Gender Differences in Dry-EEG Manifestations During Acute and Insidious Normobaric Hypoxia

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INTRODUCTION: Prior research suggests there may be gender differences with regards to hypoxia resilience. Our study was designed to determine whether there were differences between genders in neuronal electrical activity at simulated altitude and whether those changes correlated with cognitive and aviation performance decrements.

METHODS: There were 60 student Naval Aviators or Flight Officers who completed this study (30 women, 30 men). Participants were exposed to increasing levels of normobaric hypoxia and monitored with dry EEG while flying a fixed-base flight simulation. Gender differences in brainwave frequency power were quantified using MATLAB. Changes in flight and cognitive performance were analyzed via simulation tasks and with a cognitive test validated under hypoxia.

RESULTS: Significant decreases in theta and gamma frequency power occurred for women compared to men with insidious hypoxic exposures to 20K, with an average frequency power decrease for women of 19.4% compared to 9.3% for men in theta, and a 42.2% decrease in gamma for women compared to 21.7% for men. Beta frequency power correlated highest between genders, with an average correlation coefficient of $r = 0.95$ across seven channels.

DISCUSSION: Results of this study suggest there is identifiable brain wave suppression for both men and women with hypoxic exposure and, moreover, there are significant differences in this suppression between genders. Beta frequency power was most sensitive for both genders and highly correlative compared to other brainwave frequencies. The implications of these findings are important considerations for next-generation aviation helmets, which may employ this technology as an early warning mechanism.

KEYWORDS: sex, brainwaves, physiological episodes.

Rice GM, Snider D, Drollinger S, Greil C, Bogni F, Phillips J, Raj A, Marco K, Linnville S. *Gender differences in dry-EEG manifestations during acute and insidious normobaric hypoxia*. Aerosp Med Hum Perform. 2019; 90(4):369–377.

Wet (i.e., use of a conductive paste or gel) multichannel EEG has been used in a limited capacity to evaluate brain activity in extreme environments, such as hypobaric hypoxia,[13,21,22] hyperventilation,[24] and simulated excessive acceleration,[35] revealing unique wave form patterns suggestive of cognitive decrements. The cumbersome nature of traditional multichannel wet-EEG and their susceptibility to noise has prevented their transition to operationally relevant environments and subsequent utilization as a potential mitigation tool. The recent validation of dry EEG [4,27,37] as a reliable surrogate means of evaluating cognitive activity opens the door for evaluating these systems as viable devices for identifying cognitive performance decrements in operationally relevant environments, such as high altitude or excessive acceleration.

There is good evidence that resting and active electrical activity differ between men and women in sea-level conditions.[9,12] If we are to develop gender neutral algorithms which are predictive of real-time cognitive performance decrements in operational environments, such as high altitude, we will need to identify frequencies and channel locations which are most resistant to these differences. Of special interest is the potential for gender differences in the tolerance of the deleterious effects of hypoxia. There is evidence from animal models that females

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This manuscript was received for review in July 2018. It was accepted for publication in October 2018.

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DOI: https://doi.org/10.3357/AMHP.5227.2019

demonstrate an increased resistance to cognitive deficits due to sublethal hypoxia during preterm birth[30,36] and resistance to cardiac ischemia/reperfusion injury.[20] Although less studied, this apparent gender-related hypoxia resilience has also been demonstrated in human studies as well, where fatigue and recovery times for women following exposure to hypoxia and ischemia have been found to be reduced.[5,16] Additionally, differences have been found between human men and women in the genetic expression of hypoxia inducible factors.[31] Despite these previous findings, human research is lacking on both gender differences in brainwave activity and cognitive performance with hypoxia. The aforementioned developments in dry-EEG technology afford us the possibility of exploring both gender differences with electrical activity and aviation-related cognitive performance at simulated altitude.

The primary objective of this study was to evaluate differences in brainwave patterns between genders as detected by dry-EEG technology. Secondary objectives included evaluating whether there are gender differences in hypoxia tolerance as determined by cognitive and flight-related performance changes from baseline (sea level) compared to simulated altitude. We also gathered subjective hypoxia symptoms and physiological data such as oxygen concentration and heart rate.

METHODS

Subjects

Participants were 60 ($N = 30$ men, 30 women) aeromedically cleared, student Naval Aviators (SNAs), student Naval Flight Officers (SNFOs), and student Naval Flight Surgeons (SNFSs) awaiting training or instructing at Naval Air Station (NAS) Pensacola, FL. The study protocols and procedures were approved by the Navy Medicine Operational Training Center's Scientific Ethical Review Committee (SERC) under protocol number NMOTC2016.0016, and subsequently approved by a higher-level Institutional Review Board at the Naval Medical Research Unit-Dayton, Wright Patterson Air Force Base, OH, on November 1, 2016. Informed consents were obtained by one of our associate investigators not in their chain of command or involved with their medical care. Demographic information such as rank, age, gender, flight hours, and prior history of traumatic brain injury were obtained. Subjects were excluded from the study if they did not have a valid, aeromedical clearance known as an "upchit" or if they had over 25% of their physiological and cognitive performance data deemed as incomplete, a threshold by which was assumed not valid to impute.

