

Nikke Varis

**HYPOKSIA HANGOVER – LENTOKYKY
NORMOBAARISEN HYPOKSIA-ALTISTUKSEN
JÄLKEEN HAWK-SIMULAATTORISSA**

Lääketieteen ja terveysteknologian tiedekunta
Syventävät opinnot
Tammikuu 2020

TIIVISTELMÄ

Nikke Varis - Hypoksia Hangover
Syventävät opinnot
Tampereen yliopisto
Lääketieteen lisensiaatti
Tammikuu 2020

Johdanto: Hapenpuutteesta johtuvien onnettomuuksien määrä on ollut nousussa sotilasilmailussa. Tapaukset ovat johtuneet pääosin ongelmista happilaittejärjestelmissä tai paineistuksessa. Normobaarista hypoksiakoulutusta on järjestetty lentosimulaattorissa Ilmavoimien toimesta vuodesta 2008 lähtien. Koulutus auttaa lentäjiä tunnistamaan yksilölliset hapenpuuteoireensa sekä kertaamaan hätätoimenpiteitä realistisessa ohjaamossa.

Metodit: Tutkittavat (n=16) suorittivat Hawk-simulaattorissa kolme lentotehtävää hypoksia-altistuksella sekä paluulennon takaisin kentälle. Kesken lentotehtävän hengitysilma vaihdettiin lentäjien tietämättä vähähappiseen seokseen ja heidän tehtävänä oli tunnistaa hypoksiaoireet. Ensimmäisessä altistuksessa käytettiin 8 % happiseosta, toisessa 7 % ja kolmannessa 6 %. Paluulennon aikana lennonopettaja arvioi tutkittavien lentokykyä asteikolla 1-5 arvioidakseen hapenpuutteen vaikutuksen. Lentäjät suorittivat lisäksi kontrollilennon samoilla tehtävillä ilman hypoksia-altistusta.

Tulokset: Lentokyky heikkeni hypoksia-altistuksen jälkeen merkittävästi 4,81:stä 3,63:een. Osa lentäjistä raportoi väsymystä, päänsärkyä, muistiongelmia sekä kognitiivista heikentymistä jopa 12 tuntia altistuksen jälkeen.

Pohdinta: Hypoksialla on heikentävä vaikutus lentokykyyn paluulennon aikana, vaikka tunnistaessa oireet vaihdettaisiin 100 % happiseos päälle. Hypoksiakoulutus tarjoaa lentäjille mahdollisuuden tunnistaa ”hypoksia hangover” vaikutuksen lentokykyihinsä.

Sisällys

1. Title page	
2. Abstracts	
3. Introduction	p. 1
4. Methods	p. 3
5. Results	p. 6
6. Discussion	p. 9
7. Acknowledgements	p. 11
8. References	p. 12

Hypoxia Hangover and Flight Performance after Normobaric Hypoxia Exposure in a Hawk Simulator

Nikke Varis (B.M.)*, Kai Parkkola (M.D., Ph.D.)*,***, and Tuomo K. Leino (M.D., Ph.D.)**,***

* Faculty of Medicine and Health Technology, Tampere University, Finland

**Aeromedical Centre, Centre for Military Medicine, Helsinki, Finland

***National Defence University, Helsinki, Finland

Short title:

Hypoxia Hangover

Name and address of the author:

Nikke Varis
nikke.v@hotmail.com
Soukanlahdenkatu 19 A28
33100 Tampere
Finland

Manuscript metrics:

Abstract: 249
Main text: 2636
References: 16
Tables: 2
Figures: 3

Abstract

INTRODUCTION: The incidence of hypoxia-like symptoms in military aviators is on the rise. Cases can be related to On-Board Oxygen Generating System (OBOGS) malfunction, air contamination, loss of cabin pressurization, hyperventilation, or a combination of these issues simultaneously. Normobaric hypoxia training in tactical fighter simulations has been conducted in the Finnish Air Force since 2008. This training helps aviators to recognize their individual hypoxia symptoms and refreshes hypoxia emergency procedures in a realistic cockpit.

