

Normobaric Hypoxia Symptom Recognition in Three Training Sessions

Antti M. Leinonen; Nikke O. Varis; Hannu J. Kokki; Tuomo K. Leino

- INTRODUCTION:** Hypoxia training is mandatory for military pilots, but variability in hypoxia symptoms challenges the training. In a previous study we showed that 64% of pilots recognized hypoxia faster in their second normobaric hypoxia session conducted 2.4 yr after the first. Our aim here was to evaluate whether a third session conducted 5.0 yr after the first would provide further benefit.
- METHODS:** This study was conducted under normobaric conditions in a tactical F/A-18C Hornet simulator in three sessions in which the pilots performed visual identification missions and breathed 21% oxygen in nitrogen. The breathing gas was changed to a hypoxic mixture containing either 8%, 7%, or 6% oxygen in nitrogen without the pilot's knowledge. Data were collected from 102 military pilots. The primary outcome was the time taken for initial identification of hypoxia symptoms.
- RESULTS:** Hypoxia symptoms were recognized on average in the first session in 8% oxygen in 100 s, 7% oxygen in 90 s, and 6% oxygen in 78 s; in the second in 87 s, 80 s, and 71 s, respectively; and in the third in 79 s, 67 s, and 64 s, respectively. In 2 sessions 20 pilots and in each 3 training sessions 3 pilots had slow recognition times.
- DISCUSSION:** Hypoxia symptom recognition improved the further the repeated normobaric hypoxia training went. More emphasis should be put on the 23% group of slow hypoxia symptom recognizers and more customized hypoxia training for them should be offered.
- KEYWORDS:** military, simulation, aviation, symptoms of hypoxia, hypocapnia, normobaric hypoxia.

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High altitude military aviation predisposes to physiological events (PEs) in-flight. PEs occur when an aircrew experiences physiological symptoms which reduce flight performance.^{16,22,25} PEs can be related to insufficient oxygen (O₂)/hypoxia (e.g., due to cycling O₂ production from the On-Board Oxygen Generation System), hyper- and hypoventilation (provoked by mental stress or bulky flight gear), or depressurization (loss of cabin pressurization).^{7,14} The severity of symptoms can vary greatly, from mild dizziness to loss of consciousness and, in very rare cases, eventually death. However, even mild dizziness in a hazardous environment, such as a fighter jet in combat training, jeopardizes flight safety.

Physiological events may consist of several causes at the same time.⁹ For example, hypoxia promotes ventilation, which may lead to simultaneous hypoxia and hypocapnia.^{3,19} Connolly et al. state that for the UK Eurofighter fleet most PEs were due to hyperventilation rather than hypoxia.⁴

Hyperventilation-provoked hypocapnia causes vasoconstriction in the brain, which reduces the blood flow.^{1,17}

Hypoxia symptoms recognition training is a traditional training element in aviation medicine. Symptoms of hypoxia and symptoms of hyperventilation-induced hypocapnia are similar and overlap each other.² This is suspected to be related

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to hyperventilation and cardiovascular reflexes during hypoxia.²⁶ In general, hypoxia causes cognitive impairment and visual disturbance, but hyperventilation-induced hypocapnia causes dizziness and lightheadedness, both provoking ventilation and causing loss of consciousness.²⁰ However, the symptoms can vary among pilots and between training sessions.⁵ The most common symptoms experienced in hypoxia training are: lightheadedness, cognitive impairment, a warm sensation, dizziness, shortness of breath, and visual disturbance.^{8,10,24}

Although there is general agreement about the benefit of hypoxia recognition training, there remains uncertainty and controversy about the optimal methodology and periodicity of such training. The North Atlantic Treaty Organization Aeromedical Training of Flight Personnel requires hypoxia refresher training at least in a 5-yr cycle.¹⁵ Finland became a member of The North Atlantic Treaty Organization on 4 April 2023 and The Finnish Air Force (FINAF) has mandatory normobaric hypoxia training in a 3-yr cycle for F/A-18 Hornet pilots.

