Hypobaric Hypoxia: Effects on Contrast Sensitivity in High Altitude Environments

Nicola Pescosolido; Andrea Barbato; Dario Di Blasio

BACKGROUND: Effects of hypobarism and hypoxia on visual performance and mainly on contrast sensitivity (CS) are well known. The purpose of this study was to compare the adjustments of corneal thickness in hypobaric hypoxia conditions with changes in contrast sensitivity.

METHODS: There were 12 healthy, emmetropic subjects assigned to the 14th Wing Aircrew based in Pratica di Mare AFB (Rome, Italy) who were evaluated for changes occurring in central corneal thickness (CCT), measured by portable ultrasonic pachymeter, and CS, assessed after reading the standard Pelli-Robson charts, during modification of atmospheric pressure and, therefore, of oxygen partial pressure.

RESULTS: Hypobaric hypoxia conditions in pilots raised CCT (550 μm to 600 μm) and reduced CS (1.95 log to 1.05 log) in a statistically significant result.

DISCUSSION: The study demonstrated that hypoxia and variations of atmospheric pressure may produce corneal edema, including changes of CCT and, correlatively, CS reduction.

KEYWORDS: contrast sensitivity, pachymetry, hypobaric hypoxia, corneal edema, central corneal thickness.

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The effects of hypobarism and hypoxia on visual performance and mainly on contrast sensitivity (CS) are well known. CS is the ability to perceive not just the absolute luminance value of a surface, but also the relationship between an element and the background luminance.[17] As with any other tissue, the cornea also needs oxygen in order to carry out its vital activities. However, considering the lack of its own vascularization, the cornea fulfills its needs from various sources. When the eye is open, oxygen spreads into the cornea through the tear film ($Po_2 = 155$ mmHg) and from the aqueous humor ($Po_2 = 55$ mmHg); when the eye is closed, both the vessels of the eyelid conjunctiva and the aqueous humor provide the greatest amount of oxygen ($Po_2 = 55$ mmHg) to the corneal epithelium.[9,21]

Therefore, the performance of oxygen equivalent (EOP) achievable when the eyes are open is equal to an atmospheric concentration of 20.9%, whereas, with closed eyes, it is equal to an atmospheric concentration of 7.5%.[4,5] The reduced supply of oxygen leads to an alteration of the keratocyte metabolism: this reduces the rate of aerobic metabolism (Krebs cycle), which is typified by very high energy effectiveness, while it increases the anaerobic one, which is characterized by lower energy significance.[4,5]

As a result of this phenomenon, it has been observed that increasing lactic acid and carbon dioxide levels, when accumulated in the various corneal structures, stimulate a vigorous osmotic water increase, leading to edema onset (the average thickness of the central tip of the cornea is equal to 540 μm), with decrease in some visual performances such as CS.[9,19,21] Changes in CS performance may represent a risk in those subjects who perform specific occupational activities such as jet pilots. Therefore, the purpose of this study was to assess whether air force jet pilots exposed to hypobaric hypoxia during their flying activities may experience corneal

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edema and evaluate the effects on specific visual performance, namely contrast sensitivity.

METHODS

This research was carried out according to the guidelines of the Helsinki Declaration and the study protocol was approved by the Institutional Review Board. Informed consent was obtained from all subjects before enrollment.

Subjects

We recruited 12 young, healthy emmetropic subjects assigned to the 14th Wing Aircrew in Pratica di Mare AFB (Rome, Italy). All individuals were not affected by ocular or systemic disease, including myopia, glaucoma, macular degeneration, diabetes, multiple sclerosis, previous intraocular surgery, or trauma. When attending the aerophysiological basic courses, the young pilots were required to accomplish the planned training in the hypobaric chamber.

Equipment

The research was carried out in the hypobaric chamber using pilots' helmets and masks. They were connected to oxygen tanks equipped with an automatic preset mixer. The chamber has an altitude range from 0 to 100,000 ft (30,480 m) (maxim theoretical altitude of 200,000 ft or 60,960 m) and a capacity of 10 seats + 2.

