance during simulated flight in a hypoxic environment. Twenty private pilots (17 men and 3 women, mean  $\pm$  SD, age  $22.5 \pm 3.5$  yrs) with an average of 186 hours of flight experience, where half of the participants were randomly assigned to a hypoxia or control group. Participants were exposed to oxygen mixtures that simulated 8,000 ft (15.5%), 10,000 ft (14.3%), and 12,500 ft (13.0%) with balanced nitrogen, or 21% oxygen (sea level; breathing compressed air). Physiological variables of oxygen partial pressure ( $P_{tO_2}$ ), carbon dioxide partial pressure ( $P_{tCO_2}$ ), heart rate (beats per minute), and blood oxygen saturation ( $SaO_2$ ) were collected throughout. A single-engine general aviation aeromodel Basic General Aviation Research Simulator (BGARS) was used while sixteen flight performance variables were collected. The prescribed flight plan consisted of four days of flight. Day 1 was a familiarization and training day. Day 2 consisted of ascending to 4,000 ft while breathing compressed air for 45 minutes and climbing to 8,000 ft while breathing 15.5% oxygen for 45 minutes. Day 3 began with an ascent to 8,000 ft for 45 minutes, breathing 15.5% oxygen before climbing to 10,000 ft and breathing 14.3% oxygen for 45 minutes. The last day (day 5) consisted of the initial ascent to 10,000 ft while breathing 14.3% oxygen followed by an ascent to 12,500 ft breathing 13.0% oxygen. Questionnaires were administered pre- and post-flight: the Mood II scale, the Stanford Sleepiness Scale, and the Environmental Symptoms Questionnaire (ESQ-III). The NASA Task Load Index was administered only during post-flight. The results indicated tissue oxygen levels were different between the hypoxic and control groups, such that



oxygen level decreased with increasing altitude. The blood oxygen saturation decreased for the hypoxic group from breathing compressed air ( $99.00 \pm 0.68\%$ ), to 8,000 ft ( $95.53 \pm 2.53\%$ ), to 10,000 ft ( $92.78 \pm 2.54\%$ ), and 12,000 ft ( $89.01 \pm 4.78\%$ ), but remained the same in the control group. Heart rate data indicated an interaction effect ( $p < 0.0001$ ), but follow-up comparisons indicated no significant results. Flight performance had an altitude effect such that the altitude root mean square error (RMSE) was greater during the sea level condition than all others. There were no effects for high-frequency omnidirectional change error or heading RMSE. There was, however, a group difference at 10,000 ft during the first cruising segment at that altitude for procedural errors on day 3. During the descent to landing phases, the hypoxic group committed more procedural errors than the control group. The hypoxic group reported higher temporal stress from the NASA Task Load Index than the control group; there was no discernible difference in any of the questionnaires. Based on these results, the authors concluded that the effects of hypoxia are observable at those altitudes and that unsafe or high risk piloting behaviors were recorded during the final phases of flight in the hypoxic group, particularly at 10,000 ft and 12,000 ft. The authors also noted that, while not completely free from errors, the control group exhibited more deliberate and cautious behaviors during the last phases of flight.

Temme et al., 2010

The objective of this study<sup>26</sup> was to explore the impact of hypoxia on flight performance. Fourteen active-duty instructor pilots (mean  $\pm$  SD,  $32 \pm 3$  yrs,  $2235 \pm 737$  h of flight hours) were engaged in a flight task involving maintaining constant airspeed, altitude, and heading in a desktop flight simulator of a Cessna 172, while breathing nitrogen-mixed air to simulate an altitude of 18,000 ft. The results, presented as deviations from assigned flight instructions, revealed that hypoxic exposure led to a 53% reduction in pilots' control over altitude and airspeed. However,

there was no discernible effect of breathing hypoxic air on heading control. In summary, the authors concluded that exposure to moderate levels of hypoxic air compromised the ability of military instructor pilots to execute precise low flight tasks.

Peacock et al., 2017

The purpose of this study<sup>27</sup> was to research the impact of hypoxic exposure on human physiology, cognition, and flight simulator performance. Ten pilots (mean  $\pm$ SD, 21.5  $\pm$  2.0 yrs, 177.3  $\pm$  6.1 cm, 77.9  $\pm$  11.2 kg) participated in a flight simulator, executing routine take-off, flight, landing, and commanding procedures. Performance was assessed based on altitude, airspeed, and heading, with minor errors (ME) considered if outside federal limits and major errors (MJE) if double outside limits. Command errors were noted as an inability to respond appropriately to commands, combined with OE for an overall score (TE). Hypobaric hypoxic (HYP, simulated 3810 m or ~10,000 ft) and normoxic (NORM) conditions were administered in randomized order. Simultaneously, heart rate (HR), pulse-oximetry (SpO<sub>2</sub>), and frontal lobe cerebral oxygenation (PrO<sub>2</sub>) were measured at baseline (0 minute), immediately after entry into the chamber, 30 minutes, and 60 minutes before the flight simulation. Cognitive function was evaluated using the Profile of Mood States (POMS) and executive function testing (ANAM4) at the same pre-flight intervals. The flight simulation paused at 90 minutes for data collection, with final data collected after the simulation at 120 minutes. Results indicated an increase in HR over time during HYP, with a peak immediately after the flight simulation. SpO<sub>2</sub> decreased at 30 min, 60 min, 90 min, and 120 min during HYP. Frontal lobe oxygen saturation showed a consistent decrease during the HYP condition. POMS scores increased over time in both conditions, suggesting a declining mood state. ANAM4 results indicated a decrease in logic reasoning across time in both conditions, with a lower score immediately after HYP exposure. Additionally, the HYP condition exhibited a decline in

running memory. However, there was no significant change in flight performance between HYP and NORM conditions. In conclusion, HYP exposure altered physiological and cognitive functions, yet it did not impact pilot flight performance scores.

Steinman et al., 2017

The purpose of this study<sup>28</sup> was to research the impact of hypobaric hypoxia on flight performance under simulated altitudes of 91 m (baseline), 3048 m (10,000 ft), and 4527 m (15,000 ft). Twelve male pilots (mean  $\pm$  SD, 31.6  $\pm$  9.1 yrs, 79.1  $\pm$  9.4 kg, 182.7  $\pm$  6.3 cm, total flight hours 1268.8  $\pm$  1614.9 h) participated in instrumental flight rules within a hypobaric chamber in randomized order. Physiological parameters, including Heart Rate (HR), Peripheral Oxygen Saturation (SpO<sub>2</sub>), Ventilation Rate (VE), and Breathing Frequency (BF), were continuously monitored throughout each flight. Self-perceived states of alertness were assessed before and after each flight using the Stanford Sleepiness Scale (SSS). Flight performance was evaluated based on deviations from set flight parameters, including squawk adjustments, the number of warnings, and flight resets. Results from the study indicated no significant differences in flight performance between simulated altitudes. However, the SSS score was higher at 4572 m compared to 91 m before flights, and alertness decreased from the start to the end of the flight only at 4571 m. Physiological data revealed that HR was higher at 4571 (95.5  $\pm$  14.2 bpm) compared to baseline (81.6  $\pm$  10.5 bpm), and SpO<sub>2</sub> at 3048 m (89.3  $\pm$  2.7%) and 4572 m (71.5  $\pm$  6.3%) was lower compared to baseline (98.6  $\pm$  0.6%). Breathing frequency was lower at 4572 m (14.3  $\pm$  2.8 rate/min) compared to baseline (18.3  $\pm$  2.9 rate/min). The authors concluded that there was no significant change in flight performance due to simulated altitude exposures of 3048 m and 4572 m. However, they observed interindividual differences in flight performance, which they hypothesized were the result of individual variability in hypoxic tolerance.

Robinson et al., 2018

The purpose of this study<sup>29</sup> was to research the impact of sequential exposures to moderate and mild hypoxia, comparing it to a single altitude exposure. The study involved 21 active-duty U.S. Air Force personnel at Wright-Patterson Air Force Base, OH, who underwent normobaric hypoxic exposures at baseline ground level, 7620 m (25,000 ft), and 3048 m (10,000 ft) in a counterbalanced order, using a Reduced Oxygen Breathing Device. Four exposure profiles were employed: a control condition at ground level, a mild condition involving 30 minutes at 3048 m, a moderate condition with 5 minutes at 7620 m, and a combined condition of mild and moderate exposures. The flight task required participants to maintain straight and level flight while performing a secondary task of estimating 10-second intervals. Results indicated that flight simulator errors were greater in the combined condition compared to the mild condition. Lapses per minute during the secondary task were also more prominent in the combined condition compared to the mild condition. Average peripheral oxygen saturation was lower in the combined condition ( $90.06 \pm 2.77\%$ ) compared to the moderate ( $99.59 \pm 1.06\%$ ) and mild ( $90.91 \pm 2.45\%$ ) conditions. Additionally, the average heart rate was higher in the combined condition ( $78.92 \pm 10.14$  bpm) compared to only the moderate condition ( $73.71 \pm 9.91$  bpm). The authors concluded that performance may be impaired during mild exposure to hypoxia when preceded by a moderate exposure, and noted that physiological recovery did not necessarily indicate cognitive recovery.

Bouak et al., 2019

The primary purpose of this study<sup>30</sup> was to assess the impact of extended hypobaric hypoxic exposure on simulated flight performance. Seventeen military helicopter pilots (15 men and 2 women; mean  $\pm$  SD,  $34 \pm 9$  yrs,  $81.9 \pm 14.2$  kg,  $1.77 \pm 0.09$ ,  $1815 \pm 1670$  h flight experience) participated in the study, undergoing hypobaric exposure at altitudes of 8,000 ft and 9,900 ft for 6

hours on two separate days. During the exposure, participants engaged in a rotary wing flight task, with continuous monitoring of heart rate, cerebral and finger pulse oxyhemoglobin saturation levels. A cognitive test battery assessed short-term memory (matching-to-sample test), working memory (n-back), executive function (Stroop task), and multi-tasking (multi-attribute task battery). Questionnaires were also administered to evaluate hypoxic symptoms, simulator sickness, fatigue, and mood. Results showed a decrease in cerebral and finger pulse oxyhemoglobin from baseline to hypoxia at both altitudes. Heart rate was higher after approximately 4 and 6 hours spent at altitude compared to 2 hours, and at 3 hours compared to 4 hours in both conditions. More participants reported hypoxic symptoms at altitude compared to ground level, but there was no difference between conditions. Positive mood decreased between 1-hour, 3-hours, 4-hours, and 5-hours of exposure regardless of hypoxic level. Additionally, positive mood after 4- and 5-hours of exposure was lower than after 2-hours. General and mental fatigue increased between 1-hour and 4-hours of exposure and between pre- and post-exposure. Altitude did not affect simulator performance or multi-tasking cognitive tests; however, low accuracies indicated a greater impairment in short-term memory, working memory, and executive function cognitive assessments. In conclusion, the authors determined that helicopter pilots flying between 8,000 ft and 9,900 ft for up to 6-hours exhibited decreased blood oxygen saturations without adverse effects on performance.

#### Steinman et al., 2021

The objective of this study<sup>31</sup> was to assess environmental awareness (AoE) in helicopter pilots operating at 11.4% fraction of inspired oxygen (FiO<sub>2</sub>; equivalent to 4572m or 15,000 ft) while flying a flight simulator. Sixteen pilots (mean  $\pm$  SD, 30  $\pm$  5.2 yrs and 12166  $\pm$  842.8 flight hours) underwent flights exposed to either normoxia or normobaric hypoxia. The missions

included 14 environment items and 37 technical skills in Flight 1, and 16 environment items and 37 technical skills in Flight 2. Each participant performed 5 missions in each flight, while heart rate and oxygen saturation were monitored, and pilots noted environmental items, making adjustments accordingly during the flight. The results revealed a greater cumulative number of missed AoE items in the hypoxic condition (28) compared to normoxia (12). However, there was no difference in the number of forgotten or incorrectly performed technical skills for either condition or mission. Pilots' alertness, as measured by the Stanford Sleepiness Scale, indicated higher sleepiness at the end ( $2 \pm 0.61$ ) compared to the start ( $3 \pm 1.02$ ) in the hypoxic condition, a trend not observed in normoxia. The sleepiness score at the end of the hypoxic condition ( $3 \pm 1.02$ ) was also higher compared to the end of the normoxic ( $2 \pm 0.86$ ) flight but did not differ at the start. Furthermore, there was a lower peripheral oxygen saturation in the hypoxic condition ( $81 \pm 3\%$ ) compared to normoxia ( $97 \pm 1\%$ ), with no difference in heart rate ( $90 \pm 14$  bpm vs  $87 \pm 15$  bpm, respectively). In conclusion, the authors determined that exposure to 11.4% FiO<sub>2</sub> impaired AoE and decreased alertness in pilots.

### **Hypoxic Cognition**

Ballardin et al., 2007

The purpose of this study<sup>32</sup> was to assess the impact of prolonged exposure to mild hypoxia on cognitive function and visual performance. Thirty active-duty personnel (mean age 33.0 years) participated in a 12-hour ground-level exposure and a hypobaric exposure at 10,000 ft. During the hypobaric exposure, 15 participants engaged in moderate cycling exercise for 10 minutes at 70% maximum heart rate every other hour. Researchers collected data on oxygen saturation (SaO<sub>2</sub>), heart rate, cognitive performance, and visual performance. The results revealed a main effect for SaO<sub>2</sub>, which was lower at 10,000 ft (range 89.2-90.5%) compared to ground level (range 96.4-

97.4%). SaO<sub>2</sub> was consistently lower at 10,000 ft across exercise sessions, decreasing over time in both conditions (-0.9% and -0.2% respectively). While there was no altitude effect on heart rate, it increased with exercise in both conditions. Subjects reported a higher occurrence of symptoms at 10,000 ft compared to ground level, including headache (36.7% vs. 13.3%), lightheadedness (20.0% vs. 0%), fatigue (56.7% vs. 30.0%), and altered concentration (33.3% vs. 13.3%). Regarding cognitive performance, there was a time effect for 11 of the 14 outcome measures, indicating an overall improvement over time regardless of altitude condition. The exercise by altitude interaction for mean reaction time of the Continuous Performance Test (CPT) suggested the most significant improvement occurred in the exercise group at 10,000 ft, while the non-exercise group at ground level showed the smallest improvement. In terms of visual performance, high contrast visual acuity improved during the 12-hour ground-level session but remained near baseline or below at 10,000 ft, with no significant effects of exercise on the Bailey-Lovie test. The Pelli-Robinson test showed contrast vision improvement over the 12 hours at ground level, while at altitude it remained below or near baseline. The non-exercise Unaided night vision high contrast performance slightly improved compared to baseline, but the exercise group remained slightly below baseline. The low contrast had a significant main effect of altitude, with slightly better vision at altitude than ground level, but this was only significant at the 7-hour mark, which was not clinically significant. In conclusion, the authors determined that mild hypoxia at 10,000 ft for 12 hours had minimal influence on cognitive performance and night vision goggle (NVG) vision.

#### Malle et al., 2013

This study<sup>33</sup> examined the impact of acute hypobaric hypoxia on working memory during hypoxia training. Fifty-seven young male pilots were randomly assigned to either a control group (n=29, age 23.9 ± 2.8 yrs, 13.8 ± 1.6 yrs of schooling) or an experimental group (n=28, 23.9 ± 1.7

yrs,  $14.5 \pm 2$  yrs of schooling) exposed to a simulated altitude of 10000 m (31,000 ft) in a hypobaric chamber. Working memory (WM) was evaluated using the Paced Auditory Serial Addition Test (PASAT), along with measurements of Peripheral Oxygen Saturation ( $SpO_2$ ) and heart rate. Results from the WM assessment showed a higher percentage of correct responses in the control group ( $95.4 \pm 0.9\%$ ) compared to the hypoxic group ( $69.7 \pm 2.6\%$ ). The quantification of errors revealed a greater percentage of omissions and miscalculations in the hypoxic group ( $8.6 \pm 1.3\%$  and  $18.3 \pm 2.3\%$ , respectively) compared to the control group ( $0.7 \pm 0.2\%$  and  $3.1 \pm 0.9\%$ ). Physiological results indicated a lower  $SpO_2$  in the hypoxic group ( $79.2 \pm 1.0\%$ ) compared to the control group ( $98.9 \pm 0.3\%$ ), along with a higher mean heart rate in the hypoxic group ( $115 \pm 4$  bpm) compared to the control group ( $81 \pm 5$  bpm). The authors concluded that working memory is impaired in acute hypobaric hypoxia. They suggested that recognizing the significance of working memory in aircraft piloting, the PASAT could enhance both hypoxia training and comprehension of the effects of hypoxia on memory .

Legg et al., 2016

The objective of this study<sup>34</sup> was to investigate the impact of hypobaric hypoxia at altitudes of 8,000 ft and 12,000 ft on mood and complex cognition in thirty-six air force personnel. Participants were exposed, in a randomized balanced order, to 30 minutes of sea-level breathing, followed by 30 minutes at sea level, 8,000 ft, or 12,000 ft altitude, immediately succeeded by 100% oxygen breathing at altitude before descent. Physiological measures, including Peripheral Oxygen Saturation ( $SpO_2$ ), were recorded, and a battery of seven mood and six complex cognitive tests from the Automated Neurophysiological Assessment Metrics (ANAM) were administered. The mood tests covered anger, anxiety, depression, fatigue, happiness, restlessness, and vigor, while the complex cognitive tests included logical relations, 3-dimensional spatial rotation



(Manikin test), mathematical processing, memory search, selective attention/inhibition (Stroop test), and problem-solving (decision-making/mental flexibility) (Tower puzzle test). Results indicated no baseline SpO<sub>2</sub> differences between altitudes, but a significant drop from baseline (99 ± 1%) to 8,000 ft (95 ± 3%) and 12,000 ft (88 ± 3%), returning to 100 ± 1% after 100% oxygen administration. In mood tests, fatigue and vigor levels remained constant at 8,000 ft but increased, and vigor decreased at 12,000 ft, with restoration upon supplemental oxygen. The only significant cognitive impact was noted in logical relations, although it was suggested to be influenced by a single outlying high mean score in the second trial of the zero-altitude condition. The authors concluded that their findings did not support previous evidence suggesting that mild hypoxia impairs complex cognition. However, certain aspects of mood were affected at 12,000 ft, and these effects could be remedied by breathing 100% oxygen .

Malle et al., 2016

This study<sup>35</sup> explored the impact of acute normobaric hypoxia on physiological variables and working memory, considering the effects of oxygen breathing both before and after hypoxia exposure. A total of 86 healthy men (29.4 ± 0.9 years, 15.1 ± 2.4 years of school) were randomly assigned to four groups: normoxia-air (n=23), hypoxia-air (n=22, where hypoxia was preceded and followed by normal air breathing), normoxia-O<sub>2</sub> (n=21, where normoxia air was preceded and followed by breathing 100% oxygen), and hypoxia-O<sub>2</sub> (n=20, where hypoxia air was preceded and followed by breathing 100% oxygen). Physiological variables, including arterial blood oxygen saturation (SpO<sub>2</sub>) and heart rate (HR), were continuously monitored using a pulse oximeter on the forefinger throughout each phase of hypoxia. Working memory was assessed using a modified version of the Paced Auditory Serial Addition Task (PASAT) with 105 items and an interstimulus interval of 4 seconds to cover the entire hypoxic exposure and recovery period. Physiological

results demonstrated a typical response to hypoxic exposure, characterized by a decrease in SpO<sub>2</sub> and an increase in HR. When comparing the hypoxia-air and hypoxia-O<sub>2</sub> groups, mean SpO<sub>2</sub> was higher when breathing 100% oxygen compared to air in the control phase ( $\Delta 1.2\%$ ) and desaturation delay ( $\Delta 0.8\%$ ). The normoxia-air group exhibited a higher percentage of correct responses ( $88.2 \pm 2.1\%$ ) compared to the hypoxia-air group ( $70.3 \pm 3.9\%$ ). The hypoxia-air group showed a greater percentage of omissions ( $9.2 \pm 2.4\%$ ) and miscalculations ( $16.4 \pm 2.3\%$ ) compared to the normoxia-air group. The authors concluded that acute normobaric hypoxia significantly impaired working memory, and this impairment was exacerbated by oxygen breathing following hypoxia exposure.

### **Hypoxic Electromyography (EMG)**

Felici et al., 2001

The purpose of this study<sup>36</sup> was to investigate the impact of altitude exposure on muscle endurance during isometric contractions. Six sedentary men ( $33 \pm 6$  years,  $68.9 \pm 6.7$  kg,  $176.8 \pm 5$  cm) engaged in elbow flexion at 80% of maximal voluntary isometric contraction until fatigue, utilizing visual feedback. Surface electromyography (EMG) was recorded, and median frequencies of consecutive 1-second epochs of the biceps brachii, along with the force signal of the elbow flexors, were computed. The experiment was conducted before, during, and six months after a 12-day stay at an altitude of 5050 meters above sea level. The only observed change during the altitude stay was a decrease in arterial oxygen saturation, with no other alterations noted. The results revealed a decline in mean endurance time from  $22.4 \pm 4$  seconds to  $18.3 \pm 4.7$  seconds during contractions, progressively reducing throughout the altitude stay. Following altitude exposure, variations were observed in median frequency and the percentage of determinism slope, both of which returned to normal after the altitude stay. In conclusion, during the initial acclimatization

period, there was evidence of impaired isometric muscle endurance performance and a modified myoelectric activity pattern, suggesting increased fatigability of the neuromuscular system .

Casale et al., 2004

The objective of this study<sup>37</sup> was to evaluate alterations in muscle-fiber membrane properties and motor unit (MU) control properties during acute exposure to hypobaric hypoxia at high altitude (HA) and subsequent acclimatization. Six men, aged 25-49, performed three maximal voluntary contractions (MVC) of the biceps brachii at an altitude of 5050 meters, while surface electromyography (EMG) was recorded. Following the MVCs, participants underwent two electrically elicited contractions of 20 seconds each, and two voluntary contractions at 40% and two at 80% MVC. The findings indicated no significant changes in hemoglobin saturation or arterial pressure over the 10-day period at HA, and there was no difference in MVC produced at HA compared to sea level. Additionally, there was no distinction in EMG amplitude during two voluntary contractions at 40% and 80% MVC of the biceps brachii at HA compared to sea level. However, a noteworthy observation was a higher EMG spectral frequency at HA than at sea level, indicating that spectral frequencies and conduction velocity were greater at HA. In conclusion, acute exposure to hypobaric hypoxia did not impact muscle-fiber membrane properties but did affect motor unit control.

McKeown et al., 2019

The purpose of this study<sup>38</sup> was to investigate how severe acute hypoxia affects the firing rate of motor units (MU) in the biceps brachii during isometric contractions. Ten healthy subjects ( $22 \pm 1$  yrs,  $171 \pm 9$  cm,  $73 \pm 15$  kg, 4 men) had oxygen flow adjusted to reduce Peripheral Oxygen Saturation ( $SpO_2$ ) to 80% during a 35-minute desaturation period, after which they continued breathing the reduced oxygen levels for 2 hours. Subjects wore a sealed facemask to control airflow

and had SpO<sub>2</sub> and heart rate continuously monitored. Participants performed maximal voluntary contractions (MVC) at 25% of maximum. Surface electromyography (EMG) data from the biceps brachii was collected and analyzed for motor unit action potential trains (MUAPT) and root mean square (RMS). The study also assessed parameters such as SpO<sub>2</sub> and heart rate. SpO<sub>2</sub> showed a decrease during the acclimation phase, notably 20 minutes into the phase. Heart rate also increased, particularly 10 minutes into the acclimation phase. There was no time effect on MVC force. The EMG RMS signal and the firing rate of decomposed motor units didn't differ between the initial and final 5-second intervals of each steady-state region during the contraction protocol, implying that fatigue did not influence the data. A total of 865 MUs were extracted across all subjects and contractions. The number of detected MUs decreased post-hypoxia exposure, which was hypothesized to result from either fewer active MUs during contraction or fewer discriminated MUs by the PD III algorithm. Regarding motor unit firing rate and recruitment threshold, a main effect was observed for recruitment threshold, where each threshold was higher than the preceding one. However, no main effects were identified for the firing rate about time or interaction with recruitment threshold. Individual analysis indicated a mixed pattern, where some subjects exhibited decreased firing rates while others displayed increased rates post-desaturation. Moreover, subjects who displayed decreased MU firing rates experienced faster desaturation of SpO<sub>2</sub> compared to those with increased rates. This difference was significant during the hypoxia phase, showing distinct response patterns in desaturation among subjects. The authors concluded that there was no overall effect of hypoxia on MU firing rates, but rather a subject-specific response to the presented intervention.

Nell et al., 2020

The purpose of this study<sup>39</sup> was to research and compare the impact of acute hypoxia exposure on muscle deoxygenation and the recruitment of the flexor digitorum superficialis (FDS) during submaximal intermittent handgrip exercise. Twenty-four participants (mean  $\pm$  SD, age  $25 \pm 3$  yrs, height  $172 \pm 10$  cm, weight  $70.1 \pm 12.0$  kg) performed handgrip exercises (HGE) without knowing that the oxygen percentages were 21% FiO<sub>2</sub> (normoxic) or 12% FiO<sub>2</sub> (normobaric hypoxia). Throughout the trials, various physiological parameters, including heart rate, oxygen saturation, and blood pressure, were monitored. Ratings of perceived exertion for dyspnea and forearm fatigue were assessed using a 10-point Borg scale before and after the trials. The experimental protocol involved determining maximum voluntary contraction (MVC) for handgrip force, setting a target range of 45-55% of MVC, and guiding participants through the protocol using visual and audio cues. Participants continued the protocol until they were unable to sustain the required force for three consecutive contractions. Electromyography (EMG) was employed to assess the electrical activity in the flexor digitorum superficialis (FDS) muscle during HGE. Surface electrodes were placed over the FDS muscle, and the signal was processed to measure root mean square and mean power frequency, comparing the initial and final contractions during the exercise. During hypoxic HGE, the FDS muscle exhibited decreased tissue oxygen saturation (SmO<sub>2</sub>) compared to normoxic HGE ( $63.8 \pm 2.2$  vs.  $69.0 \pm 1.5$ ) at different task durations, except for the 20% mark. EMG data indicated that root mean square values for FDS increased from the initial contractions to task failure under hypoxic and normoxic conditions. Mean power frequency decreased overall from the first contractions to task failure, with lower values during hypoxia than normoxia. No differences were observed in task duration or tension-time index between gases. Additionally, no correlation was found between SmO<sub>2</sub> and Peripheral Oxygen Saturation (SpO<sub>2</sub>) when an outlier in the dataset was excluded. Physiological measures like heart rate and diastolic

blood pressure were notably higher at task failure during both hypoxic and normoxic HGE compared to baseline. However, there were no substantial differences in systolic blood pressure across trials or between gases. Ratings of perceived exertion for dyspnea and forearm fatigue were higher at task failure compared to baseline but were not different between normoxic and hypoxic conditions. The authors concluded that acute exposure to normobaric hypoxia resulted in a greater decline in  $SmO_2$  and greater muscle fatigue, as evidenced by decreased mean power frequency.

Jenkins et al., 2021

The purpose of this study<sup>40</sup> was to investigate the impact of acute normobaric hypoxic exposure with fraction of inspired oxygen ( $FiO_2$ ) levels at 15% and 13% on neuromuscular activation of the biceps brachii muscle during dynamic constant external resistance exercise. Thirteen adults (10 men and 3 women, mean  $\pm$  SEM,  $23.3 \pm 1.3$  yrs,  $80.0 \pm 6.5$  kg,  $175.4 \pm 1.8$  cm) participated in the study and performed repeated arm curls at 70% of their 1 repetition maximum for 2 sets to exhaustion. Electromyography (EMG) data were collected from the biceps brachii and analyzed for root mean squared (RMS), mean power frequency (MPF), and repetition duration. Pulse oxygen saturation ( $SpO_2$ ) was assessed using a finger pulse oximeter. The results revealed a reduction in the number of repetitions from the first set ( $18.2 \pm 1.4$ ) to the second set ( $9.5 \pm 1.0$ ), irrespective of hypoxia. Repetition duration increased from the first ( $1.12 \pm 0.09$  s) to the second set ( $1.25 \pm 0.09$  s), with a continuous increase throughout each repetition. EMG RMS was higher during the first set ( $330.05 \pm 37.48$   $\mu$ V) compared to the second set ( $318.76 \pm 37.34$   $\mu$ V), exhibiting a decline from 50-100% of repetitions to failure within each set. EMG MPF declined between 75-100% of repetitions to failure ( $126.17 \pm 3.41$  Hz to  $116.86 \pm 3.98$  Hz).  $SpO_2$  decreased in both hypoxic conditions compared to baseline before and after the fatiguing protocol ( $97.08 \pm 0.31\%$  and  $97.42 \pm 0.34\%$ ).  $FiO_2$  13% resulted in lower  $SpO_2$  ( $88.15 \pm 1.21\%$  and  $93.17$

$\pm 0.86\%$ ) compared to  $\text{FiO}_2$  15% ( $91.85 \pm 0.59\%$  and  $93.77 \pm 0.85\%$ ). Following the fatiguing exercise protocol,  $\text{SpO}_2$  increased only in hypoxic conditions. The authors concluded that acute hypoxic exposure did not influence the rate of fatigue development or neuromuscular parameters of the biceps brachii during dynamic constant external resistance exercise .

## CARDIOVASCULAR ACTIVITY

Boucsein et al., 2007

This study<sup>41</sup> utilized a closed-loop adaptive system to vary the strength of turbulence in a professional simulator and evaluated nonspecific skin conductance responses (NS.SCRs) and heart rate variability (HRV) as root mean square of successive differences (RMSSD). Forty-eight students (24 males, 24 females, mean  $\pm$  SD;  $26.42 \pm 5.34$  yrs) flew in a flight simulator using instrument flight rules (IFR), in three blocks based on different autonomic measures combinations: NS.SCRs only, NS.SCRs & heart rate (HR), and NS.SCRs & HRV. Under NS.SCRs only turbulences were modified according to deviations from a participants predefined setpoint based on NS.SCRs. During NS.SCRs & HR turbulences were triggered by deviations of both parameters from the predefined setpoint in the same direction as the deviations. The NS.SCRs & HRV condition triggered changes in turbulence in the opposite direction of their deviations from the individual setpoints. Participants were divided into two groups, the experimental condition where parameters were calculated every 2 minutes and triggered the strength of turbulences dependent on subject setpoint. The yoked control condition received the same block order and sequence of turbulences as the matched experimental subject, regardless of their setpoint. The electrodermal activity (EDA) was collected from the left hand using two electrodes at a sampling rate of 20 Hz, sensitivity of 0.001  $\mu$ S, and 0.3 low pass filter. Data was calculated as both frequency and sum of amplitudes of NS.SCRs. Electrocardiogram was obtained using Einthoven II-lead on the right wrist and left ankle at 200Hz and calculated for mean HR and root mean square of successive differences (RMSSD) for HRV. The results of this study indicate that the setpoint deviations of NS.SCRs were smaller for the experimental group than the yoked control group, especially in the second half of the flying segments. The HRV data were not different between groups. When



comparing the three conditions among the second half of the flight block, there were smaller deviations in setpoint of NS.SCRs in experimental participants when compared to NS.SCRs & HRV. Within the experimental group only, the frequency of turbulence switches were greater in NS.SCRs than NS.SCRs & HR and NSC.SCRs & HRV. The findings showed that as a result of adaptive control, experimental participants whose physiological parameters attenuated turbulence remained close to their respective threshold for arousal compared with those unaffected. The NS.SCRs & HRV showed a marked differentiation between the two experimental conditions compared to (NS.SCRs & HR and NS.SCRs alone).

Lahtinen et al., 2007

The purpose of this article<sup>42</sup> was to research the relationship of change in heart rate ( $\Delta$ HR) and flight performance. Fifteen Finish Air Force male fighter pilots (25-34 yrs) on active flying status with a total of 570-1400 total flying hours, with 170-650 of those hours in an F-18. Pilots were divided into two groups: experienced ( $>300$  Hornet flight hours;  $n = 7$ ) and less experienced ( $<300$  Hornet flight hours;  $n = 8$ ). Pilots performed a combat flight scenario in the F-18 Hornet Weapons Tactics Trainer simulator. The scenario consisted of the following phases: 1 (seated 5 min rest), 2 (2 minute reading task - Reading Task 1), 3 (flight mission start), 4 (tactical maneuver), 5 (beyond visual range enemy fighter interception), 6 (tactical maneuver), 7 (beyond visual range interception of enemy aircraft formation), 8 (tactical maneuver), 9 (enemy fighter interception), 10 (break from combat), 11 (return to base at high altitude), 12 (return to base at low altitude), 13 (initial instrument landing system (ILS) approach), 14 (intermediate ILS approach), 15 (final ILS approach and landing), and 16 (20-min reading period - Reading Task 2). The total flight lasted an average of 27 minutes. Heart Rate was continuously monitored using electrocardiogram leads V1, V5, and aVF for calculations of R-R intervals, where  $\Delta$ HR was calculated subtracting HR at seated

rest from HR obtained during flight. The results indicated an increase in  $\Delta$ HR during the flight phase compared to rest. The  $\Delta$ HR was also greater at the start of the flight compared to seated rest and Reading Task 1. Then was further increased in phase 6-8, which was higher than the start of the flight mission and higher than phase 5. There was also a decrease in  $\Delta$ HR during the break from combat (phase 10) and the return to base at high altitude (phase 11). In addition,  $\Delta$ HR was lower in phase 10-11 than during the interception of a formation (phase 9). In the final ILS approach and landing (phase 15)  $\Delta$ HR was higher than during Reading Task 2. During seated rest HR was not different between experienced (mean 78.5 bpm) and less experienced (mean 79.4 bpm). Flight performance was evaluated by the same flight instructor for each subject. There were no correlations between flight phase performance and  $\Delta$ HR in any of the flight phases. There was, however, an association between Hornet flight hours and overall flight performance score during simulated flight. The authors concluded that since HR changes reflected the cognitive load during the simulated flight, they could be used to evaluate the psychological workload of military simulator flight phases.

Sauvet et al., 2009

The purpose of this study<sup>16</sup> was to evaluate linear and non-linear heart rate variability (HRV) parameters and vigilance in response to a high mental workload induced by a complex flight and subsequent recovery. Ten male French military pilots (mean  $\pm$  SE; 40.4  $\pm$  2.7 yrs, 178.2  $\pm$  1.5 cm, 81.2  $\pm$  3.5 kg, and 115.8  $\pm$  15.7 h flying experience) participated in a 3.5-hour multi-leg cross-country flight in a Piper Pa28. The flight plan encompassed eight stages: 1) lining-up, 2) instrument flight rules, 3) simulated flap failure and touch and go, 4) simulated airspeed indicator failure and touch and go, 5) rerouting, 6) simulated engine failure, 7) high-speed approach, and 8) post-landing rest. Before the flight, pilots underwent a stand test and a 6-minute sitting ground

baseline (GB). Electrocardiogram data were collected during ground and flight testing for the analysis of mean R-R interval, standard deviation of normal R-R intervals (SDNN), root mean square of successive differences of successive normal R-R intervals (RMSSD), standard deviation of the Poincaré plot perpendicular to the line-of-identity (SD1), standard deviation of the Poincaré plot along the line-of-identity (SD2), normalized low power frequency band (0.04-0.15 Hz) (LF), normalized high power frequency band (0.15-0.4 Hz) (HF), and the ratio of the low frequency to high-frequency power (LF/HF). Vigilance parameters were assessed using the Mackworth 'clock test' to measure the ability to sustain attention during monotonous stimulation and the Karolinska Sleepiness Scale to measure sleepiness. The results indicated a decrease in mean R-R interval during in-flight sequences compared to GB, with differences observed after stages 4 and 7. SDNN exhibited a flight sequence effect, with lower values at stage 4 compared to GB and lower values at stages 4-8 compared to the preflight checklist (PF; before stage 1). SD1 was higher during PF than GB and decreased during stages 4, 6, and 7 compared to PF. SD2 was lower at stages 4-8 compared to GB. LF and HF were lower during stages 3-7 than PF, while LF/HF ratio was higher during stages 4, 6, and 7 than during GB and PF. Normalized LF was higher during stages 6 and 7 than GB and PF. During recovery, the mean R-R interval decreased in both supine and standing positions immediately, 2 h, and 5 h after the flight. SDNN was lower immediately and 5 h after in both supine and standing positions. A decrease in SD1 and RMSSD was observed immediately and 5 h after in the supine position and immediately and 2 h after in the standing position. SD2 parameter only decreased immediately after the flight in both supine and standing positions. The LF/HF ratio increased after the flight at 2 h compared to before. Mackworth 'clock test' results indicated an increase in the number of omissions to the number of jumps and reaction time immediately and 2 h after the flight. The Karolinska sleepiness score was higher 2.5 h after the

flight ( $6.5 \pm 0.35$ ) than before ( $5.1 \pm 0.46$ ). No linear relationships were found between HRV parameters and vigilance indices. The study concluded that a multi-leg cross-country flight resulted in reduced pilot vigilance and alterations in autonomic activity, which persisted for up to 5 h after the flight, and there was no correlation between increased sympathetic activity and impaired vigilance.

Di Rienzo et al., 2010

This study<sup>43</sup> examined the impact of the push-pull (PP) effect on cardiac rhythm during actual flights. Three pilots participated in a 1 hr flight protocol in an Aermacchi MB 339-CD aircraft. Throughout the flight, electrocardiogram (ECG) and respiratory data were recorded using MagIC smart garments. The flight protocol comprised two maneuvers conducted with the anti-G suit activated. The first maneuver involved a +5 Gz acceleration for 15 seconds (Ref+5Gz), followed by a push-pull maneuver. The push-pull maneuver included a 5-second acceleration with a 1 G/s onset, followed by a 15-second acceleration at +5 Gz (PP+5Gz). ECG data were analyzed for mean R-R interval (RRI), standard deviation of normal R-R intervals (SDNN), and root mean square of successive differences of successive normal R-R intervals (RMSSD). When comparing the ECG results during the push-pull inducing maneuver to the reference isolated Ref+5Gz, significant changes were observed. There was a notable reduction in RRI mean (mean  $\pm$  SEM;  $581.0 \pm 14.1$  ms to  $522.9 \pm 32.3$  ms), SDNN ( $45.2 \pm 10.7$  ms to  $20.6 \pm 5.3$  ms), and RMSSD ( $15.5 \pm 1.6$  ms to  $8.5 \pm 1.5$  ms). These findings suggested that the push-pull maneuver induced sympathetic stimulation to the heart, as evidenced by the decrease in RRI mean and SDNN, while concurrently deactivating parasympathetic control, as indicated by the reduction in RMSSD.

Sharma et al., 2011

The purpose of this study<sup>44</sup> was to assess the psychophysiological and subjective measures of pilots to understand mental workload during simulated instrument meteorological conditions (IMC), such as flying into clouds or at night. Twenty-one male students (mean  $\pm$  SD;  $33.09 \pm 6.09$  years and  $1775.33 \pm 1297.38$  hours of flying experience) from the Institute of Aerospace Medicine participated in the study. They flew in an Airfox® DISO Translational Motion Control simulator while their heart rate (HR), respiration rate, and Galvanic Skin Response (GSR) were monitored using the Nexus-10 physiological monitoring and feedback platform. The National Aeronautics and Space Administration Task Load Index (NASA TLX) served as a subjective measure of mental workload. The participants had an 8–10-minute free flight for familiarization with the controls, followed by two experimental phases: 1) ‘Day Clouds,’ where they flew in clear visibility but entered simulated intermittent IMC, and 2) ‘Evening Night,’ where they took off during dusk in poor visibility with instructions to fly on instruments alone, and Coriolis illusions were simulated. Both experimental phases were divided into stages, including baseline, cruise, pre-Coriolis, Coriolis (360° turn till straight and level), post-Coriolis, pre-leans, leans (120° turn till straight and level), post-leans, approach till landing, post-landing, and post-run baseline. The results indicated no significant difference in HR, respiration rate, or GSR between Day Clouds and Evening Night flying conditions. However, all parameters of the NASA TLX were higher during Evening Night (total workload  $65.39 \pm 15.68$ ) compared to Day Clouds ( $47.65 \pm 16.72$ ) flying. Correlation analysis revealed a moderately positive correlation between respiration rate and the Baseline NASA TLX overall workload score during both Day Clouds (Pearson  $r=0.46$ ) and Evening Night (Pearson  $r=0.44$ ) flying. A moderate negative correlation was observed between HR and pre-Coriolis (Pearson  $r=-0.45$ ), Coriolis (Pearson  $r=-0.46$ ), and post-Coriolis (Pearson  $r=-0.49$ ) overall workload score of the NASA TLX. During pre- and post-leans in the Evening Night condition,

there was also a moderate negative correlation between HR and NASA TLX overall workload score (Pearson  $r=-0.45$  and  $-0.46$ , respectively). Heart rate was negatively correlated with NASA TLX overall score for approach to land (Pearson  $r=-0.45$ ), post-landing (Pearson  $r=-0.49$ ), and post-run baseline (Pearson  $r=-0.45$ ) during Evening Night flight. In conclusion, the authors found that psychophysiological measures in isolation did not provide significant information. However, subjective measures indicated a significant workload under test conditions (Evening Night) during simulated IMC flight. Furthermore, the negative correlation between HR and NASA TLX suggests that HR could potentially be the most useful psychophysiological variable for quantifying workload .

Oliveira-Silva & Boullosa, 2015

This study<sup>18</sup> explored the autonomic control of heart rate (HR; beats per minute) in pilots before, during, and after a training flight. Eleven male fighter pilots (mean  $\pm$  SD; age:  $33.2 \pm 3.2$  yrs, body mass:  $76.0 \pm 8.5$  kg; height:  $1.75 \pm 0.05$  m, body fat:  $16.9 \pm 5.4\%$ ; with over 500 hours of flight experience and a minimum of 5 years flying high-performance aircraft) from the Brazilian Air Force participated in HR recordings on both a control day, involving routine administrative duties in the office, and a flight day, which included an operational flight (mean duration  $63:09 \pm 02:16$ ), with the same administrative duties 1-hour pre- and post-flight. Heart rate variability (HRV) parameters were measured using a chest HR monitor at pre-flight, during the flight, and post-flight intervals on the flight day and at the same time on the control day, separated by a 48-hour interval. The findings indicated an increase in mean HR ( $\Delta 18.0\%$ ) and standard deviation of all R-R intervals (SDNN;  $\Delta 40.9\%$ ) and a decrease in root mean square of successive differences between normal sinus R-R intervals (RMSSD;  $\Delta -71.4\%$ ), short-term beat-to-beat R-R variability from the Poincaré plot (SD1;  $\Delta -77.8\%$ ), and long-term beat-to-beat variability from the Poincaré

plot (SD2;  $\Delta$ -49.4%) during the flight compared to the same time of day on the control day. Additionally, there was a decrease in RMSSD ( $\Delta$ -52.9%) 1-hour post-flight compared to the same time of day on the control day. On the flight day, there was an increase in mean HR ( $\Delta$ 12.6% and  $\Delta$ 6.8%), a decrease in RMSSD ( $\Delta$ -30.8% and  $\Delta$ -12.4%), and SD1 ( $\Delta$ -38.9% and  $\Delta$ -31.0%) compared to 1-hour pre- and post-flight, respectively. In conclusion, the authors found that an operational flight lasting approximately 1-hour induced vagal withdrawal during and after the flight compared to a control day.