In a previous study, we showed that hypoxia recognition was shortened by 10–20 s (depending on the hypoxic gas mixture) in a second training session conducted a mean of 2.4 yr after the first.¹³ However, 36% of the pilots who did not recognize hypoxia faster are an urgent concern in normobaric hypoxia (NH) training. Hypoxia ventilatory response varies between individuals. In clinical observations, calm and slow ventilators have problems with hypoxia symptom recognition compared to those who hyperventilate due to the psychological workload and hypoxia.

The aim of this study was to assess the value of adding a third hypoxia training session (mean 2.6 yr later) in shortening the time to hypoxia symptoms recognition, with NH training conducted in a military flight simulator. The data collected in this third training session were compared with that collected in the previous two training sessions.

METHODS

Subjects

Data were available for 102 pilots (101 men and 1 woman). All subjects were healthy military pilots, ages between 25 and 35 yr, not on medication, and they were on active flight status in the FINAF and had passed an aeromedical evaluation in the aeromedical center (Helsinki, Finland) within the previous 12 mo. Total flight experience ranged between 400 and 2000 flight hours. These pilots were not hypoxia-naïve subjects, all pilots had also participated earlier in hypobaric chamber hypoxia training, but not previous NH training. The subjects had a hypoxia refresher briefing before the training. Each pilot had an individual briefing with the Flight Surgeon before the hypoxia refresher training, where individual hypoxia symptoms, as well as training documentation, were repeated. The study was approved by the Committee on Research Ethics of the University of Eastern Finland, Joensuu, Finland (no. 24/2018). The study had the institutional approval of the Defense Command Finland.

Equipment

A fixed-based tactical F/A-18C Hornet Weapons Tactics and Situational Awareness Training Systems flight simulator (Boeing Corporation, Chicago, IL, United States) was used with a field of view of 180°, including 100% instrumentation compared to a real cockpit. The pilots' flight gear consisted of a Joint Helmet Mounted Cueing System helmet (Collins Aerospace, Charlotte, NC, United States) with a mask (Gentex Corporation, Zeeland, MI, United States) and flight vest with a regulator as normally worn while flying a fighter aircraft. Resuscitation drugs and equipment were available in the simulator as they are mandatory during NH training.

We used five breathing gases with different concentrations of O₂ to provide differences in the hypoxia onset rate. The gases contained: 100% O₂ (emergency O₂), 21% O₂ (equal to sea level), and 8%, 7%, and 6% O₂ (hypoxic gas mixtures) in nitrogen (N₂). Gas cylinders were connected to the simulator via a gas selection box (Hypcom, Tampere, Finland) and allowed a Flight Surgeon to manually change the gas from normoxic to hypoxic and vice versa. The following concentrations of O₂ were used to induce hypoxia in a simulated high-altitude phase of flight under normobaric simulator conditions:

- 8% O₂ and 92% N₂ at 760 mmHg to simulate conditions at 20,341 ft (6200 m).
- 7% O₂ and 93% N₂ at 760 mmHg to simulate conditions at 22,966 ft (7000 m).
- 6% O₂ and 94% N₂ at 760 mmHg to simulate conditions at 25,919 ft (7900 m).

Before breathing the hypoxic gas mixtures, the subjects used the flight mask to breathe 21% O₂ in 79% N₂ at 760 mmHg.

Peripheral capillary oxygen saturation (S_pO₂) was measured from the forehead (Nonin Medical Inc., Plymouth, MN, United States) and wireless electrocardiograms were monitored by the Flight Surgeon to assure the safety of the training. S_pO₂, heart rate, and subjective symptoms were manually saved to a data sheet by an experienced flight nurse, and later from the data sheet to Excel for Mac (version 15.24, Microsoft Corporation, Albuquerque, NM, United States) and SPSS (IBM SPSS Statistics, version 27, International Business Machines Corporation, Armonk, NY, United States) spreadsheets. The training protocol was identical between training sessions.

