Lack of Significant Audiometric Changes Under Hypobaric Hypoxia at 15,000 ft

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BACKGROUND: The aim of this study was pure tone audiometry (PTA) evaluation in normal individuals exposed to hypobaric hypoxia, taking into account the influence of air rarefaction on sound transmission via a standard earphone.

METHODS: The study was conducted in a hypobaric chamber using a standard audiometer and a TDH-39P earphone whose performance at altitudes was analyzed in a previous research. Eight male volunteers underwent PTA testing at ground level and at 15,000 ft under normoxia (via an oxygen mask) and after 20 min of hypoxia. Auditory threshold at 500, 1000, 2000, and 4000 Hz was recorded from the right ear while monitoring arterial oxygen saturation (S_ao_2). The PTA data obtained at high altitude were corrected according to a specific recalibration table.

RESULTS: During hypoxia, a significant threshold shift was observed only at 4000 Hz, with respect to ground level recording, for the sole not-corrected data. At the same frequency a significant threshold shift was also observed between the ground level recording and normoxia at 15,000 ft, confirming the presence of a hypobaric effect not related to hypoxia. After the recalibration procedure, this hearing impairment was not significant. No correlation with S_ao_2 levels was observed.

DISCUSSION: The mild and not significant presence of high altitude-induced PTA derangements in healthy normal individuals was documented, although a stimulus recalibration was needed for a correct interpretation of our data.

KEYWORDS: audiometry, hypobaric, hypoxia, auditory, threshold.

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Hypobaric hypoxia represents an outstanding topic in aviation medicine, although the analysis of its effects on the human auditory system has been the object of a relatively low number of investigations. However, although within the aviation community it is well known that vision is the first of the special senses to be altered by the lack of oxygen,[22] Fowler and Prlic observed similar effects of normobaric hypoxia on P300 latency/amplitude and reaction times generated by visual and acoustic stimuli.[9] The hypoxia-induced cognitive impairment following auditory stimulation was further confirmed by other studies from different laboratories.[10,26] Such evident findings were apparently in contrast with other reports, where the effects of hypobaric hypoxia on the human auditory system were analyzed with pure tone audiometry (PTA)[3,16] or other forms of short and middle latency auditory evoked potentials,[2,13,23] and only minor derangements, if any, could be observed. Such PTA findings were also confirmed under normobaric conditions.[8,24] Nevertheless, Carlile et al. reported a significant latency increase of the auditory brainstem response (ABR) for normobaric hypoxia exposures lasting more than 20 min,[4] evidencing a discrepancy between the relatively rapid decrease under hypoxia of arterial oxygen saturation (S_ao_2)[18] and the slower variation of the auditory response.[4,14]

The critical role of the duration of hypoxia to detect significant electrophysiological changes was also confirmed by other studies, including chronic environmental exposures to high altitudes[5,6] or subsequent exposures.[14] When the hypoxic condition is obtained under hypobarism, the potential influence of the environmental pressure reduction is a further parameter that must be taken into account, especially when mild threshold changes are expected, since the lower ambient pressure may itself alter the mechanisms of sound transmission and

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transduction on the part of earphones, and potentially interfere with a correct auditory threshold detection, independently from the presence or not of any hypoxia-induced auditory derangements.[12]

Taking into account such variables, in this study a standard PTA from normal individuals exposed to acute mild hypobaric hypoxia lasting more than 20 min was evaluated, correcting the data recorded under hypobarism according to the parameters of a recalibration table developed during a previous investigation.[12] Moreover, an attempt to sensitize the auditory test with a reduction of the standard intensity sequencing was performed, aiming at detecting minor forms of auditory derangements, as in the case of past investigations.[16,24] Eventually, an additional PTA recording at high altitudes while breathing oxygen via an oxygen mask (i.e., maintaining normoxic conditions) was also performed to better evaluate the actual impact of oxygen deprivation, as well as the role of the adopted recalibration parameters.

METHODS

The study was conducted in agreement with the declaration of Helsinki and was approved by the local ethical board. Moreover, a written consent was signed by each subject before undergoing the test session.

Eight male volunteers (ages between 27 and 53 yr), qualified as aerospace physiologists and certified as fit for flight duties according to Italian Air Force rules, participated in this study. Each individual underwent a preliminary ENT investigation and an impedance test that both showed normal results, in agreement with the Italian Air Force (ItAF) selection criteria for exposure to the hypobaric chamber environment.[11] Moreover, at the return to ground level following the exposure to hypobarism, all subjects underwent an otoscopy.

During the experimental session, the subject was seated inside the chamber and the PTA was performed at ground level (i.e., normoxia at ground level: NGL), at a simulated altitude of 15,000 ft (4600 m) while breathing 100% oxygen via an aviation mask (i.e., normoxia at high altitude: NHA), and after 20 min of ambient air breathing (i.e., hypoxia at high altitude: HHA). Therefore, the total duration of the exposure to hypobaric hypoxia was slightly less than 30 min (i.e., 20 min. of preliminary ambient air breathing + the PTA testing duration under the HHA condition).

Air temperature and humidity, along with the percentage of oxygen within the ambient air, were continuously monitored and kept constant throughout the experiment.[7] Due to ItAF safety protocols, a hypobaric chamber operator who was not participating in the experiment was also present inside the chamber, while the S_aO_2 and the electrocardiogram were monitored in each test subject with a wireless device. During the HHA condition, the PTA recordings were all performed under stable S_aO_2 levels.