Equipment

Participants were fitted with a standard naval aviation mask (MBU-23) which interfaces with the Reduced Oxygen Breathing Device 2 (ROBD2, Model 6202, Environics®, Inc., Tolland, CT). The ROBD2 is a normobaric, hypoxia-producing device that works by altering the concentration of oxygen an individual breathes with inert nitrogen gas. Through validated algorithms, the device simulates altitude by providing precise concentrations of oxygen and nitrogen via mass flow-controlled sensors.[1] The device is calibrated daily and used to train thousands of aircrews each year regarding the deleterious effect of hypoxia without the side effects of reduced pressure.

Once appropriately fitted with their aviation mask and connected to the ROBD2, breathing sea-level equivalent oxygen, they were connected to oxygen saturation sensors on the finger and forehead, then to the DSI-7 System by Wearable Sensing® (DSI-7, Wearable Sensing, LLC, San Diego, CA). This is a 7-channel, dry electroencephalogram which uses sensors located within the International 10/20 electrode placement system locations: F3, F4, C3, C4, P3, P4, and linked ears.[8,34] The DSI-7 has a sampling rate of 300 Hz and a band pass rate between 1–50 Hz. The device uses software that classifies various cognitive states and has been validated for mental engagement, workload, and fatigue.[6,15,17] Although the DSI-7 has the ability to measure cognitive workload by using its proprietary software "Qstates", we independently evaluated each channel frequency and magnitude during various normobaric hypoxic exposures via MATLAB (The Mathworks, Natick, MA)[14] using Fast Fourier transformation (FFT).

Appropriately connected to the ROBD2, oxygen saturation monitors, and fitted with the DSI-7 for brainwave monitoring, the participant was acquainted with the X-Plane version 10.5 simulator.[38] X-Plane simulates the performance and handling of most aircraft, and is a tool for pilots to keep up their skills in a simulator which flies like a real plane, for engineers to predict how a new airplane will fly, and for aviation enthusiasts to explore the world of aircraft flight dynamics. For the purposes of this protocol, subjects "flew" over Montana in a fixed-wing, single-engine Cessna aircraft, and the simulation provided altitudes and heading each second of the flight which were used to determine flight performance and any changes to flight performance while wearing the dry-EEG system.

To assess cognitive performance during baseline and normobaric hypoxic exposures we used a computerized neurocognitive task called Visual Sequence Comparison (VSC). VSC is a subtest of the Cogscreen-Hypoxia Edition that has been validated to be sensitive to the effects of hypoxia at levels above 12,000 ft (3658 m).[25] The task challenges the participant to compare two simultaneously presented, alphanumeric sequences and it specifically measures visual attention, working memory, verbal-sequential processing, and visual-perceptual speed, with a test-retest reliability (stability) of 0.85–0.89.[3,11]

Procedures

Following informed consent, participants were fitted with the MBU-23, which interfaces with the ROBD2. During mask fitting, one of the researchers would give the participant a description of the common symptoms of hypoxia and told the participant to pull a "green ring" beside the chair which would signify they recognized these symptoms were occurring to them. In the study the green ring pull was simulated, but in an operational Naval aircraft the green ring represents a functional

Table I. Demographics.

	WOMEN ($N = 30$)		MEN ($N = 30$)	
	MEAN	SD	MEAN	SD
Age	24	2.5	23.8	1.7
Height	65.6	2.2	70.5	3.0
Weight	148.5	17.9	177.6	23.2
BMI	24.2	2.5	25.1	2.5
Flight Hours	22.9	52.3	9.96	17.4
Concussions	No		No	
Tobacco	No		No	
Rank	29-O1's, 1-O3		30-O1's	

handle which, when pulled, provides the aviator 100% oxygen. In our study protocol, although participants may have felt they recognized their symptoms, they were allowed to continue with their normobaric hypoxic exposure until their oxygen (O_2) saturation fell below 60%, or until they were not comfortable with continuing the exposure, and at that time were provided 100% oxygen.