METHODS: A flight mission included three set-ups and a return to base (RTB) after the third set-up. In tactical Hawk simulator different concentrations of oxygen were used (8%, 7%, and 6% oxygen in nitrogen) to create normobaric hypoxia exposures. During the RTB, the flight instructor evaluated the subjects' flight performance (n=16) in order to estimate cognitive functions after hypoxia. A control flight was evaluated before or after the flight with normobaric hypoxia exposure.

RESULTS: Instrumental flight rule performance during RTB decreased significantly from 4.81 to 3.63 after normobaric hypoxia and emergency procedures. Some pilots reported fatigue, headache, memory problems, and cognitive impairment as adverse effects up to 12 hours after normobaric hypoxia training.

DISCUSSION: Hypoxia has a significant effect on flight performance during RTB, even 10 minutes after hypoxia emergency procedures. Since 100% oxygen was used as emergency oxygen, as in a real aircraft, the oxygen paradox may decrease flight performance. Hypoxia training in tactical fighter simulations provides an opportunity for pilots to also understand the effects of the "hypoxia hangover" on their flight performance.

Keywords: hypoxia training, normobaric, flight performance, SpO₂

Introduction

Lack of oxygen is one of the most serious incidents that a military pilot can face during a high-altitude flight mission. Hypoxia – defined as the condition in which the body's tissues are deprived of adequate oxygen supply – impairs cognition, working memory, and vision, and can ultimately result in death. An increasing number of hypoxia-like symptoms (i.e. physiological episodes) have occurred in military aviation, which may be related to On-Board Oxygen Generating System (OBOGS) malfunction, air contamination (e.g. CO intoxication), hyperventilation, or loss of cabin pressurization.⁹ Furthermore, a combination of these factors is common. For example, hypoxia and hyperventilation may occur simultaneously.

Incidence of physiological episodes is 45 / 100 000 flight hours in the Finnish Air Force. It is similar in other nations using Hornet and Goshawk. E.g. Naval Safety Center reported 115 physiological episodes during the flight year 2015 in the US Navy.⁹ There has also been reported a steady upward trend in the number of physiological episodes from the year 2010 (12 / 100 000 F/A-18AD flight hours) to 2017 (over 101 / 100 000 flight hours) regarding to the US Navy.¹¹

Hypoxia training is a mandatory part of military pilots' aeromedical training across the world. An increasing amount of hypoxia training is conducted using normobaric hypoxia devices instead of hypobaric chambers. The reason for this is the removal of the risk of decompression sickness and white matter brain lesions.¹³ Hypoxia training helps pilots to recognize their individual hypoxia symptoms.⁴ The most commonly reported symptoms are lightheadedness, dizziness, tingling, mental confusion, and visual impairment.¹⁶ Normobaric hypoxia training is seldom conducted in tactical flight simulators, even though it has been recognized to be more realistic and effective than traditional training.¹ Tactical flight simulation enables decision-making training, the implementation of the actual emergency procedures, and the continuation of the hypoxia-training mission all the way to landing.

Auditory and mathematical processing have been found to be particularly vulnerable to severe hypoxia while operating a multitask workstation at hypobaric chamber altitudes of 18,000 ft and 25,000 ft (5,486 m and 7,620 m). Findings have suggested that care should be taken when trusting purely auditory hypoxia warning alerts.²

Normobaric hypoxia has been hypothesized to have an adverse effect on the central executive memory.⁵ Furthermore, acute hypobaric hypoxia has been found to impair cognition, especially the executive functions responsible for conflict resolution.¹⁴ In prior research, using a Cessna 172 flight simulator, hypoxia has been noticed to degrade the pilot's precision of altitude and airspeed.¹⁵

Reaction time values and regional cerebral oxygen saturation have been observed to return to the baseline level only 24 hours after hypoxic exposure.¹⁰ Subjects performing simple and choice reaction time tests had significantly increased total response times due to hypoxia, and mild deterioration may occur as low as 10,000 ft (3,048 m). Hyperoxia has not been found to show any positive effects.³