Mansikka, Virtanen, et al., 2016a

The purpose of this study<sup>45</sup> was to investigate the performances of fighter pilots and their Pilot Mental Workload (PMWL) during an Instrument Flight Rules (IFR) proficiency test conducted in an F/A-18 simulator. A total of 26 male Finnish Air Force F/A-18 pilots, all possessing a 1st class IFR qualification and with an average flight experience of  $781 \pm 390$  hours, participated in an official check ride using a Boeing-built Weapon Tactics and Situational Awareness Trainer. The check ride consisted of seven mission segments: takeoff and ingress, maneuvering, level turns, single-engine maneuvering (SEM), very high-frequency omnidirectional radio range (VOR) approach, instrument landing system (ILS) approach, and precision approach radar (PAR) approach. The entire mission was flown in instrument meteorological conditions, with cloud base adjustments below the 1st class decision height for the ILS approach and below the 1st class minimum descent altitude for the VOR approach, necessitating go-arounds after reaching approach-specific descent minimums. A moderate, variable, and gusty wind was maintained throughout the slightly over an hour check ride. Electrocardiogram data for heart rate variability (HRV) calculations were recorded using a three-electrode arrangement with the Mind Media Nexus-10 MKII system. The data was exported in 5-minute epochs for each segment and

analyzed using Kubios HRV 2.2 software. The HRV parameters included mean R-R interval (MEANRR), standard deviation of normal R-R intervals (SDNN), root mean square of successive R-R interval differences (RMSSD), number of successive R-R intervals differing by more than 50 ms (NN50), percentage of successive RR intervals differing by more than 50 ms (pNN50), integral of the density of the R-R interval histogram divided by the maximum of the distribution (HRVTRI), normalized low-power frequency band (0.04-0.15 Hz) (LFnu), normalized high-power frequency band (0.15-0.4 Hz) (HFnu), and the ratio of low frequency to high-frequency power (LF/HF). The results revealed that the Maneuvering segment had the lowest mean performance score ( $89.8 \pm 5.5\%$ ), whereas SEM had the highest ( $97.3 \pm 4.0\%$ ), followed by takeoff and ingress ( $96.3 \pm 3.1\%$ ), level turns ( $95.0 \pm 9.6\%$ ), VOR approach ( $94.4 \pm 6.3\%$ ), and ILS approach ( $93.8 \pm 4.3\%$ ). The performance score from SEM was also higher than that of the ILS approach. The mean values of HRVTRI during maneuvering were lower than during segments with higher performance scores. Additionally, SDNN during level turns was lower ( $\Delta -14.4$  ms), and LF/HF during the VOR approach was greater ( $\Delta 1.7$ ) than during maneuvering. The MEANRR of SEM ( $686.7 \pm 114.0$  ms) and level turns ( $689.4 \pm 126.8$  ms) were both greater than that of the VOR approach ( $661.8 \pm 103.6$  ms) and ILS approach ( $666.2 \pm 105.1$  ms). Furthermore, MEANHR was lower for SEM ( $90.2 \pm 13.7$  1/min) compared to the VOR approach ( $93.5 \pm 13.5$  1/min) and ILS approach ( $92.7 \pm 13.4$  1/min), but level turns ( $90.2 \pm 15.4$  1/min) was only less than ILS approach. In conclusion, the study demonstrated that differences in pilots' PMWL between check ride mission segments can be discerned by HR and HRV parameters. Moreover, these parameters could identify distinctions between mission segments even when there were no performance differences.

Mansikka, Simola, et al., 2016b



This study<sup>46</sup> examined the relationship between heart rate (HR), selected time domain components of heart rate variability (HRV), and variations in pilot performance during a simulated flying mission. Specifically, the study sought to determine whether these physiological measures could identify the level of task demands leading to sub-standard performance. A total of 35 Finnish Air Force F/A-18 pilots, with an average flight experience of  $598 \pm 445$  hours, participated in the study. The pilots performed an instrument landing system (ILS) approach in a Boeing-built weapon tactics and situational awareness trainer under specific simulated conditions. The simulation included an ILS task and additional flying-related subtasks, such as setting up cockpit instruments, flying from decision height to touchdown, communicating with air traffic control, and responding to in-flight emergencies. The starting ranges for landing using ILS varied, and each trial was separated by a 3-minute rest period. The electrocardiogram data were recorded, and various HR and HRV parameters were extracted using Kubios HRV 2.2 software. The study categorized values of HR and HRV into groups, including baseline rest, high-performance category (baseline ILS mission), sub-standard performance category (trials with the highest sub-standard ILS performance score), and low-performance category (trial with the weakest ILS performance score). An experienced F/A-18 examiner pilot rated the ILS task performance based solely on deviations from target flight parameters. Results showed differences in HR and HRV between baseline rest and the high-performance category. However, the study did not find differentiation in task demand and ILS performance changes between sub-standard and low-performance categories based on HR and HRV parameters. Specifically, values of MEANRR, SDNN, MEANHR, RMSSD, NN50, pNN50, and HRVTRI were all different between baseline rest and the high-performance category. Interestingly, the high-performance category was only differentiated by MEANRR and MEANHR when compared to the sub-standard performance

category. The authors concluded that the MEANRR parameter could effectively differentiate between high-performance ILS approaches and sub-standard performance approaches.

Hidalgo-Muñoz et al., 2018

This study<sup>47</sup> aimed to explore the influence of emotion and cognitive workload on pilots' mental states by monitoring heart rate variability. Twenty male pilots holding private pilots' licenses participated (mean  $\pm$  SD; 22.7  $\pm$  3.7 yrs, 141.3  $\pm$  139.5 h of flying experience) and completed two dual-task flights in an AL-50 simulator. Each flight involved a pre-established flight plan and a secondary task, with cognitive workload modulated to be either low or high. Performance was assessed by monitoring heart rate variability for any deviation  $\pm$ 5 units from the requested flight parameters. Emotional state was manipulated from low arousal (LA), where pilots were alone in the simulator, to high arousal (HA), where participants were informed about being filmed, voice recorded, closely monitored by researchers, and in competition with other participants. Anxiety related to competition was measured using the Competitive State Anxiety Inventory-2R before the HA condition, and general anxiety was measured using the State-Trait Anxiety Inventory (form Y) after completing the second dual-task scenario. Cognitive workload was manipulated as low (LCW) or high (HCW). LCW involved participants pressing a touch screen when numbers heard met a simple rule, and HCW required participants to evaluate numbers based on color cues. Electrocardiogram data were collected and analyzed for heart rate (HR) and heart rate variability (HRV) parameters: standard deviation of R-R interval (SDRR), root mean square of the successive differences between normal R-R intervals (RMSSD), and proportion of R-R intervals differing more than 20 ms from the adjacent previous R-R interval (pNN-20). Results showed main effects for emotion and cognitive factors, with faster reaction times for HA compared to LA and LCW compared to HCW. Omissions were higher in LA (10.8%) than HA (5.68%). HR

was greater during HCW ( $86.55 \pm 15.18$  bpm) than LCW ( $85.14 \pm 15.47$  bpm). HR decreased from the first ( $89.19 \pm 8.93$  bpm) to middle ( $86.06 \pm 6.44$  bpm) and first to the last ( $81.87 \pm 2.32$  bpm) flight segments. RMSSD increased from the first ( $0.03 \pm 0.01$  ms) to middle ( $0.04 \pm 0.01$  ms) and first to the last ( $0.04 \pm 0.01$  ms) flight segments. pNN-20 increased between the first ( $0.46 \pm 0.17$ ) and last ( $0.60 \pm 0.03$ ) flight segments. The study concluded that moderate social stress could enhance motivation and performance by reducing omission errors, but high mental workload negatively affected performance by increasing reaction times. The authors also observed that HR was sensitive to cognitive demand and time-on-task, with higher HR during more challenging tasks.

Cao et al., 2019

The purpose of this study<sup>48</sup> was to evaluate how the sympathetic stress response as indicated by heart rate variability (HRV) metrics impact the performance of commercial airline pilots. Thirty male active commercial airline pilots qualified to fly an Airbus A320 aircraft, completed three simulated segments tests in a Federal Aviation Administration (FAA) certified A320 flight simulator for 3 hours. Pilots were divided into pairs. The pilot flying and the pilot monitoring worked as a team, each having different responsibilities during each maneuver. Their individual and team skills were scored by an FAA examiner who sat at the control console directly behind the pilots. A Movisens EcgMove3 sensor was used to record electrocardiogram data of each pilot and calculated in 30 s intervals for standard deviation of normal beat to beat variation (SDNN), root mean square of successive R-R interval differences (RMSSD), low frequency power (LF), high-frequency power (HF), and LF/HF ratio. The results indicated a decrease in SDNN (mean  $\pm$  SD;  $40.0 \pm 11.7$  ms to  $34.1 \pm 12.7$  ms) and RMSSD ( $26.7 \pm 9.4$  ms to  $23.8 \pm 10.2$  ms) during flight compared to pre-flight. There was no change in LF/HF ratio ( $5.5 \pm 2.4$  to  $5.7 \pm 2.8$ ).

The lowest average SDNN and RMSSD values were reported during two of the most difficult maneuvers with an overall passing rate of 73% (steep turns) and 67% (circle to land). Higher variability values were observed during cruising periods, where pilots could be more relaxed than when conducting flight maneuvers. Results showed that pilots flew more accurate maneuvers when their stress response was lower. Lower stress levels are marked by higher SDNN and RMSSD scores and lower LF/HF ratios. Furthermore, an interquartile range (IQR) increase in SDNN (21.97 ms) and RMSSD (16.00 ms) values and an IQR decrease in LF/HF ratio (4.69) were associated with an increase in the odds of passing a maneuver of varying difficulty by 37%, 22% and 20% respectively.

Hormeño-Holgado & Clemente-Suárez, 2019

The purpose of this study<sup>49</sup> was to measure selected psychophysiological responses of military jet fighter pilots in air-to-air close combat engagements using basic fighter maneuvers (BFM). BFM involves fundamental maneuvers performed by fighter aircraft to gain an advantage in combat. These maneuvers include turns, rolls, climbs, dives, and reversals. Twenty-nine Spanish Air Force pilots (mean  $\pm$  SD; 28.3  $\pm$  7.4 yrs; 178.5  $\pm$  7.4 cm; 75.3  $\pm$  8.1 kg) with 9.4  $\pm$  6.0 yrs of professional experience equipped with 10 kg of standard flight gear performed one offensive and one defensive combat engagement. F5 combat aircrafts were used to fly at a block altitude of 8,000 - 18,000 ft. The engagement began with the offensive fighter and defensive fighter were flying at co-altitude at 400 knots, from opposing headings, with 1-mile separation. When both aircraft were simultaneously visually acquired at the merge point (the “3-9” line), both turned at a sustained rate of 410 knots at 5.5 Gs until the offensive fighter was within gun range of the defensive (“bandit”) aircraft. The defensive fighter now flying at 350 knots, turned to one side to keep the offensive fighter behind in sight. Immediately, the defensive fighter executed a breaking turn at 4 G’s while

monitoring the pursuit curve and continued until gravity forces decreased progressively from 3.5 to 2 Gs to a speed of 200-250 knots. Measures of forced vital capacity (FVC), isometric hand strength (IHS), body temperature, blood oxygen saturation (BOS), heart rate (HR), and blood lactate (BLa) were taken two hours before and 30 minutes after each air-to-air combat flight. The results indicated an increase in HR ( $74.5 \pm 14.0$  bpm to  $83.7 \pm 14.8$  bpm) during offensive but not defensive maneuvering. Pilots BOS decreased during offensive ( $97.6 \pm 1.2\%$  to  $96.6 \pm 0.7\%$ ) and defensive ( $97.6 \pm 0.8\%$  to  $96.0 \pm 2.2\%$ ) maneuvering. In addition, FVC was decreased during defensive ( $4.9 \pm 1.4$  to  $4.3 \pm 0.9$  ml). There was no change in IHS, body temperature, or BLa during offensive or defensive maneuvers (all  $p > 0.05$ ). Heart Rate Variability (HRV) were measured before, during, and after flight, which indicated that mean HR was greater during ( $101.9 \pm 19.4$  bpm) offensive maneuvering compared to post-flight ( $92.8 \pm 16.2$  bpm). During defensive maneuvers, mean HR ( $98.5 \pm 14.3$  bpm) was greater than pre-flight ( $92.5 \pm 13.7$  bpm). Maximal HR was only greater during flight ( $152.3 \pm 22.8$  bpm) in the defensive maneuvers compared to post-flight values ( $123.6 \pm 12.6$  bpm). The authors concluded that both offensive and defensive air combat maneuvers elicited similar physiological responses.

Kutilek et al., 2019

The purpose of this study<sup>50</sup> was to test the use of heart rate variability (HRV) to estimate the physical and psychological state of fighter pilots. Two Czech Republic Air Force pilots (male, 32 and 26 years old) participated in the study. The research employed the FlexiGuard modular biotelemetry system, specifically its heart rate sensor, to capture electrocardiogram (ECG) data during training missions conducted in a flight simulator. The training missions comprised three submissions, each involving a mix of stressful events and mid-level events, with intermittent rest intervals termed "calm periods." Nonlinear analysis, particularly Poincaré plot analysis, was

utilized to assess HRV based on beats per minute (BPM), standard deviation perpendicular to the line-of-identity (SD1), and standard deviation along the line-of-identity (SD2). The results indicated a increase in BPM during stressful events. SD1 and SD2 were found to be lower during both stress and mid-level events compared to calm periods. The findings suggest that HRV, as analyzed through the proposed methodology, can effectively quantify the physical and mental load, or stress, experienced by fighter pilots during flight simulator training. The study recommended further testing with a larger sample size to enhance the robustness of the methodology and its potential integration into practical training scenarios for fighter pilots.

Bustamente-Sánchez & Clemente-Suárez, 2020a

The purpose of this study<sup>51</sup> was to study the effects of night and instrument helicopter flights on the psychophysiological response of aircrew. Twelve male aircrew members (mean  $\pm$  IQR, age  $30.4 \pm 4.4$  yrs, height  $173.8 \pm 2.3$  cm, weight  $72.2 \pm 8.0$  kg, flight experience  $742.2 \pm 481.6$  h) flew in two-night flights of  $90.6 \pm 13.3$  minutes and two instrument flights of  $94.2 \pm 8.9$  minutes. Psychophysiological responses were measured before and after flights. Measures were taken that assessed Subjective Stress Perception (SSP), Ratings of Perceived Exertion (RPE), Critical Flicker Fusion Threshold (CFFT), Isometric Handgrip Strength (IHS), hamstring flexibility, blood oxygen saturation and heart rate variability (HRV), spirometry values, body temperature, lower body strength, anxiety, and a digit span. The results indicated that RPE increased from  $6.0 \pm 2.0$  to  $9.0 \pm 5.0$  for all flights. Flexibility increased in instrument flight conditions from  $21.0 \pm 22.8$  cm to  $23.0 \pm 19.3$  cm. There was a decline in peak expiratory flow only in the night flight condition ( $12.0 \pm 3.3$  l/s to  $11.1 \pm 5.7$  l/s). Measures of HRV indicated that preflight square root of the mean of the sum of the squared differences between adjacent normal R-R intervals (RMSSD) and the percentage of differences between R-R intervals higher than 50

ms were higher in instrument flying conditions ( $93.4 \pm 71.1$  ms and  $33.9 \pm 31.9\%$ , respectively) compared to night flying conditions ( $42.7 \pm 20.2$  ms and  $10.0 \pm 10.3\%$ ). The Stay-Trait Anxiety Inventory revealed a higher anxiety score before flights involving instruments compared to night flying. Additionally, cognitive anxiety, assessed through the Competitive State Anxiety Inventory, was higher after instrument flights than after night flights. The authors concluded that aircrew experienced different psychophysiological responses during night flights compared to flights involving instruments.

Bustamante-Sánchez & Clemente-Suárez, 2020b

The purpose of this study<sup>52</sup> was to research how disorientation training affects the psychophysiological response in helicopter pilots, transport pilots, and F-18 fighter pilots. Male pilots ( $n = 39$ ) of the Spanish Army and Air Force underwent a 25-minute vestibular and visual disorientation training session in a flight. Before and after disorientation training, we measured subjective stress perception (SSP) on a 0-100 scale, perceived exertion using Borg's 6-20 rating (RPE), cortical arousal with the Critical Flicker Fusion Threshold (CFFT), isometric handgrip strength (IHS), and forced vital capacity (FVC). Heart rate variability measures were obtained using a chest-mounted heart rate (HR) monitor. The SSP was increased in helicopter pilots ( $8.78 \pm 10.8$  to  $49.4 \pm 22.7$ ) and transport pilots ( $5.29 \pm 7.46$  to  $30.7 \pm 25.6$ ), but not in fighter pilots after training. RPE scores increased after training in helicopter pilots ( $6.7 \pm 1.27$  to  $11.9 \pm 2.04$ ) and transport pilots ( $6.86 \pm 1.57$  to  $9.29 \pm 1.98$ ), but not in fighter pilots. Helicopter pilots did have higher RPE post-training ( $11.9 \pm 2.04$ ) compared to both transport ( $9.29 \pm 1.98$ ) and fighter pilots ( $9.20 \pm 2.22$ ). The IHS was greater in transport pilots ( $50.7 \pm 4.46$  kg) compared to helicopter pilots ( $44.8 \pm 6.22$  kg) after training. Furthermore, FVC was greater in fighter pilots both pre- ( $5.44 \pm 0.41$  L) and post-training ( $5.39 \pm 0.33$  L) compared to pre- and post-training values of helicopter

pilots ( $4.73 \pm 0.547$  L and  $4.67 \pm 0.489$  L, respectively). There was no change and no difference between groups for blood oxygen saturation, heart rate, or the critical flicker fusion threshold. The HRV analysis revealed a general decrease in the root mean squared of successive differences between adjacent R-R intervals (RMSSD) for all pilots after training, dropping from  $42.0 \pm 21.7$  ms to  $37.6 \pm 16.5$  ms in the overall group. Specifically, transport pilots experienced a decrease in RMSSD from  $50.7 \pm 26.5$  ms to  $41.7 \pm 24.1$  ms. No differences were observed in other HRV variables. The study's conclusion was that disorientation training increased stress, exertion, and sympathetic activation. Notably, helicopter pilots were more adversely affected in terms of strength, breath capacity, and perceived exertion compared to transport and fighter pilots.

Tornero Aguilera et al., 2020

The purpose of this study<sup>53</sup> was to investigate the psychophysiological stress response and autonomic modulation of pilots and medical aircrew during disorientation exposure. A total of 47 Spanish Air Force soldiers participated, including males ( $n = 37$ , mean age  $35 \pm 10.2$  yrs, height  $175.7 \pm 6.9$  cm, weight  $74.4 \pm 10.7$  kg) and females ( $n = 10$ , mean age  $41 \pm 9.1$  yrs, height  $171.1 \pm 2.1$  cm, weight  $68.3 \pm 13.1$  kg). The participants comprised pilots ( $n = 25$ ) and medical aircrew personnel ( $n = 22$ ) who underwent 25 minutes of disorientation exposure training involving vestibular, proprioceptive, and visual disorientation. Assessments of isometric hand-grip strength (HS), perceived subjective stress (PSS), rating of perceived exertion (RPE), and heart rate variability (HRV) were conducted before and after disorientation. Pilots demonstrated increases in HS ( $\Delta 3.9\%$ ) and PSS ( $\Delta 51.8\%$ ), while medical aircrew personnel exhibited increases in HS ( $\Delta 4.0\%$ ), PSS ( $\Delta 63.4\%$ ), and RPE ( $\Delta 20.0\%$ ) during disorientation training. In medical aircrew personnel, HRV analysis revealed an increase in mean HR ( $\Delta 10.2\%$ ), max HR ( $\Delta 20.0\%$ ), and low frequency ( $\Delta 19.6\%$ ), and a decrease in root mean square of the successive differences (RMSSD;



$\Delta$ -45.5%), percentage of differences between R-R intervals higher than 50ms (PN50;  $\Delta$ -28.3%), and Poincaré plot standard deviation perpendicular (SD1;  $\Delta$ -43.3%) and along the line of identity (SD2;  $\Delta$ -28.0%) during disorientation exposure. Additionally, medical aircrew personnel displayed higher baseline values for mean HR ( $\Delta$ 2.6%), RMSSD ( $\Delta$ 6.3%), LF ( $\Delta$ 12.2%), SD1 ( $\Delta$ 19.4%), and lower SD2 ( $\Delta$ -39.8%) compared to pilots. The study's findings suggested that pilots did not perceive disorientation training as a stressful stimulus compared to medical aircrew personnel, as indicated by RPE and PSS. The reported increase in HS in both groups suggested sympathetic activation, which was further supported by HRV analysis in response to disorientation exposure.

Mohanavelu et al., 2020

The purpose of this study<sup>54</sup> was to explore the correlation between fighter pilots' attention (performance) and cognitive load during dynamic workload using physiological (electrocardiogram; ECG) and subjective measures (National Aeronautics and Space Administration Task Load Index; NASA TLX) while flying in a high-fidelity fighter aircraft simulator. The study involved 20 participants (mean  $\pm$  SD; age  $28.1 \pm 1.4$  years), all declared "fit to the level of combat flying." The participants underwent four different workloads separated by a 20-minute washout period in the flight simulator: 1) normal visibility condition as normal workload (NWL), 2) low visibility as moderate workload (MWL), 3) normal visibility with a secondary cognitive task as high workload (HWL), and 4) low visibility with a secondary cognitive task as very high workload (VHWL). Signal quality allowed for the analysis of 16 subjects. The results revealed that, in terms of heart rate variability (HRV) measures, overall autonomic activity, sympathetic activation, standard deviation of RR intervals, and slow changes in heart rate were lower at the start and take-off compared to the cruise and landing segments in most workload

conditions. Performance measures indicated that take-off and landing performance were more challenging ( $86-88 \pm 3.5\%$ ) in MWL compared to VHWL conditions. HRV parameters suggested that increased task performance was associated with heightened sympathetic activity and reduced parasympathetic activity during the execution of secondary cognitive tasks. Additionally, NASA TLX scores indicated an increased cognitive demand during flight. However, MWL and VHWL conditions (low visibility) indicated that effort, performance, and frustration were greater compared to NWL. In conclusion, the authors asserted that changes in HRV measures and pilot performance served as indicators of the dynamic workload environment experienced by pilots in a flight simulator.

Alaimo et al., 2020

This study<sup>55</sup> examined the connection between heart rate variability (HRV) biometric data collected from pilots and subjective data obtained through the National Aeronautics and Space Administration Task Load Index (NASA TLX) questionnaire. Twenty-three pilots (mean  $\pm$  SD; age  $31.8 \pm 8.1$  years, height  $1.74 \pm 0.06$  m, weight  $75.4 \pm 11.7$  kg) participated in a high-fidelity flight simulator classified by the European Aviation Safety Agency, simulating the CESSNA Citation C560 XLS. The flight sequence included take-off, climb to 10,000 ft, left and right turns, a stall maneuver, upset recovery, and a holding circuit. Following this approximately 30-minute flight, pilots executed an approach and landing on the same runway. The flight was segmented into two phases: take-off with initial climb (TO) and final approach with landing (LA). HRV data were collected using a heart rate monitor chest strap (Movisens EcgMove3) and analyzed for R-R interval, yielding measures such as standard deviation of normal R-R intervals (SDNN), Poincaré plot standard deviation perpendicular to the line of identity (SD1), and low to high-frequency ratio (LF/HF ratio). NASA TLX was administered in both TO and LA phases, providing an overall

workload (OW) score. The authors observed a heightened workload during the LA phase, evident in an increased LF/HF ratio and decreased SD1 and SDNN. In the TO phase, a reduction in SDNN and SD1 HRV parameters suggested a potential increase in workload, followed by an SD1 increase as pilots reached a level flight altitude, indicating reduced mental effort. The elevated workload during LA was substantiated by higher scores on the NASA TLX OW component. However, correlation analysis revealed no connection between OW and HRV indices in either the TO or LA phase. In conclusion, objective workload measures indicated higher OW during the LA phase compared to TO, but a linear relationship between OW and HRV was not observed

Kang et al., 2020

The purpose of this study<sup>56</sup> was to assess the influence of pilots' verbal reports during different types of recognized spatial disorientation. Thirty male Air Force fighter pilots ( $30.6 \pm 3.7$  years) were randomly assigned to either a verbal report group ( $n = 15$ ) or a non-verbal report group ( $n = 15$ ). The pilots encountered six types of spatial disorientation (somatogravic illusion, Coriolis, leans, graveyard spin, false horizon, and black hole illusion) in a GL-4000 simulator. Flight performance was evaluated based on self-perceived performance ability and instructor assessments. These assessments focused on the pilots' ability to manage flight specifications in each phase, considering elements such as altitude, speed, and attitude in relation to standard specifications. Mental stress was assessed using electrocardiogram (ECG) measurements and perceived distress scores. ECG data were collected using the BioPac system, analyzed with Kubios Heart Rate Variability (HRV) v. 3.3.0, and presented as low frequency (LF), high-frequency (HF), and LF/HF ratio in the frequency domain. Simulator sickness was evaluated using the Simulator Sickness Questionnaire (SSQ), including scores for nausea, oculomotor issues, disorientation, and overall severity. The results revealed group differences, with the verbal report execution group

scoring 8% higher in altitude ( $7.62 \pm 0.10$ ) and 10% higher in airspeed ( $7.63 \pm 0.10$ ) compared to the non-verbal report group (altitude:  $7.07 \pm 0.10$ , airspeed:  $6.96 \pm 0.10$ ). The altitude score for the graveyard spin was lower ( $6.63 \pm 0.18$ ) than other disorientation types, while the attitude score for graveyard spin ( $5.90 \pm 0.15$ ) was also lower compared to other disorientation types. Self-evaluation scores were lower for Coriolis ( $2.37 \pm 0.25$ ) than for other disorientation types. Verbal report execution did not significantly affect any HRV parameter, although the verbal report group tended toward higher HF and a lower LF/HF ratio. Perceived distress scores were lower in the verbal report group ( $4.83 \pm 0.16$ ) than the non-verbal report group ( $5.42 \pm 0.13$ ). Coriolis induced higher perceived distress scores ( $6.53 \pm 0.12$ ) compared to other disorientation types. There was no main effect on verbal report execution for SSQ variables. In conclusion, the findings support the idea that verbal report execution during spatial disorientation situations can contribute to improved flight safety.

Clément-Coulson et al., 2021

The purpose of this study<sup>57</sup> was to explore the utility of electrocardiogram (ECG) as a workload indicator within an aviation context, particularly when workload is induced by heightened difficulty in performing the same type of maneuver. The study included a sample of 12 pilots (5 commercial and 7 airline pilots, comprising 12 males and 2 females, with a median age of 26.5 years). The participants underwent an experimental flight sequence in the Ascent XJ flight training fixed base simulator, involving the following maneuvers: 0) take-off, 1) normal turn (NT), 2) simple approach to stall (SAS), 3) steep turn (ST), 4) complex approach to stall (CAS), and 5) landing. Electrocardiogram (ECG) data were collected using a Polar H10 heart rate monitor and analyzed using Kubios Heart Rate Variability 3.3.1 for heart rate (beats per minute or bpm) and the standard deviation of successive R-R intervals (SDNN). The National Aeronautics and Space

Administration Task Load Index (NASA TLX) was employed to assess subjective workload after each maneuver. Objective performance was quantified by flight path deviations, with turns measured as the time spent outside acceptable airspeed and altitude, and stalls assessed based on the interval between stall warning onset and the attainment of safe airspeed and altitude. The study's findings revealed that mean flight path deviations were higher during steep turns (ST) (median  $\pm$  SD;  $13.29 \pm 18.47$  s) compared to normal turns (NT) ( $6.50 \pm 12.60$  s). The mean recovery time for complex approach to stall (CAS) was greater ( $43.50 \pm 11.95$  s) than for simple approach to stall (SAS) ( $17.50 \pm 5.37$  s). A moderate increase ( $d = 0.53$ ) in heart rate was observed between NT ( $82.70 \pm 7.52$  bpm) and ST ( $84.47 \pm 7.63$  bpm), as well as between SAS ( $79.20 \pm 7.34$  bpm) and CAS ( $81.21 \pm 7.03$  bpm). There was no significant difference in SDNN between NT and ST, or between CAS and SAS. However, SDNN was lower during turns compared to stalls ( $d=0.93$ ;  $\Delta 8.76 \pm 1.87$  ms). Subjective workload, as measured by NASA-TLX, differed between NT ( $40.56 \pm 14.69$ ) and ST ( $49.58 \pm 16.39$ ), as well as between CAS ( $50.49 \pm 16.26$ ) and SAS ( $37.99 \pm 13.33$ ). In conclusion, the authors suggested that a combination of cardiac measures and subjective evaluations provides a comprehensive methodology for understanding workload in aviation settings.

Villafaina, et al., 2021

The objective of this study<sup>58</sup> was to examine the physiological response of professional pilots during various phases of a flight, including takeoff, landing, air-air attack, and air-ground attack conducted in a flight simulator. Eleven military pilots (mean  $\pm$  SD;  $33.36 \pm 5.37$  yrs,  $176 \pm 5.51$  cm,  $77.36 \pm 7.10$  kg,  $13.45 \pm 5.35$  years of military service) from the Spanish Air Force participated in the study. Electroencephalographic (EEG) and heart rate variability (HRV) were measured during different segments of the simulation, namely 1) takeoff, 2) air-air mission, 3) air-

ground attack, and 4) landing without a reduction in visibility in an F-5 M flight simulator. The ECG data were analyzed using Kubios HRV 2.1 software to measure HRV parameters. These included mean heart rate (HR), R-R intervals, standard deviation of normal beat-to-beat variation (SDNN), percentage of successive RR intervals that differ by more than 50 ms (pNN50), root mean square of successive R-R interval differences (RMSSD), low-frequency power (LF), high-frequency power (HF), LF/HF ratio, standard deviation of the Poincaré plot perpendicular to the line-of-identity (SD1), and the standard deviation of the Poincaré plot along the line-of-identity (SD2). The authors reported that mean HR and time between R-R intervals were different at baseline ( $69.24 \pm 10.91$  bpm and  $890.94 \pm 135.92$  ms, respectively) compared to takeoff ( $73.33 \pm 13.94$  bpm and  $849.38 \pm 140.78$  ms) and landing ( $80.62 \pm 15.47$  bpm and  $773.03 \pm 141.38$  ms), with differences also noted between takeoff and landing. Takeoff exhibited higher values than landing for HRV parameters, including pNN50 ( $20.35 \pm 13.67\%$  to  $7.69 \pm 5.84\%$ ), RMSSD ( $43.37 \pm 12.63$  ms to  $28.50 \pm 7.27$  ms), and SDNN ( $46.67 \pm 14.86$  ms to  $34.89 \pm 11.19$  ms). Frequency parameters showed differences where baseline was lower than takeoff for HF ( $29.14 \pm 15.93$  ms<sup>2</sup> to  $40.02 \pm 15.76$  ms<sup>2</sup>), but baseline was greater than takeoff for LF ( $70.83 \pm 15.92$  ms<sup>2</sup> to  $59.60 \pm 15.50$  ms<sup>2</sup>) and LF/HF ratio ( $3.43 \pm 2.17$  to  $1.81 \pm 0.95$ ). Non-linear HRV measures also reduced during takeoff for SD1 ( $30.74 \pm 8.96$  ms) and SD2 ( $57.79 \pm 20.44$  ms) compared to landing ( $20.20 \pm 5.15$  ms and  $44.42 \pm 16.23$  ms, respectively). HRV comparisons among baseline, air-air missions, and air-ground maneuvers revealed an increase in mean HR from baseline ( $69.24 \pm 10.91$  bpm) to air-air missions ( $77.67 \pm 13.19$  bpm) and air-ground maneuvers ( $79.75 \pm 17.74$  bpm), but no significant differences when comparing between flight maneuvers. Similarly, R-R intervals were greater at baseline ( $890.94 \pm 135.92$  ms) compared to air-air missions ( $796.98 \pm 128.07$  ms) and air-ground maneuvers ( $789.95 \pm 149.25$  ms), with no significant differences between flight

maneuvers. No other HRV parameters exhibited significant differences during baseline, takeoff, air-air missions, air-ground maneuvers, and landing segments. Based on the reported results, the authors concluded that takeoff, landing, and air-air and air-ground attack maneuvers had an impact on the autonomic regulation of professional pilots, leading to reduced HRV during landing compared to takeoff. Flight simulator tasks such as takeoff, landing, air-air attacks, or air-ground attack maneuvers led to significant alterations in EEG activity and autonomic modulation among professional pilots. Changes in the beta EEG power spectrum indicated that landing maneuvers elicited greater attentional resources compared to takeoff. Additionally, a decrease in HRV during landing was observed in contrast to takeoff. These findings are important for training applications.

Fuentes-García et al., 2021

The purpose of this study<sup>59</sup> was two-fold: first, to examine the immediate effects of both simulated and actual flights on heart rate variability (HRV), anxiety, perceived exertion, and self-confidence; and second, to compare autonomic modulation during real and simulated flights. Twelve experienced military pilots (mean  $\pm$  SD; 33.08  $\pm$  5.21 yrs, 13.25  $\pm$  5.15 yrs of military experience) were assessed before, during, and after flights, involving a real flight with an F5 aircraft and a simulated flight with an operational F-5 M flight simulator. HRV parameters were collected using a Polar RS800CX heart rate chest strap and analyzed with Kubios HRV software 3.3, covering mean heart rate (mean HR), R-R intervals, root mean square of successive R-R interval differences (RMSSD), percentage of successive RR intervals that differ by more than 50 ms (pNN50), low power frequency band [0.04-0.15 Hz, LF], high power frequency band [0.15-0.4 Hz, HF], ratio of the low frequency to high-frequency power (LF/HF), total power, standard deviation of the Poincaré plot perpendicular to the line-of-identity (SD1), and the standard deviation of the Poincaré plot along the line-of-identity (SD2). Anxiety levels were measured using

the Competitive State Anxiety Inventory-2R (CSAI-2R) in Spanish, with 17 items assessing cognitive anxiety, somatic anxiety, and self-confidence. The State-Trait Anxiety, consisting of 20 items, gauged participants' current state of anxiety, and Borg's 6-20 scale assessed perceived exertion. The study found differences in baseline mean HR ( $69.82 \pm 10.70$  bpm) and R-R interval ( $885.54 \pm 136.14$  ms) compared to post real-flight ( $98.06 \pm 11.89$  bpm and  $631.91 \pm 77.11$  ms). Post real and simulated flights showed distinctions in mean HR ( $98.06 \pm 11.89$  bpm vs.  $74.56 \pm 13.39$  bpm, respectively) and R-R interval ( $631.91 \pm 77.11$  ms vs.  $837.70 \pm 144.35$  ms, respectively). No other HRV parameters exhibited differences between baseline and post-flight conditions. Perceived exertion (RPE) increased after a real flight ( $11.17 \pm 2.33$ ) compared to baseline ( $8.42 \pm 1.88$ ), but not after a simulated flight. Cognitive anxiety, as measured by the CSAI-2R, decreased after a real flight ( $6.17 \pm 2.37$ ) compared to baseline ( $6.92 \pm 3.15$ ). The authors conducted a comparison of average HRV parameters during real and simulated flights and reported a higher mean HR during a real flight ( $93.81 \pm 15.41$  bpm) than in a simulated one ( $70.83 \pm 12.48$  bpm), while the R-R interval was shorter during a real flight ( $660.30 \pm 106.86$  ms) compared to a simulated flight ( $875.58 \pm 139.10$  ms). In conclusion, the authors found that real flights led to a reduction in R-R interval and cognitive anxiety, an increase in mean HR and RPE, whereas simulated flights did not elicit the same responses.

Maciejewska & Galant-Gołębiewska, 2021

The purpose of this study<sup>60</sup> was to assess the psychophysical changes in a pilot handling a Pilot Private License (PPL) during airfield traffic patterns and to compare their heart rate variability (HRV) parameters with normative values for the average healthy individual. The study involved three participants: Pilot 1, a student in the PPL program; Pilot 2, an individual with a PPL; and Pilot 3, an experienced flight instructor with several years of experience. The flight took



place in a Cessna 152 aircraft at an altitude of 800 ft, with visibility greater than 10 km, no clouds below 1500 m, a wind speed of 3 knots, and a temperature range of 15-25°C. HRV parameters, including standard deviation of NN (SDNN), root mean square of successive differences (rMSSD), standard deviation perpendicular to the line of identity (SD1), and standard deviation along the line of identity (SD2), were recorded using a Polar H10 chest heart rate monitor. The recorded data revealed that the RR interval for the pilots ranged from 480 to 520 ms, whereas the normative value for a healthy person should be greater than 750 ms. For SDNN, the normal range is 50-70 ms; Pilot 1 (44.86 ms) and Pilot 2 (30.81 ms) were close to this range, while Pilot 3 (24.36 ms) had a lower but nonsignificant value. The normal range for rMSSD is 27-57 ms; Pilot 1 (5.17 ms) and Pilot 3 (5.81 ms) had lower values, and Pilot 2 (23.23 ms) had a higher value but still below normative values. SD1 values were below normative values (50-82 ms) for all pilots: Pilot 1 (3.65 ms), Pilot 2 (16.43 ms), and Pilot 3 (4.11 ms). The values obtained for SD2 were close to normative values. The study concluded that parameters such as the length of the R-R interval, rMSSD, and SD1 differed from normative HRV scores. However, parameters like SD2 and SDNN were similar to normative values during short-term measurements. The values below the norm suggested parasympathetic withdrawal, while lower R-R interval values indicated an appropriate sympathetic nervous system response to the flight.

## **ELECTRODERMAL ACTIVITY (EDA)**

Lindholm et al., 1984

The primary objective of this study<sup>61</sup> was to assess pilot workload in complex flight environments which closely approximate real-world situations through use of non-intrusive, physiological metrics. The study had 12 males set to begin Undergraduate Pilot Training at Williams AFB weeks after study participation, perform a 120 s carrier landing task on a desktop simulator of a Navy A-7 aircraft. During this, participants had to perform five runs of a tone discrimination task, which required them to respond to tones higher than the reference tone. The tones could be presented in two pitches of either close (1250 and 1750 Hz) to the reference tone (1500 Hz) as the hard discrimination or further in pitch (1000 Hz and 2000 Hz) from the reference. Errors were recorded if the subject responded to a tone lower than the reference tone (error of commission) or failed to respond to the higher tone (error of omission). Reaction times were recorded to the nearest 4 ms. Each subject was given a flight termination score according to the following scale: 1) Splash – aircraft reached 0 altitude and impacted with water, 2) Time-out - subject lost orientation and could not reach carrier deck within 150 s, 3) Ramp strike – aircraft struck stern of carrier below landing area, 4) Crash - aircraft made contact with carrier deck in a state of excessive roll and vertical speed, 5) Bolter – aircraft contacted carrier deck but with a bounce and subsequent miss of tail-hook cables, and 6) Landing – aircraft contacted carrier deck in designated landing area with optimal roll and speed. Heart rate (HR) was quantified as inter-beat-interval (IBI) from leads on the left lateral ribcage and sternum. Skin conductance was collected on the middle finger of the left hand and referenced to the back of the same hand. Study procedure involved starting with the tone discrimination task, a 10-minute break, carrier landing task, 10-minute break, and combined carrier landing and tone discrimination tasks. There were

five runs of the tone task alone, 10 runs of the carrier landing task (tones were presented but participants were instructed to not respond), and 10 runs of the combined tasks. This study found slower reaction times during the hard discrimination (809 ms) compared to the easy discrimination (715 ms) during the tone task alone. During the Carrier task alone the most common error was gross and violent stick movement resulting in total loss of aircraft control and an early splash. Although, the percentage of disastrous terminations decreased with practice (Splashes 32% to 20%, Ramp strike & crash 25% to 22%), while the percentage of landings and bolters increased (36% to 42% and 7% to 17%, respectively). Participants were able to improve their flight approach score from the first five to the last five, relative to the last five flights of the carrier alone task. The percentage of disasters (Splashes 12%, Ramp strikes and crashes 15%), bolters (61%), and landings (12%) was not different in the last five flights of the combined task compared to the carrier alone task. Participants tended to treat tone discrimination as a secondary, low-priority task during the combined task, such that reaction times and discrimination errors increased relative to the tone-alone condition. The increase in reaction times and errors also became greater as the subject flew closer to the carrier landing area. Physiological measures were averaged into four blocks of six-tone trails each (each block represents a 30-segment of the 2-minute tasks). Heart rate decreased during the tone task alone over the four trial blocks (IBI: 851 ms to 876 ms to 897 ms to 901 ms; HR: 70.5 bpm to 68.4 bpm to 66.8 bpm to 66.8 bpm) and increased as participants approached the carrier landing area in the carrier alone (IBI: 829 ms to 773 ms; HR: 72.4 bpm to 77.6 bpm) and combined task (IBI: 843 ms to 801 ms; HR: 71.2 bpm to 74.9 bpm) conditions. There was no change in skin conductance levels as a function of any of the task variables. The authors concluded HR to be a reliable metric for quantifying workload during final approach to landing.