Inside the chamber, subjects first breathed a gas mixture at sea level (20.95% oxygen and 78.08% nitrogen). Then, when simulating high altitude conditions (18,000–25,000 ft/5486–7620 m), they breathed a reduced oxygen mixture while experiencing hypobarism. An individual pulse oxymeter monitored the oxygen saturation levels.

The assessment of contrast sensitivity in basal conditions and during hypobarism has been done with Pelli-Robson® charts (**Fig. 1**; **Table I**).[12] Those variable contrast charts show 16 groups of 3 letters (triplets) presented through 16 contrast values (8 rows). The contrast is the difference in luminance between the letter and the background divided by the luminance of the background itself. This luminance ratio is knows as Weber contrast: the lower visible contrast is the contrast threshold.[10,17]

The tests were performed with binocular vision, an overhead illumination of 85 $\mathrm{cd \cdot m^{-2}}$, and at a standard distance of 40″. In order to achieve results, a value of 0.05 log was assigned to each letter recognized after the first three (corresponding to 100% contrast) in a contrast ranging from 100 to 0.56%.

The central corneal thickness of the subjects were measured with a portable ultrasonic corneal pachymeter (Tomey®, Nagoya, Japan), which has a measurement range of 150–1200 μm and an accuracy of ±5 μm. The calibrated probe was used to obtain three measurements from the central cornea, with the mean value being used for analysis.

Procedure

The day before the investigation, oxybuprocaine 0.4% (Novesina®) drops were applied to the eyes of the pilots and a CS examination was performed before and after the drops in order to assess whether the anesthetic might have a toxic effect on the cornea (keratitis) and might cause CS alterations. Subjects having abnormal results were ruled out of the study.

Fig. 1. Pelli-Robson® contrast sensitivity charts.

The day of the investigation, the pilots entered the hypobaric chamber and underwent the CS test using standard Pelli-Robson® charts (at a standard distance of 40″ and illumination of 85 $\mathrm{cd \cdot m^{-2}}$). After application of anesthesia to the eyes, the pilots underwent corneal pachymetry measurements in both eyes. This measurement procedure lasted approximately 6 min. Topical anesthesia was applied only once for the first pachymetry measurement.

A re-examination of the CS with standard Pelli-Robson® charts and a further ultrasound pachymetry examination were performed on the aircrew members after climbing to an altitude of 18,000 ft (5486 m) at a rate of 4000 ft/min (1219 m/min) and wearing a mask for oxygen delivery. The above-mentioned tests were repeated after climbing up to 25,000 ft (7620 m) at a rate of 4000 ft/min (1219 m/min). Individual oximetry during measurement achieved about 55–60% of oxygen saturation.

When descending to 18,000 ft (5486 m), CS examination and pachymetry were completed in conditions of hypoxia and hypobarism after removing the oxygen supply masks. The oximetry reference was set on 60–68% of S_pO_2 values for about 8 min. When returning to normobaric conditions, about 28 min after the start, the same tests were performed again. **Table II** shows the variations of oxygen partial pressure in ambient air and inside the oxygen mask (100% oxygen) as the altitude changed.

Table I. Pelli-Robson® Contrast Sensitivity Charts: on Both Sides Numbers of Triplets Indicate the Logarithmic Contrast Sensitivity Value.

C%	CONTRAST SENSITIVITY	LOG	PELLI-ROBSON®		C%	CONTRAST SENSITIVITY	LOG
90	1	0.00	VRS	KDR	63	1.58	0.15
44	2.2	0.30	NHC	SOK	31	3.32	0.45
25	4.5	0.60	SCN	OZV	15	6.66	0.75
11	10	0.90	CNH	ZOK	7.8	12.8	1.05
5.6	17.8	1.20	NOD	VHR	3.9	25.6	1.35
2.8	35.7	1.50	CDN	ZSV	1.9	52.6	1.65
1.4	71.4	1.80	KCH	ODK	1	100	1.95
0.75	133	2.10	RSZ	HVR	0.5	200	2.25

Log 0.60 next to the letters SCN in the list of Pelli-Robson triplets indicates a contrast value equal to 1/100.60 = 0.25 = 25%.