During real in-flight hypoxia emergency procedures (EPs), 100% oxygen is always used, and 100% oxygen breathing following normobaric hypoxia exposure has been noted to induce slowing in the EEG, which is associated with a deterioration of working memory compared to normal air breathing after hypoxia.⁷

It should be noted that the OBOGS is the most common bleed air pressure-sensitive subsystem of the environmental conditioning system in fighter aircraft. Thus, reported cabin pressure fluctuations can have an effect on the partial pressure of oxygen in the fighter cockpit.⁶

In this study, we evaluated flight performance during return to base (RTB) following a hypoxia incident treated with 100% oxygen in a military flight simulator. The aim of this study was to analyze how hypoxia with emergency procedures affects the pilot's flight performance 10 min after hypoxic exposure.

Methods

Subjects

The study was performed in Fighter Squadron 41 (Tikkakoski, Finland). The study protocol followed the tenets of the Declaration of Helsinki, and it was approved by the Defence Command Finland and the Ethics Committee of Tampere University Hospital. Sixteen qualified Hawk pilots on active flight status participated in this study on a voluntary basis. The study group consisted of male subjects only, because no female pilots reported for hypoxia training during the study. Informed consent was given by each subject before the study. In terms of experience, the subjects had 160–2,100 flight hours in a Hawk, and all had completed hypoxia training in a hypobaric chamber. The subjects had received earlier theoretical training on the subjective and objective signs of hypoxia, and they also had a hypoxia re-brief before the mission. The pilots were seated in a tactical Hawk MK51A MLU simulator cockpit, which is 100% identical to a real cockpit.

Equipment

A tactical Hawk Mk51A MLU flight simulator with full military flight gear, including helmet and oxygen mask, were used in this study. The flight instructors had audio-visual access to the subjects via cameras, flight monitors, and front sector screens. A hypoxia gas selection box was connected to the simulator. In each set-up, different concentrations of oxygen were used: 8% O₂ (equal to a physiological altitude of 6 200 meters), 7% O₂ (equal to a physiological altitude of 7 000 meters), and 6% O₂ (equal to a physiological altitude of 7 900 meters). Maximum exposure times for 8% O₂, 7% O₂ and 6% O₂ were 10 min, 5 min and 3 min, respectively. Arterial oxygen saturation (S_pO₂) measured by pulse oximetry from forehead and a wireless electrocardiogram (ECG) were monitored continuously during the experiment by a flight surgeon. S_pO₂ was manually saved to data sheet by flight nurse.

Design

The study design was counterbalanced by the incoming subjects. To eliminate the first-time effect, half the subjects had the control flight mission in simulator prior to the hypoxia experiment, and the other half had the control flight mission at least one day after the hypoxia experiment. The evaluation was based on the standardized Finnish Air Force (FINAF) grading system for flight performance found in the FINAF Hawk Standard Operations Manual. Similar flight performance

grading is also used in civil aviation by TRIs (type rating instructor). The maximum performance score is 5 and minimum performance score is 1.⁸

The flight performance evaluations were done by two experienced flight instructors (Patria Pilot Training, Finland), who were not blinded for the gas mixture used during the simulated flight. The evaluation consisted of two categories: situational awareness and instrumental flight rule (IFR) performance during the RTB.

Procedure

The procedure was part of normal hypoxia training in the FINAF, which must include three hypoxia set-ups. Thus, the subjects were briefed to perform three set-ups for the line-oriented flight training scenarios. After take-off, the first two set-ups included tactical maneuvering at high altitude, starting at 25,000 ft. At the beginning of each set-up, subjects were given pressurized air, but at some point without the subjects' knowledge, this was changed to 8% or 7% oxygen in nitrogen (in the first two set-ups). The subjects continued the mission until they recognized hypoxia symptoms without system warnings (no MASTER CAUTION or OXY warning). Emergency procedures (EPs) with 100% oxygen were performed and the set-ups ended at low altitude after emergency descent.