Procedure

This is a retrospective analysis of pseudonymized data from mandatory NH training of Hornet pilots in the FINAF. Data for this study were collected from the pilots' first three career NH training sessions. In our previous article we have described the pilots' first two NH training sessions¹³ and, thus, this and the previous article include overlapping data for the first and the second training sessions. The hypoxia training was performed in Hornet squadron 11 (642 ft/196 m above mean sea level, Rovaniemi, Finland) and in Hornet squadron 31 (323 ft/98 m above mean sea level, Siilinjärvi, Finland) between November 2008 and December 2021. The training sessions were part of normal mandatory NH training in the FINAF, and the training

was held during working hours between 08:00 and 17:00. The duration of the training sessions was 50 min on average. The same methodology and training set-up remained constant throughout the study.

The subjects were performing a tactical identification flight mission in a flight simulator when a hypoxic gas was applied. The subjects were advised to abort the mission as soon as they recognized hypoxia symptoms (no system warnings, i.e., Master Caution or OBOGS DEGD light), and then execute hypoxia emergency procedures. The emergency procedures in hypoxia were: 1) a green ring pull, i.e., emergency O₂ (100%) on; 2) turn the oxygen flow knob off; 3) carry out an emergency descent at 20° nose-down attitude below a cabin altitude of 10,000 ft (3048 m); and 4) to send transponder code 7700 (emergency squawk). **Fig. 1** presents the experimental setup. The primary flight mission task was to visually identify unknown aircraft and actively fly, maintaining speed, altitude, and heading according to the fighter controller via radio. The subjects were told to treat all tasks as equally important (visual identification and hypoxia symptoms recognition).

Each training session was planned to include exposure to three hypoxic gas mixtures (set-ups). O₂ mixtures were given in a specific order in the training session. The first set-up was executed with a cylinder containing 8% O₂, the second with a 7% O₂ cylinder, and the third with a 6% O₂ cylinder. For the pilots' safety, the maximum exposure times of the set-ups were limited to 600 s for 8% O₂, 300 s for 7% O₂, and 180 s for 6% O₂. To avoid any negative consequences of training, the Flight Surgeon could abort or cancel the hypoxia set-up if necessary. An overly deep hypoxia exposure will not support the hypoxia training goals because of the risk that the pilot will not remember what happened during deep hypoxia. NH exposures may cause memory problems and more adverse effects which need to be considered after the simulator training.²⁴ Thus, not all pilots completed all three hypoxia exposures if limited by the Flight Surgeon.

Our primary outcome was the hypoxia symptom recognition time in each of the three hypoxia training sessions. For a secondary outcome, we evaluated the proportions of slow hypoxia recognizers, defined as those pilots who had recognition times longer than 1.5 times the median in the whole study sample.

Statistical Analysis

The data were entered in an Excel spreadsheet which was exported to an SPSS spreadsheet for statistical analyses. The distribution of continuous data was checked visually and the normal distribution assumption was checked using the Shapiro-Wilk test. As the recognition times were not normally distributed, differences in the recognition times and S_pO₂ values between three training sessions were analyzed with a related samples Friedman's two-way analysis of variance (the two factors were gas mixture used and training session number) and a related samples Wilcoxon signed rank test for pairwise comparisons. Proportions of slow recognizers were compared with a Chi-squared test. A Bonferroni correction was used to compensate multiple comparisons. Differences were regarded as statistically significant when the *P*-value was ≤ 0.05. The results are expressed as mean values with an SD and the median with a minimum and maximum, as appropriate.