RESULTS

Table III and **Fig. 2** illustrate the results, showing a gradual increase of central corneal thickness (CCT) related to altitude. In particular, the measured CCT value in the basal conditions (550 μm) does not show a statistically significant increase after climbing to an altitude of 18,000 ft (5486 m; 570 μm, with $t = 1.99$, degrees of freedom = 22, $P = 0.06$). Instead, the transition from 18,000 to 25,000 ft (5486 to 7620 m) raised the CCT (590 μm) and this increase was statistically significant ($t = 2.25$, $P = 0.037$). The achieved hypobaric hypoxia at an altitude of 18,000 ft after removing the oxygen supply mask for about 8 min (S_aO_2 60–68%) lead to a further CCT increase, reaching the value of about 600 microns (Fig. 2). Consequently, the hypoxic damage (hypoxia) associated with low air pressure at high altitude is when the largest increase of CCT was observed ($t = 2.36$, $P = 0.027$).

The results of the CS measurements are reported in Table III and in **Fig. 3** and **Fig. 4**. Similarly to the CCT observations, both altitude and hypobarism adversely affected contrast sensitivity performance: as the distance from sea level rises, CS decreases from the baseline. In fact, the first CS measurement (1.95 log; 1.12%) did not show a statistically significant decrease after climbing to the altitude of 18,000 ft (5486 m) (1.65 log; 2.23%, with $t = 1.55$, degree of freedom = 10, $P = 0.15$). Instead, the transition from an altitude of 18,000 to 25,000 ft (5486 to 7620 m) further reduced CS (1.35 log; 4.46%) in a statistically significant way ($t = 2.40$, $P = 0.025$). The conditions of hypobaric hypoxia at 18,000 ft (5486 m) after removing the oxygen supply mask resulted in lowering the CS to its lowest value (1.05 log; 8.91%) (Figs. 3 and 4). Therefore, as demonstrated for CCT, hypoxemia associated with high altitude hypobarism is where the greatest CS variation may be noticed ($t = 2.485$, $P = 0.021$).

DISCUSSION

CS is the ability to assess the needed minimum amount of contrast in order to identify an observed object. CS varies between individuals and its reduction may also occur in subjects having normal visual acuity and may indicate the involvement of the retinal receptive fields.[16,17] Furthermore, its preservation is essential for specific occupational activities such as flying for pilots, who require excellent visual performance. As far as we know, no data are available in scientific literature showing a relationship between CS changes and hypobaric-hypoxic damage occurring during high-altitude flights. The purpose of our study is to explain how the above-mentioned conditions may affect and decrease such visual function.

It is widely recognized that corneal tissue has a high metabolic activity requiring a large oxygen supply.[16] This requirement is essential in order to maintain corneal integrity and also is a prerequisite for good nonedematous tissue. The reduced supply of oxygen occurring in hypobaric conditions is responsible for corneal edema onset.[9,15] Hypoxia is a pathological condition caused by lack of oxygen in the body (generalized hypoxia) or in a specific area (tissue hypoxia). The low-level of oxygen concentration in plasma is called hypoxemia (P_aO_2 lower than 80 mmHg). The first tissue affected by both reduction and lack of oxygen is the nervous tissue, especially the brain and the auditory and visual systems.[16,23] A reduced supply of oxygen to the brain usually causes a visual field narrowing, central vision reduction, altered color perception, and

Table II. Ambient Air Pressure, Oxygen Partial Pressure and Oxygen Mask Pressure Related to Altitude.