The EPs considered in oxygen failure are: 1) Left hand immediately to emergency oxygen handle (PULL); 2) Oxygen main valve – OFF; 3) Emergency descent – EXECUTE; 4) Transponder code 7700 for emergency.

The third set-up consisted of breathing 6% oxygen for 100 seconds; the EPs, including 100% oxygen; and RTB. Three minutes after EP execution, the emptying of the emergency oxygen bottle was simulated by closing the breathing valve. After this, subjects had to open the breathing tube on the flight vest to breathe normally. Mask-open flying is not permitted in the FINAF. No radar vectors were given to the subjects, so a procedural IFR approach including ARC flying was performed. Subjects were informed about bad weather, including cumulonimbus clouds and lightning, which had to be taken into account on execution of the RTB. The subjects were required to calculate new fuel minimum calculations (BINGO) for an alternative airfield according to the new situation. The mission ended with an instrument landing system (ILS Z 30) approach to Jyväskylä (EFJY) with a minimum runway visual range of 700 meters. The flight time was approximately 40 minutes.

Ten-minute intervals between set-ups were used, and during the wash-out period, the flight simulation was frozen at a minimum sector altitude of 880 meters above mean sea level.

Statistical Analysis

Data analysis was performed using SPSS (IBM SPSS Statistics 25). Flying performance was graded on a non-linear scale of 1 to 5, with 1 being the worst and 5 being the best result, as in check flights in the FINAF (Table I). The association between hypoxia and flight performance was calculated using a Wilcoxon test. Data are presented as the mean \pm the Standard Error of the Mean (SEM). The correlations between experienced flight hours, recognition of symptoms and flight performance during hypoxic RTB were evaluated using Spearman's rank correlation coefficients. A p -value below 0.05 was deemed to be statistically significant.

Table I. Flight performance grading. (In ILS approach scale deviation of one dot is marked with X.)

5	The pilot was able to complete the given task without mistakes or external help, analyze his/her performance, and maintain the level of learned skills. ILS approach: heading within $\pm 0,25X$, glide slope $\pm 0,25X$ and AOA (angle of attack) at DA (decision altitude) 4-5.
4	The pilot was able to complete the given task, with minor mistakes. The pilot was able to analyze his/her performance, fix possible mistakes, and improve the level of his/her performance during the flight. ILS approach: heading within $\pm 0,5X$, glide slope $\pm 0,5X$ and AOA at DA 3.5-5.5.
3	The pilot was able to complete the given task, with minor mistakes. The pilot needed some amount of verbal support from the instructor (correcting mistakes and correct technique) to analyze and fix his/her performance. The pilot is able to complete the task safely during a solo flight. ILS approach: heading within $\pm 0,75X$, glide slope $\pm 0,75X$ and AOA at DA 3-6.
2	The pilot was able to complete the given task with active verbal support from the instructor, thus avoiding major mistakes. Further practice is needed, but the pilot can perform the task during a solo flight. ILS approach: heading within $< 1X$, glide slope $< 1X$ and AOA at DA 2-7.
1	The pilot was not able to complete the given task alone and needed active verbal and/or physical assistance from the instructor to avoid major mistakes. Further practice is needed in order to perform the task safely during a solo flight. ILS approach: heading within $> 1X$, glide slope $> 1X$ and AOA at DA $< 2, > 7$.

Results

In the first set-up, the mean duration of 8% O₂ (slow hypoxia onset rate) was 123 seconds (SEM 22.462, range 55–416) before the participants noticed hypoxia symptoms. At that point, the mean SaO₂ was 77% (SEM 1.611, range 66–89%). During the second set-up with 7% O₂ (moderate hypoxia onset rate), the mean duration was 92 seconds (SEM 10.105, range 53–184), and the mean SaO₂ was 74% (SEM 1.641, range 62–86%).

During the third set-up with 6% O₂ (fast hypoxia onset rate), the subjects recognized hypoxia symptoms at a mean duration of 69 seconds (SEM 9.908, range 33–160), and the mean SaO₂ was 77% (SEM 1.550, range 66–88%). The set-up was purposely continued to moderate hypoxia. Therefore, the exposure ended with a mean duration of 115 seconds (SEM 6.570, range 85–186) and a mean SaO₂ of 68% (SEM 1.298, range 61–79%).