RESULTS

Our study population included 102 FINAF pilots who had registered data for the first 3 career NH training sessions. In all training sessions, participants received one, two, or three hypoxic exposures (with 8%, 7%, and 6% O₂), based on the Flight Surgeon's evaluation and decisions during the training. A total of 748 hypoxic gas exposures were administered: in the first training session 300 gas exposures (with 8% O₂, *N* = 101; 7% O₂, *N* = 100; and 6% O₂, *N* = 99); in the second training

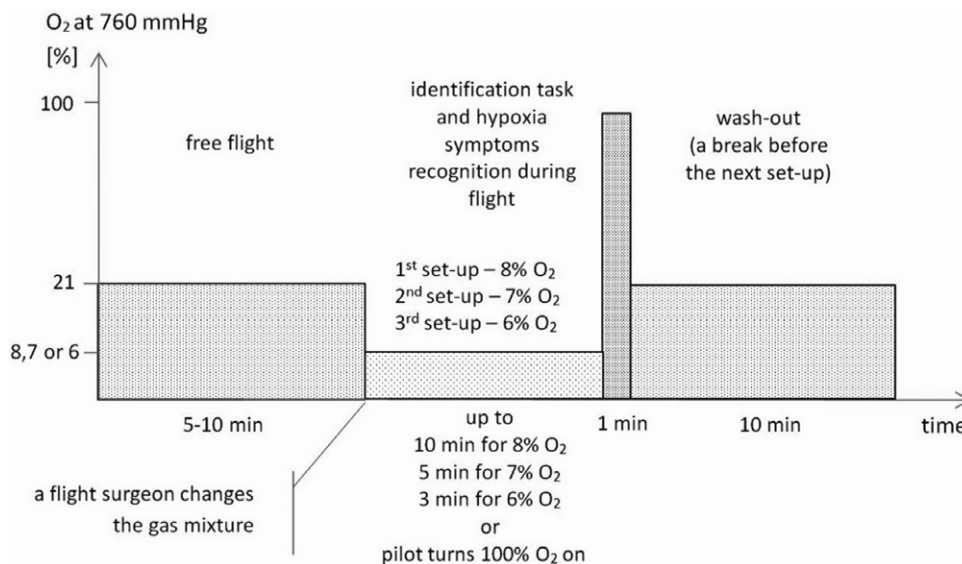


Fig. 1. Experimental setup description.

248 gas exposures ($N = 89$, $N = 71$, and $N = 88$); and in the third training 200 gas exposures ($N = 75$, $N = 41$, and $N = 84$), respectively. In seven cases the pilot reported symptoms before hypoxic gas exposure and in six cases the pilot did not recognize hypoxia during the safety limits of 600 s for 8% O₂, 300 s for 7% O₂, and 180 s for 6% O₂. These 13 exposures were excluded from further analysis.

The mean time between the first and the second training sessions was 2.1 (SD 1.4) yr, between the second and the third 3.0 (SD 1.2) yr, and between the first and the third training sessions it was 5.0 (SD 1.9) yr. The mean (SD) recognition times, S_pO₂, heart rate, and exposure data in the three NH training sessions are listed in **Table I**, and recognition times are in **Fig. 2**. The recognition times were significantly faster the further the repeated NH training progressed ($P = 0.005$, Friedman test, df 2, test statistic 10.686). Compared to the first training session, where the median recognition time was 80 (interquartile range 56) s, recognition time was shorter in the second [median 78 (41) s, $z = -3.686$, $P < 0.001$, Wilcoxon signed rank test] and third [64 (36) s, $z = -3.820$, $P < 0.001$] training sessions, respectively. The difference between the second and third training session was also significant ($z = -2.443$, $P = 0.045$). In all training sessions the 8% O₂ mix was recognized as the slowest and the 6% O₂ mix was recognized as the fastest. The mean S_pO₂ also stayed the highest with the 8% O₂ mixture and the lowest with the 6% O₂ mixture.

We also evaluated the proportion of pilots who recognized hypoxia symptoms faster, similar, and more slowly in the repeated training sessions. Less than a 5-s difference in recognition time was classified as a similar recognition time. In the second training session pilots recognized the hypoxia symptoms in 79 out of 144 set-ups (55%) faster, in 44 set-ups (31%) more slowly, and in 21 set-ups (15%) the recognition time was similar compared to that in the first training session. In the third training session, in 73 out of 135 set-ups (54%), the recognition time was faster, in 42 set-ups (31%) it was slower, and in 20 set-ups (15%) it was similar compared to the first training session. Comparing the third and the second training session, in 49 out of 90 set-ups (54%) the recognition time was faster, in 29 set-ups (32%) it was slower, and in 12 set-ups (13%) it was similar.