ALT (FT)	MMHG	P_{PO_2}	P_{PO_2} (100% O_2)
Sea level	760.00	159.6	760.00
1000	732.93	152.0	732.93
2000	706.66	148.3	706.66
3000	681.15	143.0	681.15
4000	656.40	137.8	656.40
5000	632.38	132.7	632.38
6000	609.09	128.0	609.09
8000	564.58	118.5	564.58
10,000	522.75	109.7	522.75
12,000	483.48	92.0	483.48
14,000	446.63	93.7	446.63
16,000	412.10	86.5	412.10
18,000	379.77	79.7	379.77
20,000	349.53	73.4	349.53
23,000	307.86	64.6	307.86
25,000	282.40	59.3	282.40

Table III. Summary of Measurements Performed vs. Altitude.

ALTITUDE	CCT	CS	MMHG	P_AO_2	% OXYGEN	INTRAOCULAR P_AO_2	TIME (APPROX.)
Sea level	550 ± 25.84 μm	1.95 Log 1.12% 90 CS score	760 mmHg	160 mmHg	100%	55 mmHg	Start
18,000 ft (oxygen mask on: oxygen 100%)	570 ± 23.29 μm (+3.63%)	1.65 Log 2.23% 45 CS score (−2%)	380 mmHg	80 mmHg	100%	55 mmHg	6 min
25,000 ft (oxygen mask on: oxygen 100%)	590 ± 20.23 μm (+7.27%)	1.35 Log 4.46% 22 CS score (−4,5%)	282 mmHg	59 mmHg	100%	55 mmHg	12 min
Return to 18,000 ft (oxygen mask off: oxygen 60–68%)	600 ± 29.73 μm (+9.09%)	1.05 Log 8.91% 11 CS score (−9%)	380 mmHg	80 mmHg	60–68%	35.75 mmHg	20 min
Return to normobarism	550 ± 25.84 μm	1.95 Log 1.12% 90 CS score	760 mmHg	160 mmHg	100%	55 mmHg	28 min

CCT = central corneal thickness measured with a pachymeter.

impaired contrast sensitivity. Furthermore, corneal edema has also been observed.

The exchange of oxygen within the lungs occurs at the alveolar-capillary membrane level and depends on gas pressure gradient in both the alveoli (100 mmHg) and pulmonary capillaries (40 mmHg). This difference of pressure, about 60 mmHg at sea level, is adequate to sustain the gas diffusion from alveoli to pulmonary capillaries (and then from blood to tissues, where P_aO_2 has a low level) and ensures adequate tissue oxygenation.[8] However, this decreases at high-altitude barometric pressure: in fact, a reduction of the oxygen partial pressure has been observed in that environment and consequently in both alveoli and tissues. The damage to the tissues due to their reduced ematosis (hypoxemic hypoxia) starts at approximately 9842 ft (3000 m) above sea level (525 mmHg, 70% oxygen).[2,7,14]