There was no correlation (0.039) between flight hours and flight performance during RTB, meaning that experienced Hawk pilots (more than 200 Hawk hours, 7/16) were affected similarly by hypoxia. Between flight hours and time of recognition there was a statistically significant correlation (0.542, $p=0.030$) in the first set-up (8 %), meaning that the unexperienced pilots recognized and reacted faster to hypoxic symptoms, but this was not found in the second (0.041) or third (0.147) set-ups. The group of pilots with less experience (9/16) had had hypobaric hypoxia training 18 months before this experiment, which could explain this result.

There was some correlation (-0.230) between recognizing the symptoms in the third set-up and flight performance during RTB, meaning that the longer it took for subjects to recognize the symptoms the worse their flight performance was.

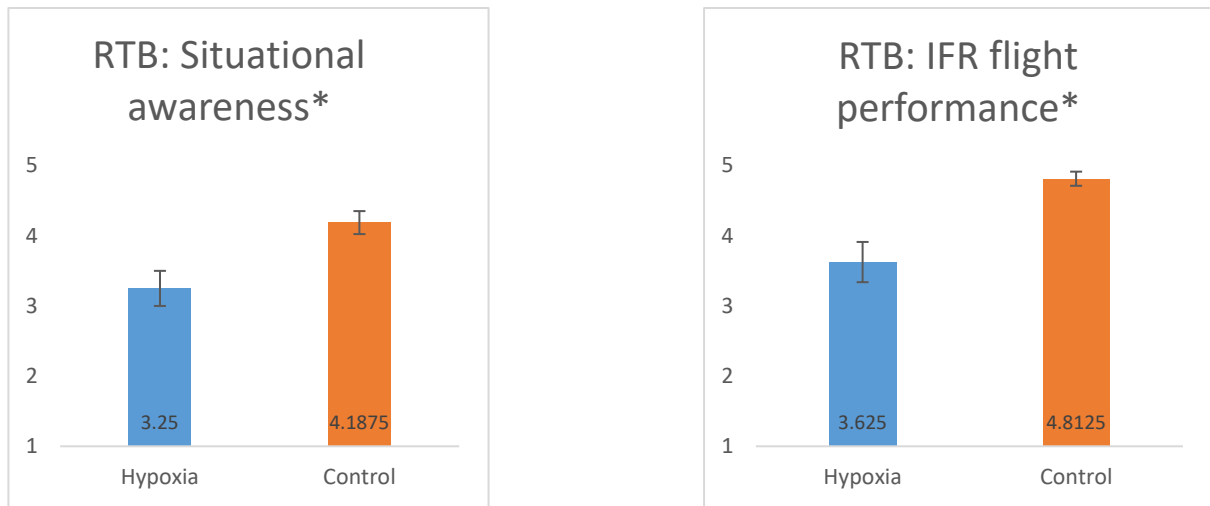


Figure 1. Mean values of flight sub-performances for hypoxic and control flights during RTB (n=16). Error bars represent standard error of the mean. *Statistically significant difference (p=0.014, p=0.005).