The median recognition time in the whole study population was 80 s for 8% O₂, 74 s for 7% O₂, and 65 s for 6% O₂, and thus the cutoff values for slow recognizers were 120 s, 111 s, and 98 s, respectively. Based on these definitions, 54 pilots had at least one slow recognition time, most of them ($N = 31$) just in one training session, but 20 pilots had slow recognition times in two sessions, and 3 pilots in each of the 3 training sessions. In the first training session 46 pilots had at least 1 slow recognition time, in the second session 21 pilots, and in the third session 13 pilots had at least 1 slow recognition time ($P < 0.001$, df 2, Pearson Chi-squared value 30.092). The median (minimum, maximum) S_pO₂ values at recognition were substantially lower in slow recognizers compared to others, with 8% O₂ at 74% (63%, 89%) vs. 80% (65%, 93%), with 7% O₂ at 68% (56%, 79%) vs. 77% (61%, 92%), and with 6% O₂ at 67% (57%, 80%) vs. 76% (59%, 92%), respectively.

Table I. Heart Rate and Peripheral Capillary Oxygen Saturation (S_pO₂) Values Before Normobaric Hypoxia Exposure, at the Moment of Recognition of Hypoxia, and During Hypoxia Emergency Procedures.

HYPOXIC GAS	TRAINING SESSION	BEFORE NH			AT RECOGNITION			DURING HYPOXIA EMERGENCY PROCEDURES		
		HEART RATE (bpm)	S _p O ₂ (%)	HEART RATE (bpm)	S _p O ₂ (%)	HEART RATE (bpm)	S _p O ₂ (%)	HEART RATE (bpm)	S _p O ₂ (%)	EXPOSURE TIME (s)
8%	First	93 (15)	97 (2)	109 (18)	78 (6)	116 (15)	68 (7)	116 (15)	68 (7)	274 (106)
	Second	94 (15)	98 (2)	104 (15)	79 (6)	112 (19)	72 (7)	112 (19)	72 (7)	173 (89)
	Third	91 (16)	98 (1)	103 (16)	80 (5)	107 (18)	74 (6)	107 (18)	74 (6)	140 (65)
7%	First	89 (14)	97 (2)	105 (19)	74 (7)	115 (15)	66 (6)	115 (15)	66 (6)	201 (62)
	Second	91 (15)	98 (2)	99 (13)	77 (7)	112 (16)	70 (7)	112 (16)	70 (7)	149 (72)
	Third	91 (14)	98 (2)	102 (16)	78 (6)	107 (15)	71 (7)	107 (15)	71 (7)	111 (48)
6%	First	88 (15)	98 (2)	104 (12)	73 (8)	108 (15)	68 (7)	108 (15)	68 (7)	106 (42)
	Second	88 (13)	97 (2)	101 (14)	74 (7)	106 (14)	71 (7)	106 (14)	71 (7)	84 (33)
	Third	86 (14)	98 (2)	99 (13)	77 (8)	105 (15)	72 (8)	105 (15)	72 (8)	83 (34)

Data are mean (SD). NH: Normobaric hypoxia.