Once appropriately fitted with their aviation mask and connected to the ROBD2, breathing sea-level equivalent oxygen, they were connected to oxygen saturation sensors on the finger and forehead, then to the DSI-7 System. Appropriately connected to the ROBD2, oxygen saturation monitors, and fitted with the DSI-7 for brainwave monitoring, the participant was acquainted with the X-Plane version 10.5 simulator. Upon becoming familiar with the operations of the X-Plane simulator, the participant was instructed to start at a heading of 360° and a simulated altitude of 10,000 ft (3048 m) and began a standard rate climb of 250 ft · min^{-1} (76.2 m · min^{-1}) and standard rate turn for 180°, then performed a standard rate decent of 250 ft · min^{-1} and continued their turn back to the original heading of 360°. This maneuver was performed for 3 min at sea level and then performed at a normobaric hypoxic exposure of 25,000 ft (25K; 7620 m) for 3 min (i.e., the acute phase in the study). Brainwave frequency power was determined for all frequencies and channels and compared between sea level and 25K. Participants were provided 100% oxygen if their O_2 saturation fell below 60%.

Following this acute 25,000-ft normobaric exposure, the participant was provided 100% oxygen until their O_2 saturation was greater than 97%, and then they began a 20-min hypoxia "washout" or recovery period before the next phase of the study. During this washout period they were taught the VSC task. The participant took this test five times during the washout period to ensure there was no learning effect during the rest of the protocol.

After completion of the hypoxia washout, the participant then began an insidious (i.e., gradual) normobaric hypoxic exposure toward 20,000 ft (20K; 6096 m) simulated altitude. Starting at sea-level equivalent oxygen concentrations, the participant was exposed to 5-min intervals of sea level, 8000 ft (2438 m), 12,000 ft (3658 m), 16,000 ft (4877 m), 20,000 ft (6096 m), 100% oxygen, and back to sea level for a total of 35 min. During each 5-min interval, 150 s were spent performing the VSC and the second half was spent performing the simulated flight task of climbing at a constant rate and turning 180°, followed by descending at a constant rate and turning to complete a full circle. Outcome measures analyzed at each interval included reaction time, omission errors, and throughput during the VSC, while mean deviation from heading, altitude, and GPS deviations were monitored during the X-Plane simulation. Brainwaves were monitored via the DSI-7 during each interval and computed frequency magnitude via FFT (3-min windows of frequency power for the acute phase, and 5-min windows of frequency power for the insidious phase) and average frequency power were determined at each interval. Oxygen saturations and heart rate were monitored through the 35-min exposure, and study duration runtimes within the 35 min were recorded when the subject pulled the green ring. It was emphasized

Table II. Women and Men's S_pO_2 and Heart Rate (HR) at Simulated Altitude.

S_pO_2	WOMEN ($N = 30$)		MEN ($N = 30$)		GENDER × S_pO_2
ALTITUDE	MEAN	SD	MEAN	SD	$P = 0.217$
0KA	97.99	0.54	97.81	0.56	–
25KA	83.50	3.72	83.66	2.95	–
100% O_2	88.16	6.26	90.27	4.71	–
Washout	97.82	0.50	97.68	0.43	–
00K	97.57	0.88	97.55	0.47	–
08K	95.83	1.07	95.44	1.35	–
12K	91.00	2.07	91.21	2.80	–
16K	83.35	3.86	84.53	5.33	–
20K	74.13	5.64	76.24	7.40	–
100% O_2	94.66	4.29	96.22	1.08	–
End	98.16	0.67	97.92	0.49	–
HR	**WOMEN (30)**		**MEN (30)**		**GENDER × HR**
ALTITUDE	**MEAN**	**SD**	**MEAN**	**SD**	$P = 0.000$
0KA	79.6	10.9	83.4	10.9	0.186
25KA	95.4	11.8	99.0	10.3	0.209
100% O_2	86.9	11.1	87.6	13.7	0.814
Washout	78.4	8.8	80.5	9.3	0.376
00K	79.6	8.7	80.2	8.7	0.791
08K	83.0	10.0	82.4	9.2	0.8
12K	86.8	10.4	85.2	8.8	0.526
16K	92.9	10.7	90.3	8.9	0.311
20K	99.8	10.6	95.9	12.2	0.19
100% O_2	76.7	9.5	77.4	10.3	0.809
End	74.7	8.8	74.9	9.0	0.937

Using subgroup averages (men/women), 151/1320 (11%) missing data points were imputed.
Note: 64/660 (10%) missing data points were imputed using subgroup averages (men/women).

to the subjects throughout the protocol that they could discontinue at any time and were immediately provided 100% oxygen if they discontinued, or if their O_2 saturation fell below 60%.

Statistical Analysis

Statistical power analysis had been performed using differences found in prior studies between men and women exposed to fatigue and ischemia,[5] so we anticipated a potential 35% reduction in reaction time change from baseline to altitude exposure of 20,000 ft (6096 m) for women compared to men. For our smallest sample size comparison, assuming there was a 0.5-ms standard deviation within subject reaction time for subjects, and setting $\alpha = 0.05$ and $\beta = 0.80$, and an estimated effect size of 35%, we anticipated a need of approximately 25 subjects per group.