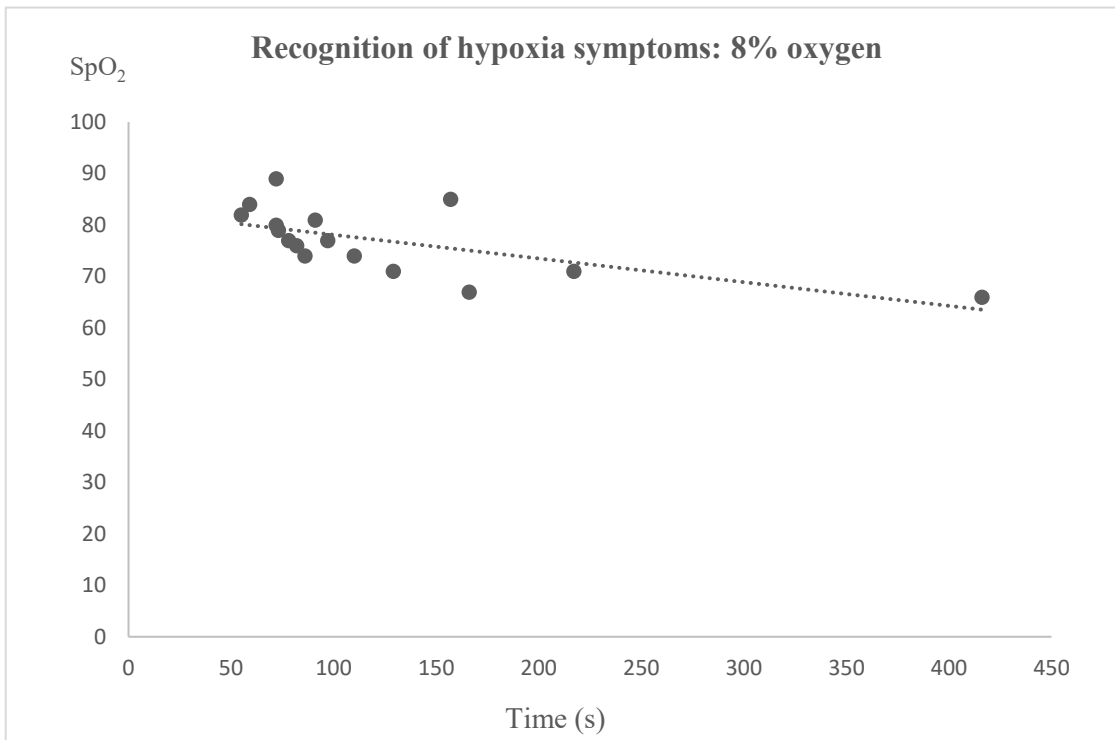
Flight performance in both of the evaluation categories was poorer during the RTB after hypoxia (Figures 1 and 2). A Wilcoxon Signed-Ranks test indicated that post-hypoxic scores were statistically significantly lower than control flight scores, Situational Awareness, $Z = -2.500$, $p = 0.014$; IFR flight performance, $Z = -2.732$, $p = 0.005$. The evaluated IFR flight performance decreased significantly from 4.81 to 3.63. Only two of the subjects (2/16) had no change in IFR flight performance compared to the control flight. Poor IFR flight performance were noted in 8/16 subjects.

Subjects reported adverse effects up to 12 hours after the training. Fatigue and tiredness were the most common symptoms, but headache, dizziness, memory problems, tingling, and hot flushes in the face were also experienced. In addition, two subjects reported narrowly avoiding car accidents when driving home. One subject reported observing the traffic at a road junction and five seconds later forgetting that a car was approaching from the left.

Table II. Instructor pilots' comments on different subjects during the RTB.

- “No decision-making capability for 6 minutes”
- “Very poor energy management during emergency decent – max power and no air brake”
- “Heads-up display cross-checking collapsed”
- “During ARC phase + 2.0 NM off the IFR route”
- “Wrong altitude pressure settings”
- “Clearance altitude violation by 250 ft”
- “Approach to wrong runway”
- “Two-time ILS wave-off limit violation”
- “Flying into thunderstorm cloud despite the received air traffic control (ATC) warning”
- “Navigation system use was extremely slow during ILS Z 30”
- “Emergency decent with 90° nose down attitude almost resulted in controlled flight into terrain”
- “Forgot to fasten mask after emergency oxygen”
- “During ILS final approach, airspeed +20 knots than recommended”
- “Speaking to operations officer before immediate actions emergency procedures – failure to follow aviate, navigate, communicate priorities”
- “Landing gear overspeed”
- “After emergency oxygen, forgot to start emergency descent”
- “Wave-off clearance was opposite direction to alternative field – could not challenge wave-off clearance although low on fuel”

Figure 3. Recognition of hypoxia symptoms during the first set-up (8% oxygen; n=16).