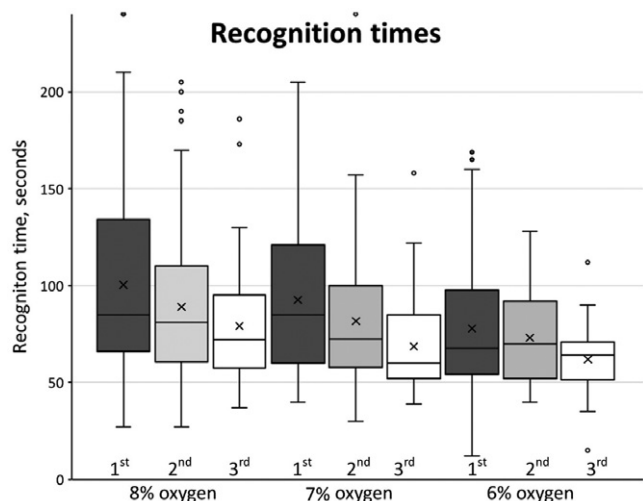


Fig. 2. Box and plot presentation of recognition times in the three normobaric hypoxia training sessions with the three gas mixtures: 8% oxygen, 7% oxygen, and 6% oxygen. Data are minimum, lower quartile, median; mean (x), upper quartile, maximum, and outliers (o). *P < 0.05.

Hypoxia symptoms reported by the pilots are listed in **Table II**. The distribution of symptoms was similar in the slow recognizers and in others. Symptoms reported were not associated with the severity of hypoxia or S_pO_2 values at recognition.

DISCUSSION

Normobaric hypoxia training in a tactical fighter simulator is engineered to teach pilots to recognize symptoms of hypoxia. In our set-ups, the pilots were on an active flight mission where there were constantly changing visual and sound stimuli to hamper hypoxia recognition, i.e., the pilots were not only waiting for hypoxia to occur.

Our data shows that NH training significantly lowers hypoxia recognition time in a tactical fighter simulator. In the present study comparing three training sessions, we found that 69% of the subjects recognized hypoxia symptoms faster or similarly in the third training session compared to the first training session, and in the third session in 68% of cases faster or similarly than in the second session. Additionally, the between-subject variability was substantially less in the third training session compared to the first and the second session, supporting the training effect. Furthermore, there was an observed training effect related to the severity of hypoxia at recognition. With the most severe hypoxia (6% O_2), there was no observed difference in hypoxia recognition times compared to the second and third training sessions, while with the 7% and 8% hypoxic mixtures, hypoxia recognition improved with training for most pilots.

However, 23% of our pilots were slow recognizers in two or three training sessions and they did not show that much improvement with repeated refresher training. In the present study there were even a few slow recognition pilots whose recognition time further slowed from the first to the second session and from the second to the third NH training session. These pilots are a concern in aviation. We assume that they may benefit from more personalized hypoxia training. Possibly, more frequent training (including NH and/or hypoxic hypoxia training), enhanced briefing, and different protocols with carbon dioxide (CO_2) enriched gas mixtures could be used in these cases. This should be evaluated in future studies.

A Flight Surgeon observed that pilots with calm and slow ventilation experienced fewer symptoms because of the lack of hyperventilation-related hypocapnic symptoms. Such pilots may benefit from enhanced briefing. A slow head-up display cross-check may be the only symptom they develop during NH.

Table II. Symptoms Reported During Normobaric Hypoxia Training.

SYMPTOM	ALL TRAINING SET-UPS (N = 748)		SLOW RECOGNIZERS' TRAINING SET-UPS (N = 102)		NONSLOW RECOGNIZERS' TRAINING SET-UPS (N = 646)	
	N	%	N	%	N	%
Warm sensation	259	37%	39	38%	220	34%
Tingling in skin	207	28%	37	36%	170	26%
Cognition impairment	207	28%	30	29%	177	27%
Dizziness	176	24%	28	27%	147	23%
Visual disturbances	169	23%	19	19%	150	23%
Lightheadedness	164	22%	22	22%	142	22%
Difficulty in breathing	157	21%	22	22%	135	21%
Feeling of pressure	115	15%	16	16%	98	15%
Anxiety	48	6%	5	5%	43	7%
Nausea	20	3%	2	2%	18	3%
Odd taste	13	2%	0	0%	13	2%
Palpitation	11	1%	3	3%	8	1%
Air hunger	10	1%	2	2%	7	1%
Muscle twitching	2	0.3%	2	2%	0	0%
Headache	1	0.1%	0	0%	1	0.2%
Odd smell	1	0.1%	0	0%	1	0.2%
Sensation of vibration	1	0.1%	0	0%	1	0.2%
Tiredness	1	0.1%	0	0%	1	0.2%
Symptoms in total, N	1559		227		1332	

Data are number of cases and percentage.