Mühlberger et al., 2001

This study<sup>62</sup> purpose was threefold: 1) examine emotional processing of individuals with a flight phobia during exposure to virtual reality (VR) flights, 2) to evaluate whether fear reduction due to repeated exposure to VR flights is comparable or even greater than fear reduction induced by traditional relaxation training, and 3) to evaluate the efficacy of exposure of flight phobics to VR flights in reducing fear of flying as assessed by psychometric measures of fear of flying and avoidance. Thirty participants who fit the criteria for simple phobia of flying with at least one previous flight were divided into two groups (n = 15 each) each of whom either exposed to VR (mean  $\pm$  SD; 43.9  $\pm$  10.6 yrs, 2 men & 13 women) or relaxation (42.2  $\pm$  9.1 yrs, 2 men & 13 women). Physiological responses of skin conductance level (SCL) were recorded on the middle phalanx of digits three and four of the non-dominant hand and electrocardiogram for heart rate (HR). The VR environment presented a head-mounted display (HMD) that used visual, auditory, and motion manipulations lasting approximately 16 minutes for all major phases of flight (leaving the parking position, reaching the take-off position, take-off, ascending, reaching flight altitude, two periods of air turbulence, descending, and landing). The three-dimensional environment within the VR simulation used the inside of a Boeing 737 with the subject seated in the left window row in the middle of the aircraft, and the seat to the right taken by a virtual passenger. A 6-minute VR test flight was conducted before and after treatment in both groups, without auditory or turbulence simulations. Fear was assessed using a 0 (no discomfort) to 100 (panic-like discomfort) Subjective Units of Discomfort (SUD) scale every two minutes during test flight. Five questionnaires were used to evaluate treatment outcomes with three assessments, pre-treatment (3 weeks [pre-1], 1 week [pre-2], and immediately before a therapy session [pre-3]), and three assessments post-treatment (immediately after treatment session [post-1], 2 weeks later [post-2],

and 14 weeks later [post-3]) assessments. The Fear of Flying scale (FFS) was used to assess fear elicited in scenarios mimicking air travel on a five-point scale. The General Fear of Flying Questionnaire (Allgemeiner Flugangstfragebogen, AFA) assesses fear of flying and avoidance of flying using an 11-point rating scale ranging from 0 (“Not at all”) to 10 (“Extreme”). The Danger Expectancy Scale (DES) aimed to evaluate the perceived likelihood that individuals would contemplate specific harmful events during flight. The Anxiety Expectancy Scale (AES) measured anxiety symptoms using ten items on a five-point scale. The Anxiety Sensitivity Index (ASI) comprises 16 items, each rated on a five-point scale, designed to evaluate fearful cognitions associated with anxiety. The treatment protocol consisted of four VR treatment flights as described above, all of which were completed in one session. The relaxation group learned deep muscle relaxation for two blocks of 32 minutes, each separated by 15 minutes in the same day. SUD peak fear responses categorized the results of this study: no fear (score 1-19), mild fear (score 20-39), moderate fear (score 40-59), strong fear (score 60-79), and extreme fear (80-100). In the VR exposure group, the strongest fear reports were observed during the first VR exposure with a mean SUD >40 after takeoff. There was a decline in SUDs both within continuing flights and repeated VR flight exposures. There was a reduction in HR with repeated VR flights, but no change within flights. The SCL responses demonstrated a decline during the course of the flight, with an initial increase before gradually decreasing across successive flights. When comparing treatment outcomes, there was a greater effect of reducing fear during VR test flights of VR exposure treatment (SUD  $35.8 \pm 26.1$  to  $10.1 \pm 13.6$ ) than of relaxation treatment (SUD  $30.2 \pm 23.4$  to  $19.6 \pm 19.8$ ). The VR exposure and relaxation group both saw a change in HR within VR test flights from pre- to post-treatment (VR exposure:  $4.2 \pm 10.3$  bpm to  $-1.9 \pm 3.5$  bpm, Relaxation:  $6.3 \pm 14.1$  bpm to  $-1.5 \pm 4.2$  bpm). There was also a change in SCL response within VR test flights from

pre- to post-treatment (VR exposure:  $4.0 \pm 3.0 \mu\text{S}$  to  $-0.9 \pm 2.0 \mu\text{S}$ , Relaxation:  $3.0 \pm 1.2 \mu\text{S}$  to  $0.4 \pm 2.0 \mu\text{S}$ ). There was also a general decline in pre- to post-psychometric assessments of AES, DES, and ASI scales for both groups. It was concluded that exposure to VR flights elicited subjective and physiological fear responses in individuals with a simple phobia of flight. These fear responses decreased with exposure and repeated exposures, such that repeated VR exposures were more effective in reducing subjective as well as physiological fear responses compared to a relaxation training of comparable duration.

#### Wilson, 2002

The main goal of this project<sup>63</sup> was to determine the reliability of psychophysiological data recording during flight and record electrodermal activity (EDA) to ascertain its utility for flight research. Ten male general aviation pilots aged 30-64 yrs (mean = 43) with 158-5400 h (mean = 1,317) of flight experience and 13-270 h (mean = 114) of experience in the aircraft used for testing, flew a Piper Arrow single-engine raft in a prescribed scenario for 90 minutes on two occasions. The flight scenario was broken into visual flight rules (VFR), instrument flight rules (IFR), and high-speed (HS) IFR parts, where IFR conditions were created using vision restriction goggles to only view the aircraft instrument panel impairing forward vision. Both days included 22 two-min segments of flight protocols: preflight baseline, preflight checklists, engine start, VFR takeoff, VFR climb-out, VFR cruise, VFR air work, VFR approach, VFR touch and go, VFR climb-out, IFR air work, IFR cruise, IFR hold, IFR distance measuring equipment (DME) arc, IFR instrument landing system (ILS) tracking, IFR missed approach, IFR climb-out, IFR HS hold, IFR HS DME arc, IFR HS ILS tracking, landing, and postflight baseline. The electrocardiogram (ECG) was collected from two electrodes, one over the sternum and another over the intercostal space on the left side of the chest and analyzed for heart rate (HR), mid-frequency power (0.06-0.14 Hz), and

high-frequency power (0.15-0.40 Hz). The EDA was recorded from electrodes placed under the right foot and analyzed using the EDR\_Para 3.6 software for number of EDA responses, rise times, recovery times, and tonic levels. Subjective mental workload was assessed at the end of each segment on a 0-100 scale, 100 being extremely high workload. Post-baseline for heart rate and IFR ILS tracking was different for subjective rating. Heart rate was able to discriminate among three groups of segments. Peak HR occurred during takeoffs and landings. The high HR group included touch and go and missed approach segments. An intermediate HR was during preflight checklists, engine start, VFR cruise, VFR air work, IFR cruise, IFR hold, IFR DME arc, IFR climb-out, HS hold, and HS DME arc. The lowest HR was observed during pre- and postflight baselines. There was a decrease in variability for both mid-frequency and high-frequency power during VFR takeoff and VFR touch and go. The preflight baseline was associated with higher levels in both frequencies. The greatest number of EDA responses was observed in the VFR takeoff, touch and go, and final landing, whereas the pre- and postflight baseline had the fewest. There was a correlation of  $r=0.83$  between HR and number of EDA responses. The EDA tonic level showed an increase during VFR takeoff, VFR touch and go, and final landing. The recovery time during VFR takeoff, VFR touch and go, and final landing were shorter than during preflight baseline, preflight checklists, VFR climb-out, IFR air work, IFR DME arc, IFR ILS tracking, HS holding, and HS DME arc. The mean subjective mental workload was highest during IFR ILS tracking and HS ILS tracking, and the easiest segments were the first six VFR associated segments. In summary, it was concluded that cardiac and electrodermal measures were highly correlated and exhibited changes in response to the various demands of flight, but present reported parameters of heart rate variability were less sensitive than heart rate.

Jang et al., 2002

The purpose of this study<sup>64</sup> was to investigate the physiological reactions to flying and driving in virtual environments (VE). Eleven participants (mean  $\pm$  SD 24.9  $\pm$  5.82 years) engaged in two virtual environments. After a 5-minute eyes-open baseline, participants utilized a head-mounted display (HMD), occupied a flight seat with a subwoofer generating vibrations, and experienced a flying scenario, including sitting in the passenger cabin with the engine on, taxiing on the runway, taking off, flying in good and bad weather, and landing. Following a 60-minute wash-out period and another 5 minutes of eyes-open baseline, participants engaged in a driving scenario, now featuring a physical steering wheel. The driving task required participants to follow traffic and directional signs, steering with only their right hand. Electrodermal activity (EDA) was measured from the left ring and index fingers, alongside temperature measurements. Heart rate was recorded on both wrists and analyzed for heart rate variability (HRV). Various questionnaires were administered to assess simulator sickness (Simulator Sickness Questionnaire or SSQ), the sense of presence and realism experienced in the virtual environment (Presence & Realism Questionnaire or PRQ), the participants' absorption into the VE (Tellegen Absorption Scale or TAS), and their capacity for dissociation (Dissociative Experience Scale or DES). No significant differences were observed in  $\Delta$ EDA or  $\Delta$ skin temperature response between flying and driving simulations ( $\Delta$ 0.20  $\pm$  0.29 vs  $\Delta$ -0.10  $\pm$  0.49;  $\Delta$ 0.02  $\pm$  0.06 vs  $\Delta$ 0.001  $\pm$  0.03; respectively). The EDA response during driving was higher than during flying, attributed to the active involvement required in the driving simulator. HRV showed no significant differences, except for an increase in heart rate during the driving simulation. Questionnaire analysis revealed a strong correlation between age and SSQ ( $r=0.90$ ) after driving, indicating that older participants were more sensitive to view changes from the head motion tracker while driving, which was not observed during the



flying simulation. The authors concluded that EDA and HRV can serve as objective measures to monitor sympathetic and parasympathetic activity.

Cheung et al., 2004

The objective of this study<sup>65</sup> was to investigate consistent physiological changes in mean arterial blood pressure (MAP), heart rate (HR), heart rate variability (HRV), respiration, and electrodermal activity (EDA) during a false sensation of pitch in a flight simulator. Sixteen healthy participants (14 men and 2 women, aged 21-31 years) underwent one familiarization and four experimental flight simulation trials in an integrated physiological trainer. In the four experimental trials, participants experienced a 120° per second to the right yaw rotation. In two of these trials, participants were instructed to roll their heads  $35 \pm 2^\circ$  from vertical to the right within 0.5 s and maintain the head tilt for 20 s. In the other two trials, participants rolled their heads to the left following the same procedures. For each head roll direction, participants were instructed to either ascend or descend 2000 ft to a new attitude, accompanied by a 60° change in heading, resulting in four conditions: right head roll + ascending task, right head roll + descending task, left head roll + ascending task, and left head roll + descending task. This altitude change occurred once before head movement (control) and immediately after (experimental). Continuous monitoring included arterial blood pressure using the Portapres Model-2 infrared finger plethysmograph, heart rate data obtained from electrocardiogram electrodes, respiratory activity monitored with an elastic pneumotachograph, and EDA measured as skin conductance between finger electrodes. The results showed no change in respiration from regular paced breathing (12-15 breaths per minute). Mean HR was higher during experimental conditions compared to control, and MAP decreased during the initial head roll. MAP returned to normal during the altitude change after head roll, with no differences between conditions. HR during the change in altitude and the subsequent straight level

flying interval was greater in the experimental condition compared to control. HRV differed between experimental and control conditions after the return of the head to the upright position and before the change in altitude. EDA response was higher during the experimental condition compared to control and varied before, during, and after the change in altitude. In terms of flight performance, participants better maintained airspeed during the control condition in the first 10 seconds compared to experimental conditions. There were fewer errors in the control condition, with participants executing appropriate power adjustments much faster in control ( $4.31 \pm 0.9$  s) compared to experimental ( $6.48 \pm 0.8$  s). The authors concluded that changes in cardiovascular responses appear to be correlated with the onset of disorientation in a simulator.

Koglbauer et al., 2009

The purpose of this study<sup>66</sup> was to investigate the impact of different arousal types on anticipatory processes, task performance, and post-task reflection, specifically in the context of pilots' threat and error management (TEM) performance. A total of twenty-eight male pilots, with a mean age of  $38.04 \pm 11.45$  years and flight experience ranging from 40 to 430 hours, holding a private pilot license for visual flight rules (VFR), were randomly assigned to either an experimental group ( $n = 16$ ) or a control group ( $n = 12$ ). The pilots undertook four flight maneuvers in a fixed-base, two-seater generic light aircraft simulator, comprising extreme pitch, overbanked attitude, power-off full stall, and left spin with two rotations. Each maneuver was analyzed across four phases: anticipation (15 seconds before each maneuver), onset, recovery, and post-recovery. The experimental group received specific recovery exercises, while the control group underwent VFR terrestrial and radio navigation training with a comparable level of difficulty. TEM performance was assessed by a flight instructor using a scale from 1 (not acceptable) to 4 (very good), and pilots self-assessed their workload using the National Aeronautics and Space Administration Task Load

Index (NASA TLX). Electrodermal Activity (EDA) was measured using the Varioport system from the medial sites of the left foot, adjacent to the plantar area, and reported as skin conductance level (SCL), non-specific skin conductance reactions frequency (NS.SCR freq.), and mean amplitude of skin conductance reactions (SCR amp). Instructor ratings revealed higher performance in the training group ( $3.21 \pm 0.07$ ) compared to the control group ( $2.65 \pm 0.08$ ). Further analysis of individual maneuvers demonstrated superior performance in the training group, particularly in recovering from extreme pitch attitude, overbanked attitude, and power-off full stall compared to the control group. Self-ratings of workload were more favorable in the training group, and subjective experiences of the physical and temporal demands of the flight task were lower in the training group than in the control group. The mean SCL response indicated higher arousal levels in the training group during the anticipation, recovery, and post-recovery phases, with notable differences influenced by the type of recovery maneuver. Conversely, NS.SCR freq. was greater in the control group across all phases. In conclusion, the study suggests that anticipative flight instructions, involving hands-on simulator exercises and recovery procedures divided into distinct anticipation-action-comparison units, can enhance pilots' TEM performance capabilities and neurophysiological adaptability during challenging maneuvers such as unusual attitudes, full stalls, and spins in real flight scenarios.

Koglbauer et al., 2011

The primary objective of this study<sup>67</sup> was to assess the effectiveness of an anticipation-based simulator training program for visual flight rules (VFR) pilots in dealing with threats, evaluated through simulator and real flight tests. The study involved 29 active male pilots with a private pilot license for VFR and no instrument flight rules experience, divided into experimental (mean  $\pm$  SD;  $33.8 \pm 10.62$  yrs) and control ( $41.77 \pm 11.96$  yrs) groups. During the initial flight,

participants flew a Pitts Special S-2B light aerobatic aircraft, with each maneuver demonstrated by the instructor first, followed by participants attempting the first recovery trial. The experimental group underwent nine training trials for each maneuver in a fixed base simulator, structured in three training sections, while the control group performed runway approaches and radio-navigation tasks. After training, all pilots completed a simulator test and a real airplane evaluation, consisting of extreme pitch maneuvers and power-off full stalls. Performance ratings by instructors increased for both groups from the initial flight to the final test flight, with a more significant improvement in the experimental group. Overall performance ratings for the experimental group increased from the initial flight to the simulator test, slightly decreasing in the first trial of the test flight and peaking in the second trial. In contrast, the control group showed minimal improvement. Recovery times decreased across different flight times for both groups, with the experimental group consistently demonstrating faster recovery durations. There was a time effect for self-rated performance and effort, with the experimental group showing improvements over time. Time pressure decreased in the experimental group for all maneuvers, while the control group experienced an increase from the initial flight to the simulator test. Participants reported increased excitement, strength, pride, and enthusiasm, as assessed by PANAS, with a decrease in heart rate (HR) and an increase in skin conductance level (SCL) observed across measurements for both groups. The authors concluded that the anticipative training, applied through a combination of simulator and real flight, can effectively transfer to flight instruction practice.

Wagner et al., 2015

The purpose of this study<sup>68</sup> was to explore the potential link between grip force and stress in the context of a stick-controlled task. Forty-two male participants (mean  $\pm$  SD, 26.17  $\pm$  2.12 yrs) were initially recruited, but only 13 successfully completed all sessions—four in the control

group and nine in the stress manipulation group. A force-sensitive resistor (FSR) embedded in the finger recess of the control stick (sampling at 60 Hz, 0-110 N) was utilized to measure grip force, while electrodermal activity (EDA) was measured on the left index finger. Participants engaged in a primary and secondary task on a 21.5-inch monitor using a handheld control stick in their right hand. The primary task involved tracking a moving circle with a stick-controlled crosshair, featuring three target velocities and three movement patterns. Simultaneously, the secondary task displayed a small moving rectangle that had to be kept within a larger stationary rectangle, with the control stick trigger returning the moving rectangle to the stationary one. Bonus points were awarded in a human factors class for participation, and stress manipulation occurred by informing the experimental group during the latter half of sessions that the number of bonus points depended on task performance. The results revealed that the mean standardized grip force was lower in the control group (-0.48) during the second half of the experiment but higher in the experimental group (0.15). There was an increase in the experimental group from the first to the second half of the experiment (stress manipulated) from -0.18 to 0.15. The mean standardized EDA response was lower in the control group (-0.35) during the second half of the experiment but higher in the experimental group (-0.04). Grip force and EDA measures demonstrated a positive correlation ( $r=0.65$ ). Subjective stress ratings, assessed using the National Aeronautics and Space Administration Task Load Index (NASA TLX), indicated that the control group (-0.30) had lower scores during the second half of the experiment compared to the experimental group (-0.17). In conclusion, the authors proposed that grip force serves as a potential indicator of stress, showing increased grip force during more stressful situations compared to less stressful ones .

Tamura et al., 2018

The purpose of this study<sup>69</sup> was to explore electrodermal activity (EDA) utilizing a wrist-worn device, concurrently assessing subjective autonomic symptoms during spatial disorientation training, and investigating potential correlations between variables. A cohort of 177 healthy pilot candidates (mean age 22.7 yrs, male/female 170/7) from the Japan Air Self-Defense Force participated in spatial disorientation training using the GYROLAB GL-4000 device. The training comprised two simulations: 1) a daytime scenario with visual elements like a runway, towns, forests, mountains, clouds, and a blue sky, and 2) a nighttime simulation replicating the same scenes but with reduced visual information, causing outlines to disappear due to diminished brightness. Participants were exposed to visual illusions, vestibular illusions, or a combination of both for 30 minutes. The visual illusion involved the somatogravic illusion, simulating a sudden forward linear acceleration during level flight, creating the perception of the aircraft's nose pitching up. The Coriolis illusion induced sudden tilting of the pilot's head while the aircraft turned, stimulating both semi-circular canals. Electrical conductance across the skin, measured by a Q-sensor 2.0, was used to quantify EDA over the left wrist. Various EDA parameters, such as maximum change, number of peaks, mean and median amplitude, and area under the curve (AUC), were analyzed. Subjective autonomic symptoms and Graybiel diagnostic scores were evaluated by two examiners. Participants were categorized into three groups based on total Graybiel score (0 points [n=59], 1-2 points [n=64], and  $\geq 3$  points [n=54]) and two groups (0 points or  $\geq 1$  point) for each assessed autonomic symptom (nausea, skin color, cold sweating, increased salivation, drowsiness, and pain). Results indicated that the maximum change in EDA was higher in the  $\geq 3$  points group compared to the other two groups. However, no correlation ( $r=-0.059$ ) was found between the maximum change in EDA and the total Graybiel score. There was no change in the number of EDA peaks during spatial disorientation for any group. The mean EDA amplitude was

higher in the  $\geq 3$  points group compared to the 0 points and 1-2 points groups. No differences were reported in AUC values for the EDA data. Evaluation of EDA data and subjective autonomic symptoms revealed that the maximum EDA change was higher in the  $\geq 1$  points group compared to the 0 points group for cold sweat and increased salivation, with no differences reported for the other five autonomic symptoms. Based on these findings, the authors concluded that autonomic nervous system activity can be functionally evaluated during spatial disorientation training.

Islam et al., 2019

The objective of this study<sup>5</sup> was to research user responses on different driving simulator settings, driving events, and situations based on user electrodermal activity (EDA) signal. Twenty-three university students (9 male, 14 females, mean  $\pm$  SD;  $20.9 \pm 2.3$  yrs) with normal or corrected to normal vision underwent five different task configurations in a City Car Driving simulator. Each task consisted of combinations of 2 controllers and 3 displays conducted in a randomized order: 1) keyboard and single monitor (KS), 2) keyboard and triple monitor (KT), 3) driving set (steering wheel, pedal set, and shifter) and single monitor (DS), 4) driving set and triple monitor (DT), and 5) driving set and virtual reality head mounted display (DH). Participants EDA was collected using a wristband device and sampling rate of 4Hz and processed for maximum, minimum, mean, median, standard deviation, variance, number of zero crossings, and root mean square. Driving conditions were set to perform 3 Emergency and 1 Normal driving events consisting of 1) hitting/almost hitting a pedestrian, 2) hitting/almost hitting an object, 3) hitting/almost hitting a car, and 4) normal driving/stopping, respectively. The results indicated mean EDA and Task (testing configuration) was different between keyboard (Task 1 and 2) and driving set (Task 3, 4, and 5), where there was greater variability in mean EDA using the driving set. In addition, using the Head mounted (Task 5) display resulted in greater mean EDA variability compared to monitor

display (of Task 3 and 4). Additional reported findings included female participants tended to have higher mean EDA compared to males and participants with glasses had a lower mean EDA response than those without. A prediction accuracy using all features extracted from the signals was used as the indication of strong impact of the configuration setup on EDA readings. The driving set and single/triple monitor were the highest (DS 87.3% and DT 90.0%), followed by the KT (80.0%), DH (77.3%) and KS (63.6%). The authors speculate the lack of visible arms in the DH condition for the reduced classification accuracy, indicating a deviation from realism immersion. The results of this study<sup>5</sup> indicate the realism of the simulator during emergency situations had less influence on EDA signals compared to normal driving situations. The stress experienced in emergency situations is stronger than the effect on EDA readings due to differences in configuration setups, such that engagement is greater with realistic controls and participants are less affected by visible context during emergency driving situations.

Gao & Wang, 2020

The purpose of this study<sup>70</sup> was to investigate pilot's mental workload and risk perception in risk operations based on physiological indicators using wearable and portable wireless physiological equipment to minimize the extent of interruption during operations. The study utilized 19 cadets (mean  $\pm$  SD; 20.47  $\pm$  3.405 yrs) with simulator experience of the Flight Technology College of the Civil Aviation University of China. The cadets flew in a desktop simulator with throttle controller and a pair of rudder pedals and performed a flying task with the Cessna SP-G1000. The flight began above RW16R Tianjin/Binhai airport, 3000 ft, 110 knots and 80° heading. There was a marginal scattered cloud ceiling at 5000 ft and visibility 20 statute miles (32 km). The first weather change involved a descent in cloud ceiling to 3000 ft, ground visibility to 12 statute miles (19 km), and mild rain and storm. The second weather change caused the



weather to get worse with marginal ground visibility to 7 statute miles (11 km), heavy rain and storm, with occasional lighting and turbulence. The experiment lasted approximately 30 minutes and ended with a landing (or crash) at Tianjin airport. The flying segments were divided for analysis into Baseline (3 minutes before simulation start), Segment 1 (3 minutes after simulation start), Segment 2 (3 minutes after first weather change), Segment 3 (3 minutes after second weather change), and Segment 4 (3 minutes before the aircraft touched down on the runway). The ErgoLAB Human-Machine-Environment platform was used to analyze mean variables of photoplethysmography (inter-beat intervals or IBI) and electrodermal activity (skin conductivity level or SCL and skin conductivity resistance or SCR). Based on flight performance participants were divided into normal and abnormal groups, the latter of which had unsafe performances including stall warnings, runway overshoot, bounced landing, overspeed landing, wrong runway landing, and crashed. The results indicated no difference in groups for IBI of any segment but did show a decline in IBI during flight. The SCL results indicated the normal group had higher values during Segment 2 ( $13.82 \pm 7.72 \mu\text{s}$ ), 3 ( $14.49 \pm 8.34 \mu\text{s}$ ), and 4 ( $16.14 \pm 7.86 \mu\text{s}$ ) compared to the abnormal group ( $6.10 \pm 4.71 \mu\text{s}$ ,  $6.17 \pm 4.72 \mu\text{s}$ ,  $7.11 \pm 4.72 \mu\text{s}$ , respectively). In addition, SCR was greater in the normal group ( $0.41 \pm 0.24 \mu\text{s}$ ) compared to the abnormal group ( $0.20 \pm 0.18 \mu\text{s}$ ) only after the second the weather change. The IBI variability indicated the greatest variability in both normal ( $69.63 \pm 48.68 \text{ ms}$ ) and abnormal ( $109.31 \pm 87.22 \text{ ms}$ ) was observed in Segment 4. The SCL variation in the normal group was higher after the appearance of bad weather ( $2.24 \pm 1.06 \text{ ms}$ ,  $2.91 \pm 1.32 \text{ ms}$ , and  $4.56 \pm 1.31 \text{ ms}$ ) than in the abnormal group ( $0.72 \pm 1.76 \text{ ms}$ ,  $0.78 \pm 0.78 \text{ ms}$ , and  $1.73 \pm 1.39 \text{ ms}$ , respectively). This study were that mental workload and risk perception affected safety performance in adverse weather conditions and risk perception is more

obvious; and the cause of change in physiological parameters were not related to pilots flying skills but rather their risk perception and adaptability.

Vallés-Catalá et al., 2021

The objective of this study<sup>3</sup> was to explore the impact of stress during highly demanding conditions in a flight simulator training on electrodermal activity (EDA). The participant group comprised 41 student pilots, consisting of 35 men and 6 women. These individuals underwent multiple flight simulator sessions, graded by experienced flight instructors based on their performance. Electrodermal activity was recorded at 4 Hz from the dominant wrist using a wristband during highly demanding tasks (HDT). These tasks were categorized as either OK (correctly performed) or NOK (poorly performed). The statistical analysis utilized the mean of all EDA values within an HDT. Results revealed that 64.3% of EDA responses were higher during OK tasks compared to NOK tasks in HDT. In comparison to baseline (low demanding tasks or LDT), 56.5% of EDA values were greater in OK tasks, and 50.7% were greater than during NOK tasks. Further examination demonstrated a correlation between EDA values of NOK tasks and overall marks, with students scoring above the mean (7.26) in NOK tasks exhibiting lower EDA values (Spearman rank  $r=-0.52$ ,  $p<0.001$ ). The authors concluded that elevated EDA values are associated with performance under high-demand conditions. Interestingly, poor performance in HDT was also linked to low EDA values

Kriklenko & Kovaleva, 2021

The purpose of this study<sup>71</sup> was to demonstrate the feasibility and practicality of real-time skin conductance assessment during participants' engagement in a standard task using a home-based flight simulator. The objective was to evaluate the system's capability to differentiate stress levels and mental workloads in various situations. The authors conducted a case study involving a

45-year-old male with over 5 years of experience using a home-based simulator similar to the Microsoft Flight Simulator 2021. The participant operated the virtual Cessna CJ4 aircraft using specific flight equipment, and skin conductance (SC) signals were recorded using the ThoughtTechnology polygraph. The experimental flight scenario, lasting approximately 20 minutes, included phases such as start, take-off, climb, cruise, U-turn, descent, and landing. Flights were conducted under normal weather conditions and extreme weather conditions, introducing complexities like wind and gusts. The analysis of SC revealed that pilot workload during different flight phases under normal conditions could be differentiated, with the U-turn and descent phases showing the highest variability in SC. Interestingly, changes in SC amplitude occurred before the pilot executed specific maneuvers. In contrast, SC could not effectively distinguish between individual stages of flight in severe weather conditions. However, three distinct peaks in SC amplitude aligned with the busiest flight phases: take-off, U-turn, and descent. The authors concluded that SC can effectively differentiate between phases of a flight, reflecting varying stress levels and mental workloads. They suggested that as flight conditions become more complex, there is a more pronounced change in the dynamics of SC.

## **ELECTROMYOGRAPHY (EMG)**

### Lindstrom et al., 1970

The purpose of this article<sup>72</sup> was to investigate alterations in frequency and motor unit action potential conduction velocity (MUAP CV) within the electromyographic (EMG) signal during biceps brachii exercise. Six men, aged 24-30, engaged in fatiguing biceps exercises, involving resistance against a 2 kp force for 20 seconds, followed by a 30-second maximal voluntary isometric contraction, and concluding with another 2 kp load for 20 seconds. The results revealed a frequency shift and a dip in the power spectrum at the initiation of the maximal contraction. The observed MUAP CV was believed to be linked to this spectral shift. The power spectrum's maximum increased during maximal effort but shifted towards lower frequencies. Additionally, the frequencies subsequent to the observed dip displayed a reduction in amplitude. Consequently, the authors concluded that, as muscle fatigue increased, there was a greater decline in EMG frequency, indicating a slowing of MUAP CV.

### Bigland-Ritchie et al., 1983

The purpose of this study<sup>73</sup> was to assess the force, contractile speed, and electromyographic (EMG) activity of the adductor pollicis muscle during a 60-second maximal voluntary isometric contraction (MVIC). Eight participants, both men and women aged 25-55, underwent the MVIC protocol three times. The second repetition involved interruptions every 10 seconds for 2-5 seconds, and blood flow was occluded with a cuff around the upper arm to prevent recovery during force decline. The findings revealed a decline in force over time, showing an approximate linear pattern with reductions ranging from 30-50% of the initial value. As the contractions progressed, the EMG spike frequency decreased, with no change in duration or amplitudes but an observed increase in synchronization. There was a substantial 50-70% reduction

in motor unit action potential conduction velocity (MUAP CV) during the sustained 60-second MVIC, suggesting diminished motor drive from the central nervous system. While twitch contraction times remained constant, total twitch duration increased by 50% after fatigue. Twitch amplitudes were potentiated by 25-30% after a brief 5-second MVIC twitch, with consistent contraction times before and after. After fatiguing contractions, times averaged  $54.1 \pm 9.1$  ms when amplitude had declined by  $29.6 \pm 14.0\%$ , indicating prolonged relaxation times. In summary, the authors concluded that during sustained 60-second MVIC, there is a progressive slowing of MUAP CV, resulting in a reduced excitation rate necessary for maximal force production. Additionally, the decline in EMG may be attributed to a continuous reduction in motor neuron discharge rate, although this decline does not necessarily contribute to force loss.

Roy et al., 1986

The purpose of this study<sup>74</sup> was to explore the sensitivity of the frequency spectrum parameter, median frequency (MF), and motor unit action potential conduction velocity (MUAP CV) estimates across different locations of surface electrodes along the length of a muscle. Ten healthy males, aged 21-53, were seated in a modified dental chair with hip, knee, and ankle joints secured at right angles. They performed dorsiflexion for three repetitions at 20% and 80% of maximal voluntary contractions (MVC) while an array of surface electrodes was placed on the tibialis anterior at various muscle locations. The study revealed that the number of motor points for the tibialis anterior muscle varied from one to five, with a mean of 2.44, and the locations were highly variable. The highest MF value occurred at the region of the motor point, decreasing proportionally with distance. As participants approached the muscle tendon, the MF value increased. A high MUAP CV was observed at the most distal location of the muscle in the majority of participants. Increasing the force level of the contraction from 20% to 80% did not alter the

relationship, maintaining higher MF values closer to innervation zones. In conclusion, the authors found that estimates of MUAP CV were most reliably obtained between the distal tendon and the adjacent innervation zone in the tibialis anterior muscle.

Arendt-Nielsen & Mills, 1988

The objective of this study<sup>75</sup> was to explore submaximal fatiguing contractions equal to or greater than 60% of maximal voluntary isometric contractions (MVIC). Five healthy men (ages 22-39) performed three isometric knee extensions at randomly assigned 10% increments for the measurement of electromyographic (EMG) motor unit action potential conduction velocity (MUAP CV), mean power frequency (MPF), mean EMG voltage, and force of the vastus lateralis. The average MVIC force was 520 N (range 511-529 N). The MUAP CV exhibited a decrease over time for all force levels, and up to the point of endurance (after the force began to decline), MUAP CV decreased for higher forces. After the endurance point, there was a greater decrease in MUAP CV than before. During the 60-90% MVIC range, MUAP CV tended to decrease faster for higher forces. Still, at 100% MVIC, it decreased less than at 90% MVIC, which was not different from 80% MVIC. The MPF declined for all forces with time, and up to the endurance point, it decreased linearly with increasing initial force. After the endurance point, the decline in MPF was greater at 60-80% MVIC than before the endurance point. The decline in MPF after the endurance point at 90 and 100% MVIC was less than that of 80% MVIC but did not differ from 70% MVIC. There was a linear increase in mean EMG voltage during the period up to the endurance point for greater % MVICs ( $-4.11 \text{ mV} \cdot \text{s}^{-1} + 0.084 \text{ mV} \cdot \text{s}^{-1} \cdot \%^{-1}$ ,  $r=0.98$ ). After the endurance point, mean EMG voltage fell linearly with greater initial force ( $4.52 \text{ mV} \cdot \text{s}^{-1} - 0.088 \text{ mV} \cdot \text{s}^{-1} \cdot \%^{-1}$ ,  $r=-0.99$ ). Mean time to the endurance point decreased with increasing MVIC (52 s, 43 s, 29 s, and 20s, for 60, 70, 80, 90, 100% MVIC, respectively). The force decline after reaching the endurance point fell

linearly for increasing initial force ( $-1.684 \text{ mV} \cdot \text{s}^{-1} - 0.00421 \text{ mV} \cdot \text{s}^{-1} \cdot \%^{-1}$ ,  $r=-0.83$ ). In conclusion, the study suggests that during submaximal contraction of the human vastus lateralis, the average MUAP CV and MPF are influenced by both a slowing of fiber velocity, impacted by the accumulation of intramuscular metabolites, and recruitment of less fatigued motor units with a faster MUAP CV.

Bouissou et al., 1989

The purpose of this study<sup>76</sup> was to explore the connection between intramuscular pH and the frequency components of the electromyogram (EMG) power spectrum of the vastus lateralis in eight men (mean  $\pm$  SD, age  $23.7 \pm 4.0$  yrs, height  $186.2 \pm 7.5$  cm, weight  $78.0 \pm 4.7$  kg) during cycle ergometer exercise at 375 watts. Participants were randomly assigned to either the placebo or alkalosis group, where they ingested either  $\text{CaCO}_3$  or  $\text{NaHCO}_3$ , totaling 0.3 g/kg of body weight, respectively. Endurance time tended to be higher in the alkalosis group ( $82.6 \pm 3$  s) compared to the placebo group ( $69.3 \pm 2$  s). At the onset of exercise, plasma pH was 0.08 units higher in the alkalosis group than in the placebo group. The end exercise blood pH and lactate concentrations were greater in the alkalosis group ( $7.13 \pm 0.03$  and  $7.02 \pm 0.5$  mM, respectively) than in the placebo group ( $7.08 \pm 0.003$  and  $8.67 \pm 0.37$  mM). Muscle pH at the point of exhaustion did not differ; however, muscle lactate was higher in the alkalosis group ( $32 \pm 5$  mmol/kg wet wt) than in the control group ( $17 \pm 4$  mol/kg wet wt). This increase in muscle lactate concentration was correlated with muscular endurance ( $r=0.62$ ). There was a continued increase in total EMG power during exercise, and increasing myoelectrical activity was associated with a decrease in mean power frequency (MPF). The decline in MPF was higher in the alkalosis group ( $19 \pm 2\%$ ) than in the placebo group ( $10.1 \pm 0.9\%$ ). The fall in MPF as a percentage of the initial value was linearly associated with muscle lactate concentration, but there was no correlation between

changes in muscle hydrogen ion concentration and MPF during exercise in either group. The authors concluded that alkalosis results in a greater reduction in MPF associated with higher muscle lactate accumulation, although the observed correlation does not necessarily imply a causative effect.

Cady et al., 1989

The purpose of this study<sup>77</sup> was to research the interplay between intracellular phosphorus concentrations, hydrogen ions (H<sup>+</sup>), and force during fatiguing contractions in the first dorsal interosseous muscle of the hand. The study involved four normal participants (2 men and 2 women, ages 21-43 yrs) and a 65-year-old female subject with myophosphorylase deficiency (MPD). The first dorsal interosseous muscle underwent fatigue through three sets of 15s maximal voluntary isometric contractions (MVIC), with blood flow occluded by an upper arm cuff during the first contraction and for three minutes before subsequent MVICs. Metabolites were measured before and after using an NMR spectrometer. The results revealed differences between the first and third sets, with force decreasing by approximately 10%. Force could recover to at least 90% of the resting value after a 5-minute recovery with restored circulation. The MPD subject exhibited similar force loss patterns during rest intervals and recovered to 96% of the resting value. In normal participants, tetanic force declined to  $64 \pm 2.3\%$  of the control value after 45 s MVIC, while the MPD subject declined to  $49 \pm 5\%$  after only 21 s MVIC. Phosphocreatine in the normal subjects fell from  $38.3 \pm 0.4$  mM to  $6.3 \pm 0.5$  mM over the three sets, with an equimolar rise in phosphate from  $6.1 \pm 0.3$  mM to  $32.9 \pm 1.0$  mM. ATP concentration remained constant, and pH fell from  $7.03 \pm 0.01$  to  $6.51 \pm 0.02$ . In the MPD subject, muscle metabolites changed similarly, while pH did not change ( $7.06 \pm 0.02$  to  $7.11 \pm 0.03$ ). Changes in tetanic force production were not associated with changes in free ATP, but the MPD subject showed a greater percentage loss of force compared



to normal participants. Force declined roughly in proportion to the increase in monobasic phosphate, but the MPD subject exhibited a greater loss of force for an equivalent increase in monobasic phosphate. Force also declined in proportion to the increase in hydrogen ion concentration, except in the MPD subject. The authors concluded that the buildup of metabolic byproducts caused a decrease in force production, indicating a slowing of motor unit action potential conduction velocity

Solomonow et al., 1990

This study<sup>78</sup> explored the impact of electromyography (EMG) force relationships on joint angles within the physiological range of motion. The investigation involved the gastrocnemius muscles of six cats, which underwent isometric muscle actions through sciatic nerve stimulation at fixed joint angles (45°, 60°, 75°, 90°, 105°, 120°, and 135°). The findings revealed that the initial activation was consistent across all joint angles. However, the maximal terminal force occurred at a 90° joint angle. From these results, the authors concluded that joint angle influences EMG-force relationships, emphasizing that caution should be exercised when using the EMG signal to predict muscle force.

Farina et al., 2002

The purpose of this study<sup>79</sup> was to explore the potential and limitations of utilizing global surface electromyography (EMG) variables as indicators of motor unit recruitment strategies. The investigation involved both a simulation model and an experimental study with ten men (mean  $\pm$  SD, age 26.3  $\pm$  4.3 yrs). Participants performed a training session comprising three 3s ramp contractions with linearly increasing torque from 0-80% of maximal voluntary isometric contractions (MVIC), followed by two constant force contractions lasting 11s at 80% MVIC. The study findings revealed a continuous increase in motor unit action potential conduction velocity

(MUAP CV) throughout the entire contraction, irrespective of motor unit location. The maximum mean power frequency (MPF) occurred at  $61.0 \pm 15.1$ ,  $72.3 \pm 24.0$ , and  $71.2 \pm 22.2\%$  of the contraction time for recruitments equal to 50, 75, and 95% of the contraction, with a standard deviation of MUAP CV set at 0.7 m/s. When the standard deviation for MUAP CV was reduced to 0.3 m/s, the maximum point of MPF shifted to  $49.0 \pm 20.5$ ,  $66.0 \pm 31.7$ , and  $57.4 \pm 22.0\%$  of the contraction time for 50, 75, and 95% of recruitment. Additionally, the data suggested that MUAP CV increases with force, while other frequency parameters may exhibit different behaviors in response. In conclusion, the authors stated that relying solely on surface EMG frequency provides insufficient indications of motor unit recruitment strategies.

Kuiken et al., 2003

The overarching purpose of this study<sup>80</sup> was to investigate the impact of subcutaneous adipose tissue on electromyographic (EMG) amplitude and Crosstalk using a model replicating the human upper arm. The study involved transmitting motor unit action potentials (MUAP) through muscle fibers with varying subcutaneous adipose thickness (0, 3, 9, and 18 mm) to simulate voluntary EMG activity. The findings revealed a reduction in the surface MUAP amplitude by 31.3%, 80.2%, and 90.0% for subcutaneous adipose thicknesses of 3 mm, 9 mm, and 18 mm, respectively. As the thickness increased, the decline in surface potential amplitude around the model slowed, leading to an increase in crosstalk over the inactive muscle region. Crosstalk diminished to 5% of the maximum MUAP value at angles of 14, 17, 34, and 47 degrees from the active muscle edge for 0 mm, 3 mm, 9 mm, and 18 mm thicknesses, respectively. Reducing adipose thickness from 9 mm to 3 mm resulted in a 241% increase in EMG amplitude and a 68% decrease in EMG crosstalk at a location 45 degrees away. In summary, the study concluded that

subcutaneous adipose tissue diminishes surface EMG signal amplitude and enhances EMG crosstalk at nearby surface recording sites.

Dimitrov et al., 2006

The objective of this study<sup>81</sup> was to assess the suitability and sensitivity of a new electromyography (EMG) spectral index in examining peripheral muscle fatigue during dynamic knee extension exercise. Seven adults, comprising 6 men and 1 woman, with a mean age of  $28.7 \pm 7$  years, height of  $180 \pm 10$  cm, and body mass of  $78 \pm 12$  kg, performed leg extension exercises involving 10 sets of 15 repetitions at 50% of their one-repetition maximum. Torque, knee joint angle, and EMG data (analyzed for median frequency, MDF, and a newly introduced spectral index of muscle fatigue) were recorded for each repetition of the rectus femoris muscle. The findings revealed that both the rate and range of relative changes for both measures increased with each repetition compared to the initial repetition of each set. The maximum observed change in the new spectral index was approximately 8-fold, while MDF showed a change of only 32%. Consequently, the authors concluded that the novel EMG spectral indices demonstrated greater sensitivity to peripheral muscle fatigue, establishing them as a valid and reliable tool for assessing muscle fatigability during dynamic muscle actions, regardless of natural signal variability.

Fortune & Lowery, 2007

The purpose of this study<sup>82</sup> was to investigate the impact of variations in extracellular potassium (K<sup>+</sup>) concentration on motor unit action potential conduction velocity (MUAP CV) in a simulated model based on skeletal mouse muscle fibers developed in MATLAB 7.0.1. The study involved increasing extracellular K<sup>+</sup> concentration and subsequently blocking each channel to assess its influence on MUAP CV at different levels of extracellular K<sup>+</sup> concentrations. The findings revealed that, with the elevation of extracellular K<sup>+</sup>, the resting membrane potential

increased, leading to a broadening of the transmembrane action potential and a reduction in its amplitude. Specifically, when  $K^+$  was increased from 5 to 10 mM, the peak-to-peak amplitude of the transmembrane action potential decreased from 130.08 mV to 99.92 mV at 20°C. As the  $K^+$  concentration increased from 5 mM to 10 mM, the broadening of the transmembrane potential resulted in a progressive decrease in MUAP CV from 2.64 m/s to 2.09 m/s. Additionally, there was a nonlinear increase in MUAP CV with rising temperature. Based on these results, the authors concluded that the reduction in MUAP CV during sustained fatiguing contractions may be attributed to the increased accumulation of extracellular  $K^+$ .