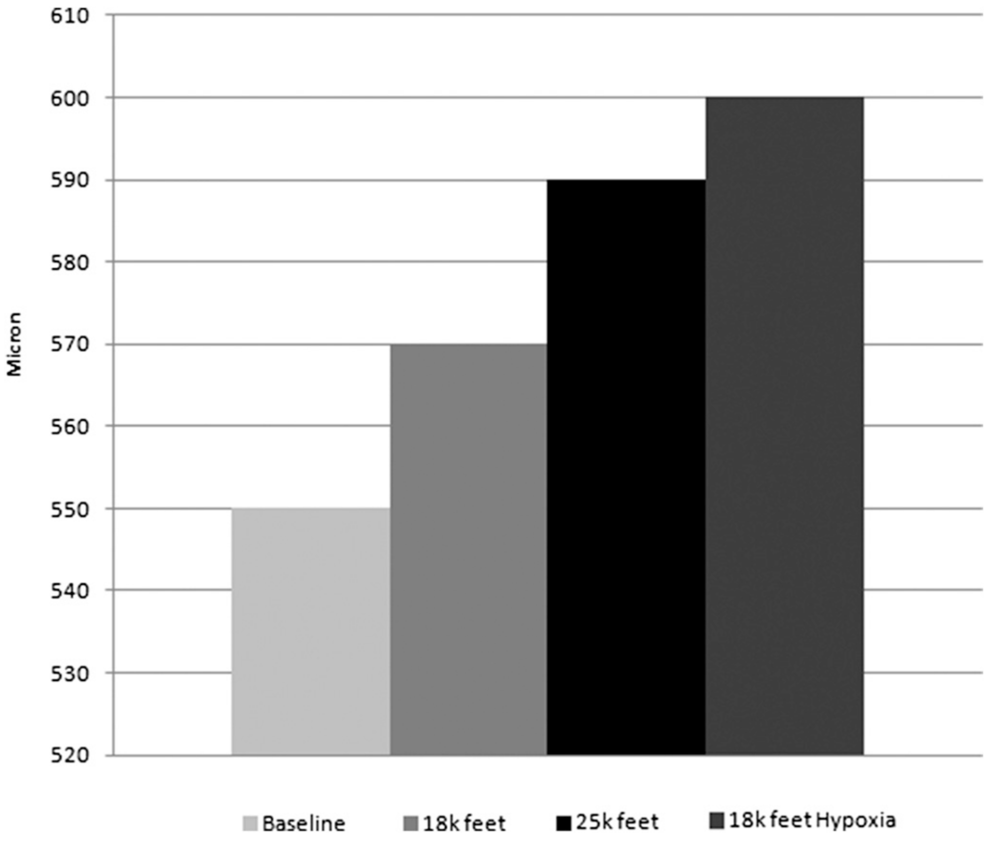

Fig. 2. Pachimetric value changes related to altitude modifications: 18,000 ft = +3.63%; 25,000 ft = +7.27%; 18,000 ft hypoxia = +9.09%.

This study observed that CCT significantly increased up to 590 μm (25,000 ft or 7620 m). The increase (CCT = 600 μm) was more significant during the hypoxic event than the high altitude event at an altitude of 18,000 ft (5486 m) when the oxygen supply mask was removed for 8 min. CS changes are also related to the CCT increase, the modifications of atmospheric pressure, and the oxygen partial pressure in ambient air (Fig. 4). The results showed