For the EEG analyses, a series of logistic regression analyses were used to identify if any altitude changes predicted gender differences in the EEG. Pearson correlations were used to determine which of the seven channels best showed correlations between genders. For the other variables (O_2 saturation, cognitive performance, simulated flight performance) repeated measures ANOVAs were also performed to identify any interactions with gender across the altitude changes. For the self-reported hypoxia symptoms, a series of nonparametric Chi-square (χ^2) analyses were performed. All statistical analyses were conducted using the statistical package for the social sciences (IBM© SPSS®).

Table III. Brainwave Changes [Mean (M) Frequency Power and 95% Confidence Intervals (±CI)] and Significance* ($P < 0.05$) Between Gender at Each Frequency.

FREQUENCY	**WOMEN**			**MEN**			**SIGNIFICANCE**
THETA	**M**	**+CI 95%**	**−CI 95%**	**M**	**+CI 95%**	**−CI 95%**	***P* =**
0K A	81	89	73	83.9	94.4	73.5	0.735
25K A	29.4	32.8	26.1	38.7	48.8	28.6	0.394
Washout	115.6	128.6	102.6	123.4	139.9	106.8	0.5
00K I	111.8	123.6	100.1	124.8	140.6	109.1	0.55
08K I	108.4	120.5	96.4	124.5	142.2	106.8	0.264
12K I	105.8	115.7	95.9	124.2	139	109.3	0.243
16K I	111.2	128.5	93.9	128.9	146.3	111.4	0.915
20K I	85.3	99.7	70.9	113.2	134	92.5	**0.049 ***
O_2	128.1	150.7	105.4	112.1	123.6	100.6	0.252
End	114	128.1	99.9	104.8	113.8	95.7	0.688
GAMMA							
0K A	5.5	6.4	4.6	5.6	6.7	4.4	0.953
25K A	1.5	1.9	1.2	1.6	2	1.2	0.494
Washout	11.9	13.8	10.1	11.0	13.0	9.1	0.4
00K I	12.6	14.7	10.5	11.5	13.5	9.4	0.42
08K I	13.1	14.9	11.3	11.2	13.3	9.1	0.192
12K I	13.2	15	11.3	11.1	13	9.3	0.241
16K I	11	13.1	9	10.6	12.5	8.7	0.194
20K I	7.1	8.5	5.7	9	11	7	**0.029 ***
O_2	13.5	15.9	11	17.3	26.1	8.5	0.559
End	12.4	14.7	10.1	16.7	24.7	8.7	0.977
ALPHA							
0K A	28.7	33.8	23.6	27.7	31.1	24.2	0.742
25K A	10.3	12	8.6	11.4	13.7	9.1	0.68
Washout	45.2	52.2	38.2	43.6	48.5	38.8	0.5
00K I	44.3	49.6	39.1	43.7	47.7	39.8	0.737
08K I	45.3	52	38.5	47	52.8	41.3	0.152
12K I	46.9	54.3	39.5	47	52.8	41.3	0.985
16K I	47.3	56.4	38.1	46.7	52.7	40.6	0.642
20K I	43.6	54.1	33	43.4	49.8	36.9	0.744
O_2	39.2	43.8	34.6	47.9	54.5	41.3	0.867
End	40.7	45.9	35.4	51.8	59.4	44.1	0.225
BETA							
0K A	57.6	63.1	52.1	57.5	64.2	50.8	0.992
25K A	16.5	18.9	14.2	17.3	20.7	13.8	0.497
W01-04	107.0	116.9	97.0	100.1	111.8	88.3	0.6
00K I	112.7	122.1	103.4	102.3	114.3	90.3	0.731
08K I	115.3	125.3	105.3	101.1	114.1	88.1	0.911
12K I	116.5	124.9	108.2	100.3	111.5	89.1	0.128
16K I	104	117.6	90.4	97.3	110.1	84.4	0.335
20K I	74.1	85.6	62.5	83	96.2	69.9	0.308
O_2	106	117.7	94.3	106.8	116.9	96.8	0.932
End	103.6	115.3	92	110.3	120.1	100.5	0.646

Note: Imputed 0.3% (56/21,840) missing data points using subgroup averages (men/women). Bolded and asterisked numbers represent a statistically significant difference in the EEG frequency comparison of men vs. women at the 20,000 normobaric altitude.

RESULTS

A total of 73 subjects volunteered for this project. There were 13 subjects who were excluded for incomplete S_pO_2 analysis or incomplete cognitive performance results, leaving the total $N = 60$ (30 women, 30 men). No subjects were excluded for incomplete brainwave acquisition. The population was homogenous with no significant differences in average age, body mass index (BMI), or flight hour history (**Table I**).