Rainoldi et al., 2008

The purpose of this study<sup>83</sup> was to investigate whether electromyography (EMG) analysis of myoelectric manifestation of muscle fatigue could distinguish between the vastus lateralis (VL), vastus medialis longus (VM), and vastus medialis obliquus (VMO) muscles. Nine participants, with a mean age of  $31.3 \pm 8.6$  years, performed isometric knee extensor contractions at 60% and 80% maximal voluntary isometric contractions (MVIC) for durations of 10 and 60 seconds, respectively. Recordings of VML, VMO, and VL were analyzed for mean power frequency (MPF), average rectified value (ARC), and motor unit action potential conduction velocity (MUAP CV). The initial values of ARV, MPF, and MUAP CV differed between the vasti muscles at both force levels. Specifically, MUAP CV was lower for VMO compared to VL at 60% MVIC and lower than VML and VL at 80% MVIC. MPF values were greater for VL compared to both VML and VMO at 80% MVIC. Additionally, ARV was higher for VMO compared to VML at both force levels. During the sustained contraction at 80% MVIC, VL exhibited a greater increase in MUAP CV over time compared to VMO. Furthermore, VL also demonstrated a greater decrease in MUAP CV over time compared to VMO. Comparisons between force levels indicated that initial values

of MPF for VL were greater at 80% MVIC compared to 60% MVIC. In conclusion, the authors suggested that VML, VMO, and VL muscles exhibit distinct EMG variable parameters during sustained isometric knee extension contractions. They proposed that this information could be valuable for describing the functional characteristics of the vasti muscles.

González-Izal et al., 2010

The objective of this study<sup>84</sup> was to research various electromyographic (EMG) fatigue indices associated with muscle power loss during dynamic high-fatiguing tasks. Fifteen active men, with a mean age of  $34.2 \pm 5.2$  years, height of  $177.3 \pm 5.6$  cm, and body mass of  $73.1 \pm 6.4$  kg, participated in the study. The participants performed five sets of 10 repetitions maximum (10RM) bilateral leg press exercises, with muscle power output measured during the concentric movement phase. EMG activity was recorded for the right vastus medialis (VM), vastus lateralis (VL), and biceps femoris (BF). The recorded data included mean average voltage (MAV), median frequency (MF), mean power frequency (MPF), and the EMG power spectrum calculated using Fourier Transform (FI). The findings revealed that muscle power output decreased in the last five repetitions compared to the first five, with a 45% reduction in power during the last repetition of the fifth set compared to the initial two repetitions of the first set. The average MAV (averaged for both VM and VL) during the last five repetitions of each set and the first five of the fifth set was greater than during the first five contractions. MF during the last repetitions of each set was lower than during the first five repetitions. The average FI parameter of the last five repetitions of each set was higher than the first five repetitions of the first set, and the average log of FI during the first five repetitions of the third, fourth, and fifth sets was greater than the first five repetitions of the first set. The MAV of the BF increased during the last five repetitions of the first, second, and third sets compared to the corresponding five repetitions of the first set. Additionally, the average

log FI values of the BF during the third, fourth, and fifth sets were greater than the first five repetitions of the first set. Mechanical power changes (averaged for VM and VL) exhibited the strongest correlation with log FI ( $r=-0.59$ ), MPF ( $r=0.57$ ), MF ( $r=0.50$ ), and MAV ( $r=-0.39$ ). Muscle power changes of the BF were most correlated with log FI ( $R=-0.315$ ), MAV ( $r=-0.23$ ), MF ( $r=0.11$ ), MPF ( $r=0.20$ ), instantaneous mean frequency ( $r=0.18$ ), and MF variance ( $r=-0.01$ ). In conclusion, the study suggested that in a high-intensity dynamic protocol with natural velocity slowing as fatigue increases, the logarithm of the spectral index is the most accurate fatigue index reflecting changes in muscle power compared to other frequency or amplitude EMG parameters.

Äng & Kristoffersson, 2013

The purpose of this study<sup>85</sup> was to assess the impact of head-worn night vision equipment on neck muscle activity during controlled, simulated flights in a dynamic flight simulator. The study involved five senior fast-jet test pilots actively engaged in flying duty, with an average age of 40 years, weight of 85 kg, and height of 1.84 m. These pilots had accumulated an average flight time of 2570 hours. During the study, each pilot completed a 2.5-hour session in a dynamic flight simulator, flying with and without night vision goggles (NVG). The flight protocol included a 1-hour simulation at 1 Gz, followed by 1.5 hours of dynamic flight involving repeated Gz profiles ranging from 3 to 7 Gz, including aerial combat maneuvers (ACM) at 3-5 Gz. Surface electromyography (EMG) was employed to measure the activity of the sternal sternocleidomastoid, upper neck extensors, and upper shoulder muscles. The EMG signals underwent various processing steps, including preamplification, band-pass filtering, common-mode rejection, and sampling at 1 kHz. Normalization of neck EMG values was achieved as a percentage of root mean square (RMS) of preflight voluntary maximal contractions. The results highlighted that erector spine activity (7%) surpassed that of all other muscles (2%). Overall neck

muscle activity was more pronounced in the NVG session than in the control session during the first ACM episodes (10% vs. 8%). Furthermore, muscle activity was greater at 7 Gz (20%) and 5 Gz (10%) compared to 3 Gz (6%), with 7 Gz exhibiting higher activity than 5 Gz and ACM at 3-5 Gz (9%). In conclusion, the authors inferred that the use of helmet-mounted NVG equipment led to increased neck muscle activity during sustained combat maneuvers, indicating heightened muscle strain.

#### Clausen, 2013

The primary objective of this study<sup>86</sup> was to explore the impact of potassium (K<sup>+</sup>) and sodium (Na<sup>+</sup>) ion concentrations on membrane excitability in rat extensor digitorum longus muscles. The experimental setup involved stimulating rat muscles for 60 seconds at 60 Hz and 300 seconds at 5 Hz, with ion concentrations measured before and after stimulation. The study's findings revealed notable changes in ion concentrations, specifically an increase in total Na<sup>+</sup> content ( $4.6 \pm 1.2 \mu\text{mol/g wet wt}$  after 5 Hz and  $9.8 \pm 0.7 \mu\text{mol/g wet wt}$  after 60 Hz) and a decrease in total K<sup>+</sup> content ( $5.5 \pm 2.3 \mu\text{mol/g wet wt}$  after 5 Hz and  $10.0 \pm 2.7 \mu\text{mol/g wet wt}$  after 60 Hz). This decrease in K<sup>+</sup> adversely affected Cl<sup>-</sup> uptake, contributing to excitation-induced depolarization and a deceleration of motor unit action potentials. In conclusion, the author inferred that the accumulation of extracellular K<sup>+</sup> following fatiguing exercise resulted in muscular fatigue, primarily attributed to a reduction in membrane excitability.

#### Beck et al., 2014

The purpose of this study<sup>87</sup> was to investigate alterations in electromyography (EMG) spectral shape in the vastus lateralis (VL), rectus femoris (RF), and vastus medialis (VM) during 50 nonconsecutive maximal concentric isokinetic contractions at 180°s<sup>-1</sup>. The study involved 12 men (mean  $\pm$  SD, age  $22.2 \pm 1.3$  yrs, height  $179.2 \pm 5.2$  cm, body weight  $79.0 \pm 10.3$  kg) and 7

women (age  $22.7 \pm 2.1$  yrs, height  $161.1 \pm 6.0$  cm, body weight  $63.0 \pm 11.6$  kg). The findings revealed a consistent decrease in EMG mean power frequency from the VL, RF, and VM during the course of fatiguing contractions. Specifically, the spectral decomposition components of VL, RF, and VM exhibited a linear increase in the low-frequency spectrum accompanied by a linear decrease in the high-frequency spectrum. In essence, the observed decrease in EMG mean power frequency during fatiguing muscle actions was attributed to concurrent reductions in high-frequency power and increases in low-frequency power. The authors concluded that these alterations signify specific changes in muscle activation patterns associated with fatigue.

Pousette et al., 2016

The purpose of this study<sup>88</sup> was to investigate the impact of Night Vision Goggles (NVG) on peak neck muscle strain during controlled simulated flights. The study involved five senior fast-jet test pilots (mean  $\pm$  SD;  $40 \pm 4.2$  yrs,  $85 \pm 4.2$  kg,  $1.84 \pm 0.04$  m, total flight time  $2570 \pm 758$  h) with experience flying the JAS 39 Gripen while using NVGs. These pilots performed two 150-minute flight programs, one with a helmet and NVG and another with only a helmet, in randomized order on separate days (mean 16 days apart). The flight protocol included a 60-minute simulation of Earth's gravity, followed by 90 minutes of flight simulations involving 5 minutes of free warm-up flight and 17 unique Gz maneuvers ranging from 3 to 7 Gz, including active combat maneuvers. Physiological recovery involved a 2-minute rest at 1.4 Gz, and the rate of increase between exposures was 6 Gz/s. Electromyographic data were collected from specific neck muscles—sternocleidomastoid (anterior neck), splenius capitis (upper posterior neck), erector spinae (lower posterior neck), and trapezius descendens (upper shoulders). The data were processed, including rectification, smoothing, and normalization as a percentage of reference activity (MVE), obtained through maximal voluntary force against manual resistance in extension (upper/lower posterior



neck), flexion (anterior neck), and shoulder elevation (upper shoulders), held for 3 seconds. Analysis was conducted on data from four participants due to data loss. The results revealed a total of 157 and 118 muscle strain activities during NVG and helmet-only programs, respectively. There were more peak activations in the anterior neck during NVG (18 peaks) compared to helmet-only (1 peak), with no differences observed in other muscle values. The authors concluded that the additional load of helmet-mounted NVGs increases neck muscle strain in anterior stabilizing muscles.

Honkanen et al., 2017

The purpose of this study<sup>89</sup> was to compare Electromyographic (EMG) activation differences in neck and shoulder muscles between two groups of pilots one experienced and one inexperienced, during controlled +Gz exposure in a centrifuge. The participant pool consisted of 29 Finnish Air Force pilots, with the experienced group (n = 15; mean  $\pm$  SD, 23.0  $\pm$  0.4 yrs, 75.6  $\pm$  9.7 kg, 178.4  $\pm$  5.8 cm) having flown Hawk Mk 51 Jet trainers capable of +8 Gz, and the inexperienced group (n = 14; 22.3  $\pm$  0.6 yrs, 77.6  $\pm$  6.7 kg, 180.3  $\pm$  2.9 cm) having experience limited to early trainers not exceeding +4 Gz. The +Gz exposure took place in a dynamic flight simulator centrifuge, implementing a standardized gradual onset of +8 Gz at a rate of +0.1 Gz/s. EMG activity of specific muscles (right and left sternocleidomastoid - SCM, right and left trapezius - TRA, and right and left cervical erector spinae - CES) was recorded and normalized to maximal voluntary contractions for cervical flexion (SCM), shoulder rise (TRA), and cervical extension (CES), expressed as a percentage of the maximal voluntary contraction. During the exposure, two inexperienced participants and one experienced participant stopped the gradual onset at +7.0 Gz. Passive G tolerance (PGT) was also assessed by the centrifuge instructor. The results revealed increased mean EMG activity in all measured muscles and both groups. In the

inexperienced pilots, higher muscle activity in the left SCM ( $30.0 \pm 13.4\%$ ) and left CES ( $49.2 \pm 27.6\%$ ) during the last 5 seconds beyond +7.4 Gz was observed compared to the experienced group (SCM  $20.4 \pm 7.8\%$  and CES  $31.5 \pm 10.0\%$ ). The combined mean EMG% for both sides was higher for SCM ( $29.5 \pm 29.0\%$ ) and CES ( $45.7 \pm 24.7\%$ ) in the inexperienced group compared to the experienced group ( $21.6 \pm 12.7\%$  and  $32.7 \pm 11.4\%$ , respectively). PGT was greater in the experienced group ( $5.0 \pm 0.2$  Gz) compared to the inexperienced group ( $+4.6 \pm 0.6$  Gz). In conclusion, the authors found that muscle activity increased with rising +Gz forces, and inexperienced pilots exhibited higher neck and shoulder muscle activity than their experienced counterparts.

Ghasemi et al., 2021

The purpose of this study<sup>90</sup> was to assess whether a head-locked view or world-locked view is more effective for presenting information in an augmented reality (AR) environment. Eighteen participants (14 males and 4 females, mean age = 21.9 yrs, SD = 1.87) engaged in a data entry task using the Magic Leap One head-mounted display. The task involved completing a US Passport Application and University Faculty Advising form, with information presented in a randomized order and condition through the AR device. In the world-locked view, images were displayed above the data entry device, and if participants moved their heads, the information would disappear or become partially visible. In the head-locked view, the image moved along with participants' head movements. Participants were instructed to fill out the NASA Task Load Index (TLX) to assess their perceived workload. Muscle activation was measured using electromyography of the upper left and right trapezius, recorded at 1260 Hz and expressed as a percentage of maximal voluntary contraction (%MVC). The findings revealed that typing speed was faster in the head-locked position compared to the world-locked view (mean rank Mann-Whitney U test 42.20 vs

27.81, respectively), while the error rate did not differ between the two conditions. The time taken to complete the task was higher in the world-locked view (113.3 s) compared to the head-locked view (110.5 s). However, there was no difference in the perceived workload for either view. The electromyography analysis showed no variation between the two conditions in terms of %MVC. In conclusion, the authors determined that participants exhibited improved performance in the head-locked view, particularly in terms of time to task completion and typing speed.

## QUESTIONNAIRES

### Hypoxic Symptoms Questionnaire (HSQ)

Smith, 2005

The primary purpose of this study<sup>91</sup> was to conduct a survey assessing the experienced symptoms of hypoxia at altitudes below 10,000 ft in physically active helicopter aircrew. During aviation medicine refresher training, 75 anonymous surveys were distributed among Australian Army helicopter aircrew with experience operating in high-density altitude locations. The aircrew were tasked with identifying hypoxic symptoms they had personally experienced (symptoms) or observed in colleagues (observations). They were specifically instructed to recall situations where they perceived a decline in their or other crew members' performance during routine flight operations. The analysis included 53 surveys, representing loadmasters (n=25), pilots (n=23), and aircrewmen technicians (n=5) associated with Black Hawks (n=34), Chinook (n=12), Kiowa (n=5), and Iroquois (n=2). On average, the participants had 1678 hours of flying experience, with pilots having the most extensive experience. The findings revealed that 88.7% of aircrew had either experienced (mean  $\pm$  SD;  $4.8 \pm 3.2$  symptoms) or observed ( $5.7 \pm 4.4$  symptoms) one or more of the listed hypoxic symptoms. Non-pilot aircrew reported a higher number of hypoxic symptoms and reported them more frequently compared to pilots. Approximately 41.5% reported four or more symptoms, with a higher prevalence among non-pilot aircrew (60%) compared to pilots (17.4%). It was observed that while aircrew were more likely to report unusual behavior in colleagues, they were less likely to notice these changes in themselves. Cognitive impairment emerged as the most commonly observed hypoxic symptom, differing from other reported symptoms. Both cognitive and psychomotor impairments were notable in both reported symptoms and observations, with a slightly higher frequency in symptoms (56.6% and 45.3%, respectively)

than in observations (50.9% and 41.5%, respectively). Aircrew who had undergone aviation medicine refresher training within the previous 3 years reported hypoxic symptoms more frequently compared to those who had received training more than 3 years ago, although the difference was not statistically significant. Smokers also reported a higher number of hypoxic symptoms compared to non-smokers, but this difference was also not statistically significant. The author concluded that Army helicopter aircrew reported hypoxia symptoms at altitudes where hypoxia is not typically considered a significant threat, and loadmasters reported more symptoms more frequently than pilots.

#### Smith, 2008

The purpose of this study<sup>92</sup> was to document the hypoxic symptoms reported by military aircrew following an acute exposure to 25,000 ft and to assess whether the aircrew's recollection of their individual hypoxic profile from prior training corresponds to the symptoms experienced after the acute exposure. A total of 58 aircrew members operating non-rotary wing aircraft, previously trained in hypoxia awareness, underwent an aviation medicine refresher training, including a hypobaric chamber ascent simulating 25,000 ft (7620m) for 3 minutes. Participants, comprising 53.1% pilots and weapon systems operators and 46.9% loadmasters, flight engineers, and specialist technical and mission crew, rated the severity of 22 hypoxia symptoms on a scale from "not at all" to "extreme" after experiencing neurocognitive impairment and reaching final oxyhemoglobin saturation levels between 60-70%. The most commonly reported hypoxia symptoms after awareness training were cognitive impairment (58% overall), with poor concentration (73%), confusion (67%), memory impairment (57%), making mistakes (57%), and drowsiness (35%); psychomotor impairment (55% overall) with slowed response (67%), incoordination (55%), and tremors (43%); visual changes (54% overall) including reduced color

vision (59%), reduced light intensity (57%), and blurred vision (45%); and psychological disturbance (40% overall) with anxiety (51%), depression (35%), and euphoria (33%). Nonspecific hypoxic symptoms (shortness of breath, paresthesia, feeling weak or warm, headache, tachycardia, dizziness, and light-headedness) were reported 50% of the time. Feelings of warmth were the most commonly reported "extreme" symptom during acute hypoxic exposure. Recalled symptoms included psychomotor impairment (67% overall), with slowed response (69%), incoordination (69%), and tremors (63%); cognitive impairment (65% overall), with poor concentration (71%), confusion (71%), memory impairment (71%), making mistakes (59%), and drowsiness (51%); visual changes (51% overall), including reduced light intensity (55%), reduced color vision (51%), and blurred vision (47%); and psychological disturbance (46% overall), with anxiety (51%), depression (45%), and euphoria (43%). Recalled nonspecific symptoms were reported by 52% of aircrew, with "poor concentration" being the most commonly reported as "extreme." The pattern and distribution of reported hypoxia symptoms were similar to previously recalled symptoms. Aircrew remembered psychomotor impairment (67%) and cognitive impairment (65%) more frequently than these occurred during the acute exposure (55% and 58%, respectively). On average, participants reported  $16.1 \pm 4$  symptoms out of the possible 22, and typically  $12.7 \pm 6.7$  of those symptoms were within one severity point of the recalled survey of symptoms. Participants reporting only a single symptom or none at all were older ( $39.7 \pm 8.1$  years) compared to those reporting one or more symptoms ( $32.6 \pm 7.4$  years), with no difference in flight experience between the two groups. The authors concluded that most aircrew exhibited a high level of agreement between the symptoms experienced during the recent acute exposure and those recalled from their previous training up to 3 years ago. However, they noted that it could not be determined whether

those reporting none or only one symptom had a true absence of hypoxic symptoms or experienced hypoxia-related amnesia.

Self et al., 2011

The purpose of this study<sup>93</sup> was to compare the physiological effects of normobaric and hypobaric hypoxic exposure. Participants, consisting of 17 men and 3 women with a current Class II Airman Medical Certificate (mean  $\pm$  SD,  $42 \pm 10.8$  years,  $1.8 \pm 0.09$  m,  $85.2 \pm 18.3$  kg), underwent 5-minute exposures to hypobaric hypoxia in the morning and normobaric hypoxia in the afternoon at 25,000 ft. Various measurements, including gas alveolar samples, heart rate, peripheral oxygen saturation, and a hypoxic symptom questionnaire, were taken at 1, 3, and 4 minutes during each exposure. The results showed that the initial heart rate was higher in the hypobaric condition ( $104.9 \pm 14.3$  bpm) compared to the normobaric condition ( $96.6 \pm 14.6$  bpm). Peripheral oxygen saturation at 4 minutes was greater in the normobaric condition ( $69.5 \pm 4.9\%$ ) compared to the hypobaric condition ( $62.3 \pm 8.4\%$ ), with a slower rate of decline over the 5 minutes of normobaric exposure ( $0.14 \pm 0.03\%/s$  vs.  $0.16 \pm 0.03\%/s$ ). Alveolar oxygen tension at 4 minutes was higher in the hypobaric condition ( $33.5 \pm 2.4$  mmHg) compared to the normobaric condition ( $31.4 \pm 3.6$  mmHg), while alveolar carbon dioxide tension was lower in the hypobaric condition ( $28.2 \pm 3.1$  mmHg vs.  $32.1 \pm 2.6$  mmHg). The respiratory quotient was higher in the hypobaric condition ( $2.37 \pm 0.53$ ) at minute 4 of exposure compared to the normobaric condition ( $1.41 \pm 0.15$ ) at the same time point. There was an interaction effect of exposure condition and time on the number of reported symptoms, showing an average difference of 2.36, 3.4, and 4.89 at 1, 3, and 4 minutes, respectively. Follow-up comparisons indicated more reported symptoms at minute 1 in the hypobaric condition, while at minutes 3 and 4, there were more reported symptoms during normobaric exposure. The authors concluded that although alveolar gas composition and arterial

hemoglobin oxygen desaturation patterns differed between normobaric and hypobaric exposures at 25,000 ft, the similar occurrence pattern of symptoms suggests that normobaric exposures may be a useful alternative modality.

Johnston et al., 2012

The purpose of this study<sup>94</sup> was to evaluate the ability of aircrew to remember their hypoxic symptoms after a lapse of 3 years. The study involved 26 participants from the Royal New Zealand Air Force, all of whom had undergone prior hypoxia training. During routine refresher training, participants (mean age 31.6 years, average time since last training 4.5 years) were exposed to a simulated altitude profile, starting with a 30-minute de-nitrogenating pre-breathe at ground level with 100% oxygen. Subsequently, they ascended to 18,000 ft (5486 m) for 11 minutes without oxygen, followed by an ascent to 25,000 ft (7620 m) for a maximum of 4 minutes. Symptom questionnaires, requiring participants to rate 12 hypoxia symptoms on a severity scale ranging from "not at all" to "severe – an inability to function effectively," were administered before and after the training. Of the 26 participants, 25 reported experiencing hypoxia symptoms during their previous training, and all 26 reported some degree of hypoxic symptoms in the current refresher training. Cognitive impairment was the most frequently recalled symptom from previous training and did not differ in reported frequency during the refresher training. The recall of slurred speech was more frequent from previous training compared to the refresher, while hot/cold flushes were less frequent during the refresher. Comparing the severity between recalled and refresher training, cognitive impairment, visual changes, hot/cold flushes, shaking limbs/tremors, lightheaded/dizzy, tingling/numbness, and loss of consciousness showed an increase. Feeling unwell and headaches increased in severity, while lethargy/tiredness decreased in severity. The average hypoxia score from recalled training (mean  $\pm$  SD;  $8.3 \pm 4.9$ ) was lower compared to the refresher training (10.3



± 5.6). No difference in hypoxia scores was found based on the years since the last training (less than 2 years 9.43, 2-4 years 8.17, 4-6 years 10, greater than 6 years 6.5). The authors concluded that individuals can accurately recall their hypoxia symptoms even after a period longer than 3 years.

Kryskow et al., 2013

The purpose of this investigation<sup>95</sup> was threefold: 1) to identify the threshold altitude (within the range of 2500-4300 m) at which simple and complex military task performance is impaired, 2) to explore whether the extent of degradation is associated with changes in altitude illness, fatigue, or sleepiness at a given altitude, and 3) to examine the impact of hypoxemia levels on simple and complex military task performance. Fifty-seven lowlanders (mean ± SD: 22 ± 3 years, 79 ± 12 kg, 177 ± 8 cm) were exposed to hypobaric elevations of 2500 m, 3000 m, 3500 m, or 4300 m while engaging in weapons dis/re-assembly (DsAs) and rifle marksmanship (RM). Acute mountain sickness (AMS) was assessed using an environmental symptoms questionnaire, and measurements of fatigue, sleepiness, and arterial oxygen saturation (SaO<sub>2</sub>) were taken at sea level, 8 hours, and 30 hours into the exposure. Results showed no differences in DsAs or RM speed (targets per minute) at sea level among altitude groups. There were also no changes in RM speed at 2500 m, 3000 m, and 3500 m between sea level and 8 hours to 30 hours of exposure. Accuracy did not vary with time or between conditions. AMS severity and prevalence did not differ between groups at sea level, and there were no changes at 2500 m across time. However, at 3000 m, 3500 m, and 4300 m, both severity and prevalence of AMS increased from sea level to 8 hours to 30 hours of exposure. While fatigue and sleepiness did not differ at sea level between conditions, fatigue increased at all altitudes from sea level to 8 hours of exposure and remained elevated at 30 hours at 3000 m and 4300 m. Sleepiness increased at 2500 m, 3000 m, and 4300 m from sea level

to 8 hours and remained elevated at 30 hours only at 4300 m. A negative correlation was observed between individual changes in RM speed and changes in sleepiness from sea level to 30 hours ( $r=-0.66$ ). Resting SaO<sub>2</sub> was not different between groups at sea level ( $98 \pm 1\%$ ) but decreased at 8 hours and 30 hours after exposure at 2500 m ( $93 \pm 3\%$ ,  $94 \pm 3\%$ ), 3000 m ( $91 \pm 2\%$ ,  $92 \pm 2\%$ ), 3500 m ( $90 \pm 3\%$ ,  $91 \pm 2\%$ ), and 4300 m ( $78 \pm 8\%$ ,  $79 \pm 6\%$ , respectively). Hypoxemia levels, independent of altitude condition, were correlated with RM speed after 30 hours ( $r=0.27$ ) but not after 8 hours. Additionally, no correlation was found with DsAs performance at any time point. Based on these findings, the authors concluded that simple psychomotor performance was unaffected by exposures between 2500-4300 m, but complex psychomotor performance was degraded at 4300 m.

Pilmanis et al., 2016

The purpose of this study<sup>96</sup> was to research the impact of short-term, mild hypoxia on cognitive function in 91 active military personnel with a U.S. Air Force class II flight physical. Participants were exposed to four altitude conditions: ground level (GL), 1524 m (5,000 ft), 2438 m (8,000 ft), and 3658 m (12,000 ft), each for 105 minutes at a rate of 1524 m/min (5,000 ft/min). The soldiers underwent testing using seven tasks from the Automated Neuropsychological Assessment Metrics (ANAM) battery, including Choice Reaction Time, Tower, Continuous Performance, Grammatical Reasoning, Mathematical Processing, Match to Sample, Spatial Processing, and Manikin Test. Physiological measures, such as blood oxygen saturation and heart rate, were recorded using finger pulse oximetry. A survey with 65 symptoms, 33 of which were relevant to hypoxia, was administered to assess the subjective experience of the participants. Oxygen saturation decreased from  $97.5 \pm 0.8\%$  at GL to  $86.6 \pm 2.9\%$  at 3658 m, and heart rate increased from  $66.5 \pm 9.2$  bpm at GL to  $74.4 \pm 9.7$  bpm at 3658 m. Cognitive performance,

particularly in the continuous performance test, showed a decline in accuracy from  $97.4 \pm 2.5\%$  at GL to  $95.9 \pm 4.3\%$  at 3658 m. Reaction time increased slightly with altitude, and there was a decrease in grammatical reasoning accuracy from  $91.8 \pm 7.8\%$  at GL to  $89.5 \pm 10.3\%$  at 3658 m. While the study revealed small decreases in cognitive performance under low-grade hypoxia, the operational significance of these changes remains to be determined.

Bouak et al., 2018

The authors<sup>97</sup> purpose was to explore the impact of mild hypoxia on various physiological and cognitive parameters, as well as flight simulator performance, at altitudes ranging from 8,000 to 14,000 feet under different exercise intensities. Sixteen male military helicopter pilots, with an average age of 32.5 years and flight experience of 860 hours, underwent altitude exposures and exercise sessions on a cycle ergometer at rest (0 W), light (30 W), and moderate (60 W) intensities. During each exposure, participants followed a standardized testing sequence, including physiological monitoring using pulse oximetry at the fingertip ( $SpO_2$ ) and forehead ( $rSO_2$ ), heart rate, and respiration rate measurements. The flight simulation task involved maintaining specific flight parameters while detecting vehicles along the route. Additionally, a cognitive testing battery was administered, and participants completed questionnaires on hypoxic symptoms, affect, and fatigue. Results showed a decline in  $rSO_2$  with increasing altitude, accentuated by exercise, with supplemental oxygen increasing  $rSO_2$ .  $SpO_2$  decreased with altitude, and heart rate increased with both altitude and exercise. Reported hypoxic symptoms peaked at 12,000 and 14,000 feet. Flight simulator accuracy declined at all altitudes, while cognitive performance in tasks such as the Delayed Matching-to-Sample Test (dMTS), dual n-back, and Stroop task was affected at 14,000 feet. In conclusion, the study revealed mild hypoxia affected subjective and objective measures

above 10,000 feet, which highlight the absence of hypoxia's influence on performance at lower altitudes of 8,000 and 10,000 feet.

### **Simulator Sickness Questionnaire (SSQ)**

Kennedy et al., 1992

This study<sup>98</sup> examined the original scoring key of the Pensacola Motion History Questionnaire (MHQ) and formulate a new scoring key for predicting susceptibility to simulator sickness in Navy and Marine Corps pilots, which was then cross-validated. A sample of n = 457 Navy and Marine Corps pilots participated by answering the MHQ and Motion Sickness Questionnaire (MSQ) during regularly scheduled simulator exercises. The simulator sickness (SS) scoring key was derived by identifying correlations ( $p < 0.05$ ) between individual MHQ items and both post-simulator MSQ scores and the difference between pre- and post-simulator MSQ scores. Cross-validation involved correlating scores of the SS key with the severity of sickness experienced. The authors recommended the use of the SS scoring key for assessing simulator sickness when administering the MHQ in military and commercial pilots.

Kennedy et al., 1993

The purpose of this study<sup>99</sup> was to develop a Simulator Sickness Questionnaire (SSQ) derived from the Pensacola Motion Sickness Questionnaire (MSQ) to establish a scale indicating the onset of motion sickness under less severe conditions of stimulation. The study analyzed 1,119 pairs of pre- and post-simulator exposure data collected from MSQs during on-site studies at 10 different Navy simulator sites using factor analysis. Out of the 28 symptoms recorded in the MSQ, 16 were selected for further analysis, eliminating symptoms selected too infrequently or showing no change in frequency/severity. Factor analysis, exploring three-, four-, five-, and six-factor solutions of the selected 16 symptom variables, revealed that a three-factor solution provided the

best interpretation with clinical relevance. These three distinct symptom clusters were identified as Oculomotor, Disorientation, and Nausea. The authors concluded that the analysis indicated at least three separate dimensions underlying motion sickness and simulator sickness. As a result, they suggested that the patterns of symptom presence and severity associated with simulator sickness justify the use of a separate measuring system. The presented SSQ offered straightforward scoring, improved detection of problematic simulators, and enhanced diagnostic ability for sickness.

Kennedy et al., 1997

The purpose of this study<sup>100</sup> was to validate self-report of disorientation from the Simulator Sickness Questionnaire (SSQ) by comparing it with a physiological measure of postural instability. The research analyzed SSQ data collected from experienced Naval aviators operating the Device 2F114 Weapon Systems Trainer for the A-6E and Device 2F143 Operational Flight Trainer for the EA-6B. Concurrently, tests for standing and walking unsteadiness were conducted. The findings revealed a correlation between post-simulation disorientation scores and standing on the non-preferred leg ( $r=-0.34$ ) as well as standing on the preferred leg ( $r=-0.38$ ). The authors concluded that these results provide support for the validity of the disorientation subscale of the SSQ. Furthermore, they suggested that postural instability following simulator exposure might be attributed to disorientation.

Stanney et al., 1997

The purpose of this study<sup>101</sup> was to explore distinctions between cybersickness in a virtual environment (VE) and simulator sickness in simulator systems. Through the analysis of 8 empirical studies employing VE systems and the Simulator Sickness Questionnaire (SSQ), the authors observed an average total SSQ score for VE environments at 29 (range 16-55), while the

average for flight simulators was 10 (range 7-20). The study highlighted that the "best" simulators triggered one symptom in 20% of the population, contrasting with the "worst" military simulators, which caused symptoms in 60% of individuals. Additionally, 10% of pilots experienced aftereffects persisting for several hours, posing a potential safety hazard. The authors introduced a symptom categorization system based on central tendencies, classifying scores as negligible (<5), minimal (5-10), significant (10-15), concerning symptoms (15-20), or indicating a "bad" simulator (>20). The analysis revealed that simulators primarily induced Oculomotor symptoms, followed by Nausea, with Disorientation-like symptoms being the least common. In contrast, VE-induced symptoms exhibited more disorientation than Nausea, and Oculomotor disturbances were the least prevalent. The study's conclusion emphasized the distinct nature of VE-induced cybersickness and simulator sickness, hinting at different underlying causes for each .

Mourant & Thattacherry, 2000

The purpose of this study<sup>102</sup> was to explore simulator sickness in a fixed-base virtual environment driving simulator. A diverse sample of 30 participants (15 males and 15 females) aged 18 to 36, with normal or corrected-to-normal vision, was randomly assigned to highway, rural, or city simulator driving groups, each consisting of 5 males and 5 females. Participants underwent a 2-minute practice session using the driving simulator and computer monitor display before donning the Virtual Research VR8 helmet-mounted display (HMD) for a 5-minute driving simulation. During the simulation, highway and rural routes required participants to maintain a speed of 60 mph, while the city route involved driving at 25 mph. Postural stability was assessed by having participants stand on their preferred leg (SOPL) with eyes closed and arms folded across their chest for a maximum of 30 seconds, with an average of two trials recorded. The simulator sickness questionnaire (SSQ) was administered before and after simulator exposure, as well as

before the SOPL assessment for each condition. Results revealed a decrease in SOPL time for females after HMD exposure (16.1 s to 13.3 s), while males showed no change (24.0 s to 21.4 s). Males exhibited longer SOPL times both before and after exposure compared to females. SOPL scores decreased in the highway (21.1 s to 18.4 s) and rural (16.2 s to 13.5 s) environments but remained relatively stable in the city (23.0 s to 19.8 s). When comparing driving environments, the city had higher scores than rural, both before (23.0 s vs. 16.2 s) and after (21.4 s vs. 13.4 s) HMD exposure. Average SSQ oculomotor discomfort scores were greater for both males (4.0 and 14.1) and females (1.0 and 8.1) before and after HMD exposure, with differences observed for each environment in both instances. The authors concluded that males exhibited greater postural stability than females in the SOPL test. Although males had higher SSQ oculomotor discomfort scores than females, the latter experienced a change in SSQ scores from before to after HMD exposure. Notably, participants in the highway or rural environment (driving at 60 mph) experienced a decrease in SOPL, whereas those in the city environment (driving at 25 mph) did not.

Stoffregen et al., 2000

The purpose of this study<sup>103</sup> was to assess the relationship between postural instability and subjective symptoms reported in the Simulator Sickness Questionnaire (SSQ) within a fixed-base flight simulator. Fourteen participants aged between 20 and 42 years were exposed to a flight simulator that visually oscillated in the roll axis, mimicking the motion experienced during flight simulation and resembling postural sway during normal stance. Among the participants, 6 were classified as experiencing motion sickness, with 2 self-reporting and 4 identified by the experimenter. Pre-exposure total severity scores did not show differences between those who later became motion sick (sick group) and those who did not (well group). However, immediately after

exposure, the sick group had higher scores (mean 34.75) compared to the well group (mean 4.27). This difference in SSQ scores persisted between the sick and well groups even after 1-hour (mean 14.96 vs. 0.0, respectively) and 2 hours after leaving the laboratory (mean 13.36 vs. 0.53, respectively). Analysis of postural motion, measured by head movement during visual oscillations, indicated greater motion in the group that later experienced motion sickness. The authors concluded that postural instability preceded the onset of motion sickness symptoms.

Oskarsson & Nählinder, 2006

The purpose of this study<sup>104</sup> was to assess the severity of simulator sickness in a virtual reality (VR)-based air combat simulator. The participants included 12 military flight instructors (mean age 34.6 years), 8 military student pilots (24.3 years), and 12 novices (31.7 years) engaging in a simulation of a Swedish fighter jet SAAB JA 37 Viggen equipped with a head-mounted display (HMD) system. A Simulator Sickness Questionnaire (SSQ) was administered before the simulation, after simulator setup, every fifteen minutes during the 60-minute simulation, immediately after, and at 1-, 6-, 12-, and 24-hours post-simulation. Postural stability was measured by head movement while standing quietly heel-to-toe with folded arms at arrival (pre-1), directly before the simulation (pre-2), immediately after the simulation (post-1), and one hour after the simulation (post-2). The SSQ results indicated that symptoms of nausea were elevated from baseline at 15 to 60 minutes during the simulation, oculomotor symptoms were elevated after installation up to one hour after the simulation, and disorientation symptoms were elevated from 30 to 60 minutes during the simulation. No differences were observed between participant groups. Results regarding postural stability indicated that pre-1 was higher than pre-2, and post-1 was higher than pre-2. The authors concluded that the simulation induced low levels of VR sickness symptoms and postural stability changes, with no notable differences between experience groups.



Webb et al., 2009

The purpose of this study<sup>105</sup> was to evaluate reports of simulator sickness in a newly developed rotary-wing flight simulator among instructor pilots (IP) and student pilots (SP). The Simulator Sickness Questionnaire (SSQ) was administered immediately after each simulator session, with a total of 950 questionnaires collected over five days of training (referred to as the "pre-study"). Another set of 225 SSQs was gathered over three days of training following the implementation of a set of recommendations aimed at reducing simulator sickness (referred to as the "post-study"). The results revealed that eyestrain, general discomfort, headache, and difficulty focusing were the most commonly reported symptoms. Regardless of severity, 72% of IP and 91% of SP reported at least one symptom during the pre-study. Before the recommendations, difference scores for total and subscores increased over the five days of training, indicating a worsening of symptoms. In the post-study, the most common reported symptom remained eyestrain, along with general discomfort, nausea, and burping, with 64% of IP and 90% of SP reporting at least one symptom, regardless of severity. Oculomotor and disorientation SSQ subscores increased over the three days, but not to the same magnitude as in the pre-study. Nausea SSQ scores decreased over the course of training, indicating symptom improvement. There was no change in the total SSQ score from the first to the last days of test administration. The authors concluded that implementing training recommendations reduced sickness in the new simulators, emphasizing the importance of addressing simulator sickness during the design stage for optimal effectiveness.

Patterson & Muth, 2010

The purpose of this study<sup>106</sup> was to assess the frequency and intensity of head-mounted display (HMD) virtual reality sickness in an operational shipboard setting. Active-duty participants (mean  $\pm$  SD, aged  $36 \pm 6$  years) engaged in flight simulations using an HMD display, both on land

and aboard a U.S. Navy Yard Patrol Boat. Flight performance parameters and head positions were recorded, and Simulator Sickness Questionnaires were administered before and after the simulations. The results revealed no difference in completion times between land ( $60.5 \pm 1.5$  minutes) and shipboard ( $59.4 \pm 2.0$  minutes) virtual reality flights. While both conditions induced head movement in coronal and sagittal planes, only head yaw movement increased in the shipboard condition. The SSQ score before simulation was elevated in the shipboard condition but did not differ from the land condition. Additionally, there was no difference between shipboard ( $23.7 \pm 28$ ) and land ( $26.6 \pm 15$ ) post-trial SSQ scores. In conclusion, the authors found that while shipboard HMD virtual reality simulation induced more head yaw movement, there was no difference in reported simulator sickness symptoms.

Stein & Robinski, 2012

The authors<sup>107</sup> examined simulator sickness in jet simulators configured as cockpit training (CT) and full mission simulator (FMS). A total of 42 male Eurofighter pilots (aged 32-45 years) with varying experience levels, up to 50 hours in the CT simulator and 51-100 hours in the FMS configuration, participated. The Simulator Sickness Questionnaire (SSQ) and the National Aeronautics and Space Administration Task Load Index (NASA TLX) workload questionnaire were administered before and after each simulation session. The study found no difference in SSQ total scores between simulations or simulator configurations. Simulator sickness was observed in 21.4% of pilots ( $SSQ \geq 20$ ), and this occurrence correlated positively with workload ( $r=0.39$ ,  $p=0.014$ ). The NASA TLX subscale scores were comparable between simulator conditions, with average workload scores falling in the medium range for both CT (64.2%) and FMS (66.2%). The frustration subscale, reflecting simulator quality, showed low scores for both CT (25.8%) and FMS (25.0%), indicating no differences and suggesting that both conditions did not hinder or disrupt

activities. Subscales for physical and temporal demand were not reported due to the study's experimental design. However, a positive correlation was observed between SSQ and the oculomotor subscale of the NASA TLX ( $r=0.92$ ,  $p<0.001$ ), suggesting that simulators could induce simulator sickness more easily, and higher workload positively correlated with simulator sickness.

Newman et al., 2013

The purpose of this study<sup>108</sup> was to determine whether a once-daily sustained G training session could decrease incidence of motion sickness in nine participants (8 men and 1 woman, mean 44.4 yrs old). Participants underwent simulated 3-Gz turning maneuvers in an Authentic Tactical Flight Simulator model 400, incorporating precise head movements representing to-target and return-to-center head movements. Subjective ratings of motion sickness (MS) on a scale of 0 to 10 and the Simulator Sickness Questionnaire (SSQ) were evaluated before and after acceleration exposure. The normalized MS scores were 58% lower on day 5 compared to day 1, and retention on day 22 after the initial centrifuge exposure was also lower than on day 1. A decrease in total SSQ scores was observed across days, with reductions in both nausea and disorientation subscores. Retention of total SSQ and nausea subscores was evident on day 22. The authors concluded that repeated exposure to Coriolis-inducing head movements in a sustained G simulator resulted in an overall reduction in the development of motion sickness symptoms and cumulative motion sickness intensity.

Oberhauser et al., 2018

The purpose of this study<sup>109</sup> was to explore disparities in pilots' movement time to reach cockpit controls, ideal flight path deviations, workload, and Simulator Sickness Questionnaire (SSQ) outcomes between a virtual reality flight simulator (VRFS) and a conventional flight simulator, involving 28 pilots (mean age 42.5 yrs and mean flight experience 2,485 h). In VRFS,

the movement time for rotary knobs was prolonged, with a mean difference ranging from (mean  $\pm$  SEM)  $1.11 \pm 0.31$  seconds and  $1.68 \pm 0.68$  seconds during ground maneuvers and between  $0.95 \pm 0.20$  seconds and  $1.17 \pm 0.27$  seconds during flight. Pilots also exhibited longer movement times for setting flaps for landing in VRFS. Kinematic flight performance data indicated larger deviations in flight paths within the VRFS environment. Workload analysis using the National Aeronautics and Space Administration Task Load Index revealed higher mental, physical, temporal demand, effort, and frustration in the VRFS condition. Additionally, pilots' self-rating of performance was lower in the VRFS compared to the conventional flight simulator. Symptoms reported in the SSQ were greater in VRFS for nausea ( $28.96 \pm 6.48$  vs  $8.18 \pm 2.18$ ), oculomotor ( $40.93 \pm 5.56$  vs  $19.93 \pm 3.98$ ), and disorientation ( $53.69 \pm 8.40$  vs  $23.37 \pm 5.59$ ) subscores. The authors concluded that despite differences in flight performance, pilots were able to complete the flight task safely and reliably in both environments. However, VRFS presented higher workload and greater incidence of simulator sickness, which could potentially impact performance negatively.