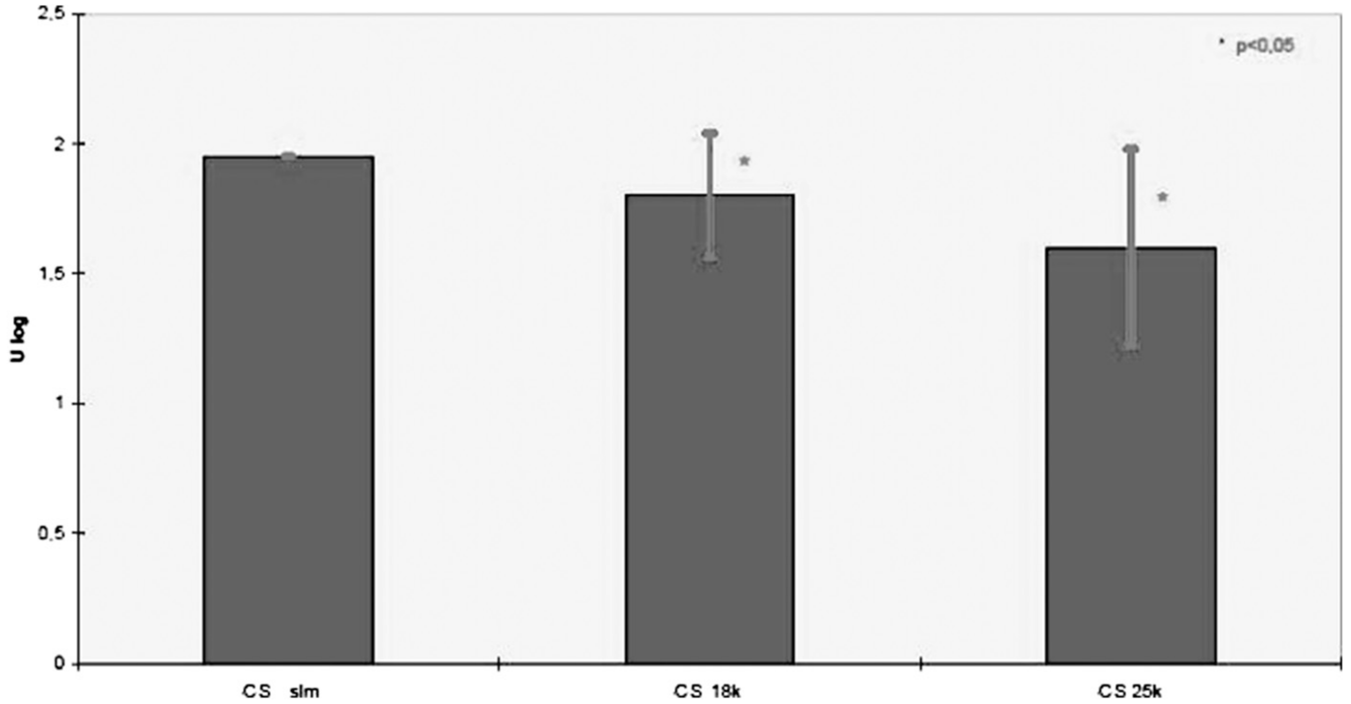

Fig. 3. Contrast sensitivity changes related to altitude in three different experimental conditions: 18,000 ft = −2%; 25,000 ft = −4.5%.

that this visual performance decreases as the distance from sea level increases. Furthermore, it worsens when hypoxemia is connected to hypobarism.

However, we should consider some limitations that could affect this study. First of all, the experiment was not able to distinguish between neural and corneal effects on CS. The huge need for oxygen and nutrients required by both the brain and retina has already been observed: this means that hypoxic conditions can lead to a diminished visual capacity (and in particular CS) based on both retinal and cerebral cortex changes. Nevertheless, recent studies have demonstrated that changes in visual evoked potentials induced by hypoxemic hypoxia are minimal in young healthy subjects:[3,22] indeed, the central nervous system would ensure a high resistance against hypoxic insult thanks to compensatory mechanisms.[6,18,20] Furthermore, the latest researches have shown that in healthy subjects, inner retinal oxygen extraction remains constant during systemic hypoxia.[11]

Secondly, CS decrease may be closely related to a refractive change induced by the corneal edema. To remedy this problem, the subjects would have to be optically corrected at altitude (not an easy option) before the CS test. In reference to this, recently Pescosolido et al. have carried out research on corneal topographic changes in hypobarism examining the corneal surface using a Keratron® Scout topographer before and after hypobaric hypoxia (18,000 ft or 5486 m and 25,000 ft or 7620 m).[13] Results did not show any significant variation of corneal indexes after climbing to the altitude of 18,000 ft (5486 m), while slight changes in simulated keratometry and best fit cylinder indexes occurred after transition to 25,000 ft (7620 m). Any change occurred in other indexes, namely best fit sphere and topographic irregularity. Furthermore, Aaron et al.[1] have clinically examined at altitude (22,000 ft) 12 subjects treated with laser-assisted in situ keratomileusis (LASIK); the results did not show any statistically significant refractive changes on keratometry and/or spherical refractive error shift greater than ±0.25.[1] Further longitudinal studies are required in order to examine this matter in depth.

In conclusion, this study reveals how hypobaric hypoxia may produce a corneal edema in correlation with a reduced CS performance on Pelli-Robson® charts. This is a risk factor for jet pilots' safety because the preservation of good visual performance is an essential requirement for them. Contrast sensitivity assessment may be useful in the study of corneal edema produced not only in recurrent ophthalmological conditions (use of contact lenses), but also in order to evaluate the damage to corneal tissue related to clinical situations producing hypoxemic conditions, such as chronic obstructive pulmonary disease and heart failure. The use of the Pelli-Robson® CS test is recommended due to its easy performance, cost-effectiveness, and easy repetition in the evaluation of hypoxemia-related corneal edema so as to accomplish an early correction of this change.