Table II shows the mean the S_pO_2 levels (and standard deviations) and heart rate (HR) across the acute, washout, and insidious phases of the study as described in the previous paper.[26] In this case, gender differences were examined. In the repeated measures ANOVA, Mauchly's test of sphericity had been violated, therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity and adjusted in the *F* statistic. The ANOVA showed a significant main effect for S_pO_2 [$F_{Greenhouse\text{-}Geisser}$ (3.01, 174.8) = 372.6, $P = 0.000$, partial eta squared = 0.87, large effect size]. However, the interaction with gender was not significant.

Table II also illustrates the effect of normobaric hypoxia on mean HR between genders. Mean HR comparisons from baseline and between genders were made by ANOVA, revealing a significant main effect for HR [$F_{Greenhouse\text{-}Geisser}$ (4.8, 278.2) = 151.1, $P = 0.000$, partial eta squared = 0.72, large effect size]. The interaction with gender was also significant [$F_{Greenhouse\text{-}Geisser}$ (4.8, 278.2) = 3.6, $P = 0.004$, partial eta squared = 0.06, medium effect size]. However, independent *t*-tests comparing men and women at each altitude level did not show significant gender differences at each level. The interaction reflected HR differences across the altitudes within each group.

Table III displays the mean frequency power and 95% confidence intervals about each mean for both genders at each EEG frequency across the study's altitude phases. The means are then illustrated in **Fig. 1**. Notice in Fig. 1, theta and gamma frequencies show a potential gender difference beginning in the washout phase through the insidious phase. Logistic regression analyses were used to identify gender differences at each frequency beginning in the washout phase (WO2) to the end of the study (END). These data were inputted as a set of predictor variables with gender as the dichotomous outcome variable with all variables entered simultaneously into the regression equation.

A series of Pearson correlations were conducted to identify which of the seven EEG recording channels were highly correlated between genders. That is, the frequency power data were collapsed across the entire study (acute, washout, insidious to end) to look at which of the seven channels were highly correlated between women and men at each of the EEG frequencies. **Table IV** shows the correlations. Note at the theta and gamma frequencies, not all channels significantly correlated between women and men. However, for the alpha and beta frequencies, all channels were significantly correlated between the genders.

A series of repeated measures ANOVAs were used to examine cognitive performance with the VSC test and flight performance with the X-Plane data. There were significant main effects in VSC performance across the altitude changes [Reaction Time $F_{Greenhouse\text{-}Geisser}$ (4.1, 235) = 12.98, $P < 0.000$; Accuracy $F_{Greenhouse\text{-}Geisser}$ (3.3, 193) = 7.89, $P < 0.000$; Throughput $F_{Huynh\text{-}Feldt}$ (5.1, 293.8) = 17.78, $P < 0.000$], but no significant interactions with gender (see **Table V**). X-Plane performance showed a significant main effect across the altitude changes [$F_{Greenhouse\text{-}Geisser}$ (3.8, 80.5) = 3.0, $P < 0.05$], but no significant interaction with gender (**Fig. 2**). Of note, although there were statistical differences during various normobaric hypoxic exposures between women and men, deviations of a few feet from assigned altitude is unlikely to be of operational significance.

With regards to time of awareness of hypoxia symptoms, we observed no significant difference in time to pull the green ring during acute and insidious