Stróžak et al., 2018

The purpose of this study<sup>110</sup> was to research the impact of visual and vestibular spatial disorientation on cognitive performance in twenty male military pilots (mean  $\pm$  SD, age  $32.31 \pm 6.6$  yrs, flight experience  $970.75 \pm 831.11$  h). Participants underwent a flight profile involving three visual illusions (false horizon, shape constancy, size constancy) and three vestibular illusions (somatogyral illusion, Coriolis effect, the leans) in a GYRO-IPT while concurrently engaging in an auditory discrimination task (Experiment 1) and the N-back sequential letter memory task (Experiment 2). Flight performance was evaluated in both experiments, and the Simulator Sickness Questionnaire (SSQ) was administered after each session. In both experiments, task accuracy

declined for flight profiles featuring the leans illusion, while the number of control reversal errors increased for the false horizon illusion and somatogyral illusion. The total SSQ score ( $1.88 \pm 2.72$ ) and the nausea ( $3.63 \pm 2.42$ ), oculomotor ( $1.81 \pm 1.52$ ), and disorientation ( $2.44 \pm 1.55$ ) subscales showed negligible effects in Experiment 1. Similarly, Experiment 2 demonstrated a minimal impact on the total SSQ score ( $1.38 \pm 1.41$ ) and nausea ( $2.88 \pm 2.31$ ), oculomotor ( $1.81 \pm 1.72$ ), and disorientation ( $2.02 \pm 1.59$ ) subscores indicating similar symptom severity. The authors concluded that spatial disorientation, particularly the vestibular illusion of leans, can hinder selective attention and the working memory process in military aviators.

Ishak et al., 2018

The purpose of this study<sup>111</sup> was to explore the impact of attenuating visual sensory input on motion sickness. Eleven participants (7 men and 4 women, mean age 27.7 yrs) were seated in a motion platform-mounted cockpit simulator programmed to execute sinusoidal pitch, heave, and roll movements for 10 minutes to induce motion sickness. Participants were then administered the Simulator Sickness Questionnaire (SSQ). In the visual occlusion condition, participants wore blackout goggles and instructed to close their eyes while in the simulator. The results revealed that the control condition exhibited a higher mean total SSQ (30.90 vs 2.38), nausea subscore (22.60 vs 0.87), oculomotor subscore (24.10 vs 3.45), and disorientation subscore (38.00 vs 1.27) compared to the occluded vision condition. The authors concluded that visual input plays a crucial role in motion sickness, and eliminating visual input to mitigate sensory conflict aligns with the sensory conflict theory of motion sickness.

Pettijohn et al., 2020

The primary objectives of this study<sup>112</sup> were twofold: a) to investigate potential differences in simulator sickness symptoms between virtual reality (VR) and augmented reality (AR) headsets,

and b) to assess the impact of physical motion on the severity of sickness symptoms. Fourteen participants (mean  $\pm$  SE;  $30.17 \pm 1.98$  yrs) of the Department of Defense visited the laboratory on six separate occasions, experiencing one of three physical motion conditions and one of two headset conditions, each separated by 24-hour interval. In the VR condition, participants wore the HTC Vive headset with 1080x1200 resolution per eye, 110° field of vision, and 90 Hz refresh rate. In the AR condition, images were projected onto three screens (65 x 48.5 in or 165.1 x 123.2 cm), joined at a 45° angle to mimic the 110° field of vision in the VR condition. Participants sat 10 ft (3 m) away, wearing the Microsoft HoloLens projecting a 2.3-megapixel display with onscreen commands in the AR condition. A motion platform induced pitch and roll motion, mounted with a mock 0.50 caliber machine gun, with the objective in each 15-min motion profile to destroy approaching hostile ships. The three physical motion conditions were: 1) no physical motion, 2) synchronous motion where the platform motion matches the visual display, and 3) asynchronous motion where the platform motion was delayed by 10 seconds after the simulated visual motion. The simulator sickness questionnaire (SSQ) was administered before, between motion profiles, and after to assess the severity of motion sickness symptoms. Shooting metrics were reported as behavioral measures for each condition to identify performance differences. The results of the within-participants ANOVA indicated significance in the time domain ( $F=4.68$ ,  $p=0.020$ ,  $\eta_p^2=0.30$ ), suggesting that the motion profiles were able to elicit motion sickness symptoms. There was no difference between SSQ scores of the VR ( $5.02 \pm 2.02$ ) and AR ( $4.57 \pm 2.01$ ) headsets, and no difference in scores in the no physical motion ( $2.49 \pm 0.88$ ), synchronous ( $4.93 \pm 2.48$ ), or asynchronous ( $6.96 \pm 3.11$ ) motion profiles. Performance metrics indicated a main effect of headset, where participants had a greater accuracy in the VR condition ( $45.92 \pm 2.41\%$ ) compared to AR ( $35.94 \pm 2.36\%$ ). The main effect of physical motion showed participants exhibited greater

accuracy in the no physical motion profile ( $58.99 \pm 2.10\%$ ) compared to synchronous ( $29.88 \pm 1.13\%$ ) and asynchronous ( $33.92 \pm 1.40\%$ ), with no difference between synchronous and asynchronous profiles. The study found no differences in simulator sickness, as measured by the SSQ, between VR and AR devices or motion profiles, suggesting feasibility for use in the operational environments where the simulation does not precisely match the real motion.

Fussell & Hight, 2021

The purpose of this study<sup>113</sup> was to explore the usability of both a 2D and virtual reality (VR) simulation in a pilot study of an experimental flight training course. Fourteen undergraduate students (aged 18-24 yrs) enrolled in the Aeronautical Science program underwent training modules covering seven specific flight maneuvers and basic flight skills necessary for a private pilot certification. The training was delivered through either a 2D simulation on gaming computers or the VR group, which included the HTC Vive Pro VR Head Mounted Display (HMD). At the end of the semester, participants completed surveys, including the System Usability Scale (SUS), Game User Experience Satisfaction Scale (GUESS), National Aeronautics and Space Administration Task Load Index (NASA TLX), and the Simulator Sickness Questionnaire (SSQ). Results revealed no differences in perceived comfort, confidence, or difficulty of use between simulation types. However, the SUS scores for the VR group (mean  $\pm$  SD,  $64.64 \pm 12.20$ ) were lower than those for the 2D group ( $78.93 \pm 8.27$ ). Neither the composite score or subscale average scores differed between groups for the GUESS and NASA TLX questionnaires. The total weighted score of the SSQ showed no difference between the 2D group ( $0.13 \pm 0.38$ ) and the VR group ( $0.53 \pm 0.71$ ). Although SSQ subscores for nausea, oculomotor, or disorientation-related symptoms did not differ between groups, a direct comparison of symptoms indicated eye strain was greater in the VR group. In conclusion, the authors determined that both simulations were

beneficial for learning of flight maneuvers, and the VR simulation was comparable to the 2D simulation in terms of usability and user satisfaction for flight training.

Auer et al., 2021

The purpose of this study<sup>114</sup> was to investigate whether consumer-grade virtual reality flight simulators (VRFS) could be comparable to a Boeing 737-800NG physical flight simulator (PFS) during cockpit familiarization training. Eleven participants (8 men and 3 women, mean  $\pm$  SD,  $31.64 \pm 7.13$ ) engaged in the study. The VRFS condition involved using the Pimax5k+ with two control schemes: finger tracking leap motion (VRL) and using the HTC Vive controller (VRC). Performance, error rate, and task completion time were evaluated while participants read aloud various aircraft parameters and manipulated switches for a checklist that included engine start (check 1), after engine start (check 2), and engine shutdown (check 3). Participants also completed questionnaires, including the National Aeronautics and Space Administration (NASA TLX) and Simulator Sickness Questionnaire (SSQ). The results indicated no difference between PFS and VRFS in reading performance and error rate. However, task completion time was longer in the VR condition compared to the PFS in the check 2 task (VRL  $34.45 \pm 7.12$  s, VRC  $34.20 \pm 9.54$  s, PFS  $7.73 \pm 1.82$ ) and check 3 task (VRL  $56.91 \pm 8.53$  s, VRC  $50.49 \pm 8.21$  s, PFS  $19.81 \pm 8.19$  s). Perceived workload was greater in physical demand and effort in both VR conditions, with mental demand being higher in VRC ( $53.64 \pm 18.04$ ) compared to PFS ( $32.73 \pm 18.76$ ). The change in the total score of SSQ was greater in the VRFS condition ( $14.59 \pm 18.87$ ) compared to PFS ( $-1.02 \pm 8.54$ ), and also in the oculomotor (VRFS  $16.48 \pm 21.37$  vs PFS  $-5.51 \pm 9.03$ ) and disorientation (VRFS  $18.98 \pm 18.96$  vs PFS  $-3.80 \pm 9.00$ ) subscores. However, the change in nausea subscore was greater in the PFS ( $6.94 \pm 11.36$ ) condition compared to VRFS ( $3.47 \pm 11.51$ ). The authors concluded that the VRFS cannot fully replace PFS for cockpit familiarization training.



Nevertheless, with improvements in software and hardware for interacting with simulated switches, VRFS can serve as alternatives to PFS.

Polak et al., 2022

The purpose of this study<sup>115</sup> was to evaluate the psychophysical state of novice pilots following exposure to a flight simulator. Twenty-seven men, qualified to operate airplanes under instrument flight rules and in instrumental meteorological conditions, participated in a 2h flight session included procedural flight exercises, training in take-off and approach to landing, flights in conditions of limited visibility, and exercises in emergency procedures using an Alsim ALC-30 flight simulator. The simulator sickness questionnaire (SSQ) was administered both before and immediately after the simulation, assessing total score and its three factors: nausea, oculomotor disturbance, and disorientation. The authors reported an increase in the total score after simulation exposure (median  $\pm$  inter-quartile range;  $7.5 \pm 9.4$  to  $33.7 \pm 22.4$ ). Subscale analyses indicated an increase in simulator-associated sickness in the nausea ( $0 \pm 0$  to  $19.1 \pm 19.1$ ), oculomotor ( $7.6 \pm 7.6$  to  $37.9 \pm 26.5$ ), and disorientation ( $13.9 \pm 13.9$  to  $27.8 \pm 41.8$ ) domains. The authors concluded that the observed changes in the psychophysical state of novice pilots after flight simulator exposure confirm the occurrence of simulator sickness symptoms.

**NASA Task Load Index (TLX)**

Moroney et al., 1992

The purpose of this study<sup>116</sup> was to compare unweighted National Aeronautics and Space Administration Task Load Index (NASA TLX) results with previously reported weighted outcomes under immediate and delayed rating conditions. Twelve university students (10 men and 2 women) completed flying tasks in a Cessna 182 using the Microsoft Flight Simulator, featuring varying difficulty levels. The NASA TLX or a matching form was completed after each task. In

the delayed reporting conditions, the matching form involved selecting a matching radio call sign from a series of options. The study results indicated that mean flight task performance decreased with increasing difficulty, particularly in the presence of crosswinds of 2, 9, and 16 knots. There was no difference in performance between the no-delay and 15-minute rating delay conditions for the matching task. A strong positive correlation ( $r=0.94$ ) was observed between weighted and raw mean subscale scores of the NASA TLX, suggesting a high level of agreement between the two scoring procedures. Furthermore, there was no difference between NASA TLX rating delay and no-delay conditions. It was found that the time-consuming use of weighting scales was not necessary and that delaying TLX reports up to 15-minutes did not significantly interfere with recall of workload ratings.

Karavidas et al., 2010

The purpose of this study<sup>117</sup> was to evaluate mechanical respiratory activity (volume and frequency) and end-tidal carbon dioxide ( $PCO_2$ ) levels during varying levels of workload in a flight simulator. Seven professional pilots (aged 34-60 yrs old) operated a Boeing 737B flight-800 Level D simulator while wearing the Vivo Metrics LifeShirt to capture physiological respiration variables across 11 flight tasks categorized as low, moderate, and high FAA staff-described task loads. Pilot performance was assessed on a 5-point scale by an experienced test and check pilot, and the National Aeronautics and Space Administration Task Load Index (TLX) scale was administered after each task. The findings revealed an increase in respiration rate from baseline, with respiration during high task load (mean  $\pm$  SEM,  $22.90 \pm 1.04$  breaths/min) exceeding the combined rates of medium and low loads ( $21.12 \pm 0.97$  breaths/min). Minute ventilation was also higher during high task load ( $19.79 \pm 1.71$  l/min) compared to the combined medium and low ( $17.21 \pm 1.64$  l/min). The  $PCO_2$  values consistently decreased during all flight tasks from baseline,

with instances of hypocapnia (value  $<32$  mmHg) being most prevalent during high demand tasks, aligning with evaluator scores  $\leq 2$ . Higher NASA TLX scores correlated with elevated minute ventilation and respiration rates. The authors concluded that ventilation serves as a sensitive measure of mental workload demands during flight.

Mansikka et al., 2019

The purpose of this study<sup>118</sup> was to investigate measures of pilot mental workload using the National Aeronautics and Space Administration Task Load Index (NASA TLX), modified Cooper-Harper (MCH) scale, and inter-beat-interval (IBI) of successive heartbeats in a flight training device. Twenty-seven Finnish Air Force pilots conducted a series of instrument landing system approaches, spanning from 8-15 nautical miles in 1 nautical mile increments. These approaches involved various triggered tasks necessitating immediate pilot action, acknowledgement, or altimeter settings. Following each trial, the NASA TLX and MCH were administered, accompanied by performance measures and continuous electrocardiogram monitoring. The pilots' trial scores were categorized into low (mean  $\pm$  SD,  $2.43 \pm 0.84$ ), medium ( $3.72 \pm 0.36$ ), and high ( $4.73 \pm 0.11$ ) performance levels. Analysis revealed that IBI mean values differed among performance categories (low  $678.20 \pm 127.63$  ms, medium  $682.67 \pm 121.78$  ms, high  $730.17 \pm 157.56$  ms) and pre-testing baseline ( $851.80 \pm 175.52$  ms). Only the high-performance category exhibited a greater IBI than both low and medium performance categories. Workload, as measured by the NASA TLX, was highest in the low-performance category ( $39.04 \pm 7.86$ ) compared to both the medium ( $33.48 \pm 9.36$ ) and high ( $14.93 \pm 6.42$ ) performance categories. The medium and high categories also differed from each other. Subscale scores of the NASA TLX consistently increased with decreasing performance scores, with the low-performance category subscores higher than the high-performance category. However, only mental demand,

temporal demand, and self-rated performance of the NASA TLX showed differences between low and medium performance scores. MCH results indicated that low ( $6.67 \pm 1.92$ ), medium ( $5.37 \pm 1.57$ ), and high ( $2.44 \pm 1.12$ ) performance categories were all distinct from each other. Furthermore, a positive correlation between NASA TLX and MCH scores existed in all performance categories. The authors found that all measures effectively differentiated task conditions and characterized pilot performance.

Arce-Lopera et al., 2021

The purpose of this study<sup>119</sup> was to explore grip force dynamics using force sensitive resistors during gaming tasks with varying mental workloads and difficulties. Five participants (2 women and 3 men, aged 23-28 yrs) engaged in a mobile game with both low and high difficulty levels, utilizing a Bluetooth-connected gamepad while grip force was recorded. The National Aeronautics and Space Administration Task Load Index (NASA TLX) was recorded after each task to measure workload. The findings revealed that the low difficulty task resulted in a lower workload ( $56.5 \pm 8.8$ ) compared to the high difficulty task ( $78.8 \pm 11.5$ ). While a higher grip force was observed during the high difficulty game, however the low difficulty level exhibited a greater magnitude of different frequency components. The authors concluded that an increased mental workload may be associated with a diminished attention to handgrip force.

Galant-Gołębiewska et al., 2021

The purpose of this study<sup>120</sup> was to research the relationship between task difficulty and the level of operator workload. The participants, divided into two groups -one holding a private pilot license (Group A) and the other without (Group B) – operated a flight simulator, engaging in easy, moderate, and difficult tasks while researchers recorded pulse oximeter readings and brain activity measures. At the conclusion of all three tasks, participants completed the National

Aeronautics and Space Administration Task Load Index (NASA TLX) and a post-task questionnaire evaluating the difficulty level of each stage. Analysis of the results revealed that the average heart rate during the moderate difficulty task was lower than that during both the easy and hard tasks. Additionally, the heart rate during the easy task was lower than during the hard task. Concentration levels. On average, were lower during the hard task compared to both the easy and moderate tasks. The NASA TLX scores indicated that the workload during the moderate difficulty task was higher than during the easy task, and the hard task had a higher workload score than both the easy and moderate difficulty tasks. The post-task questionnaire ratings of difficulty supported these findings, indicating that the hard task was perceived as more challenging than the moderate and easy tasks. The authors concluded that heart rate, concentration levels, and subjective measures of workload can effectively serve as psychophysical indicators of operator workload.

Chiossi et al., 2022

The purpose of this study<sup>121</sup> was to assess the usability of a physiological adaptive virtual reality (VR) system within a social VR scenario, focusing on eliciting and maintaining a consistent level of arousal. The experiment involved 18 participants (9 men and 9 women, mean  $\pm$  SD, 27.9  $\pm$  2.9 yrs) who engaged in a visual working memory n-back test and a visual detection using the HTC VIVE VR head-mounted display. The experiment comprised five testing blocks, each with predetermined parameters of increasing difficulty, and the sixth block introduced an adaptive condition. In this adaptive condition, the visual complexity of the detection task is adjusted based on the subject's arousal levels, determined through electrodermal activity (EDA), electrocardiogram (ECG), and electroencephalogram (EEG) measurements. Post-testing block questionnaires included the National Aeronautics and Space Administration Task Load Index (NASA TLX), the Game Experience Questionnaire (GEQ), and the Fast Motion Sickness scale

(FMS). Results indicated a correlation between an elevated NASA TLX score and increased EDA during fixed difficulty increments in the five non-adaptive conditions. However, the physiologically adaptive condition showed no increase in EDA activity or NASA TLX score, demonstrating successful adaptability for each participant. Subjective assessments revealed a heightened sense of immersion (GEQ) in the adaptive condition ( $1.56 \pm 0.71$ ) compared to a computed expected value for the non-adaptive conditions ( $1.03 \pm 0.32$ ). In conclusion, the authors determined that adaptive virtual reality enhanced subject comfort by tailoring physiological arousal to the complexity of the tasks.

Reddy et al., 2022

The purpose of this study<sup>122</sup> was to investigate cognitive load and cybersickness through a series of six flying tasks in a Boeing T-45C jet simulator. The tasks included flying straight, minor turns, 180° turns, loop maneuver, barrel roll maneuver, and nearsighted/farsighted focusing. Six male participants (mean  $\pm$  SD, age  $24.7 \pm 1.2$  yrs, game experience  $2.9 \pm 1.8$  h/week) answered two questionnaires pertaining to workload and cyber sickness. The Pilot Inceptor Workload (PIW) was used to measure aircraft control workload, utilizing duty cycle (the percentage of time the pilot changes aircraft input) and aggressiveness (root mean squared per-second average of the inceptor position rate of change with respect to time). Omnicepts, a cognitive load a machine learning model provided real-time cognitive load outputs a real time ranging from 0 to 1. Self-reported measures included the National Aeronautics and Space Administration Task Load Index (NASA TLX), virtual reality sickness questionnaire (VRSQ), motion sickness susceptibility questionnaire (MSSQ), and the motion sickness assessment questionnaire (MSAQ). The findings revealed that duty cycle and aggressiveness were impacted by task complexity. Task difficulty influenced both the NASA TLX and Omnicepts cognitive load measure. A positive correlation

was observed between PIW aggressiveness rating and scores of the Omniceps cognitive load measure ( $\rho = 0.35$ ) and the NASA TLX ( $\rho = 0.43$ ) rating. However, there was no effect of the task on MSSQ, MSAQ, or VRSQ scores. The authors concluded that the NASA TLX and Omniceps cognitive load measure effectively differentiated between levels of task complexity.

## Chapter III – Methods

### EXPERIMENTAL APPROACH SUMMARY

Participants arrived at the laboratory for a familiarization period prior to testing where they learned the controls of the simulator, became acquainted with the sensors/ equipment and familiarized with each of the questionnaires/cognitive tests. Participants arrived at the laboratory for two testing visits lasting approximately 2h each separated by at least 24h and exposed to 2 altitude conditions per visit. After familiarizing participants with the controls of the game, they are asked to perform three flying tasks while exposed to Normoxia ( $\text{FiO}_2$  21%), a hypoxic exposure of 8,000 ft (2438m or  $\text{FiO}_2$  15.4%) or 12,000 ft (3658m or  $\text{FiO}_2$  13.2%), and a Ramp Hypoxic exposure (pre-breathing at  $\text{FiO}_2$  15.4% for 5-minutes decreased to  $\text{FiO}_2$  13.2% at the start of the simulation) in a randomized blinded order using <http://www.randomizer.org/>. The environmental conditions are illustrated in **Figure 1**.

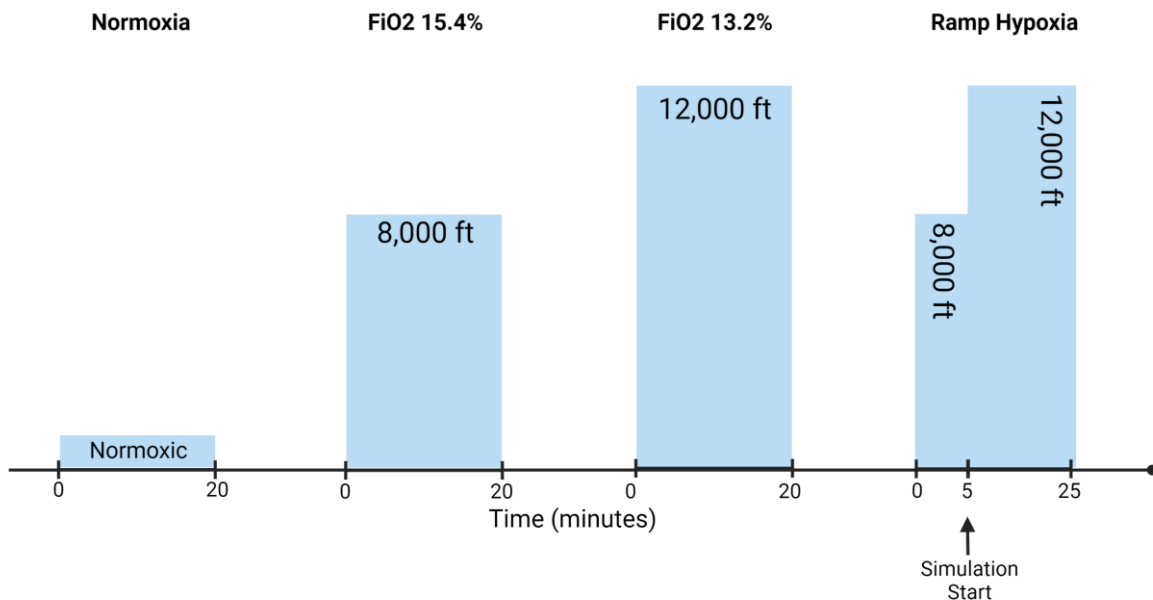


Figure 1. Simulated Environmental Conditions



Participants signed a written informed consent and completed a health history questionnaire (Appendix A) to screen for Inclusion/Exclusion criteria (Table 1). Participants who met inclusion criteria were then introduced to and familiarized with all equipment, procedures, and the virtual reality (VR) setup on their first visit.

Table 1. Inclusion and Exclusion Criteria	
Inclusion	Exclusion
Age 18-40 yrs	Respiratory Deficiency (Asthma)
Physically active for 150 min Aerobic or 2x Week of Strengthening <sup>123</sup> or have a Normal BMI	Cardiovascular Disorders
Normal 20/20 vision or corrected to normal	Neurological/Musculoskeletal Disorders
	Photosensitive Epilepsy

On the first testing day (Figure 2) and signing informed consent, participants were assessed for physical activity habits (Appendix B) and their height/weight were obtained using a standard physician’s beam scale to verify eligibility. Rewrite to improve clarity. Prior to testing, participants were administered the motion sickness susceptibility questionnaire (MSSQ – Appendix C) to assess for the likelihood of becoming motion sick during simulator use.<sup>124</sup> During initial setup electromyography (EMG) sensors, metabolic mask, and electrodermal activity sensors (EDA) were placed on the participant while they are seated in a chair. Participants were asked to perform 3 trials of a maximal strength shoulder shrug to ensure equipment was functioning normally. Participants then donned the virtual reality headset and began the three flight Tasks: 1) maintaining a cruising altitude of 5,000 ft while performing mental addition, 2) flying the aircraft through the center of a series of seven targets, and 3) flying the aircraft a short distance to land on the center of the indicated target. This evolution took approximately 20-minutes. Following each flight simulation task, participants took off their headsets. Subsequently, all measurements for post-task values were obtained while the participants were in a state of quiet sitting, including the completion

of questionnaires. Measures of piloting performance was the correct number of responses during the mental addition (Math Task), the score of flying through the center of the seven targets (Course Task), and the score of how close to the target participants were able to land the aircraft (Landing Task). The National Aeronautics and Space Administration (NASA) Task Load Index (TLX) measure of self-perceived workload was obtained after each simulator condition, along with questionnaires assessing simulator sickness and hypoxic symptoms.<sup>92, 97, 125-127</sup> Participants were given a 10-minute break period before repeating the above procedures while exposed to the second randomized simulated altitude condition. Peripheral oxygen saturation (SpO<sub>2</sub>) was monitored throughout the break in two-minute intervals. On the second visit, participants would repeat the above flight simulator testing in the simulated altitude condition that did not occur on the first testing visit.

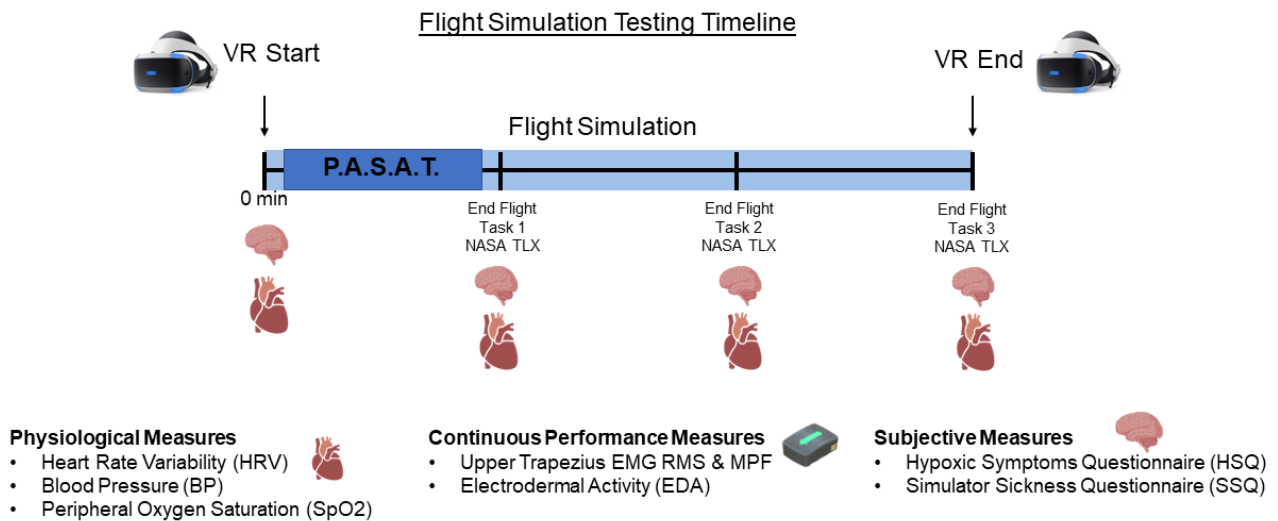


Figure 2. Flight Simulation Testing Timeline

## A PRIORI POWER ANALYSIS

An *a priori* power analysis for a repeated measures ANOVA (4 Altitude x 4 Time) using G\*Power 3.1.9.7 was conducted on pilot data ( $N_p = 5$ ) for the meanHR calculated using Kubios

HRV Standard (version 3.5.0 Kubios Oy, Kuopio, Finland) in each Altitude condition ( $\bar{X}_{\text{Normoxic}}=83.540$  bpm;  $\bar{X}_{8k\text{ ft}}=84.40$  bpm;  $\bar{X}_{12k\text{ ft}}=86.75$  bpm;  $\bar{X}_{\text{Ramp}}=84.60$  bpm) and at each Time point ( $\bar{X}_{\text{Exposure}}=83.65$  bpm;  $\bar{X}_{\text{Math Task}}=86.55$  bpm;  $\bar{X}_{\text{Course Task}}=84.70$  bpm,  $\bar{X}_{\text{Landing Task}}=84.39$  bpm) with a computed effect size of  $f = 0.4922$  from an  $\eta_p^2=0.195$ , a total sample size of 8 is required to reach a power of 0.8 (Figure 3).<sup>128-130</sup>

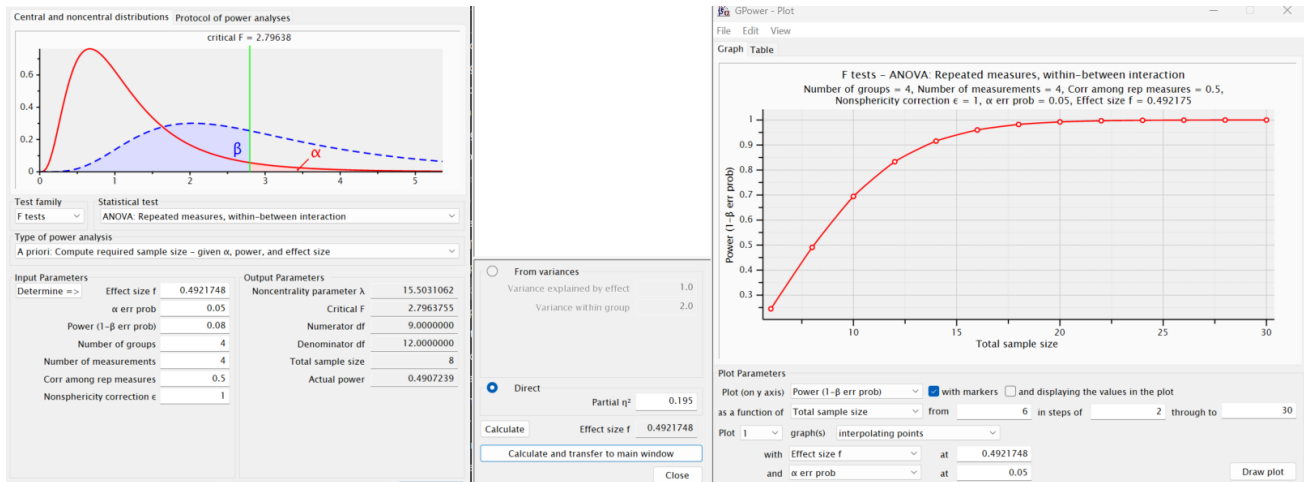


Figure 3. G\*Power 3.1 A priori to reach a power of 0.80 with an effect size of 0.49.

## HYPOXIC EXPOSURE

Participants donned a Hans-Rudolf Oro-nasal face mask connected to a two-way non-rebreathing valve. The valve is attached to a breathing hose connected to the HYP 123 altitude generator (Hypoxico Altitude Training Systems, New York, NY, USA) that takes ambient room air and alters the  $\text{FiO}_2$  to simulate higher altitudes. A set of double-Douglas bags capable of storing up to 4 liters of simulated altitude air was used so that subjects may breathe freely without the typical effects of breathing through a tube. The simulated altitudes were adjusted on the generator and monitored using an oxygen monitoring device (OxyCheq Expedition – X O2 Analyzer, Higher Peak LLC, Newburyport, MA, USA), where the Normoxic condition ( $\text{FiO}_2$  21%) was administered by opening the valves completely to allow ambient air to pass through. The two constant hypoxic

conditions administered in random order was simulated by lowering the FiO<sub>2</sub> to 15.4% (8,000 ft or 2438m) and 13.2% (12,000 ft or 3658m). The Ramp Hypoxic exposure began at an FiO<sub>2</sub> 15.4% simulating flying under normal low altitude conditions for 5-minutes, followed by a decrease to FiO<sub>2</sub> 13.2% simulating a failure of a pilot's on-board oxygen generator system (OBOGS) and breathing air at an altitude where supplemental oxygen is required simulating an uncontrolled/unmonitored ascent in altitude as seen with inexperienced pilots experiencing hypoxia symptoms.<sup>131</sup> Participants condition order was in a randomized single blinded order using <https://www.randomizer.org/>.

### **CARDIOVASCULAR ACTIVITY (HRV, & SpO<sub>2</sub>, BP)**

The SpO<sub>2</sub> was collected using a finger pulse oximeter of the right index finger before and after each simulation condition. Blood pressure (mmHg) was measured using an automated sphygmomanometer on the left arm while participants are seated with feet flat on the ground. Variables of systolic (SBP) and diastolic (DBP) pressure were recorded and used for calculation of mean arterial pressure (MAP) using the following formula [1]:<sup>8</sup>

$$MAP = DBP + \frac{1}{3}(SBP - DPB) \quad [1]$$

Electrical activity of the heart was measured using the Polar H10 Heart Rate Sensor (Polar Electro Oy, Kempele, Finland) by moistening the electrode area of the chest strap and fastened around the chest snugly centered over the sternum just below the pectoral muscles. Signals were recorded utilizing the Elite HRV app (Elite HRV, Asheville, NC, USA) on an android smartphone (Samsung S23 Ultra, Android 13.5.1, Samsung Group, Suwon, South Korea) and exported as RR interval data in .txt format to Kubios HRV Standard (version 3.5.0 Kubios Oy, Kuopio, Finland) for evaluation of meanHR (bpm), root mean squared of successive RR interval differences

(RMSSD), and ratio of relative power of the low-frequency band (0.04-0.15 Hz) to the high-frequency band (0.15-0.4 Hz) (LF/HF). The beat correction level was individually adjusted according to the guidelines provided in Kubios HRV preprocessing (<https://www.kubios.com/hrv-preprocessing/>). It was ensured that corrected beats did not surpass a specified threshold (<5% beats corrected), by first identifying any beat intervals that required correction and then selecting the necessary correction level that effectively rectified abnormal beats without excessively altering the data, as outlined in the manual guidelines.<sup>132</sup>

### **ELECTRODERMAL ACTIVITY (EDA)**

The EDA response was measured using the Grove – GSR Sensor (Seeed Studio, Shenzhen, China) connected to a SunFounder Uno R3 Microcontroller Board (SunFounder, Shenzhen, China) for data acquisition. The nickel finger contact electrodes were placed on the middle phalanges of the left index and ring finger.<sup>133</sup> Using manufacturer suggested code (Figure 4) in the Arduino IDE Software 1.8.19 (Arduino, Ivrea, Italy) and calibrated to a midpoint reference of 521, data was recorded and saved using the two-way data transfer for Excel (Data Streamer, Microsoft Corp, Redmond, WA).<sup>134</sup>

```

GSRTest | Arduino 1.8.19
File Edit Sketch Tools Help
GSRTest
const int GSR=A0;
int sensorValue=0;
int gsr_average=0;

void setup() {
  Serial.begin(9600);
}

void loop() {
  long sum=0;
  for(int i=0;i<10;i++) //Average the 10 measurements to remove the glitch
  {
    sensorValue=analogRead(GSR);
    sum += sensorValue;
    delay(5);
  }
  gsr_average = sum/10;
  Serial.println(gsr_average);
}

Sketch uses 2008 bytes (6%) of program storage space. Maximum is 32256 bytes.
Global variables use 188 bytes (9%) of dynamic memory, leaving 1860 bytes for local variables.

19 Arduino Uno on COM7

```

Figure 4. Manufacturer suggested code for the EDA sensor.

Data was analyzed in MATLAB (MATLAB v 23.2.0.2365128, The MathWorks Inc., Natick, Massachusetts, USA) by filtering values outside of measurement range 0-1024, and data points selected as 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100% for the time course of EDA response while flying the simulator. Values are analyzed as measures of skin conductance level ( $\mu\text{S}$ ) by taking the reciprocal of the calculated human resistance ( $\mu\Omega$ ) from raw signal using the below formula [2]:<sup>134</sup>

$$\text{Human Resistance } (\mu\Omega) = \frac{(1024+2 \times (\text{Serial Port Reading}))}{(521 - \text{Serial Port Reading})} \quad [2]$$

## ELECTROMYOGRAPHY (EMG)

Electromyographic amplitude and frequency responses of the neck were recorded using an active electrode arrangement. An EMG sensor was placed at 50% on the line from the acromion

to the spine on vertebra C7, after shaving and cleaning with alcohol wipes and in the direction of the line between the acromion and vertebral spine over the right upper trapezius muscle.<sup>135, 136</sup> Signals were collected at 2000 Hz using the Trigno Avanti Sensor (Trigno® Wireless Biofeedback System, Delsys Incorporated, Natick, MA, USA) with a 10 mm inter-electrode distance on a laboratory computer installed with the EMGWorks® Software (Delsys Incorporated, Natick, MA, USA).

Electromyographic signals were stored and analyzed offline using custom written software (LabVIEW v 21, National Instruments, Austin, TX, USA). The EMG signal was bandpass filtered using fourth-order Butterworth at 10-500 Hz. Measures of EMG amplitude (root mean square, RMS) and frequency (mean power frequency, MPF) signal of the upper trapezius was continuously collected throughout each condition, where the middle 33% of each epoch was considered mean muscle activation during each condition. The EMG data of the upper trapezius was normalized to the maximum value of three maximal strength shoulder shrugs separated by 2 minutes of rest.<sup>136</sup>

#### **COGNITIVE TASK (PACED AUDITORY SERIAL ADDITION)**

The Paced Auditory Serial Addition Task developed by Gronwall & Sampson (1974) involves presenting a series of single digit numbers where the two most recent digits are summed together.<sup>137</sup> For example, if the digits ‘4’, ‘9’, and ‘6’ are presented, the participant would respond with the corresponding sums of ‘13’ and ‘15’. For a response to be scored as correct the participant must respond prior to the presentation of the next digit (4.0s intervals). In the present study, 60 single digit numbers will be presented every 4 seconds in randomized order using the “P.A.S.A.T.” mobile application on an android smartphone device (total ~240s). The serial addition task was reported as the number of correct responses.<sup>138</sup>

## **QUESTIONNAIRES**

### **Hypoxic Symptoms Questionnaire (HSQ)**

Participants was asked to rate their symptoms of hypoxia as 0 for “None”, 1 for “Slight”, 2 for “Moderate”, or 3 for “Severe” after each flight simulation Task. hypoxic symptoms was taken based on research from Bouak et al., (2018) and Smith, (2005) comprised of 18 symptoms (Appendix D) calculated for cumulative (i.e., sum of) reported hypoxic symptom count and as symptom severity.<sup>91, 97</sup>

### **Simulator Sickness Questionnaire (SSQ)**

The SSQ will be used to monitor feelings of sickness after VR experiences and monitor physiological state return to Baseline after the 10-minute break period. The SSQ consists of 16 symptoms and are graded on a modified Likert scale (None, Slight, Moderate, Severe). The SSQ (Appendix E) was administered using an iPad tablet (iPad Pro 11-in 2<sup>nd</sup> gen) and an Apple Pencil (Apple Inc., Cupertino, CA, USA) given to participants immediately after each simulated altitude condition. Results were calculated as weighted Total Score, Nausea, Oculomotor Discomfort, and Disorientation subscores for each flying task during each simulated altitude condition (Appendix F).<sup>99, 139, 140</sup>

### **NASA Task Load Index (TLX)**

The National Aeronautics and Space Administration (NASA) Task Load Index (TLX) (Appendix G) was used as a subjective workload assessment comparing between each simulated altitude condition. The NASA TLX was reported as a weighted overall workload score (calculated as the sum of weighted scores and divided by 15) and subscores of Mental demand, Temporal demand, Physical demand, Effort, Frustration, and Performance.<sup>125-127</sup>



## VIRTUAL REALITY (VR) SETUP

Participants flew a flight simulator using the PlayStation Console and PSVR CUH-ZVR2 Series hardware (Sony Interactive Entertainment, Tokyo, Japan) with Ultrawings VR flight software. On the first visit, participants played through each task for the first 45 minutes of their first visit to become familiarized with the game controls (PlayStation Move Controllers) using the control stick, throttle, and rudder pedals to fly the plane. During testing participants completed the following tasks, once in each simulated altitude condition:

Math Task: Consists of an approximate six-minute period of free flight, where participants are asked to take-off from a runway, fly around a nearby statue and continue on straight towards an island in the distance while maintaining  $5,000 \pm 400$  ft of elevation (Figure 5). At this time the P.A.S.A.T. was administered immediately upon reaching the designated cruising altitude.