Discussion

The difference in individuals' symptoms creates variety in the time of recognition and the level of oxygen saturation, as described in Figure 3. While some subjects experience very minor symptoms (slowing of crosschecking) that are hard to detect, others experience distinct symptoms (warmth and tingling skin) as a result of hyperventilation. Hyperventilation might also affect blood acidity (respiratory alkalosis) and explain the non-linear decrease in oxygen saturation.

By the time pilots recognize the symptoms, hypoxia is already affecting their situational awareness, working memory, and decision-making. After hypoxia, a significant decrease in flight performance was observed during the RTB, including the ILS Z approach. The RTB lasted 10 minutes, and we named the reduction in flight performance the "hypoxia hangover." Hypoxia hangover describes the late effects of hypoxic exposure, which may remain and linger despite the exposure ending and S_pO_2 levels returning to normal level. Persisting performance deficits has also been discovered before through examining sequential hypoxic exposures in a flight simulator.¹²

Even when treated with 100% oxygen, hypoxia has a long-lasting cognitive effect on performance.⁷ The oxygen paradox theory explains why emergency 100% oxygen decreases flight performance even further. Reflexive hyperventilation causing hypercapnia can result in even worse flight performance.

One option to minimize the hypoxia hangover is holding at sector altitude (minimum altitude with clearance of 300 meters above objects in the area) for over 10 minutes, especially if fuel is not a critical factor. The pilot needs all the support available from the formation and the operations officer to complete the flight mission safely. For example, a new BINGO for the alternative airfield at low altitude was necessary because after the hypoxia incident, the pilot cannot climb to a high altitude. Assigning a chase plane to monitor airspeed, altitude, and radio communication is also a good option. In fighters, the chase plane should be 1.0 NM behind, in radar trail formation. Routine in executing hypoxia EPs is crucial, and this hypoxia refresher training in a tactical simulator should be repeated every three years in the FINAF.

The major limitation of this study is the low number of subjects: there were only 16 participants. The standard flight performance grading system is limited to 5 values, but on the other hand, it is

the same system the FINAF routinely uses. For outliers with long hypoxia recognition time, three consecutive hypoxia set-ups may also have had a cumulative effect on the subjects' cognitive performance during RTB, although we used a 10 min wash-out period between set-ups. After each wash-out period subjects reported that they have recovered from previous hypoxia exposure. Severe hypoxia, like 416 s in 8 % O₂, may need more recovery time.

The study indicates that pilots should be trained in emergency descents in a tactical simulator under normobaric hypoxia. A steep inverted dive increases the CFIT (controlled flight into terrain) risk, since the brain takes 40 seconds to become oxygenated after hypoxia.⁷ Emergency descent should be commenced with a 20° nose-down attitude. The transponder emergency code assures ATC priority during descent to a low altitude. Pilots also need to prepare for O₂ hose disconnection from the vest after the emergency O₂ bottle in the ejection seat is empty. Mask-open flying is not permitted in the FINAF, firstly to assure smooth radio communications, and secondly because of the risk of a neck injury during ejection due to asymmetric forces to the head.

It remains unclear whether breathing frequency and ventilation volume affect flight performance during RTB, and this topic needs future research. Due to the hypoxia hangover, the FINAF has ordered a 12-hour grounding following hypoxia training. This restriction should also include a restriction on driving.

In conclusion, hypoxia had a significant, long-lasting effect on IFR flight performance during RTB. As in real aircraft, 100% oxygen was used as emergency oxygen, which can make cognitive performance even worse due to the oxygen paradox. More research is needed on the ventilation effect on hypercapnia and flight performance during hypoxia.

Acknowledgments

The authors acknowledge adjunct professor Matti Mäntysaari (Aeromedical Centre, Helsinki) for his valuable comments during writing process. This work was financially supported by research grant from Centre for Military Medicine, Finland.