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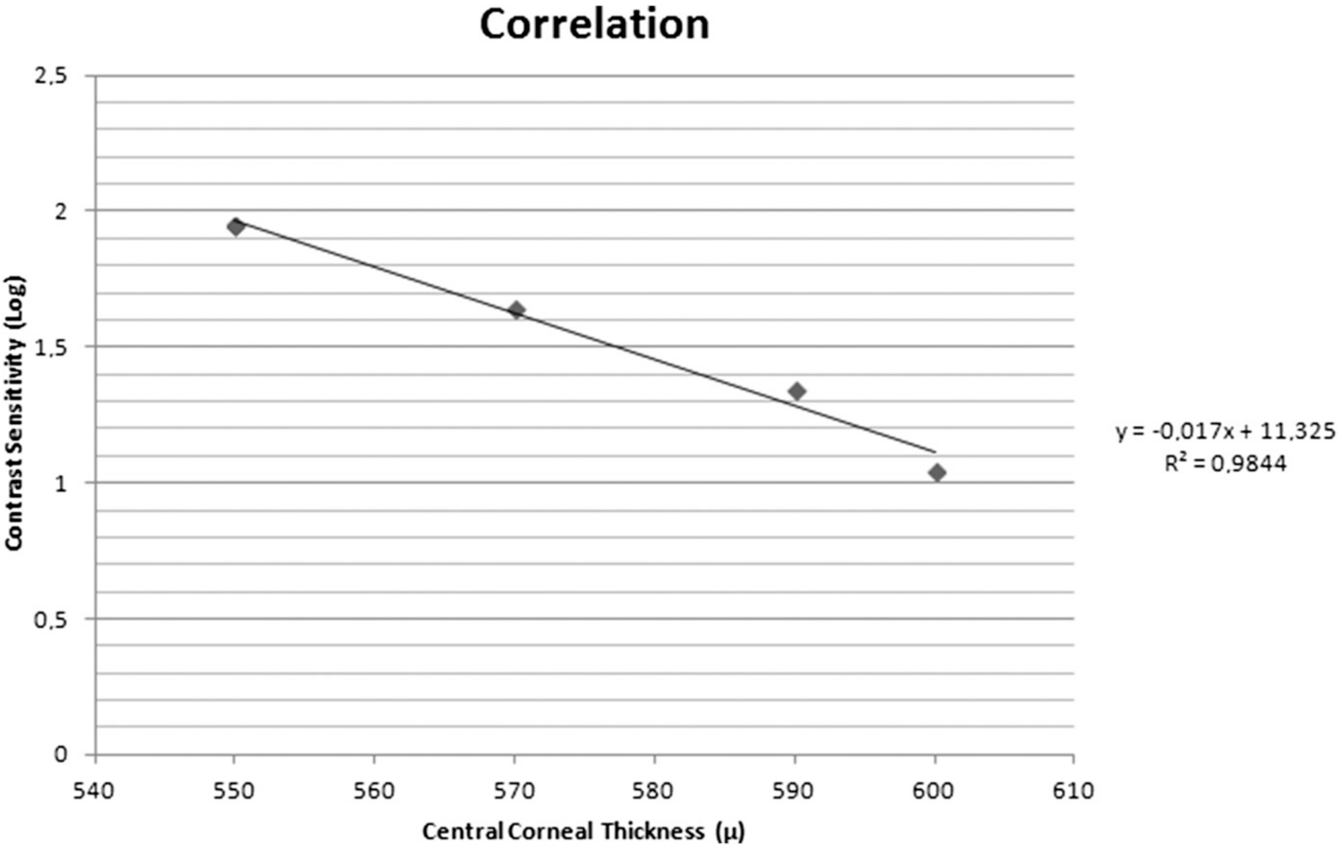

Fig. 4. Correlation of central corneal thickness vs. contrast sensitivity changes in hypobaric hypoxia.

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