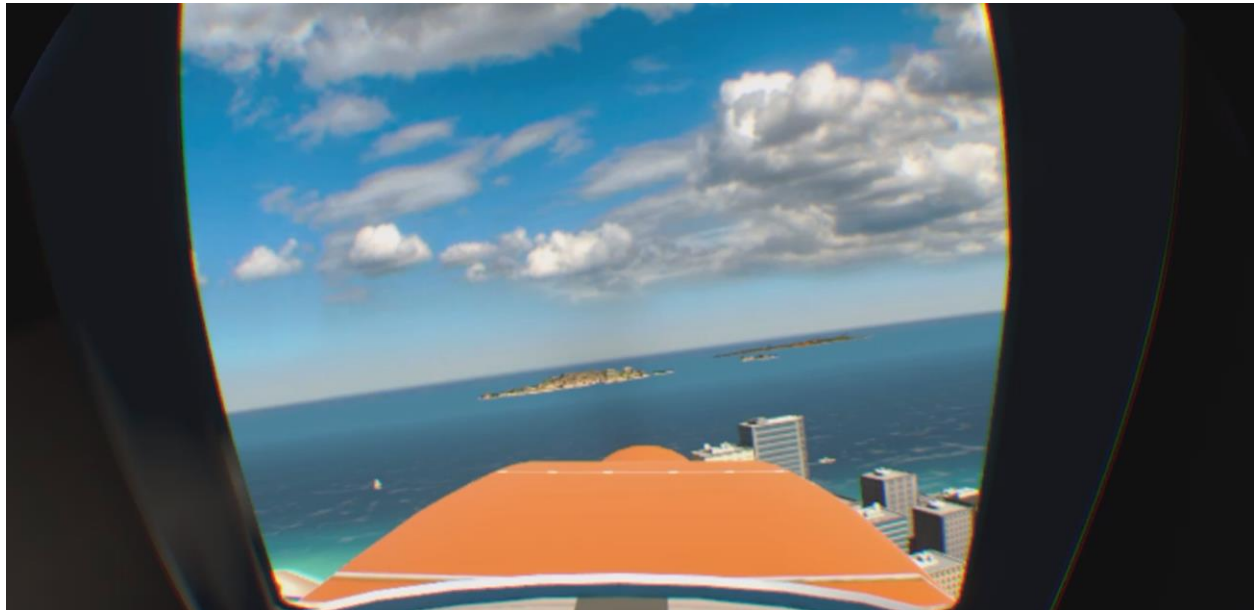


Figure 5. Screenshot of simulated flight during the Math Task. Participants were instructed to maintain altitude while heading into the direction of the distant island on the right while performing the P.A.S.A.T.

Course Task: Consists of an approximate two-minute course flight, where participants are asked to fly through a series of seven targets. Participants were scored on how close to the center of each target they were able to maneuver the plane through, where the red outer circle is scored as 2 points, and the yellow inner circle is 8 points.



Figure 6. Screenshot of simulated flight during the Course Task. Participants were instructed to fly through the center of seven of the depicted targets.

Landing Task: Consists of an approximate two-minute landing task, where participants are asked to take off from a runway and fly to a nearby island locating the ground target with the objective of “touching down” the aircraft wheels located below the chair on the center of a target and coming to a complete stop.



Figure 7. Screenshot of simulated flight during the Landing Task. Participants were instructed to land the wheels of the aircraft on the center of the above-depicted target.

Flight performance was graded based upon the following: “Math Task” will be scored based on the number of correct responses of the P.A.S.A.T. cognitive test with a maximum score of 59 correct responses. Course Task performance score will be the total number of accumulated points from flying through the centers of each of the seven targets for a maximum score of 48. In addition, “Landing Task” performance will be graded based on distance from the target, where  $<5$  m is 8 points,  $<10$  m is 4 points,  $<17$  m is 2 points, and  $>17$  m is 0 points.

### STATISTICAL ANALYSIS

All collected data was entered and organized using Microsoft Excel (Microsoft 365, Microsoft Corporation, Redmond, WA, USA) and exported as .csv to the Statistical Package for Social Sciences (SPSS version 28.0, IBM Corporation, Armonk, NY, USA) for statistical processing.

Three, 4 (Altitude: Normoxia, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, Ramp Hypoxia) by 10 (Time Course: 10, 20, 30, 40, 50, 60, 70, 80, 90, 100%) repeated measures ANOVA will be conducted to compare the time course progression of EDA between all four simulated altitude conditions for each simulated flight task.

A total of five, 4 (Altitude: Normoxic, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, Ramp Hypoxia) x 4 (Time: Exposure, Math Task, Course Task, Landing Task) repeated measures ANOVA's will be used to examine the interaction and main effects on MAP, HRV (meanHR, RMSSD, LF/HF), and SpO<sub>2</sub>. Follow-up one-way ANOVA and *post hoc* paired samples t-test will be performed when appropriate with Tukey's method for comparisons.<sup>141</sup>

Sixteen, 4 (Altitude: Normoxic, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, Ramp Hypoxia) x 3 (Task: Math Task, Course Task, Landing Task) repeated measures ANOVA will be performed to examine interaction and main effects on the weighted NASA TLX (Overall Workload, Mental Demand, Physical Demand, Temporal Demand, Effort, Frustration, & Performance), SSQ (Total Score, Nausea, Oculomotor Discomfort, & Disorientation), HSQ (cumulative number of symptoms & severity), EMG RMS, and EMG MPF.

Three, one-way ANOVA's will be conducted to compare the effects of simulated altitude conditions on the "Math Task" P.A.S.A.T. Score, "Landing" Target Accuracy Score, and "Course Task" Landing Accuracy Score.

An alpha level of  $p \leq 0.05$  will be considered significant for all statistical tests. If Mauchly's Test of Sphericity assumption is not met a Greenhouse-Geiser Correction will be applied and partial eta-squared ( $\eta_p^2$ ) effect sizes reported. All descriptive statistics are reported as Mean  $\pm$  Standard Error Mean (SEM), unless otherwise stated.

## Chapter IV – Results

### SUBJECTS

Seventeen participants (10 women and 7 men) were recruited and exposed to simulated altitude conditions in random order (Table 2). Participants were either physically active according to the ACSM physical activity guidelines or had a normal BMI (between 18.9 kg•m<sup>2</sup> and 24.9 kg•m<sup>2</sup>). This study was approved by the University of Texas at El Paso Institutional Review Board (2042946), and all subjects signed a written informed consent and completed a health history/physical activity questionnaire before participation.

	N	% of the total sample			
<b>Gender</b>					
Female	10	58.8			
Male	7	41.2			
	<b>Mean</b>	<b>SEM</b>	<b>Mean</b>	<b>SEM</b>	
Age (yrs)	24.8	1.56	<b>Activity per week</b>		
Height (cm)	169.3	2.52	Sleep (h)	6.89	0.52
Weight (kg)	74.93	4.28	Aerobic (h)	0.56	0.12
BMI (kg/m <sup>2</sup> )	25.87	0.98	Anaerobic (h)	0.30	0.11

The mean raw score of the MSSQ was  $6.242 \pm 2.051$ . The mean sub-scores did not differ between Part A child ( $3.12 \pm 1.08$ ) and Part B adult ( $3.13 \pm 1.15$ ) ( $t=-0.012$ ,  $df$  14,  $p=0.990$ , 2-tail). The female mean MSSQ raw score ( $4.19 \pm 1.61$ ) did not differ from the male mean ( $8.58 \pm 3.98$ ) (equal variances not assumed,  $t=-1.022$ ,  $df$  7.937,  $p=0.337$ , 2-tailed).

### CARDIOVASCULAR RESPONSES

#### Mean Arterial Pressure (MAP)

A 4 (Altitude: Normoxic, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia) by 4 (Time: Exposure, Math Task, Course Task, Landing Task) repeated measures ANOVA for MAP indicated

no significant interaction effect ( $p=0.121$ ,  $\eta^2 =0.103$ ). There was no significant main effect of Altitude ( $p=0.303$ ,  $\eta^2 =0.082$ ). However, there was a significant main effect of Time on MAP ( $p=0.006$ ,  $\eta^2 =0.254$ ). Follow-up pairwise comparisons indicated a decrease Exposure ( $94.31 \pm 2.82$  mm Hg) to the Course Task ( $92.23 \pm 2.64$  mm Hg,  $p=0.033$ ) and the Landing Task ( $91.73 \pm 2.39$  mm Hg,  $p=0.012$ ) (Figure 8). In addition, MAP was greater at the Math Task ( $93.96 \pm 2.72$  mm Hg) compared to Course Task ( $p=0.023$ ) and Landing Task ( $p=0.017$ ) (Figure 8).

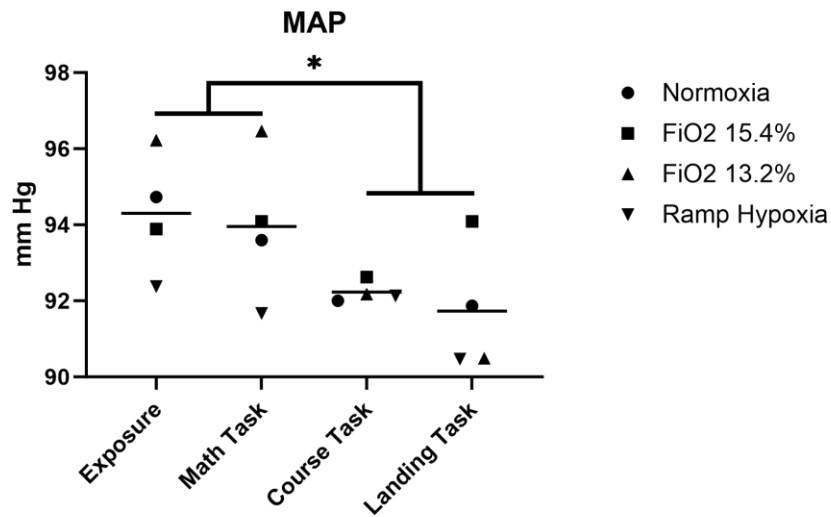


Figure 8. Grand mean and individual values of the Mean Arterial Pressure (MAP). \* Significantly different at the  $p<0.05$  level

### Heart Rate Variability (HRV)

A 4 (Altitude: Normoxic, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia) by 4 (Time: Exposure, Math Task, Course Task, Landing Task) repeated measures ANOVA for meanHR indicated no significant Altitude by Time two-way interaction ( $p=0.269$ ,  $\eta^2 =0.086$ ). There was no significant main effect of Altitude ( $p=0.122$ ,  $\eta^2 =0.154$ ) or Time ( $p=0.511$ ,  $\eta^2 =0.045$ ) (Figure 9).

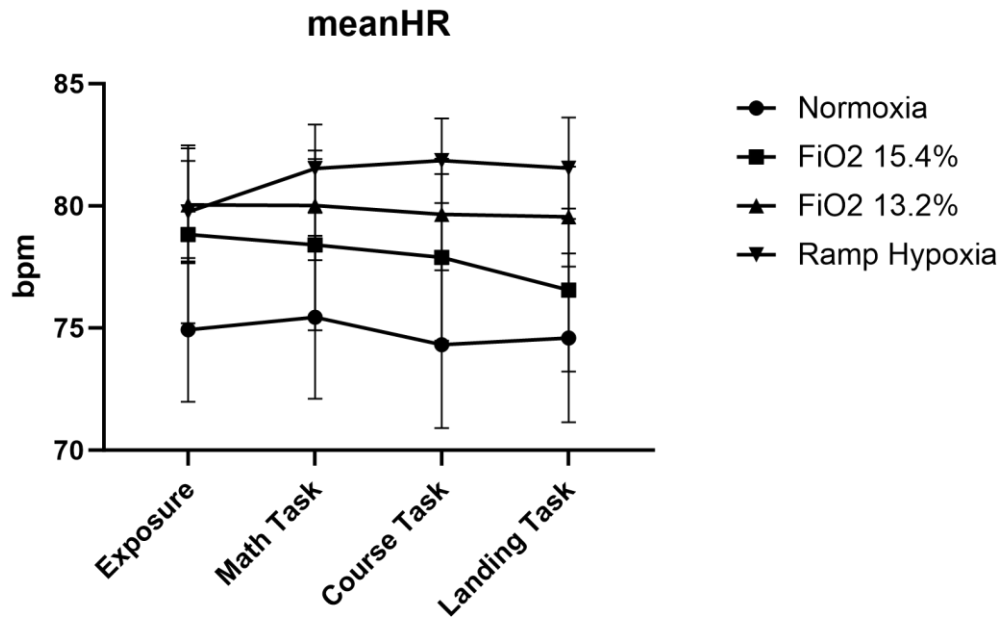


Figure 9. Mean  $\pm$  SEM for the mean heart rate collected over a 3-minute epoch.

A 4 (Altitude: Normoxic, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia) by 4 (Time: Exposure, Math Task, Course Task, Landing Task) repeated measures ANOVA for RMSSD indicated no significant Altitude by Time two-way interaction ( $p=0.330$ ,  $\eta^2=0.078$ ). There was no significant main effect of Time ( $p=0.555$ ,  $\eta^2=0.040$ ). There was, however, a significant main effect of Altitude ( $p=0.015$ ,  $\eta^2=0.218$ ) and RMSSD, which indicated RMSSD was lower in Ramp Hypoxia ( $38.18 \pm 6.61$  ms) compared to Normoxia ( $46.96 \pm 6.21$  ms,  $p=0.045$ ), FiO<sub>2</sub> 15.4% ( $48.47 \pm 7.57$  ms,  $p=0.005$ ), and FiO<sub>2</sub> 13.2% ( $44.31 \pm 7.07$  ms,  $p=0.019$ ) (Figure 10).

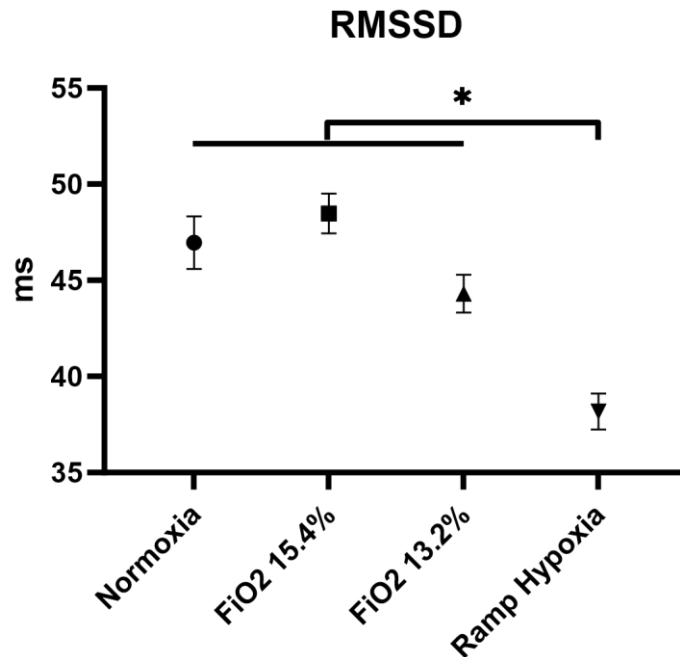


Figure 10. Mean  $\pm$  SEM of the Root Mean Square of Successive Differences (RMSSD) collected over a 3-minute epoch collapsed over conditions. \* Significantly different at the  $p < 0.05$  level

A 4 (Altitude: Normoxic, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia) by 4 (Time: Exposure, Math Task, Course Task, Landing Task) repeated measures ANOVA for LF/HF ratio indicated no significant Altitude by Time two-way interaction ( $p=0.262$ ,  $\eta^2 = 0.091$ ). There was no significant main effect of Altitude ( $p=0.439$ ,  $\eta^2 = 0.062$ ). There was a significant main effect of Time ( $p=0.025$ ,  $\eta^2 = 0.259$ ), which indicated a greater LF/HF ratio at Exposure ( $3.18 \pm 0.74$ ) compared to after the Course Task ( $2.44 \pm 0.54$ ,  $p=0.026$ ) and after the Landing Task ( $2.03 \pm 0.41$ ,  $p=0.029$ ) (Figure 11). The LF/HF ratio was greater after the Math Task ( $2.69 \pm 0.56$ ) compared to after the Landing Task ( $p=0.031$ ) (Figure 11).



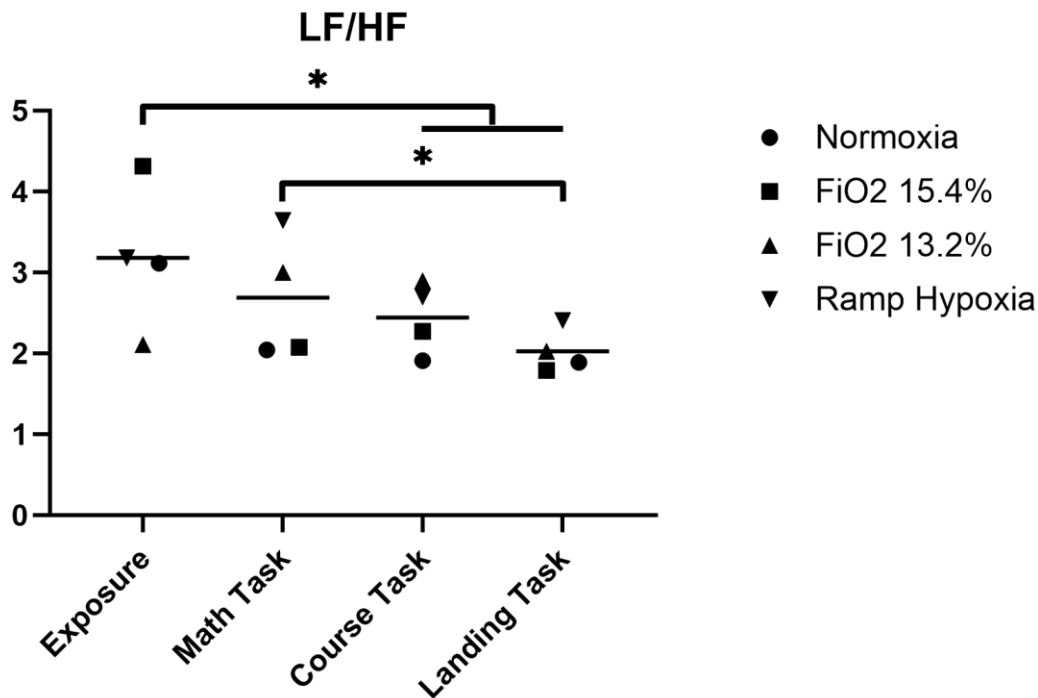


Figure 11. Grand mean and individual values of the Low Frequency to High Frequency Ratio (LF/HF). \* Significantly different at the  $p < 0.05$  level

### Peripheral Oxygen Saturation (SpO<sub>2</sub>)

A 4 (Altitude: Normoxic, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia) by 4 (Time: Exposure, Math Task, Course Task, Landing Task) repeated measures ANOVA for SpO<sub>2</sub> indicated a significant Altitude by Time interaction ( $p < 0.001$ ,  $\eta^2 = 0.259$ ) (Figure 12). The follow-up one-way repeated measures ANOVA to examine differences between conditions at Exposure was significant ( $p < 0.001$ ,  $\eta^2 = 0.402$ ), which indicated SpO<sub>2</sub> was greatest in Normoxia ( $96.50 \pm 0.37\%$ ) compared to FiO<sub>2</sub> 15.4% ( $92.25 \pm 0.96\%$ ,  $p < 0.001$ ), FiO<sub>2</sub> 13.2% ( $90.94 \pm 1.14\%$ ,  $p < 0.001$ ), and Ramp Hypoxia ( $89.06 \pm 1.11\%$ ,  $p < 0.001$ ) (Table 3).

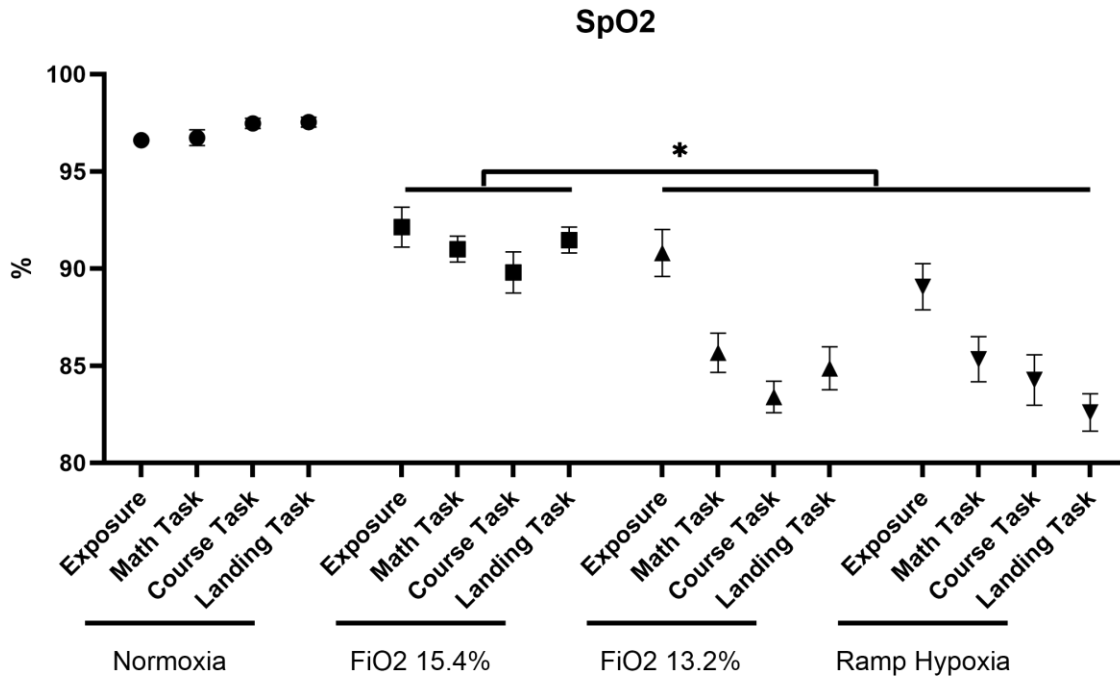


Figure 12. Mean  $\pm$  SEM of the Peripheral Oxygen Saturation (SpO<sub>2</sub>) over time and by each altitude condition. \* Significantly different at the  $p < 0.05$  level.

A one-way repeated measures ANOVA was employed to compare conditions following the Math Task. The results were significant ( $p < 0.001$ ,  $\eta^2 = 0.757$ ), indicating that SpO<sub>2</sub> levels varied significantly. Specifically, SpO<sub>2</sub> was highest at Normoxia (all  $p < 0.001$ ), decreased at FiO<sub>2</sub> 15.4% (all  $p < 0.001$ ), and further decreased at FiO<sub>2</sub> 13.2% ( $p < 0.001$ ) and Ramp Hypoxia ( $p < 0.001$ ). The SpO<sub>2</sub> at FiO<sub>2</sub> 13.2% ( $85.67 \pm 1.01\%$ ) did not differ significantly from Ramp Hypoxia ( $85.33 \pm 1.16\%$ ,  $p = 0.808$ ) (Table 3).

The one-way repeated measures ANOVA comparing conditions after the Course Task was significant ( $p < 0.001$ ,  $\eta^2 = 0.781$ ), which indicated SpO<sub>2</sub> was greatest at Normoxia (all  $p < 0.001$ ), decreased at FiO<sub>2</sub> 15.4% (all  $p < 0.001$ ), and further decreased at FiO<sub>2</sub> 13.2% ( $p < 0.001$ ) and Ramp Hypoxia ( $p = 0.008$ ). The SpO<sub>2</sub> at FiO<sub>2</sub> 13.2% ( $83.40 \pm 0.81\%$ ) was not different from Ramp Hypoxia ( $84.27 \pm 1.29\%$ ,  $p = 0.521$ ) (Table 3).

The one-way repeated measures ANOVA, conducted to compare conditions after the Landing Task, yielded a significant result ( $p < 0.001$ ,  $\eta^2 = 0.845$ ). This suggests that SpO<sub>2</sub> levels varied significantly, with the highest levels observed at Normoxia (all  $p < 0.001$ ), a decrease at FiO<sub>2</sub> 15.4% (all  $p < 0.001$ ), and a further decrease at FiO<sub>2</sub> 13.2% ( $p < 0.001$ ) and Ramp Hypoxia ( $p < 0.001$ ). The SpO<sub>2</sub> at FiO<sub>2</sub> 13.2% ( $84.87 \pm 1.10\%$ ) did not significantly differ from Ramp Hypoxia ( $82.60 \pm 0.96\%$ ,  $p = 0.140$ ) (Table 3).

Comparing the time course change of SpO<sub>2</sub> within each condition using a one-way repeated measures ANOVA indicated no significant time course change within Normoxia ( $p = 0.077$ ,  $\eta^2 = 0.183$ ) or FiO<sub>2</sub> 15.4% ( $p = 0.243$ ,  $\eta^2 = 0.094$ ). There was a significant time course change in SpO<sub>2</sub> within FiO<sub>2</sub> 13.2% ( $p < 0.001$ ,  $\eta^2 = 0.421$ ) and Ramp Hypoxia ( $p < 0.001$ ,  $\eta^2 = 0.385$ ). In the FiO<sub>2</sub> 13.2% condition, there was a 5.13% decrease from Exposure to after The Math Task ( $p = 0.007$ ) and then a decrease of 2.27% after the Course Task ( $p = 0.041$ ). In the Ramp Hypoxia condition, only the SpO<sub>2</sub> at Exposure ( $89.07 \pm 1.19\%$ ) was greater than after the Math Task ( $85.33 \pm 1.16\%$ ,  $p = 0.012$ ), after the Course Task ( $84.27 \pm 1.29\%$ ,  $p = 0.004$ ), and after the Landing Task ( $82.60 \pm 0.96$ ,  $p < 0.001$ ) (Table 3).

	Normoxia		FiO <sub>2</sub> 15.4%		FiO <sub>2</sub> 13.2%		Ramp Hypoxia	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
<b>Exposure</b>	96.60	0.38	92.13	1.02 <sup>a</sup>	90.80	1.20 <sup>a</sup>	89.07	1.19 <sup>a</sup>
<b>Math Task</b>	96.73	0.41	91.00	0.67 <sup>a</sup>	85.67	1.01 <sup>a,b,c</sup>	85.33	1.16 <sup>a,b,c</sup>
<b>Course Task</b>	97.47	0.26	89.80	1.05 <sup>a</sup>	83.40	0.81 <sup>a,b,c,d</sup>	84.27	1.29 <sup>a,b,c</sup>
<b>Landing task</b>	97.53	0.26	91.47	0.67 <sup>a</sup>	84.86	1.11 <sup>a,b,c</sup>	82.60	0.96 <sup>a,b,c</sup>

<sup>a</sup> Significantly different from Normoxia  
<sup>b</sup> Significantly different from FiO<sub>2</sub> 15.4%  
<sup>c</sup> Significantly different from Exposure  
<sup>d</sup> Significantly different from Math Task

A repeated measures ANOVA with a 2 (Altitude) by 4 (Time: Exposure, Math Task, Course Task, Landing Task) design was employed to examine simulated altitudes for either an interaction effect or a main effect of Altitude. There was no interaction effect ( $p=0.455$ ,  $\eta^2=0.056$ ) or main effect of Altitude ( $p=0.318$ ,  $\eta^2=0.067$ ) when comparing the FiO<sub>2</sub> 13.2% and the Ramp Hypoxia conditions. A significant interaction effect ( $p=0.028$ ,  $\eta^2=0.198$ ) and a significant main effect of Altitude ( $p<0.001$ ,  $\eta^2=0.672$ ) were observed when comparing the FiO<sub>2</sub> 15.4% and Ramp Hypoxia conditions. This indicates that the average SpO<sub>2</sub> at FiO<sub>2</sub> 15.4% ( $91.10 \pm 0.51\%$ ) was significantly higher than that at Ramp Hypoxia ( $85.32 \pm 0.83\%$ ,  $p<0.001$ ). There was a significant interaction effect ( $p=0.021$ ,  $\eta^2=0.193$ ) and a significant main effect of Altitude ( $p<0.001$ ,  $\eta^2=0.767$ ) when comparing the FiO<sub>2</sub> 15.4% to Ramp Hypoxia conditions, which indicated the average SpO<sub>2</sub> at FiO<sub>2</sub> 15.4% ( $91.27 \pm 0.51\%$ ) was greater than Ramp Hypoxia ( $86.39 \pm 0.57\%$ ,  $p<0.001$ ) (Figure 12).

## ELECTRODERMAL ACTIVITY RESPONSES

There was no significant 4 (Altitude: Normoxia, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, Ramp Hypoxia) by 10 (Time: 10, 20, 30, 40, 50, 60, 70, 80, 90, 100%) interaction effect for EDA Skin Conductance during the Math Task ( $p=0.395$ ,  $\eta^2=0.092$ ) and no main effect of Altitude ( $p=0.169$ ,  $\eta^2=0.167$ ) (Appendix H: Figure 26a). There was a significant main effect of Time ( $p<0.001$ ,  $\eta^2=0.588$ ), which indicated that 10% > 40%, and that 20% > 30% > 40% > 50% > 80%, and that 60% > 70% > 90%, and that 80% > 90% > 100% time course of exposure during flight the Math Task ( $p<0.05$  for all comparisons) (Table 4).

Table 4. Means  $\pm$  SEM for EDA during the Math Task.

	Mean	SEM
10%	0.22	0.02 <sup>b,c,d,e,f,g,h</sup>
20%	0.21	0.03 <sup>a,b,c,d,e,f,g,h</sup>
30%	0.20	0.02 <sup>b,c,e,f,g,h</sup>
40%	0.20	0.02 <sup>c,f,g,h</sup>
50%	0.19	0.02
60%	0.18	0.02 <sup>e,f,g,h</sup>
70%	0.17	0.02 <sup>g,h</sup>
80%	0.17	0.01 <sup>g,h</sup>
90%	0.16	0.01 <sup>h</sup>
100%	0.07	0.03

**a-** significantly different from 30%

**b-** significantly different from 40%

**c-** significantly different from 50%

**d-** significantly different from 60%

**e-** significantly different from 70%

**f-** significantly different from 80%

**g-** significantly different from 90%

**h-** significantly different from 100%

There was no significant 4 (Altitude: Normoxia, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, Ramp Hypoxia) by 10 (Time: 10, 20, 30, 40, 50, 60, 70, 80, 90, 100%) interaction effect for EDA Skin Conductance during the Course Task ( $p=0.458$ ,  $\eta^2=0.084$ ) (Appendix H: Figure 26b). There was a significant main effect of Altitude ( $p=0.030$ ,  $\eta^2=0.254$ ), which indicated that Skin Conductance at FiO<sub>2</sub> 13.2% ( $0.21\pm0.03 \mu\text{S}$ ) was greater ( $p=0.014$ ) compared to the Ramp Condition ( $0.17\pm0.02 \mu\text{S}$ ) when comparing mean Skin Conductance between altitudes during the Course Task (Figure 13). In addition, there was a main effect of Time ( $p<0.001$ ,  $\eta^2=0.577$ ) which indicated that 10% and 20% > 30% > 40% > 80%, and that 50% > 60%, and that 60% > 80%, and that 70% > 90%, and that 80% > 90% > 100%-time course of exposure during the Math Task ( $p<0.05$  for all comparisons) (Table 5).

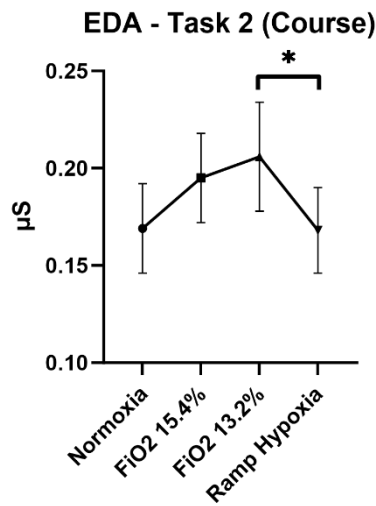


Figure 13. Mean  $\pm$  SEM altitude comparisons of Skin Conductance of the Electrodermal Activity (EDA) during the Course Task. \*Significantly different from FiO<sub>2</sub> 13.2%

Table 5. Means  $\pm$  SEM for EDA during the Course Task.

	<b>Mean</b>	<b>SEM</b>
<b>10%</b>	0.24	0.04 <sup>a,b,c,d,e,f,g,h</sup>
<b>20%</b>	0.23	0.03 <sup>a,b,c,d,e,f,g,h</sup>
<b>30%</b>	0.22	0.03 <sup>b,f,g,h</sup>
<b>40%</b>	0.21	0.03 <sup>f,g,h</sup>
<b>50%</b>	0.19	0.02 <sup>d,e,f,g,h</sup>
<b>60%</b>	0.19	0.02 <sup>f,g,h</sup>
<b>70%</b>	0.18	0.02 <sup>g,h</sup>
<b>80%</b>	0.17	0.02 <sup>g,h</sup>
<b>90%</b>	0.16	0.02 <sup>h</sup>
<b>100%</b>	0.07	0.02

**a- significantly different from 30%**  
**b- significantly different from 40%**  
**c- significantly different from 50%**  
**d- significantly different from 60%**  
**e- significantly different from 70%**  
**f- significantly different from 80%**  
**g- significantly different from 90%**  
**h- significantly different from 100%**

There was no significant 4 (Altitude: Normoxia, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, Ramp Hypoxia) by 10 (Time: 10, 20, 30, 40, 50, 60, 70, 80, 90, 100%) repeated interaction effect for EDA Skin Conductance during the Landing Task ( $p=0.527$ ,  $\eta^2=0.072$ ) and no main effect of Altitude ( $p=0.080$ ,  $\eta^2=0.199$ ) (Appendix H: Figure26c). There was a significant main effect of Time ( $p<0.001$ ,  $\eta^2=0.556$ ), which indicated 10% >50%, and that 20% >30% >40%, and that 50% >60% >70% >80% >90% >100% time course of exposure during the Math Task ( $p<0.05$  for all comparisons) (Table 6).

Table 6. Means  $\pm$  SEM for EDA during the Landing Task

	<b>Mean</b>	<b>SEM</b>
<b>10%</b>	0.24	0.04 <sup>c,d,e,f,g,h</sup>
<b>20%</b>	0.24	0.03 <sup>a,b,c,d,e,f,g,h</sup>
<b>30%</b>	0.22	0.03 <sup>b,c,d,e,f,g,h</sup>
<b>40%</b>	0.22	0.03 <sup>d,e,f,g,h</sup>
<b>50%</b>	0.20	0.03 <sup>d,e,f,g,h</sup>
<b>60%</b>	0.19	0.02 <sup>e,f,g,h</sup>
<b>70%</b>	0.17	0.02 <sup>f,g,h</sup>
<b>80%</b>	0.17	0.02 <sup>f,h</sup>
<b>90%</b>	0.16	0.02 <sup>h</sup>
<b>100%</b>	0.10	0.023

**a- significantly different from 30%**  
**b- significantly different from 40%**  
**c- significantly different from 50%**  
**d- significantly different from 60%**  
**e- significantly different from 70%**  
**f- significantly different from 80%**  
**g- significantly different from 90%**  
**h- significantly different from 100%**

## ELECTROMYOGRAPHY RESPONSES

### Amplitude Responses (EMG RMS)

There was no significant 4 Altitude (Normoxia, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, Ramp Hypoxia) by 3 Task (Math Task, Course Task, Landing Task) interaction effect of EMG RMS ( $p=0.310$ ,  $\eta^2=0.086$ ), or main effect of Altitude ( $p=0.425$ ,  $\eta^2=0.054$ ). There was a significant main effect of Task ( $p=0.034$ ,  $\eta^2=0.230$ ). Follow-up pairwise comparisons indicated a greater %MVC during the Course Task ( $21.28 \pm 34.0$  %MVC) compared to the Math Task ( $14.65 \pm 3.16$  %MVC,



p=0.017) (Figure 14). There was no difference between the Course Task and the Landing Task (p=0.360) or the Math Task and the Landing Task (p=0.053).

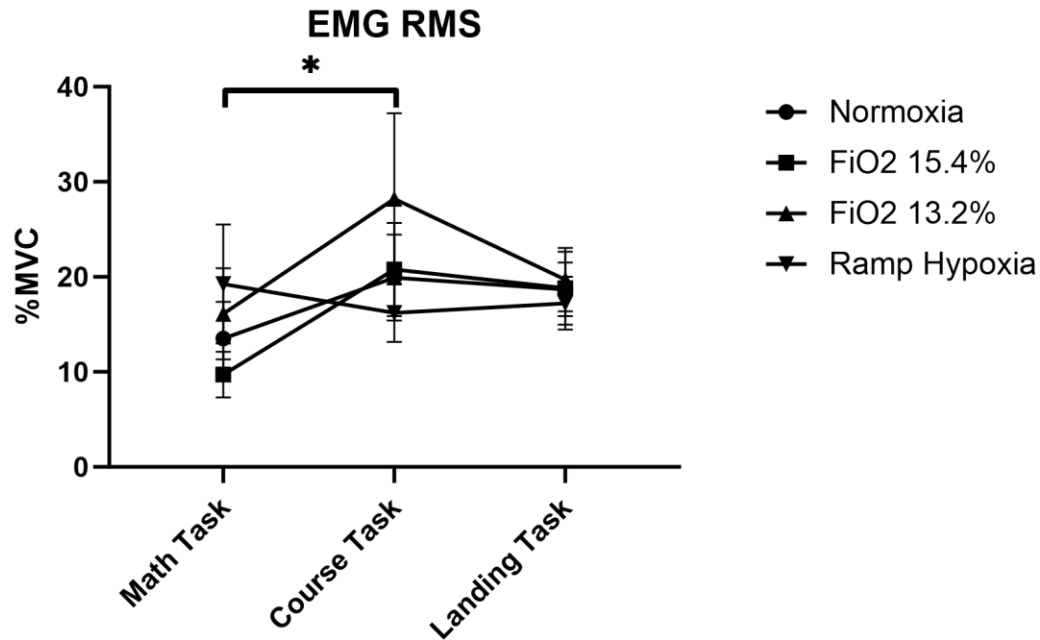


Figure 14. Mean ± SEM upper trapezius electromyographic (EMG) amplitude as measured by EMG root mean square (RMS). \* Indicates statistically significant difference (p<0.05).

### Frequency Responses (EMG MPF)

There was no significant 4 Altitude (Normoxia, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, Ramp Hypoxia) by 3 Task (Math Task, Course Task, Landing Task) interaction effect of EMG MPF (p=0.310, η<sup>2</sup> =0.085), or main effect of Altitude (p=0.570, η<sup>2</sup> =0.030). There was a significant main effect of Task (p=0.041, η<sup>2</sup> =0.226). Follow-up pairwise comparisons indicated a greater %MVC during the Course Task (18.82 ± 3.36 %MVC) compared to the Math Task (12.90 ± 2.91 %MVC, p=0.010) (Figure 15). There was no difference between the Course Task and the Landing Task (p=0.302) or the Math Task and the Landing Task (p=0.129).

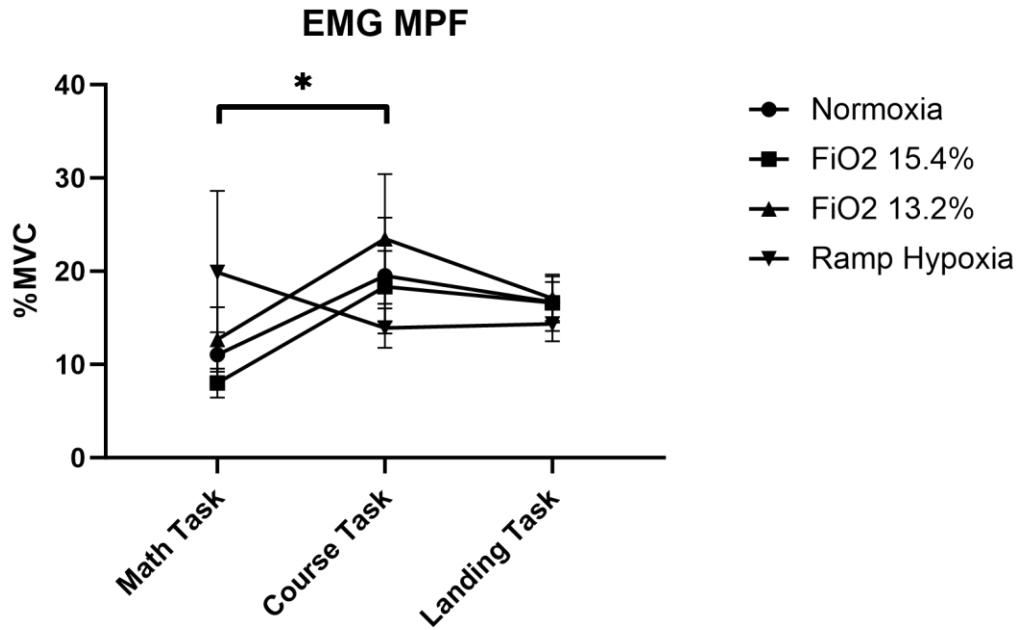


Figure 15. Mean  $\pm$  SEM upper trapezius electromyographic (EMG) frequency as measured by EMG mean power frequency (MPF). \* Indicates statistically significant difference ( $p < 0.05$ ).

#### PERFORMANCE RESPONSES

There was no significance comparing performance measures across Simulated Altitude conditions of total number of correct responses during the Math Task ( $p=0.182$ ,  $\eta^2 = 0.101$ ) (Figure 16a), number of accumulated points during the Course Task ( $p=0.290$ ,  $\eta^2 = 0.074$ ) (Figure 16b), or scores for the Landing Task ( $p=0.590$ ,  $\eta^2 = 0.044$ ) (Figure 16c).

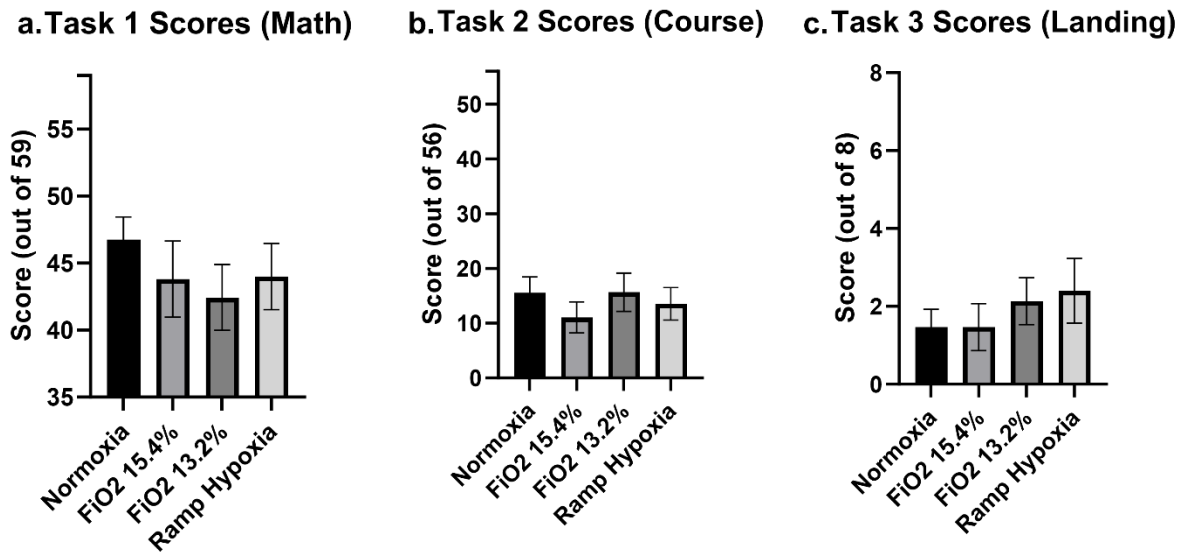


Figure 16. Mean  $\pm$  SEM for performance measures of the Math Task (a), the Course Task (b), and the Landing Task (c) scores.