References

1. Artino AR, Folga RV, Swan BD. Mask-on hypoxia training for tactical jet aviators: Evaluation of an alternate instructional paradigm. *Aviat Space Environ Med* [Internet]. 2006 August 01;77(8):857-63.
2. Beer JMA, Shender BS, Chauvin D, Dart TS, Fischer J. Cognitive deterioration in moderate and severe hypobaric hypoxia conditions. *Aerosp Med Hum Perform* [Internet]. 2017 July 01;88(7):617-26.
3. Dart T, Gallo M, Beer J, Fischer J, Morgan T, Pilmanis A. Hyperoxia and hypoxic hypoxia effects on simple and choice reaction times. *Aerosp Med Hum Perform* [Internet]. 2017 December 01;88(12):1073-80.
4. Files DS, Webb JT, Pilmanis AA. Depressurization in military aircraft: Rates, rapidity, and health effects for 1055 incidents. *Aviation, Space, and Environmental Medicine* [Internet]. 2005 Jun;76(6):523-9. Available from: <http://www.ingentaconnect.com/content/asma/ asem/2005/00000076/00000006/art00001>
5. Fowler B, Prlic H, Brabant M. Acute hypoxia fails to influence two aspects of short-term memory: Implications for the source of cognitive deficits. *Aviat Space Environ Med* [Internet]. 1994 July 01;65(7):641-5.
6. Lee KJ, Sanou AZ. Decompression sickness in the F/A-18C after atypical cabin pressure fluctuations. *Aerosp Med Hum Perform* [Internet]. 2018 May 01;89(5):478-82.
7. Malle C, Bourrilhon C, Quinette P, Laisney M, Eustache F, Pierard C. Physiological and cognitive effects of acute normobaric hypoxia and modulations from oxygen breathing. *Aerosp Med Hum Perform* [Internet]. 2016 January 01;87(1):3-12.
8. Mansikka H, Harris D, Virtanen K. An input-process-output model of pilot core competencies. *Aviation, Psychology and Applied Human Factors*. 2017;7(2):78-85.
9. Myers M. Nothing scares Hornet pilots more than losing oxygen - and it happens all the time [Internet]. May 8, cited March 2, 2019]. Available from: <https://www.navytimes.com/news/your-navy/2016/05/08/nothing-scares-hornet-pilots-more-than-losing-oxygen-and-it-happens-all-the-time/>
10. Phillips JB, Horning D, Funke ME. Cognitive and perceptual deficits of normobaric hypoxia and the time course to performance recovery. *Aerosp Med Hum Perform* [Internet]. 2015 April 01;86(4):357-65.
11. Rice GM, Snider D, Drollinger S, Greil C, Bogni F, Phillips J, Raj A, Marco K, Linnville S. Dry-EEG manifestations of acute and insidious hypoxia during simulated flight. *Aerosp Med Hum Perform* [Internet]. 2019 February 01;90(2):92-100.
12. Robinson FE, Horning D, Phillips JB. Preliminary study of the effects of sequential hypoxic exposures in a simulated flight task. *Aerosp Med Hum Perform* [Internet]. 2018 December 01;89(12):1050-9.
13. Sherman P, Sladky J. Acute and Chronic Effects of Hypobaric Exposure upon the Brain. *IntechOpen*; 2018. Available from: <https://www.openaire.eu/search/publication?articleId=intech::8074b45a1e8d3443a886f9df5c2b35ed>
14. Takacs E, Czizler I, Pato LG, Balazs L. Dissociated components of executive control in acute hypobaric hypoxia. *Aerosp Med Hum Perform* [Internet]. 2017 December 01;88(12):1081-7.

15. Temme LA, Still DL, Acromite MT. Hypoxia and flight performance of military instructor pilots in a flight simulator. *Aviation, Space, and Environmental Medicine* [Internet]. 2010 Jul;81(7):654-9. Available from: <http://www.ingentaconnect.com/content/asma/asem/2010/00000081/00000007/art00005>
16. Woodrow AD, Webb JT, Wier GS. Recollection of hypoxia symptoms between training events. *Aviat Space Environ Med* [Internet]. 2011 December 01;82(12):1143-7.