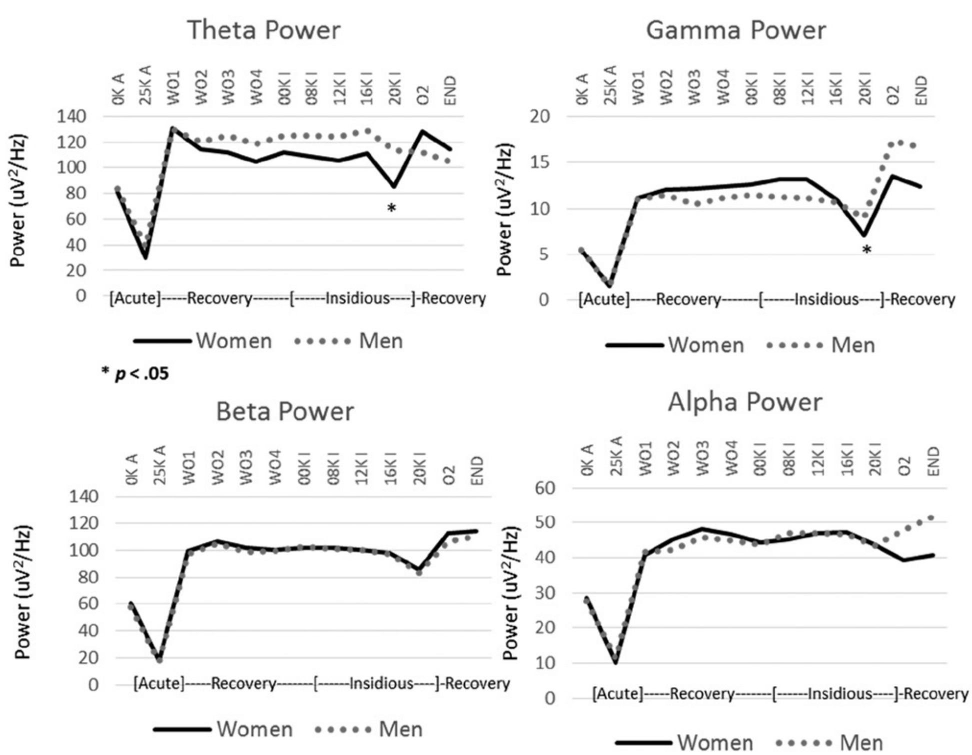

Fig. 1. Total brain wave frequency power between men and women with acute and insidious hypoxic exposures.

Table IV. Gender Correlations by Channel and by EEG Frequency Collapsed Across Altitude Phases (Acute, Washout, Insidious).

CHANNELS	THETA	GAMMA	ALPHA	BETA
F3	0.96**	0.59*	0.94**	0.95**
LE	0.87**	0.81**	0.89**	0.97**
F4	0.90**	0.33NS	0.94**	0.89**
C3	0.92**	0.87**	0.94**	0.97**
C4	0.83**	0.72**	0.90**	0.92**
P3	0.86**	0.96**	0.75**	0.97**
P4	0.46NS	0.92**	0.98**	0.96**

** Correlation is significant at the 0.01 level (2-tailed); *Correlation is significant at the 0.05 level (2-tailed); NSNot significant.

normobaric hypoxic exposure between men and women. The mean average time required for women to pull the green ring was 98 s (SD 38) vs. 109 s for men during acute hypoxia and the mean average of seconds to pull the green ring during the insidious hypoxic exposure being 1027 s for women vs. 1005 s for men (See **Fig. 3**). Regarding hypoxia symptomatology, a series of Chi-squared analyses were conducted of the symptoms reported. Women reported more numbness/tingling in the extremities than men during the acute (25K) phase of the study [χ^2 (1) = 4.6, P = 0.033, phi = 0.3, medium effect size] (**Fig. 4**). No differences were noted between men's and women's symptomatology during the insidious hypoxic exposures.

Table V. Cogscreen-HE Performance Results Between Women and Men at Simulated Altitude.

ALTITUDE	WOMEN MEAN	WOMEN SD	MEN MEAN	MEN SD	
REACTION TIME (ms)					
00K	1543.20	428.33	1527.76	323.88	Gender × RT
8K	1408.23	355.69	1433.82	272.30	P = 0.76
12K	1424.50	378.46	1469.72	282.19	
16K	1595.77	483.51	1615.55	384.42	
20K	1676.44	550.45	1679.14	420.27	
100% O_2	1503.10	431.63	1592.00	441.14	
END	1512.83	406.74	1532.72	376.50	
ACCURACY (% CORRECT)					
00K	97.47	2.96	97.43	2.90	Gender × ACC
8K	98.03	2.79	98.28	2.13	P = 0.30
12K	97.68	2.22	96.87	3.00	
16K	96.33	3.89	97.18	2.27	
20K	94.21	6.83	95.48	4.85	
100% O_2	97.14	3.95	97.38	3.01	
END	97.73	2.57	96.71	3.16	
THROUGHPUT (ACCURACY/RT)					
00K	40.62	10.55	40.06	8.82	Gender × Thru
8K	44.07	9.99	42.65	7.94	P = 0.74
12K	43.67	10.49	41.04	8.06	
16K	39.15	10.53	38.06	8.56	
20K	37.17	10.69	36.27	9.25	
100% O_2	41.64	10.60	39.18	9.31	
END	41.22	9.93	40.03	9.29	

DISCUSSION

To our knowledge this is the largest comparison of brainwave activity between genders with acute and insidious exposures to hypoxia and the first study to use dry-EEG technology as a means of monitoring this brainwave activity in this environment. The goal of this study was to determine if significant differences exist between women and men with regards to brainwave activity across various channel locations using dry-EEG technology when participants were exposed to simulated altitude. Additionally, we wanted to evaluate whether there were differences in cognitive performance and physiological responses with hypoxia between genders. Answers to both questions would ultimately be useful in developing a sensor which could potentially be used to identify hypoxia and cognitive decline during flight operations.