## QUESTIONNAIRES

### Hypoxic Symptoms Questionnaire Response

There was no significant 4 (Altitude: Normoxia, FiO<sub>2</sub> 13.2%, FiO<sub>2</sub> 15.4%, Ramp Hypoxia) by 3 (Math Task, Course Task, Landing Task) interaction effect for cumulative (i.e., sum of) reported hypoxic symptom count ( $p=0.231$ ,  $\eta^2=0.090$ ) of the main effect of Altitude ( $p=0.146$ ,  $\eta^2=0.119$ ). There was a significant main effect for Task ( $p=0.023$ ,  $\eta^2=0.276$ ), which indicated that there were a greater number of symptoms reported after the Math Task ( $3.15 \pm 0.66$ ) compared to the Course ( $2.02 \pm 0.70$ ,  $p=0.016$ ) Task and Landing ( $1.85 \pm 0.77$ ,  $p=0.033$ ) Task (Figure 17).

### HSQ Cumulative Reported Symptom Count

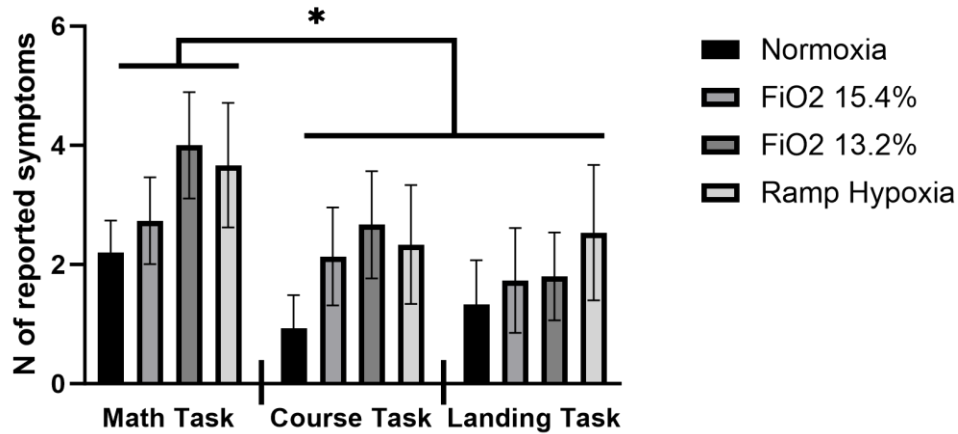


Figure 17. Mean ± SEM for the hypoxic Symptom Questionnaire (HSQ) cumulative number of reported symptoms. \* Significantly different at the  $p < 0.05$  level.

There was no significant 4 (Altitude: Normoxia, FiO<sub>2</sub> 13.2%, FiO<sub>2</sub> 15.4%, Ramp Hypoxia) by 3 (Task: Math Task, Course Task, Landing Task) interaction effect for HSQ symptom severity ( $p = 0.393$ ,  $\eta^2 = 0.067$ ), main effect for Altitude ( $p = 0.197$ ,  $\eta^2 = 0.112$ ), or main effect for Task ( $p = 0.124$ ,  $\eta^2 = 0.150$ ) (Figure 18).

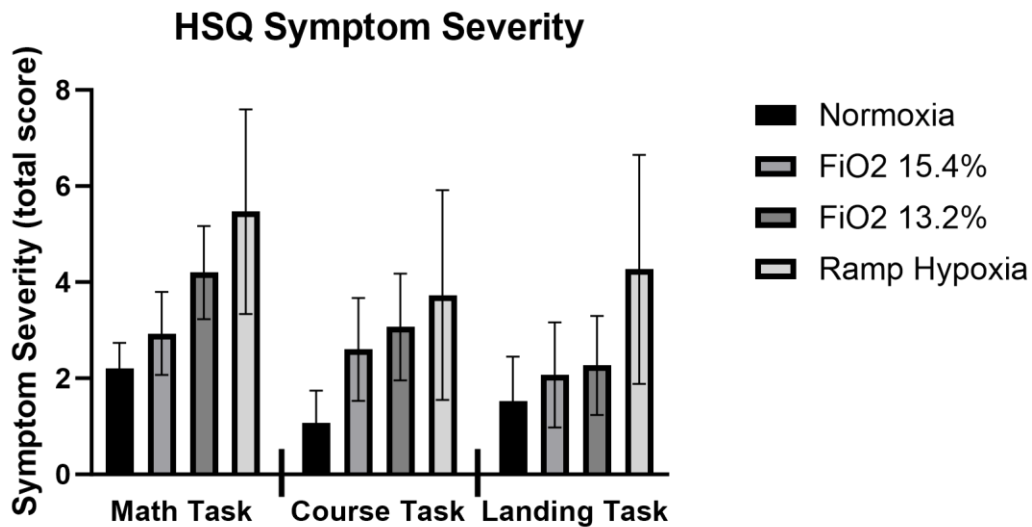


Figure 18. Mean ± SEM for the hypoxic Symptom Questionnaire (HSQ) severity of reported symptoms.

## Simulator Sickness Questionnaire Responses

There was no significant 4 (Altitude: Normoxia, FiO<sub>2</sub> 13.2%, FiO<sub>2</sub> 15.4%, Ramp Hypoxia) by 3 (Math Task, Course Task, Landing Task) interaction effect for SSQ Total Score ( $p=0.872$ ,  $\eta^2=0.017$ ) and no main effect of Altitude ( $p=0.340$ ,  $\eta^2=0.067$ ). There was a significant main effect of Task ( $p=0.022$ ,  $\eta^2=0.067$ ), indicating SSQ Total Score for the Math Task ( $19.109 \pm 4.305$ ) was greater than the Course Task ( $11.45 \pm 3.99$ ,  $p=0.006$ ). There was no difference between the Landing Task ( $12.56 \pm 5.28$ ) compared to the Math Task ( $p=0.062$ ) or the Course Task ( $p=0.539$ ) (Figure 19).

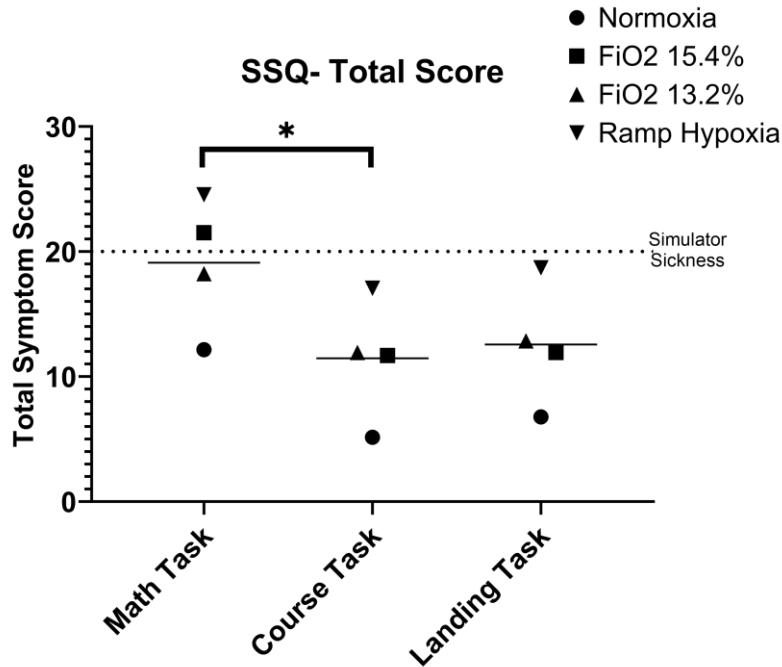


Figure 19. Grand mean of the Simulator Sickness Questionnaire (SSQ) score. \*Significantly different at the  $p<0.05$  level.

There was no significant 4 (Altitude: Normoxia, FiO<sub>2</sub> 13.2%, FiO<sub>2</sub> 15.4%, Ramp Hypoxia) by 3 (Math Task, Course Task, Landing Task) interaction effect of SSQ sub-score of Nausea ( $p=0.738$ ,  $\eta^2=0.030$ ) or main effect of Altitude ( $p=0.460$ ,  $\eta^2=0.046$ ). There was a significant main effect of Task for the SSQ sub-score of Nausea ( $p=0.003$ ,  $\eta^2=0.322$ ), which indicated a

greater score of Nausea during the Math Task ( $13.27 \pm 2.93$ ) Task compared to both the Course Task ( $7.60 \pm 2.75$ ,  $p=0.005$ ) and the Landing Task ( $8.20 \pm 3.08$ ,  $p=0.021$ ). There was no difference between the Course Task and the Landing Task ( $p=0.615$ ) (Figure 20).

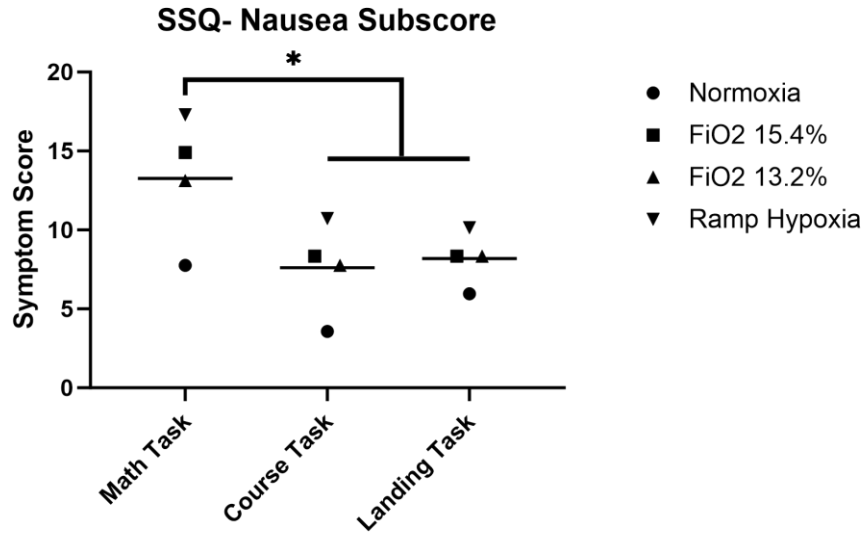


Figure 20. Grand mean of the Simulator Sickness Questionnaire (SSQ) Nausea Subscore.  
\*Significantly different at the  $p < 0.05$  level.

There was no significant 4 (Altitude: Normoxia, FiO<sub>2</sub> 13.2%, FiO<sub>2</sub> 15.4%, Ramp Hypoxia) by 3 (Math Task, Course Task, Landing the Landing Task) interaction effect for SSQ sub-score of Oculomotor Discomfort ( $p=0.962$ ,  $\eta^2 = 0.006$ ) or main effect of Altitude ( $p=0.324$ ,  $\eta^2 = 0.072$ ). There was a significant main effect of Task for SSQ sub-score of Oculomotor Discomfort ( $p=0.034$ ,  $\eta^2 = 0.232$ ), which indicated a greater score of Oculomotor Discomfort during the Math Task ( $17.65 \pm 3.96$ ) compared to the Course Task ( $10.90 \pm 3.63$ ,  $p=0.008$ ). The sub-score of Oculomotor Discomfort was not different between the Math Task and the Landing Task ( $11.61 \pm 4.92$ ,  $p=0.075$ ), or the Course Task different from the Landing Task ( $p=0.703$ ) (Figure 21).

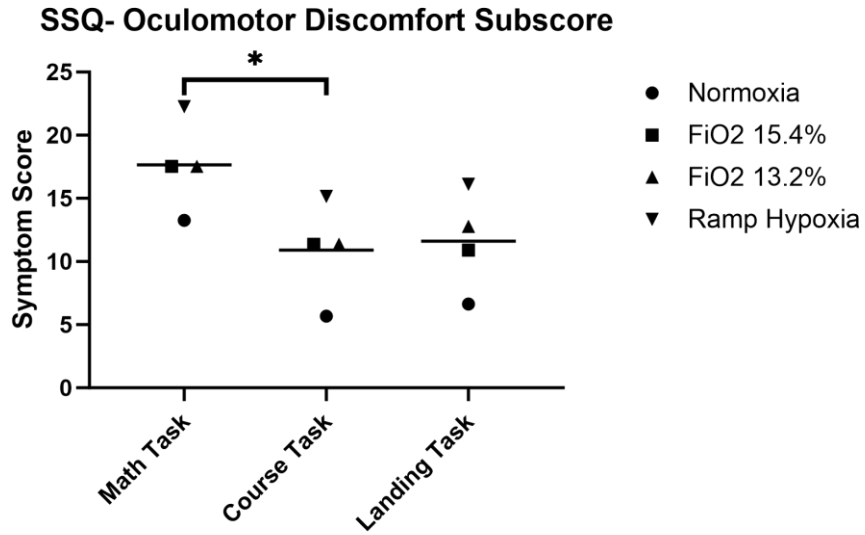


Figure 21. Grand mean of the Simulator Sickness Questionnaire (SSQ) Oculomotor Discomfort score. \*Significantly different at the p<0.05 level.

There was no significant 4 (Altitude: Normoxia, FiO<sub>2</sub> 13.2%, FiO<sub>2</sub> 15.4%, Ramp Hypoxia) by 3 (Math Task, Course Task, Landing Task) interaction effect for SSQ subscore of Disorientation (p=0.284,  $\eta^2$  =0.080), main effect of Altitude (p=0.307,  $\eta^2$  =0.073), or main effect of Task (p=0.081,  $\eta^2$  =0.173) (Figure 22).

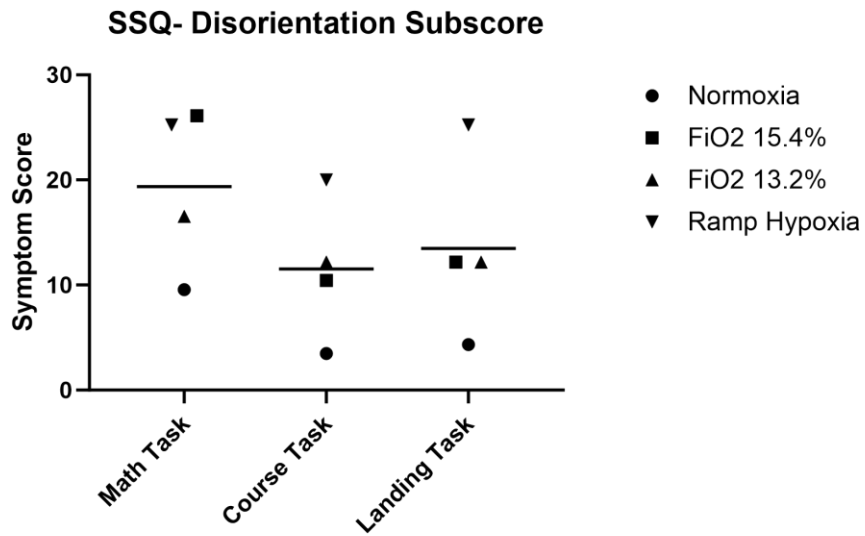


Figure 22. Grand mean of the Simulator Sickness Questionnaire (SSQ) Disorientation Subscore.

## NASA Task Load Index Workload Responses

The results of the repeated measures ANOVA, which assessed the impact of Altitude (Normoxia, FiO<sub>2</sub> 13.2%, FiO<sub>2</sub> 15.4%, Ramp Hypoxia) and Task (Math Task, Course Task, Landing Task) on the weighted overall workload of the NASA TLX, did not yield a significant effect ( $p=0.606$ ,  $\eta^2 = 0.055$ ). There was no main effect of Altitude ( $p=0.533$ ,  $\eta^2 = 0.054$ ). There was a significant main effect of Task ( $p<0.001$ ,  $\eta^2 = 0.484$ ), which indicated participants perceived the highest workload during the Math Task (Math:  $62.22 \pm 4.01$ ) compared to the Course Task (Course:  $53.21 \pm 5.57$ ,  $p=0.011$ ) and the Landing Task ( $43.41 \pm 5.12$ ,  $p<0.001$ ). The overall workload score for the Course Task was higher than the Landing Task ( $p=0.047$ ) (Figure 23).

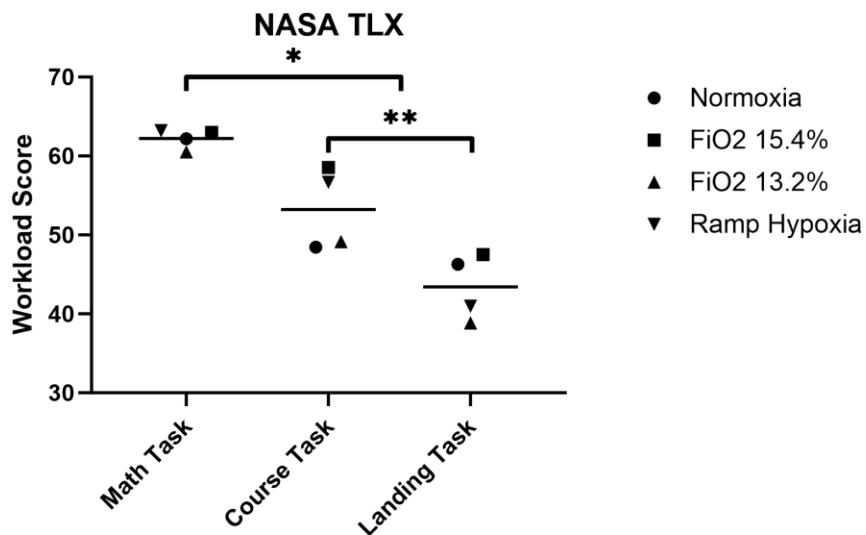


Figure 23. Grand mean of the National Aeronautics and Space Administration (NASA) Task Load Index (TLX) weighted score of Overall Workload. \*Significantly different from the Course Task and the Landing Task. \*\*Significantly different from the Landing Task

### *Demands imposed on the Subject: Mental, Physical, & Temporal*

The weighted subscore of Mental Demand (Figure 24a) indicated no significant 4 (Altitude) by 3 (Task) interaction effect ( $p=0.102$ ,  $\eta^2 = 0.124$ ) and no main effect of Altitude



( $p=0.448$ ,  $\eta^2=0.065$ ). There was a significant main effect of Task ( $p<0.001$ ,  $\eta^2=0.726$ ), which indicated Mental Demand was greatest during the Math Task ( $290.89 \pm 26.83$ ) compared to the Course Task ( $113.75 \pm 25.68$ ,  $p<0.001$ ) and the Landing Task ( $118.75 \pm 30.93$ ,  $p<0.001$ ). There was no difference in Mental Demand between the Course Task and the Landing Task ( $p=0.806$ ).

The weighted subscore of Physical Demand (Figure 24b) indicated no significant 4 (Altitude) by 3 (Task) interaction effect ( $p=0.424$ ,  $\eta^2=0.064$ ), no main effect of Altitude ( $p=0.935$ ,  $\eta^2=0.001$ ), or main effect of Task ( $p=0.550$ ,  $\eta^2=0.031$ ).

Task ( $p=0.032$ ,  $\eta^2=0.233$ ), which indicated time pressure was greater during the Math Task ( $191.96 \pm 24.15$ ) compared to the Landing Task ( $110.36 \pm 19.95$ ,  $p=0.012$ ). The score of Temporal Demand during the Course Task ( $169.82 \pm 35.42$ ) was not different when compared to the Math Task ( $p=0.521$ ) or the Landing Task ( $p=0.055$ ).

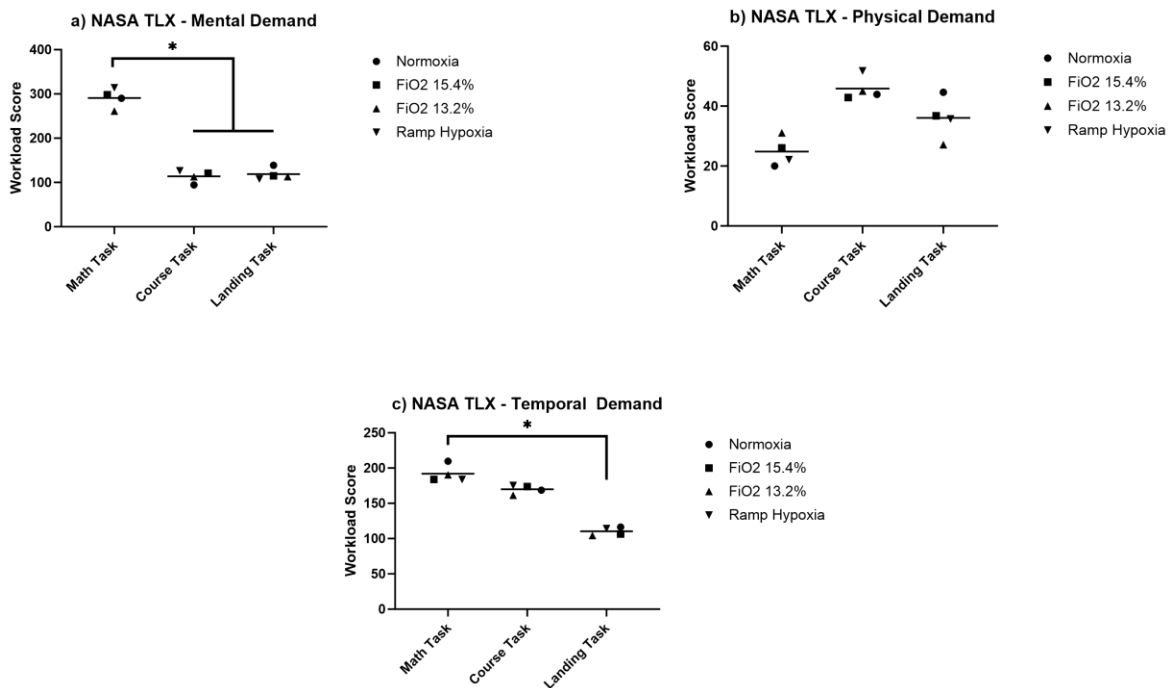


Figure 24. Grand means of the National Aeronautics and Space Administration (NASA) Task Load Index (TLX) weighted scores of Mental (a), Physical (b), and Temporal (c) Demand. \*Significantly different at the  $p<0.05$  level.

### ***Interactions of the subject with the Task: Effort, Frustration, & Performance***

The weighted sub-score of Effort (Figure 25a) showed no significant 4 (Altitude) by 3 (Task) interaction effect ( $p=0.560$ ,  $\eta^2=0.059$ ), no main effect of Altitude ( $p=0.949$ ,  $\eta^2=0.009$ ), and no main effect of Task ( $p=0.137$ ,  $\eta^2=0.142$ ).

The weighted sub-score of Frustration (Figure 25b) showed no significant 4 (Altitude) by 3 (Task) interaction effect ( $p=0.534$ ,  $\eta^2=0.051$ ), no main effect of Altitude ( $p=0.398$ ,  $\eta^2=0.072$ ), and no main effect of Task ( $p=0.079$ ,  $\eta^2=0.177$ ).

The weighted subscore of Performance (Figure 25c) showed no significant 4 (Altitude) by 3 (Task) interaction effect ( $p=0.544$ ,  $\eta^2=0.061$ ) and no main effect of Altitude ( $p=0.154$ ,  $\eta^2=0.125$ ). There was a significant main effect of Task ( $p=0.024$ ,  $\eta^2=0.249$ ), which indicated that participants self-reported score of performance during the Course Task ( $199.82 \pm 27.19$ ) was greater than the Math Task ( $119.46 \pm 19.55$ ,  $p=0.017$ ). There was no difference in self-reported performance between the Landing Task ( $173.84 \pm 22.35$ ) or the Math Task ( $p=0.068$ ) or compared to the Course Task ( $p=0.357$ ).

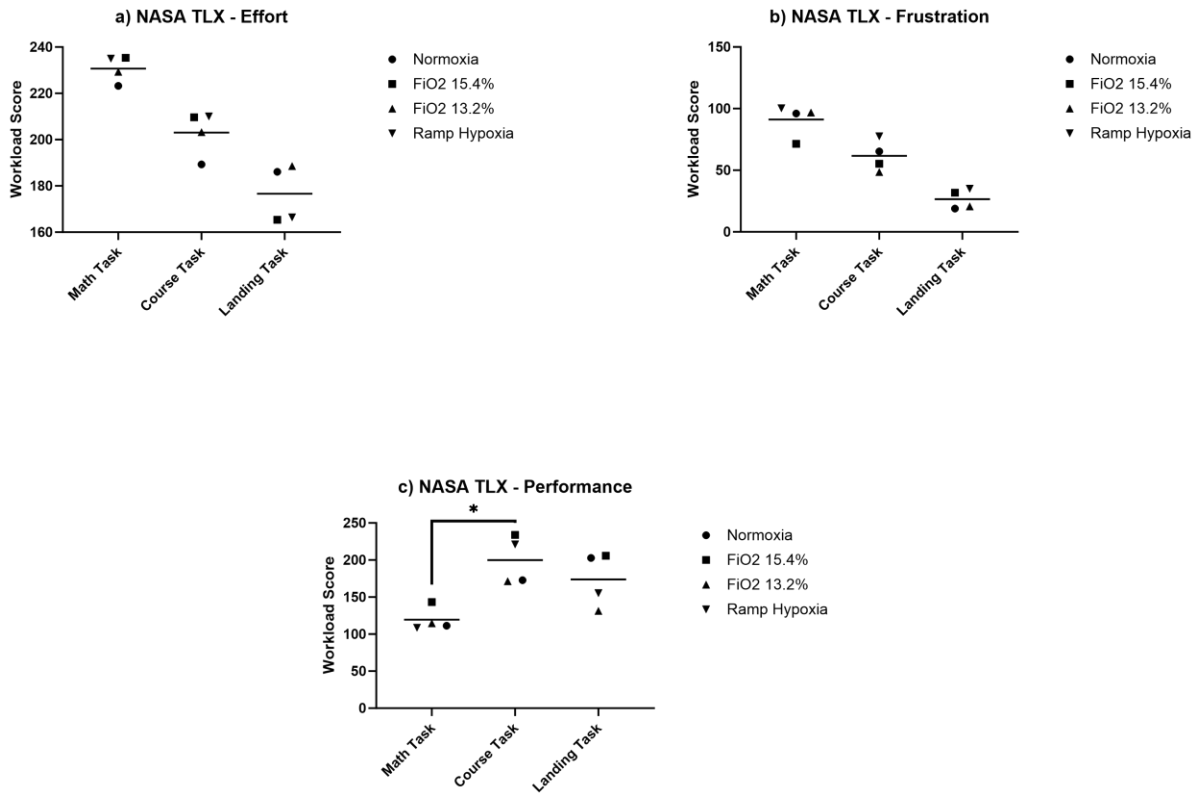


Figure 25. Grand means of the National Aeronautics and Space Administration (NASA) Task Load Index (TLX) weighted scores of Effort (a), Frustration (b), and Performance (c). \*Significantly different at the p<0.05 level.

## Chapter V – Discussion

### CARDIOVASCULAR RESPONSES

#### Mean Arterial Pressure (MAP)

In the current study, MAP exhibited no significant differences across simulated altitude conditions (Figure 8). The current study hypothesis was that MAP would demonstrate an initial increase during the Exposure phase followed by a decrease. This anticipated pattern is based on that acute hypoxia has been shown to increase blood pressure responses which then normalizes as a result of compensatory mechanisms to maintain adequate oxygen delivery.<sup>9, 142-145</sup> There were, however, decreases in MAP from the Exposure phase through the Math, Course, and Landing Tasks (Figure 8) which aligns with previous studies, such as Casale et al. (2004)<sup>37</sup> who reported consistent arterial pressure in men during a 10-day stay at 5050 m. Similarly, Bourdillon et al. (2023)<sup>146</sup> reported no change in blood pressure when exposing pilot trainees while seated to 30 minutes of normobaric hypoxia (FiO<sub>2</sub> 11.2%), hypobaric hypoxia (39.4% oxygen at PiO<sub>2</sub> 74.3 mm HG), normobaric normoxia (PiO<sub>2</sub> 141.2 mm Hg), and hypobaric normoxia (PiO<sub>2</sub> 141.5 mm Hg). In addition, Nell et al. (2020)<sup>39</sup> reported no change in systolic blood pressure in the University of Toronto general community, when exposed to FiO<sub>2</sub> 12% compared to normoxia during repeated handgrip exercise at 50% MVC for 2:1 work to rest ratio until task failure. The consistent MAP across normoxia, FiO<sub>2</sub> 13.2%, FiO<sub>2</sub> 15.4%, and Ramp Hypoxic conditions in the present study could be attributed to the cardiovagal baroreflex response to maintain adequate blood flow to important structures in a reduced oxygen environment.<sup>146</sup>

In aviation, understanding cardiovascular stability is paramount to both pilot performance and survival as disturbances to these systems may induce physiological events. In hypoxic conditions, the baroreflex adapts to a new baseline, responding to changes in blood pressure at a

higher baseline level due to reduced oxygen levels.<sup>147-149</sup> This adaptive reset allows the baroreflex to proactively maintain blood pressure stability within the new baseline range set by the reset, counteracting the anticipated decrease in oxygen levels. Notably, Halliwill et al. (2002)<sup>147</sup> found that acute exposure to hypoxia resets baroreflex control of both heart rate and muscle sympathetic nerve activity to higher pressures and higher levels of heart rate and sympathetic nerve activity without changes in sensitivity of the arterial baroreflex. Their findings, including the reduction in arterial O<sub>2</sub> saturation levels, increase in HR, MAP, and sympathetic activity, provide additional context to our observations.<sup>147</sup> Decreased baroreflex sensitivity, a measure of cardiovagal baroreflex function, is associated with orthostatic hypotension, difficulty maintaining blood pressure, and blunted cardiovascular responses to stressors, including hypoxia.<sup>147, 150, 151</sup> The stability in MAP observed in the current study suggests a well-functioning baroreflex system, contributing to the cardiovascular system's ability to maintain stable blood pressure even in reduced oxygen environments. The use of MAP for monitoring in-flight physiological events and assessing real-time performance in military pilots is supported by the current study findings, however, a multi-sensor approach is highly suggested to account for compensatory mechanisms that may not manifest as obvious changes.

## **Heart Rate Variability (HRV)**

### ***Mean HR***

The Mean HR response during simulated altitude exposures while engaging in flight tasks within a video game flight simulator, measured using a chest strap device in three-minute epochs, did not reveal a significant interaction nor main effects of heart rate (Figure 9). These findings contrast with our hypothesis that acute altitude exposure would lead to an increase in HR to enhance oxygen delivery.<sup>9, 144</sup> However, these results are consistent with previous findings that

reported no discernible difference in HR when participants were exposed to similar altitudes, ranging from  $\text{FiO}_2$  16% to 11.2%, compared to baseline normoxic conditions.<sup>24, 31, 146, 152</sup> Steinman et al. (2021)<sup>31</sup> observed no significant difference in HR of Apache helicopter crews between sea level and breathing at  $\text{FiO}_2$  11.4% for 15 minutes while flying missions in a flight simulator. Jenkins et al. (2022)<sup>152</sup> similarly found no distinction in HR in recreationally active individuals between normoxic conditions and exposures of  $\text{FiO}_2$  levels of 16% and 14.3% while participants performed the Stroop test. Additionally, Jenkins et al. (2023)<sup>24</sup> investigated the effects of moderate ( $\text{FiO}_2$  16%) and severe ( $\text{FiO}_2$  14.3%) hypoxia during events of the Army Combat Fitness Test in recreationally active soldier analogs and reported no main effect of altitude between conditions. Bourdillon et al. (2023)<sup>146</sup> also reported no differences in heart rate in pilot trainees while seated in 30 minutes of normobaric hypoxia ( $\text{FiO}_2$  11.2%), hypobaric hypoxia (39.4% oxygen at  $\text{PiO}_2$  74.3 mm Hg), normobaric normoxia ( $\text{PiO}_2$  141.2 mm Hg), and hypobaric Normoxia ( $\text{PiO}_2$  141.5 mm Hg).

The absence of an increase in HR with hypoxic exposure can potentially be a result of variations in hypoxic exposure duration and level. The absence of an increase in HR with hypoxic exposure can potentially be a result of variations in hypoxic exposure duration and level. For example, Nishi, (2011)<sup>22</sup> measured HR in male aircrew members during a helicopter test flight at various altitudes for an average exposure time of 20 minutes each: ground level, 5,000 ft, 8,000 ft, 10,000 ft, and 13,000 ft. Their findings indicated an initial increase in HR from pre-test to ground level, which persisted at 5,000 ft with partial recovery at 8,000 ft, followed by another increase at 10,000 ft and 13,000 ft.<sup>22</sup> Peacock et al. (2017) exposed Caucasian pilots to 120 minutes of hypobaric hypoxia (10,000 ft) in a flight simulator, and reported HR increased across time in the hypoxic condition. Steinman et al. (2017)<sup>28</sup> exposed male pilots to hypobaric hypoxia at altitudes

of 10,000 ft and 15,000 ft during a 37-minute flight simulation, and reported HR was higher at 15,000 ft compared to baseline but not at 10,000 ft. The findings of previous studies<sup>22, 27, 28</sup> suggest hypoxic dependent changes in HR may be dependent on the duration and level of hypoxic exposure. Therefore, the simulated low altitudes in the present study (FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia) with a total exposure duration of approximately 15 minutes may not have provided sufficient stimulus to induce HR changes. Participants likely maintained adequate blood flow to vital organs through alternative means. These findings support the need to move beyond conventional HR monitoring in flight simulations. Specifically, there is a need for more specific and advanced assessments, such as HRV parameters. These advanced measures are important for understanding individual responses and predicting performance changes in aviation.

### ***RMSSD***

The current study revealed no significant time course changes in RMSSD. However, a main effect of altitude was observed, where RMSSD during Ramp Hypoxic exposure was significantly lower than in normoxia, FiO<sub>2</sub> 15.4%, and FiO<sub>2</sub> 13.2% (Figure 10). These findings align with Aebi et al. (2020)<sup>153</sup> who exposed young pilot trainees to normobaric hypoxia at a FiO<sub>2</sub> of approximately 11% and observed a 17.1 ms decrease in RMSSD during seated rest. Similarly, Teckchandani et al. (2020)<sup>154</sup> reported a 10 ms decrease in RMSSD during exposure to FiO<sub>2</sub> 14.8%. It's worth noting that the protocol by Teckchandani et al. (2020)<sup>154</sup> included five minutes of isometric squat-stands, contributing to higher overall values compared to the present study. In seated individuals exposed to FiO<sub>2</sub> 11.2%, Bourdillon et al. (2023)<sup>146</sup> also reported a 19 ms decrease in RMSSD compared to the normoxic condition. These findings suggest that cardiac indices, such as RMSSD derived from HRV analyses, can serve as a sensitive indicator of autonomic nervous system response during acute hypoxic exposure. Specifically, the consistent

decline in RMSSD implies greater sympathetic innervation and parasympathetic withdrawal in the present study population.<sup>155</sup> The findings of the present study contribute to the growing understanding of the intricacies of cardiovascular dynamics in simulated flights tasks, highlighting that RMSSD may be a valuable metric for assessing autonomic responses and potential implications in tracking pilot well-being.

### ***LF/HF***

The findings of the present study revealed no interaction nor main effect of altitude on the LF/HF ratio which has been utilized as an index of sympathovagal balance (Figure 11).<sup>7, 156-158</sup> The LF/HF ratio was highest at Exposure (before initiating the flight simulation) and significantly higher after performing the Math Task compared to the end of the Landing Task. These results align with Aebi et al. (2020)<sup>153</sup> who reported no change in LF/HF when comparing normobaric normoxia to normobaric hypoxia at FiO<sub>2</sub> 11%. Similarly, Vigo et al. (2010)<sup>159</sup> found no change in LF/HF when exposing military pilots to hypobaric conditions equivalent to 8230 m, and Yamamoto et al. (1996)<sup>160</sup> reported no changes during rest at various altitudes up to 3500 m (~11,000 ft). The LF/HF ratio serves as a metric capturing the equilibrium between sympathetic and parasympathetic activity within the autonomic nervous system (sympathovagal balance).<sup>7, 157</sup> The maintenance of the LF/HF ratio across different altitude conditions in the present study implies stability in the autonomic nervous system's ability to maintain sympathovagal balance.<sup>7, 153, 157, 158</sup> In evaluating the potential of LF/HF ratio as a “stress tracker” in flight simulations and its usability in identifying physiological events, the current study, and previous findings provides insight into how sympathovagal balance, altitude exposure, and adaptive responses in the autonomic nervous system are interconnected. Further exploration of LF/HF ratios’ specific application in aviation



stress is needed to support its use as a valuable metric for physiological monitoring during flight scenarios.

### **Peripheral Oxygen Saturation (SpO<sub>2</sub>)**

In the present study, there was a significant decrease in SpO<sub>2</sub> with FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia (Figure 12), where SpO<sub>2</sub> was significantly greater at all time points (Exposure, Math, Course, and Landing Task) in normoxia compared to FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxic conditions. In the FiO<sub>2</sub> 13.2% condition, SpO<sub>2</sub> significantly decreased from Exposure to the Math Task and further decreased from the Math Task to the Course Task (Table 3). In the Ramp Hypoxia condition, there was a significant decrease from Exposure to the Course Task, and SpO<sub>2</sub> remained constant from the Course Task to the Landing Task (Table 3). There was no difference in SpO<sub>2</sub> between the FiO<sub>2</sub> 13.2% and Ramp Hypoxic conditions, however, SpO<sub>2</sub> in both conditions were significantly lower when compared to the FiO<sub>2</sub> 15.4% condition (Table 3). These findings support our hypothesis that simulated altitude exposures decrease SpO<sub>2</sub>, and the higher the altitude the lower the SpO<sub>2</sub>.

Comparing SpO<sub>2</sub> saturation in both FiO<sub>2</sub> 13.2% and Ramp Hypoxia to SpO<sub>2</sub> response in FiO<sub>2</sub> 15.4%, the results indicated that while SpO<sub>2</sub> was already reduced in FiO<sub>2</sub> 15.4%, it further decreased in FiO<sub>2</sub> 13.2% and Ramp Hypoxia (Table 3). For instance, Nesthus et al. (1997)<sup>11</sup> exposed military pilots to stepwise gas concentrations simulating 8,000 ft, 10,000 ft, and 12,500 ft, noting a decrease in SpO<sub>2</sub> using a finger pulse oximeter. Jenkins et al. (2021)<sup>40</sup> also reported decreased finger pulse SpO<sub>2</sub> in young generally healthy active adults from normoxic conditions compared to normobaric hypoxia FiO<sub>2</sub> 15% and FiO<sub>2</sub> 14%. Legg et al. (2016)<sup>34</sup> observed finger pulse oximetry SpO<sub>2</sub> values of Air Force personnel decreasing from normoxia upon hypobaric chamber ascent reaching altitudes of 8,000 ft and 12,000 ft in randomized order separated by 30-

minute breaks at ground level. Similarly, Bouak et al. (2018)<sup>97</sup> reported a decrease in finger pulse SpO<sub>2</sub> in male military helicopter pilots with hypobaric chamber ascent to 8,000 ft, 10,000 ft, 12,000 ft, and 14,000 ft on separate days.

In the current study, the Ramp Hypoxic condition was not significantly different from the FiO<sub>2</sub> 13.2% condition. Contrasting evidence by Robinson et al. (2018)<sup>29</sup> reported SpO<sub>2</sub> levels were lower in a normobaric combined condition (simulated altitude of 25,000 ft for 5 minutes, followed by a 5-minute rest in normoxia, and then 30-minutes at 10,000 ft) compared to a 30-minute simulated altitude exposure at 10,000 ft or a 5-minute exposure at 25,000 ft, within a population of U.S. Air Force personnel. The sequential Ramp exposures aim to replicate the conditions experienced by pilots during an emergency, initial exposure to a hypoxic environment induces symptoms and cognitive deficits, followed by mild hypoxia (10,000 ft) introduced upon removing the flight mask in the final step of emergency procedures. The absence of an additive effect of hypoxic exposure in the current study might be attributed to the mild hypoxic exposure (8,000 ft) preceding a higher exposure (12,000 ft), in contrast to Robinson et al. (2018) where a higher exposure (25,000 ft) preceded a mild exposure (10,000 ft).<sup>29</sup> SpO<sub>2</sub> monitoring could be a valuable tool for detecting physiological events during sequential exposures, but the effects of such exposures, mimicking pilot emergency situations, require further exploration.

## **ELECTRODERMAL ACTIVITY (EDA) RESPONSES**

In the current study, skin conductance results revealed a significant decrease in the time course change from 10% to 40%, then 20% to 30%, then 30% to 40% to 50% to 80%, then 60% to 70% to 90%, then 80% to 90% to 100% during the Math Task (Table 4). There was also a significant decrease in the time course change from 10% to 30%, then 20% to 30% to 40% to 80%, then 50% to 60% to 80%, then 70% to 90%, then 80% to 90% to 100% during the Course Task (Table 5). There was a significant time course change decrease from 10% to 50%, then 20% to 30% to 40% to 60%, then 50% to 60% to 70% to 80% to 90% to 100% during the Landing Task (Table 6). These findings are in line with prior research on EDA response during flight tasks, where skin conductance tends to increase in highly demanding, stressful, and arousing scenarios.<sup>3, 5, 62, 64-71</sup> Vallés-Catalá et al. (2021)<sup>3</sup> assessed EDA in second and third-year student pilots on the dominant wrists in a flight simulator. The flight simulator involved maneuvers, interceptions, cross-country scenarios (approaches/go-arounds), and emergencies.<sup>3</sup> Tasks were categorized as highly demanding in terms of how they are performed with respect to the previous task (high demand = performance was high compared to the previous task)<sup>3</sup>. The study found that 64.3% of EDA values in correctly performed tasks exceeded those in poorly performed tasks.<sup>3</sup> Additionally, 56.5% of EDA values in correctly performed tasks and 50.7% of EDA values in poorly performed tasks were both higher than in low-demanding tasks compared to highly-demanding tasks.<sup>3</sup> Lindholm et al.<sup>61</sup> assessed male pilots set to begin Undergraduate Pilot Training, participants performed a 120-second carrier landing task, a tone discrimination task, and combined task.<sup>61</sup> Their results showed no significant change in skin conductance levels of the middle finger of the left hand during the carrier landing task alone, tone discrimination task alone, or the combination of tasks.<sup>61</sup> An increase in skin conductance has been associated with heightened stress during

flying or driving tasks.<sup>5, 66</sup> The current study hypothesis was that each of the flight tasks would exhibit different EDA responses, however, the current study results did not align with these expectations. In the current study, the observed EDA response may be attributed to participants' lack of experience with flight simulators, rendering the tasks novel and unfamiliar. It is plausible that the initial elevation in EDA at the onset of the task could be indicative of heightened anticipation and anxiety stemming from the novelty of the experience.<sup>161</sup> However, as participants became more accustomed to the tasks over time, this heightened state of nervousness may have dissipated, leading to a subsequent decline in EDA levels as the tasks progressed.<sup>3</sup> This emphasizes the dynamic nature of physiological responses and the potential utility of EDA in assessing task demand in the context of aviation.