One way to organize customized hypoxia training is to use hyperventilation-provoking gas, e.g., a hypoxic mixture with 4% CO₂. Breathing CO₂ during hypoxia will provoke ventilation, and, as a physiological response, mitigate cognitive impairment and reduce cerebrovascular vasoconstriction.⁶ We have named this physiological events (PEs) training. In PEs training, pilots' ventilation increases more than in normal NH training and, thus, control of hyperventilation is one training goal.¹² We have recently validated this PEs training method with a 6% O₂ + 4% CO₂ gas mixture and, as hypothesized, ventilation was provoked during the exposure. Hyperventilation-provoking training gas may help pilots to recognize increased minute ventilation and allow them to control the ventilation.¹² Currently, there are no emergency procedures for hyperventilation.

In the first NH training session pilots were permitted to experience their severe hypoxia symptoms more explicitly after the hypoxia symptom recognition, which explains the long duration between recognition time and exposure time in the earlier training. In the two later sessions the pilots might have better recognized hypoxia from the first sensations, and they were instructed to commence corrective action as soon as hypoxia symptoms occurred. Recognition may also be enhanced by experiencing similar symptoms to those experienced in the previous training sessions, getting better at flying, and that the stress provoked by NH training is minimized in refresher training. Military pilots should understand the importance of aborting a flight mission if PEs are recognized in flight while time of useful consciousness is still available and that emergency procedures are carried out with a good safety margin. Greater safety margins are created by arranging hypoxia training and gaining more knowledge on hypoxia symptoms. PEs analysis is done after landing, combining flight data, aircraft data, pilot symptoms, and, e.g., data from the Insta Pilot's Breath Air Monitor (Insta Group Oy, Tampere, Finland).¹¹ In the future pilot physiological data could be added to this in-flight analysis.

It has been shown that pilots who have exposure to hypoxia are more likely to recognize the symptoms on subsequent exposures. Smith theorizes that this "hypoxia signature" remains for 3 to 5 yr after hypoxia training,²¹ and others have proposed that at least the most prominent symptoms remain constant for at least 4 to 5 yr for certain hypoxic exposures.^{8,23,27} However, it seems it might not be that easy for some pilots to become familiar with hypoxia symptoms. Recent study provided compelling evidence against the existence of hypoxia signatures.⁵ If hypoxia symptoms are missing, the symptoms of hypoxia might be difficult to notice.

Rice *et al.* showed that nearly half (42%) of student aviators were not able to recognize any hypoxia symptoms during their very first NH simulator training.¹⁸ This is one reason why it is recommended to have hypoxia training regularly, at least on a triannual basis. Nowadays, FINAF's student pilots receive all three hypoxic gases during initial training (8%, 7%, and 6% O₂) in a Hawk simulator to gain more knowledge of hypoxia symptoms before F/A-18 Hornet flight training.

There are limitations to the present study. First, this study is a retrospective analysis, the order of applied gas mixtures was

not randomized, and the pilots all knew that they were going to experience hypoxia during these events, and so were able to anticipate it, leading to a risk of a systematic and an order effect bias. However, our methods and personnel in hypoxia training have remained constant throughout the study years. Second, we did not include the pilots' smoking/nicotine product habits or ask how well they had slept for the last couple of nights before the training session, and their alcohol and supplement usages were not surveyed, which may influence hypoxia tolerance. However, in the FINAF, military pilots annually undergo a Flight Surgeon examination and are healthy.

In conclusion, this study shows that, for the majority of fighter pilots, repeated NH training three times within 5 yr enhanced hypoxia symptom recognition in a tactical F/A-18 Hornet simulator. However, 23% of the pilots recognized their hypoxia symptoms relatively slowly in repeated training sessions. More emphasis should be put on this group of pilots, who should be offered more customized hypoxia training to increase flight safety.

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