With regards to our first question, whether there are significant differences in brain wave activity during hypoxia between genders, we found no significant differences between men and women's brainwave activity with acute 25K exposure. Both genders' brainwave frequency power was significantly suppressed in all frequencies and all channels. Following this acute exposure, both genders significantly increased their frequency power in all frequencies and channels. As we progressed through the hypoxia washout period, significant differences between genders appeared in frequency power from their new baselines in the gamma and theta frequencies. These differences continued to manifest themselves as the participants were progressively exposed to greater simulated altitude and during the recovery period, where women demonstrated significantly lower frequency power in the theta and gamma frequencies at 20K. Of interest, Kober, when evaluating EEG power and coherence during a short-term memory task in middle-aged adults, also noted gamma and theta suppression in middle-aged women compared to their younger female counterparts, whereas middle-aged men did not show significant theta and gamma suppression compared to younger men.[12] Whether there are parallels in the response of brainwave activity to insidious hypoxia exposure and response of brainwave activity for normal aging women is potentially a topic for further investigation.

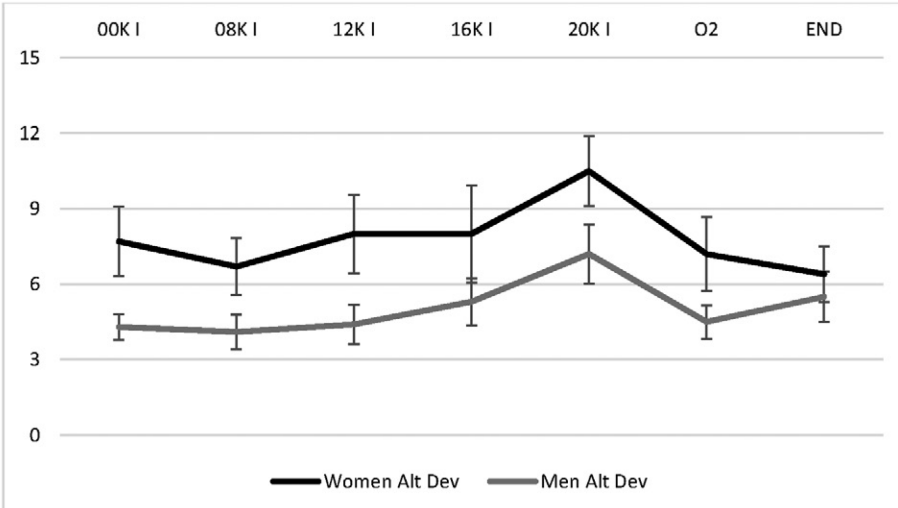

Fig. 2. X-Plane flight deviations in altitude (mean, SE) for women and men.

those involving fatigue, higher mental workload, or drowsiness that did not involve hypoxia, there is a different pattern of EEG frequency power change.

Beta and alpha frequencies did not show significant frequency power difference between genders and these frequencies correlated significantly across all channels between genders, with correlation coefficients over 0.89 in every channel except P3 (see Table IV). These very high correlations, particularly for the beta frequency, are important findings in that if we are to develop future sensors that are sensitive to cognitive decrements due to hypoxia, we must use frequencies that are most sensitive to hypoxia and further are most similar across genders.

With regards to our second question, whether there are significant differences in cognitive performance between genders when exposed to acute or insidious hypoxia, we found no significant difference in mean accuracy, reaction time, throughput, or aviation performance between genders with insidious hypoxic exposures to 20K. While there is some evidence that under normoxic conditions there are advantages in executive function and disadvantages in attentional tasks for post-ovulatory women,[32] the operational training tempo of our student population limited us from controlling for phases of the menstrual cycle. Attempts will be made in future studies to control for this previously observed pre/post ovulatory difference in cognitive performance between men and women. Another limitation in our methodology was that we did not obtain a 72-h sleep history of our subjects prior to them performing their cognitive performance exams under hypoxic conditions. Clearly if one gender averaged less sleep than the other, this may have impacted their performance with or without the additional environmental stressor of hypoxia.

More research has been performed regarding the physiological differences between men and women during hypoxic exercise. Most have found no difference in mean S_pO_2 declines and heart rate rise with acute hypoxia.[10,28,29] There have been conflicting reports on the ventilatory responses of men and women to acute hypoxia, with some studies describing no significant difference between genders,[23,33] and some literature describing significant increases in minute ventilation for men compared to women.[18] We did not measure respiratory parameters in this present study and this is a limitation of our current work; however, it would have been difficult to compare our findings to these prior reports as our exposures were different in altitude and duration. More recently, Morgagni observed 12 female pilots' responses to 25K and noted that the recognition of

Borghini, in a recent review of neurophysiological measures of aircraft pilots and car drivers for assessment of mental workload, fatigue, and drowsiness found increases in the theta band and decreases in the alpha band during higher workload states.[2] Additionally, they noted increases in the theta, delta, and alpha bands as signals between the transition of high workload states and fatigue or drowsiness. Higher workload states, fatigue, and drowsiness are cognitive conditions that often symptomatically overlap with hypoxia, yet we observed vastly different electro-physiological findings in our subjects, who were exposed to acute and insidious hypoxia. The suppression of brainwave frequency power we found in all frequencies and channels with acute severe hypoxia may be explained by a reduction in the substrate which neurons use to generate action potentials, oxygen. Under hypoxic conditions the brain may continue to use glucose, but will quickly be depleted of adenosine triphosphate (ATP) as a result of oxygen deprivation.[7] When the ATP supply eventually declines to levels insufficient to maintain the activity of the ion pumps, rapid and widespread membrane depolarization occurs, causing an extensive depression of synaptic transmission. Therefore, it is not surprising that, when comparing our findings to