In the current study, skin conductance during the FiO<sub>2</sub> 13.2% was greater compared to Ramp Exposure during the Course Task (Figure 13). This aligns with other studies indicating increased vascular conductance during simulated high altitude exposures.<sup>162-164</sup> Hohenauer et al. (2022)<sup>162</sup> assessed cutaneous vascular conductance in Swiss University students to participate in a cold-stress test under normoxia, low level normobaric – (FiO<sub>2</sub> 14.4%) and low level hypobaric hypoxia (PiO<sub>2</sub> 105.7 mm Hg). Hohenauer et al. (2022) reported no difference in cutaneous vascular conductance between normoxia, normobaric- and hypobaric hypoxic conditions.<sup>162</sup> Keramidas et al. (2019)<sup>163</sup> reported no effect of systemic hypoxia (30,000 ft) on cutaneous vascular conductance in the left forearm or fingers of male lowlanders, however, they observed decreased cutaneous vascular resistance of the right finger in Hypoxia during the rewarming phase after cold water immersion. Papparde et al. (2015)<sup>164</sup> exposed generally healthy adults to 20 minutes of acute normobaric hypoxia (pO<sub>2</sub> 12%) and reported a significant increase in forearm skin conductance in acute hypoxia compared to baseline in normoxia, but did not differ between acute hypoxia and

recovery in normoxia. The increase in EDA reflecting higher skin conductance (the inverse of skin resistance) observed at higher altitudes in both the current and previous studies<sup>162-164</sup>, aligns with known sympathetic activation associated with hypoxic exposures. This highlights the potential of EDA as a sensitive marker of sympathetic arousal.<sup>165</sup> The intricate balance between the sympathetic and parasympathetic branches in the autonomic nervous system is critical for adapting to environmental stressors.<sup>3, 166, 167</sup> The observed sensitivity of EDA to hypoxia in previous studies suggests that sympathetic dominance might play a more prominent role in the initial phases of the physiological responses to altitude-related stress.<sup>162-164</sup> In the flight environment, the relationship between sympathetic activity and task demand, as reflected in skin conductance, presents a potential avenue for quantifying hypoxia by monitoring sympathovagal balance.<sup>165</sup> Integrating electrodermal metrics with traditional vascular measures, such as blood pressure and HRV offers a more comprehensive understanding of autonomic adaptations to altitude-related stressors when developing in-flight physiological monitoring capabilities.

## **ELECTROMYOGRAPHY RESPONSES**

### **Amplitude Responses (EMG RMS)**

The current analysis revealed no significant interaction nor individual effect of altitude on motor unit activation measures assessed by EMG RMS across the Math, Course, and Landing Tasks (Figure 14). In the current study, there was an increase in EMG RMS from the Math Task to the Course Task (Figure 14). These findings support previous studies, such as Casale et al. (2004)<sup>37</sup> who reported no significant difference in two electrically elicited contractions of 20 seconds each, two voluntary contractions at 40%, and two at 80% MVC of the biceps brachii in men free from neuromuscular disorders during a 12-day stay at 5050 m (FiO<sub>2</sub> 11.2%). Similarly, McKeown et al. (2019)<sup>38</sup> found no effect of reduced SpO<sub>2</sub> (to 80%) on motor unit activation

measured by EMG RMS of the biceps brachii muscle in healthy participants during sustained isometric contractions with the forearm supinated and at 120° elbow flexion. Nell et al. (2020)<sup>39</sup> had participants from the general community perform intermittent handgrip exercise of the flexor digitorum superficialis at 50% MVC to task failure in FiO<sub>2</sub> 12%, and reported no difference in EMG RMS between normoxic and Hypoxic conditions. The authors, did report an increase in EMG RMS from Trial Start to Task Failure as a result of intermittent handgrip exercise to failure.<sup>39</sup> Jenkins et al. (2021)<sup>40</sup> further supported these results, reporting no effect of hypoxia on EMG RMS in recreationally active healthy adults during dynamic constant external resistance exercise to failure in the biceps brachii at FiO<sub>2</sub> 15% and FiO<sub>2</sub> 13%. The Math Task required participants to maintain straight and level flight while simultaneously engaging in mental serial addition, which required minimal head and neck movement. In contrast, the Course and Landing Tasks involved more dynamic movements for target observation or manipulation of aircraft controls. Therefore, the observed increase in motor unit activation, as measured by EMG RMS, from the Math Task to the Course Task in the present study can be attributed to fatigue development. This pattern aligns with findings from prior studies that have shown an increase in EMG RMS during fatiguing contractions.<sup>37-40</sup> While EMG RMS may not serve as a useful variable for quantifying physiological events related to in-flight hypoxia among pilots, it proves valuable for evaluating the impact of head-worn equipment (e.g., helmets, goggles, oxygen masks) in a cockpit environment, particularly concerning neck injury prevention and equipment ergonomics.

Drawing parallels to the use of NVGs, which have been shown to increase EMG RMS activity in trapezius muscles, the present study emphasizes the importance of task-specific nature of motor unit activation measured by EMG RMS.<sup>85, 88, 168</sup> The additional mass from NVG is typically associated with increased neck motor unit activation.<sup>85, 88, 168</sup> In the present study, the

Math Task, characterized by minimal head and neck movement, despite the similar extra mass from the HMD of the VR system to NVG, exhibited lower EMG RMS activity compared to the Course Task. This suggests that, when using a HMD or NVG without significant movement, may not result in fatigue-related increases in motor unit activation measures by EMG RMS. The task-dependent nature of this fatigue-related increase in EMG RMS highlights that muscular engagement varies based on the specific demands of the task, especially when extra mass is involved.

### **Frequency Responses (EMG MPF)**

The current study revealed no significant effect of hypoxia on EMG MPF responses across the Math, Course, and Landing Tasks (Figure 15). These data support previous studies that reported no significant impact of simulated hypoxic exposures on EMG MPF responses during discrete and repeated muscle actions.<sup>38,40</sup> For example, Jenkins et al. (2021)<sup>40</sup> had recreationally active generally healthy adults perform dynamic constant external resistance arm curl repetitions to failure at 70% MVC in FiO<sub>2</sub> 15% and FiO<sub>2</sub> 13% and reported no effect of hypoxia on EMG MPF. McKeown et al. (2019)<sup>38</sup> saw no effect of SpO<sub>2</sub> desaturation to 80% on biceps brachii motor unit firing rate in healthy adults during sustained isometric elbow flexion exercise. In contrast to these findings, other studies reported varying effects on MUAP CV under hypoxic conditions.<sup>36,37</sup> Felici et al. (2001)<sup>36</sup> reported a progressive reduction in biceps brachii muscle EMG median frequency in healthy men, during fatiguing isometric contractions at 80% MVC but only after 10 days at 5050 m. In addition, Casale et al. (2004)<sup>37</sup> observed increased EMG MPF during 20 s of voluntary contractions at 40% MVC and at 80% MVC at 5050 m in the biceps brachii. The contrast in findings between the current and previous studies may be attributed to a muscle-specific neuromuscular responses. Hypoxic exposures of the present study (FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and

Ramp Hypoxia) may not affect neuromuscular responses of the upper trapezius muscle, as indicated by no change in MUAP CV with hypoxia.

The present study observed an increase in EMG MPF from the Math Task to the Course Task suggesting greater MUAP CV during the Course Task occurred due to the study protocol and not simulated altitude (Figure 15). The present study results were in contrast to Rainoldi et al. (2008)<sup>83</sup> reported a decrease in conduction velocity of the vasti muscles during knee extensions at 60% and 80% MVIC. González-Izal et al. (2010)<sup>84</sup> reporting a decrease in EMG median frequency of the vastus lateralis and medius muscles in physically active men during fatiguing leg press exercise. Similarly, Jenkins et al. (2021)<sup>40</sup> performed dynamic constant external resistance exercise of the biceps brachii and reported a decrease in EMG MPF between 75% and 100% of repetitions to failure, independent of hypoxic exposure. Similarly, Smith et al. (2023)<sup>169</sup> reported a decrease in EMG MPF in men performing repeated leg extensions to failure at 70% 1RM. The contrast in findings, may be a result of fatiguing muscle actions typically utilized in neuromuscular investigations leading to a decrease in MUAP CV.<sup>40, 83, 84, 169</sup> The results of the present study suggest that head movement during the Math, Course, and Landing Tasks did not result in fatiguing action of the upper trapezius. However, the increase in EMG MPF in the present study could indicate stronger muscle contractions, as the frequency component of EMG has been associated with mechanical power changes in previous studies.<sup>72, 73, 84</sup> When evaluating EMG MPF for monitoring physiological parameters in pilots to predict hypoxic episodes, it is important to consider the specific tasks pilots perform. While the present study does not support the use of EMG MPF for this purpose, the findings emphasize the need to choose variables that capture the nuanced and task-dependent nature of the aviation environment.



## PERFORMANCE RESPONSES

In the current study, there were no observed decreases in the number of correct responses during the P.A.S.A.T. across any of the simulated altitude exposures (Figure 16a). These findings concur with those of Balldin et al. (2007)<sup>32</sup> reporting no impact of 12 hours at 10,000 ft on mathematical processing in active duty personnel. Legg et al. (2016)<sup>34</sup> had Air Force personnel breathe at 8,000 ft and 12,000 ft for 30 minutes and found no effects on mathematical processing. Similarly, Stephens et al. (2017)<sup>170</sup> reported no change in performance of simple computational problems (addition, subtraction, and multiplication) in generally healthy participants while exposed to normobaric simulated altitude of 15,000 ft. The present study contrasts with research by Malle et al. (2013)<sup>33</sup> reporting a decreased number of correct responses in the P.A.S.A.T. while pilots were exposed to 244 seconds of hypobaric hypoxia of 31,000 ft. Beer et al. (2017)<sup>171</sup> exposed active duty personnel to 18,000 ft and 25,000 ft in a hypobaric chamber (mean exposure duration was 17 min 45 s) and reported a “dip” in a multi-battery cognitive task performance (consisting of a memory, math, visual, and auditory task). The findings of the current study and previous research<sup>32, 34, 170</sup> indicate that the cognitive parameters assessed by the P.A.S.A.T. may not be affected by low level hypoxic exposure. The present study results and previous work suggest that the assessed cognitive process of the P.A.S.A.T. might not be a useful tool to quantify a hypoxic episode at low exposure levels. Future research is needed to pinpoint the specific cognitive process affected at low altitude levels and that can be readily assessed in an aviation environment.

In terms of simulator flight performance, as assessed through the Course (Figure 16b) and Landing Tasks (Figure 16c), there were no significant changes during simulated altitude exposures. This is consistent with previous studies that also reported no changes in flight performance metrics across altitude exposures.<sup>27, 28, 30</sup> However, these findings contrast with other

studies that reported increased piloting errors at different altitude exposures.<sup>11, 25, 26, 29, 31</sup> Variability in pilots' tolerance to hypoxia and its impact on flight performance may be attributed to individual respiratory responses, with a lower respiratory rate potentially associated with impaired cognitive performance. The psychological perception of hypoxic stress might have influenced participants more than actual performance outcomes, especially for those familiar with the effects of mild hypoxia, such as individuals from higher elevations or trained pilots.<sup>30</sup>

## QUESTIONNAIRES

### Hypoxic Symptoms Questionnaire Response

In the current study, the total number of reported symptoms (Figure 17) and their severity (Figure 18) did not exhibit significant changes with simulated altitudes of FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia exposure. Conversely, the number of reported hypoxia-related symptoms was a greater in the Math Task compared to both the Course and Landing Tasks. These findings are consistent with a study by Nesthus et al. (1997)<sup>11</sup> which exposed private pilots to FiO<sub>2</sub> 21%, 15.5%, 14.3%, and 13.0% while flying in a flight simulator, reported no effect of hypoxic conditions on hypoxia-related symptoms. Nesthus et al. (1997)<sup>11</sup> reported an increase in procedural errors during flight, descent, and approach phases at FiO<sub>2</sub> 14.3% and only during the descent phase at 13.0%. Similar to this, Pilmanis et al. (2016)<sup>96</sup> subjected military personnel analogs to hypobaric hypoxia (5,000 ft, 8,000 ft, and 12,000 ft in either ascending or descending order for 20 minutes) while conducting the Automated Neuropsychological Assessment Metrics (ANAM). Pilmanis et al. (2016)<sup>96</sup> reported an increase in the number of reported symptoms, with two symptoms at 5,000 ft, five symptoms at 8,000 ft, and 18 symptoms at 12,000 ft, compared to ground level with a small ANAM performance decrease. The presence of symptoms was not associated with a negative performance in previous research.<sup>11, 96</sup> In the context of aviation this suggests pilots may be able

to satisfactorily perform assigned tasks even while experiencing low-grad hypoxic symptoms, which suggests more research may be needed on symptoms indicative of reduced task performance.

During the Math Task, an impaired memory/recall, aligning with the cognitive demands of the P.A.S.A.T., was the most commonly reported hypoxic symptom across FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia. Following the Course Task, symptoms such as mental confusion, slowed reaction time, impaired judgment, and slowed reaction times were most commonly reported in Normoxia, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia, respectively. The Landing Task, characterized by the fewest total reported symptoms, had several symptoms that were equally common across Normoxia, FiO<sub>2</sub> 15.4%, FiO<sub>2</sub> 13.2%, and Ramp Hypoxia.

Contrasting evidence from previous studies,<sup>30, 32, 94, 97</sup> reported an increased occurrence of hypoxic symptoms during exposure to hypoxia. Balldin et al. (2007)<sup>32</sup> exposed active duty military personnel to 10,000 ft of hypobaric hypoxia for 12 hours, involving moderate workload cycling (70% VO<sub>2max</sub>) or low workload (no cycling) every 2 hours.<sup>32</sup> Their results showed a higher percentage of participants experiencing symptoms such as headache, lightheadedness, fatigue, and altered concentration at 10,000 ft compared to ground level.<sup>32</sup> In Johnston et al. (2012)<sup>94</sup> Royal New Zealand Air Force personnel completed symptom questionnaires during hypoxia awareness refresher training at 18,000 ft, and reported cognitive impairment and slurred speech as the most frequently recalled symptoms.<sup>94</sup> The severity rating increased between recalled and refresher hypoxia training for cognitive impairment, visual changes, hot/cold flushes, shaking limbs/tremors, lightheaded/dizzy, tingling/numbness, and loss of consciousness.<sup>94</sup> Similarly Bouak et al. (2018)<sup>97</sup> exposed military helicopter pilots to altitudes of 8,000 ft, 10,000 ft, 12,000 ft, and 14,000 ft on different days, combined with varying physical exertion levels (Rest: 0W,

Light: 30W, Moderate: 60W) on a bicycle ergometer, while engaging in a flight simulator and cognitive testing. They reported more symptoms at 12,000 ft and 14,000 ft compared to 10,000 ft, with an increasing number of symptoms reported from the beginning to the end of each altitude condition, with cognitive symptoms being the most common.<sup>97</sup> In a follow-up study, Bouak et al. (2019)<sup>30</sup> exposed military helicopter pilots to 8,000 ft and 9,900 ft of hypobaric hypoxia, while performing cognitive testing and a hypoxic symptoms questionnaire. They found a greater number of participants reporting more symptoms at altitude and ground level post-exposure than pre-exposure at ground level.<sup>30</sup> The number of reported symptoms increased from before the cognitive battery to after but did not differ between altitude conditions.<sup>30</sup> While previous studies<sup>30, 32, 94, 97</sup> suggest an increase in reported symptoms during simulated altitude exposures, the present study observed no such effect, possibly explained by the unfamiliar nature of hypoxic symptoms in the present study population. The existing literature, primarily involving aviation personnel accustomed to hypoxic training, might contribute to heightened symptom awareness.<sup>30, 32, 94, 97</sup> Original studies on the HSQ found that aircrew were more likely to notice symptoms in colleagues than in themselves.<sup>91, 92</sup> In the present study, participants may not have been familiar or be able to distinguish hypoxic symptoms, potentially resulting in underreporting. The lack of reported symptoms in the present study hypoxic exposures also supports the idea of incorporating multiple measures of hypoxic physiology to monitor physiological events. Future research should consider including a researcher observational questionnaire similar to the HSQ, to increase understanding of participants' experiences during hypoxic exposures.

### **Simulator Sickness Questionnaire Responses**

No previous studies were found that addressed the effects of acute low-level hypoxic exposure on feelings of simulator sickness. The results of the current study indicated that simulated

altitude exposures at  $\text{FiO}_2$  15.4%,  $\text{FiO}_2$  13.2%, and Ramp Hypoxic exposure did not significantly affect simulator sickness total scores or sub-scores (Figure 19 to 22). However, when comparing SSQ scores between flight tasks, there was a significant main effect of Task on Total Score, Nausea, and Oculomotor Discomfort. For the Total Score, follow-up pairwise comparisons suggested that the Math Task had a significantly higher score than the Course Task (Figure 19). The Nausea sub-score was significantly greater during the Math Task compared to both the Course and Landing Tasks (Figure 20), and the Oculomotor Discomfort was also significantly higher during the Math Task compared to the Course Task (Figure 22). Previous studies validating the use of various simulators with the SSQ did not include hypoxic exposures in their training evaluations.<sup>56, 64, 98-115</sup> Certain studies have reported an increase in Nausea, Oculomotor Discomfort, or all over time during simulator exposures.<sup>104, 105, 109, 113, 114</sup> Oskarsson and Nählinder, (2006)<sup>104</sup> investigated sickness symptoms in a VR HMD air combat simulator in military flight instructors, military student pilots, and novices. Oskarsson and Nählinder, (2006)<sup>104</sup> reported a peak in nausea symptoms at 15 and 60 minutes, oculomotor symptoms at the simulation's start and one hour later, and disorientation symptoms at 30 and 60 minutes. The present study results indicated no effect of hypoxia on symptoms of simulator sickness symptoms. However, symptoms were task dependent in the present study, showing higher scores after the Math Task compared to the Course and Landing Task. In the realm of aviation safety, examining simulator sickness symptoms in a hypoxic setting provides insights into whether there's an additional effect of hypoxia on symptoms related to simulator or motion sickness. This could provide more information on whether hypoxic related physiological events are affected by motion related symptoms.

## NASA Task Load Index Workload Responses

In the present study, when evaluating the workload demands using the NASA TLX the Math Task had greater time pressure compared to the Landing Task, but no difference was observed from the Course Task (Figure 24c). Additionally, the Mental Demand was greatest during the Math Task compared to the Course and Landing Task (Figure 24a). In the present study, self-perceived measures of Performance suggested that participants felt they scored better in the Course Task compared to the Math Task (Figure 25c). The Math Task had a significantly greater overall weighted workload score compared to the Course and Landing Tasks (Figure 23). Importantly, there was no effect of altitude exposure on any of the weighted scores of the NASA TLX. These findings are in contrast with earlier research by Phillips et al. (2015)<sup>172</sup> which found that active-duty personnel's workload increased during the hypoxic condition after being exposed to 18,000 feet (FiO<sub>2</sub> 9.96%) during cognitive tests. Similarly, Stephens et al. (2017)<sup>170</sup> had generally healthy participants perform a battery of written, computer-based, and flight simulation tasks in normobaric hypoxia (FiO<sub>2</sub> 11.5%) and reported an increase in overall workload, mental demand, performance, and frustration ratings of subjective workloads in only the flight simulation task. Similar to the present study results, Dahiya and Tripathi, (2009)<sup>173</sup> examined the effect of 10,000 ft and 15,000 ft on workload during a visuo-spatial working memory tasks with two difficulties in male lowlanders. The authors reported an effect of task difficulty only on weighted mental demand, temporal demand, performance, and effort, but no effect of hypoxia on ratings, weights, or overall workload of the NASA TLX. Their contrast in findings to previous work as hypothesized as the deficit in working memory was too subtle to be detected by the NASA TLX.<sup>173</sup> Previous literature, suggested that the subjective perception of workload might have been masked by the common hypoxic symptom of "euphoria."<sup>170, 172, 173</sup>

The elevated workload score during the Math Task, compared to both the Course and Landing Tasks, can be explained by the inherent nature of the P.A.S.A.T., designed to assess working memory, necessitating memorization and active information processing. The subscores underscore the distinctive Mental Demand associated with the Math Task, surpassing that of piloting the aircraft in the Course and Landing Tasks. The time component of the Math Task, requiring responses within 4-seconds of presented digits, further contributed to its complexity. Additionally, participants perceived lower Performance in the Math Task compared to the Course and Landing Tasks aligns with previous work that greater task difficulty is associated with higher workload.<sup>44, 54, 55, 57, 66, 67, 116-122</sup> It's essential to note that the current study involved generally healthy, active individuals rather than experienced pilots who routinely engage in in-flight calculations for factors like fuel, heading, and speed. Workload as quantified by the NASA TLX can be a useful tool to quantify workload, however its use in predicting hypoxic related unexplained physiological events remains elusive.

## LIMITATIONS

The present study, while contributing valuable insights into the impact of hypoxia on cognitive function, flight performance, and perceived workload, is not without its inherent limitations. A notable limitation in the present study is the lack of systematic consideration for potential practice effects associated with the Math Task or Paced Auditory Serial Addition Test (P.A.S.A.T.). Tombaugh, 2006 noted in his review highlighted a notable practice effect across various interstimulus intervals.<sup>138</sup> The presence of practice or learning effects in cognitive tests indicates participants tend to exhibit improved performance with repeated exposures.<sup>174</sup> This improvement is likely due to the development of effective strategies for tackling the complex and challenging nature of the test, as well as the reduction of anxiety and frustration associated with the initial baseline performance of the P.A.S.A.T.<sup>138, 174</sup> Practice effects seem unaffected by the duration between tests, and the emotional impact of the PASAT diminishes with repeated exposure.<sup>138</sup> In the present study, the absence of a practice trial and the inclusion of only five total trials may have allowed practice effects to potentially overshadow altitude-induced effects. Despite implementing a randomized single-blinded design to mitigate the impact of repeated testing, the definite exclusion of a learning or practice effect on participant performance cannot be guaranteed.

One notable limitation lies in the failure to systematically account for a potential practice effect associated with the Math Task or Paced Auditory Serial Addition Test (P.A.S.A.T.), a cognitive function assessment tool. The P.A.S.A.T., as noted by Tombaugh, is highly susceptible to these effects.<sup>138</sup> The absence of a practice trial for participants in the present study, combined with only five total trials, could have contributed to potential practice effects "washing out" any altitude-induced effects. Despite the implementation of a randomized single-blinded design to



mitigate the impact of repeated testing, the potential influence of a learning or practice effect on participant performance cannot be definitively ruled out.

The current study included participants with varying levels of flight experience, with the majority of participants having none. Consequently, the assessment of procedural and task-specific performance during flight was not feasible, even though such aspects have been associated with numerous civilian and military flight incidents.<sup>11, 25, 26, 29, 31</sup> Future investigations should include flight specific procedural metrics, to ensure a more comprehensive understanding of the intricate relationship between hypoxia and aviation performance.

These limitations underscore the importance of approaching the study findings with caution. They signify important areas for improvement and refinement for future investigations of the effects of hypoxia on cognitive and performance outcomes. As the field progresses, addressing these limitations will contribute to a more robust understanding of the multifaceted impacts of hypoxia on human performance.

## CONCLUSIONS

The purpose of this study was to investigate the physiological and cognitive effects of low-level hypoxic exposure and to assess whether the collected physiological variables could be used to predict flight performance during simulated hypoxic conditions. Stable flight performance in mild hypoxic exposures suggests performance impairments may manifest primarily at severe hypoxic exposures. Cardiovascular stability may result from an effective baroreflex reset in response to hypoxia, supported by autonomic nervous system adaptations, including stable heart rate, decreased skin conductance, and parasympathetic dominance. These variables could predict the physiological effects of hypoxia and flight performance in real-world aviation applications. The present study found no significant simulated altitude-induced effects on motor unit activation or motor unit action potential conduction velocity in the upper neck. Monitoring symptoms and workload is critical for understanding physiological responses in the cockpit environment, as hypoxia can downplay symptom severity. Overall, this study contributes to the understanding of the effects of hypoxia on human performance in aviation, paving the way for targeted investigations in the future. The findings of this study support the hypothesis that physiological assessments can be integrated with other measures to characterize the effects of acute and gradual hypoxic exposures.

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## Glossary

$\mu\text{S}$	micro-Siemens (Human Conductance)
$\mu\Omega$	micro-Ohms (Human Resistance)
ANOVA	Analysis of Variance
BP	Blood Pressure (mmHg)
DBP	Diastolic Blood Pressure (mmHg)
ECG	Electrocardiogram
EDA	Electrodermal Activity
EMG	Electromyography
$\text{FiO}_2$	Fraction of inspired oxygen
HF	Relative power of the high-frequency band (0.15–0.4 Hz)
HMD	Head Mounted Display
HR	Heart Rate (bpm)
HRV	Heart Rate Variability
HSQ	hypoxic Symptoms Questionnaire
LF	Relative power of the low-frequency band (0.04–0.15 Hz)
MAP	Mean Arterial Pressure (mmHg)
meanHR	Average Heart Rate
MPF	Mean Power Frequency (Hz)
MSSQ	Motion Sickness Susceptibility Questionnaire
MUAP CV	Motor Unit Action Potential Conduction Velocity
NASA TLX	National Aeronautics and Space Administration-Task Load Index
OBOGS	On Board Oxygen Generator System

P.A.S.A.T.	Paced Auditory Serial Addition Test
RMS	Root Mean Squared (ms)
RMSSD	Root Mean Square of Successive Differences Between Normal Heartbeats (ms)
SBP	Systolic Blood Pressure (mmHg)
SD1	Poincaré plot standard deviation perpendicular the line of identity
SD2	Poincaré plot standard deviation along the line of identity
SpO <sub>2</sub>	Peripheral Oxygen Saturation
SSQ	Simulator Sickness Questionnaire
TS	Total Score
VR	Virtual Reality
$\eta_p^2$	partial eta squared effect size

## Appendix A - Health History Questionnaire

Participant ID \_\_\_\_\_ Date \_\_\_\_\_

Gender \_\_\_\_\_ Age \_\_\_\_\_ (yrs) Height \_\_\_\_\_ cm Weight \_\_\_\_\_ (kg)

**A. JOINT-MUSCLE STATUS** (√Check areas where you currently have problems)

Joint Areas

- Wrists
- Elbows
- Shoulders
- Upper Spine & Neck
- Lower Spine
- Hips
- Knees
- Ankles
- Feet
- Other \_\_\_\_\_

Muscle Areas

- Arms
- Shoulders
- Chest
- Upper Back & Neck
- Abdominal Regions
- Lower Back
- Buttocks
- Thighs
- Lower Leg
- Feet
- Other \_\_\_\_\_

**B. HEALTH STATUS** (√Check if you previously had or currently have any of the following conditions)

- |  |   |
|--|---|
| <input type="checkbox"/> High Blood Pressure                             | <input type="checkbox"/> Acute Infection  |
| <input type="checkbox"/> Heart Disease or Dysfunction                    | <input type="checkbox"/> Diabetes or Blood Sugar Level Abnormality                          |
| <input type="checkbox"/> Peripheral Circulatory Disorder                 | <input type="checkbox"/> Anemia   |
| <input type="checkbox"/> Lung Disease or Dysfunction                     | <input type="checkbox"/> Hernias  |
| <input type="checkbox"/> Arthritis or Gout                               | <input type="checkbox"/> Thyroid Dysfunction  |
| <input type="checkbox"/> Edema   | <input type="checkbox"/> Pancreas Dysfunction   |
| <input type="checkbox"/> Epilepsy  | <input type="checkbox"/> Liver Dysfunction  |
| <input type="checkbox"/> Multiple Sclerosis                              | <input type="checkbox"/> Kidney Dysfunction   |
| <input type="checkbox"/> High Blood Cholesterol or Triglyceride Levels   | <input type="checkbox"/> Phenylketonuria (PKU)  |
| <input type="checkbox"/> Loss of Consciousness                           | <input type="checkbox"/> Allergic Reactions to Medication<br>please describe _____          |
| <input type="checkbox"/> Others That You Feel We Should Know About _____ | <input type="checkbox"/> Allergic Reactions to Any Other Substance<br>please describe _____ |
| <input type="checkbox"/> Pregnant  |   |

**C. PHYSICAL PERCEPTIONS** (Indicate any unusual sensations or perceptions. !Check if you have recently experienced any of the following during or soon after *physical activity* (PA); or during *sedentary periods* (SED))

- | <u>PA</u>                | <u>SED</u>   | <u>PA</u>                | <u>SED</u>                                     |
|--------------------------|--|--------------------------|--|
| <input type="checkbox"/> | <input type="checkbox"/> Chest Pain                                      | <input type="checkbox"/> | <input type="checkbox"/> Nausea                |
| <input type="checkbox"/> | <input type="checkbox"/> Heart Palpitations "fast irregular heart beats" | <input type="checkbox"/> | <input type="checkbox"/> Light Headedness      |
| <input type="checkbox"/> | <input type="checkbox"/> Unusually Rapid Breathing                       | <input type="checkbox"/> | <input type="checkbox"/> Loss of Consciousness |
| <input type="checkbox"/> | <input type="checkbox"/> Overheating                                     | <input type="checkbox"/> | <input type="checkbox"/> Loss of Balance       |
| <input type="checkbox"/> | <input type="checkbox"/> Muscle Cramping                                 | <input type="checkbox"/> | <input type="checkbox"/> Loss of Coordination  |
| <input type="checkbox"/> | <input type="checkbox"/> Muscle Pain                                     | <input type="checkbox"/> | <input type="checkbox"/> Extreme Weakness      |
| <input type="checkbox"/> | <input type="checkbox"/> Joint Pain                                      | <input type="checkbox"/> | <input type="checkbox"/> Numbness              |
| <input type="checkbox"/> | <input type="checkbox"/> Unusual Fatigue                                 | <input type="checkbox"/> | <input type="checkbox"/> Shortness of Breath   |
| <input type="checkbox"/> | <input type="checkbox"/> Heart Murmur                                    | <input type="checkbox"/> | <input type="checkbox"/> Mental Confusion      |
| Other _____              |  |                          |  |



## Appendix B – Physical Activity Recall (PAR)

		DAYS							
		Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	
Morning	<b>SLEEP</b>	1___	2___	3___	4___	5___	6___	7___	
	Moderate								
	Hard								
	Very Hard								
	Afternoon	Moderate							
		Hard							
		Very Hard							
	Evening	Moderate							
		Hard							
Very Hard									
Total Min per	Strength:								
	Flexibility:	_____	_____	_____	_____	_____	_____	_____	

<p>4a. Compared to your physical activity over the past 3 months, was last week's physical activity more, less, or about the same?</p> <p>1. More                      2. Less                      3. About the same</p>	<p>6. Do you think this was a valid PAR Interview?</p> <p>1. Yes                      O. No If NO, to the back and ex ajn.</p>
<p>5. Were there any problems with the PAR interview?</p> <p>O. No                      I. Yes If YES, go to the back and explain.</p>	<p>7. Were there any special circumstances concerning this PAR ?</p> <p>O. No                      I. Yes, If YES, what were they?(circle)</p> <p>1. Injury all week      2. Illness all week      3. Illness part week 4. Injury part week    5. Pregnancy            6. Other:</p>

Time Rounding: 10-22 min.=.25  
 23-37 min.=.50  
 38-52 min.=.75

53-1 .07 hr/min. —1 .0 hr/min.=1 .25

## Appendix C - Motion Sickness Susceptibility Questionnaire (MSSQ)

240

*J.F. Golding / Personality and Individual Differences 41 (2006) 237–248*

Table 1

Motion sickness susceptibility questionnaire short-form (MSSQ-Short)

This questionnaire is designed to find out how susceptible to motion sickness you are, and what sorts of motion are most effective in causing that sickness. Sickness here means feeling queasy or nauseated or actually vomiting

**Your childhood experience only** (before 12 years of age), for each of the following types of transport or entertainment please indicate

1. As a child (before age 12), how often you felt sick or nauseated (tick boxes)

	Not Applicable - Never Traveled	Never Felt Sick	Rarely Felt Sick	Sometimes Felt Sick	Frequently Felt Sick
Cars					
Buses or Coaches					
Trains					
Aircraft					
Small Boats					
Ships, e.g. Channel Ferries					
Swings in playgrounds					
Roundabouts in playgrounds					
Big Dippers, Funfair Rides					
	t	0	1	2	3

**Your experience over the last 10 years (approximately)**, for each of the following types of transport or entertainment please indicate

2. Over the last 10 years, how often you felt sick or nauseated (tick boxes)

	Not Applicable - Never Traveled	Never Felt Sick	Rarely Felt Sick	Sometimes Felt Sick	Frequently Felt Sick
Cars					
Buses or Coaches					
Trains					
Aircraft					
Small Boats					
Ships, e.g. Channel Ferries					
Swings in playgrounds					
Roundabouts in playgrounds					
Big Dippers, Funfair Rides					
	t	0	1	2	3

Golding JF. Predicting individual differences in motion sickness susceptibility by questionnaire. *Pers Individ Dif.* 2006;41(2):237-248

### Appendix D - Hypoxic Symptom Questionnaire (HSQ)

Please rate each item as 0 for ‘None’; 1 for “Slight”; 2 for “Moderate” and 3 for “Severe” and mark answers below.

	None 0	Slight 1	Moderate 2	Severe 3
<b>Behavioral</b>				
Change in mood				
Apprehension				
Euphoria				
<b>Cognitive</b>				
Impaired Judgment				
Impaired Memory/Recall				
Mental confusion				
<b>Physical</b>				
Fatigue or drowsiness				
Feeling light-headed				
Headache				
Hot/Cold flushes				
Loss of muscle coordination				
Numbness				
Tingling of fingers or lips				
<b>Psychological/Psychomotor</b>				
Difficulty with communications				
Impaired manual dexterity				
Slowed reaction time				
<b>Visual</b>				
Impaired peripheral vision				
Impaired visual acuity				

Bouak F, Vartanian O, Hofer K, Cheung B. Acute mild hypoxic hypoxia effects on cognitive and simulated aircraft pilot performance. *Aerosp Med Hum Perform.* 2018;89(6):526-535.

Smith A. hypoxia symptoms reported during helicopter operations below 10,000 ft: A retrospective survey. *Aviat Space Environ Med.* 2005;76(8):794-798.

## Appendix E - Simulator Sickness Questionnaire (SSQ)

### SIMULATOR SICKNESS QUESTIONNAIRE

Kennedy, Lane, Berbaum, & Lilienthal (1993)

Instructions: Circle how much each symptom below is affecting you right now:

1. General discomfort	None	Slight	Moderate	Severe
2. Fatigue	None	Slight	Moderate	Severe
3. Headache	None	Slight	Moderate	Severe
4. Eye Strain	None	Slight	Moderate	Severe
5. Difficulty focusing	None	Slight	Moderate	Severe
6. Salivation increasing	None	Slight	Moderate	Severe
7. Sweating	None	Slight	Moderate	Severe
8. Nausea	None	Slight	Moderate	Severe
9. Difficulty concentrating	None	Slight	Moderate	Severe
10. Fullness of Head	None	Slight	Moderate	Severe
11. Blurred vision	None	Slight	Moderate	Severe
12. Dizziness with eyes open	None	Slight	Moderate	Severe
13. Dizziness with eyes closed	None	Slight	Moderate	Severe
14. Vertigo*	None	Slight	Moderate	Severe
15. Stomach awareness**	None	Slight	Moderate	Severe
16. Burping	None	Slight	Moderate	Severe

\*Vertigo is a feeling of spinning around and being unable to balance

\*\*Stomach awareness is a feeling of discomfort which is just short of nausea

## Appendix F - Scoring of the SSQ

### The calculations in the Simulator Sickness Questionnaire

None = 0  
 Slight = 1  
 Moderate = 2  
 Severe = 3

Symptoms	Weights for Symptoms		
	Nausea	Oculomotor	Disorientation
General discomfort	1	1	
Fatigue		1	
Headache		1	
Eye strain		1	
Difficulty focusing		1	1
Increased salivation	1		
Sweating	1		
Nausea	1		1
Difficulty concentrating	1	1	
Fullness of head			1
Blurred vision		1	1
Dizzy (eyes open)			1
Dizzy (eyes closed)			1
Vertigo			1
Stomach awareness	1		
Burping	1		
Total*	[1]	[2]	[3]

Score  
 Nausea = [1] × 9.54  
 Oculomotor = [2] × 7.58  
 Disorientation = [3] × 13.92  
 Total Score = ([1] + [2] + [3]) \*3.74

---

\* Total is the sum obtained by adding the symptoms scores. Omitted scores are zero

Walter H, Li R, Munafo J, Curry C, Peterson N, Stoffregen T. Data from: APAL coupling study 2019. 2019. doi:10.13020/XAMG-CS69

# Appendix G - NASA- Task Load Index (TLX)

Figure 8.6

### NASA Task Load Index

Hart and Staveland's NASA Task Load Index (TLX) method assesses work load on five 7-point scales. Increments of high, medium and low estimates for each point result in 21 gradations on the scales.

Name	Task	Date

**Mental Demand**      How mentally demanding was the task?  
Very Low                      Very High

**Physical Demand**      How physically demanding was the task?  
Very Low                      Very High

**Temporal Demand**      How hurried or rushed was the pace of the task?  
Very Low                      Very High

**Performance**      How successful were you in accomplishing what you were asked to do?  
Perfect                      Failure

**Effort**      How hard did you have to work to accomplish your level of performance?  
Very Low                      Very High

**Frustration**      How insecure, discouraged, irritated, stressed, and annoyed were you?  
Very Low                      Very High

Hart SG. NASA-Task Load Index (NASA-TLX); 20 years later. Sage publications Sage CA: Los Angeles, CA; 2006:904-908.

Hart SG, Staveland LE. Development of NASA-TLX (Task Load Index): Results of empirical and theoretical research. *Advances in Psychology*. Elsevier; 1988:139-183.

## Appendix H – Electrodermal Activity (EDA) Time Course Changes

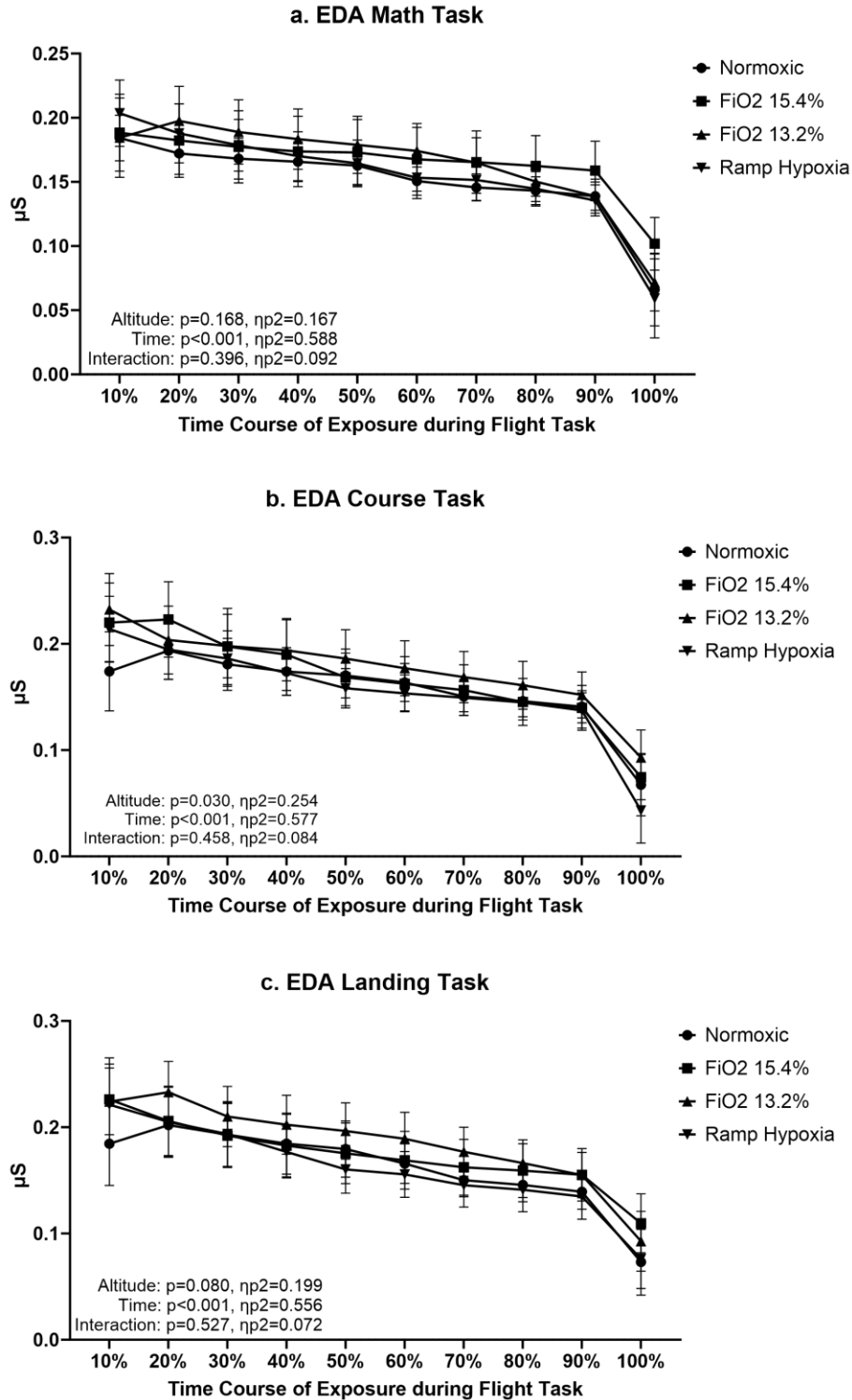


Figure 26. Mean  $\pm$  SEM Time course changes for electrodermal activity (EDA) during the Math Task (a), Course Task (b), and Landing Task (c).

## **Vita**

Jasmin Renee Jenkins received her bachelors and masters in Kinesiology from the University of Texas at El Paso. During her tenure at the University, Jasmin published scientific papers based on her research and disseminated those findings at several national and regional scientific conferences. Jasmin also has experience as a teaching assistant and adjunct professor for the Department of Kinesiology. Jasmin received gracious support from the Interdisciplinary Health Sciences PhD Program and Graduate School to fund her schooling throughout her PhD.

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