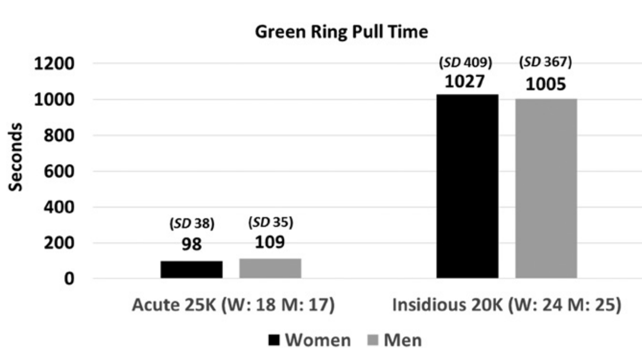

Fig. 3. Time (mean and SD) of green ring pulls to initial hypoxia symptoms at acute and insidious phases.

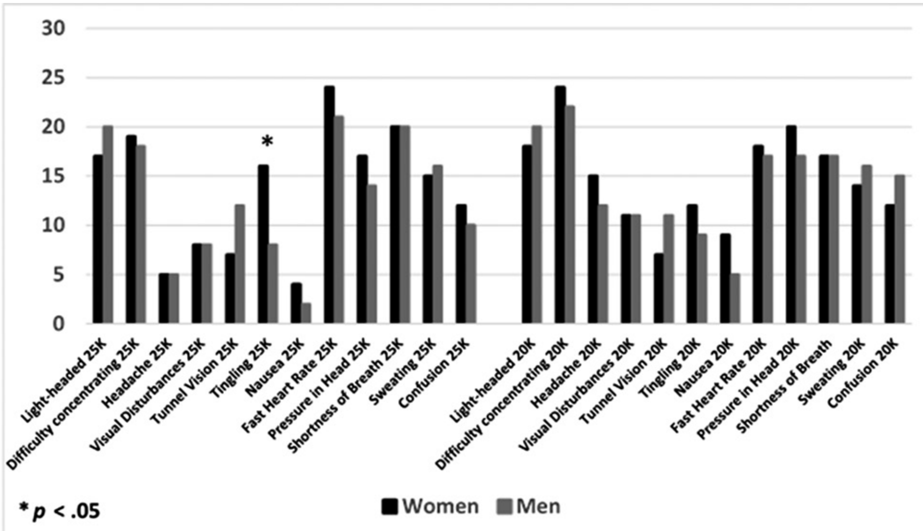

Fig. 4. Self-reported hypoxia symptomatology of women and men at acute and insidious phases.

their hypoxic symptoms was significantly quicker than men (2.4 min compared to 3.2 min for men).[19] Our study found no difference in average initial reports of hypoxia symptoms between men and women (see Fig. 2). Morgagni also observed significantly higher complaints of mental confusion for women and higher numbness/tingling for men. Conversely, we did not observe significant differences in any commonly reported symptoms for hypoxia with insidious hypoxic exposure and with acute 25K hypoxic exposures, we found only higher complaints of numbness/tingling for women ($N = 16/30$ women, 8/30 men; $P < 0.05$ two tailed). Although this finding reaches statistical significance, in our experience the subjective awareness of hypoxia symptoms is quite variable, and we are cautious as to whether this finding of increased numbness/tingling among women is of clinical significance.

Our data suggest that there are significant gender differences in dry-EEG frequency power for the frequencies of gamma and theta during insidious hypoxic exposures. Alpha and beta frequencies correlated greatest between genders during acute and insidious hypoxic exposures across all observed channels. We did not observe significant cognitive or physiological differences between genders with exposures to acute and insidious hypoxia. Dry-EEG technology has the potential to identify hypoxia prior to the subjective awareness in both genders. Future studies are underway to confirm these findings and evaluate this technology under other extreme conditions such as acceleration and fatigue.

ACKNOWLEDGMENTS

The authors would like to acknowledge the financial support of the U.S. Navy's Clinical Investigation Program and technical and human resource support from the Clinical Investigation Department, Naval Hospital Portsmouth, VA. Additionally, we appreciate the facility support from the Naval Survival Training Institute, Pensacola, FL, without which this research would not have been able to be accomplished. The authors' opinions do not necessarily reflect the views of the Department of Defense and we do not have any financial relationships to disclose.

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