The air conditioning system and related ventilation were turned off during each test session to reduce the ambient noise level. In such environmental conditions, the total mean sound pressure level from 63 to 4000 Hz (i.e., including the PTA frequencies analyzed in this study) was 50.7 dB(A). The PTA testing was performed with a calibrated audiometer (Amplaid 460) that was positioned outside the chamber, used with an ascending method, per the technical recommendations suggested by Yantis.[27]

The sole right ear threshold was evaluated at 500, 1000, 2000, and 4000 Hz, with a randomly selected frequency sequencing between subjects and within each individual for the three different test conditions (NGL, NHA, and HHA) to rule out possible bias due to a "learning effect" and/or to a different duration of the exposure to hypoxia for different test frequencies during the HHA session. To ameliorate the detection of the acoustic stimulus and make the test more sensitive, a pulsed pure tone was used along with ascending steps of 1 dB.

To reduce possible bias due to the PTA test-retest variability,[1] during each experimental session (i.e., NGL, NHA, and HHA) the individual's threshold at each frequency was recorded at least 10 times and its median was taken into account for final evaluation. This prolonged the total PTA test duration to about 8 min for each experimental session (i.e., about 2 min for each test frequency).

The choice of testing only one ear and selecting just the four central octave test frequencies was due to the preliminary observation of a long duration of PTA recordings with such a method during each test session (about 8 min). However, this methodological approach could analyze the behavior of those PTA frequencies playing a major role in speech intelligibility and communication.[19]

The audiometer was connected with a cable to a Telephonics TDH-39P headphone (Farmingdale, NY, USA) via a dedicated and sealed opening in the chamber's wall. The subject was instructed to lift his hand when the auditory stimulus was detected, and was preliminarily trained several times before performing the experimental session.

The statistical analysis was carried out on the PTA data obtained during the NGL, the NHA, and the HHA respiratory conditions, before and after threshold correction according to previous findings.[12] The median value of the audiometric responses obtained at each octave test frequency under every respiratory condition (i.e., NGL, NHA, and HHA) was taken into account and averaged, calculating the related standard deviation (SD).

A 3 by 3 (NGL-NHA-HHA vs. 1000-2000-4000 Hz) ANOVA was then carried out considering the threshold the dependent variable, with a separate analysis for non-corrected and corrected data. Post hoc Duncan test or planned comparisons were then used to analyze significant effects and interactions. Moreover, a linear regression model was used to analyze the possible relationship existing between the PTA threshold changes under hypoxia at each PTA frequency and the related S_aO_2 decrease. The criterion of significance was set at $P < 0.05$.

RESULTS

All subjects safely concluded their test sessions without the onset of clinical side effects secondary to the exposure to the hypobaric environment (e.g., hypoxia-related symptoms, any form of barotrauma, etc.). Such clinical findings, along with the normal pre- and postexposure investigations (including an otoscopic check and tympanometry) and the low ambient noise levels can substantially rule out possible bias due to middle ear disorders and/or noise-induced temporary threshold shifts. Moreover, PTA recordings conducted only after ascent further minimize the risk of middle ear derangements due to barotrauma.[11]

Unfortunately, due to a particularly high test-retest variability during the two hypobaric conditions (i.e., NHA and HHA), the data obtained at 500 Hz could not be considered as sufficiently reliable and was not included in our final analysis. Therefore, **Table I** indicates the mean S_aO_2 values recorded in our sample, along with the mean PTA threshold of the remaining three frequencies (i.e., 1000, 2000, and 4000 Hz) as obtained throughout the three experimental conditions (NGL, NHA, and HHA). The PTA data were also corrected for a TDH-39P loudspeaker at 15,000 ft, in agreement with our previous findings.[12]

As expected, S_aO_2 was reduced during the HHA session in all subjects, stabilizing after a few minutes, in agreement with previous reports where it rapidly decreased at high altitudes.[14,16] However, no significant correlation was observed between the PTA threshold variations under hypoxia and the amount of the S_aO_2 decrease. Different results were obtained with the ANOVA of noncorrected and corrected data, so they will be separately summarized.

Noncorrected Data

The ANOVA indicated a significant effect [$F(2,14) = 20.58$; $P < 0.0001$] of the stimulus frequency, with a different behavior of 4000 Hz with respect to both 1000 Hz ($P < 0.03$) and 2000 Hz ($P < 0.0001$), and of 1000 Hz with respect to 2000 Hz ($P < 0.02$). Moreover, the interaction between test condition and stimulus frequency produced significant differences [$F(4,28) = 3.78$; $P < 0.02$], with the post hoc comparison indicating that the auditory threshold at 4000 Hz significantly increased in the NHA ($P < 0.03$) and in the HHA ($P < 0.001$) conditions with respect to NGL recordings. The statistical power of the analysis comparing NGL and HHA data was 0.152 at 1000 Hz, 0.058 at 2000 Hz, and 0.694 at 4000 Hz.

Table I. Mean PTA Thresholds (in dB) and Related SD (in Brackets) Observed at Each Frequency Analyzed in This Study Under the Three Different Test Conditions (NGL, NHA, and HHA).

	S_aO_2	1000 Hz	2000 Hz	4000 Hz
NGL	98 (0.8)	13.1 (10.4)	0.6 (6.2)	7.1 (7.9)
NHA	99 (0.5)	8.1 (4.3)	−1.9 (5.3)	15.7* (11.1)
NHA (corrected)	99 (0.5)	9.3 (4.3)	2.3 (5.3)	11.5 (11.1)
HHA	75 (8.4)	8.8 (5.2)	−0.1 (4.4)	20.0** (11.1)
HHA (corrected)	75 (8.4)	10.0 (5.2)	4.1 (4.4)	15.8 (11.1)

PTA: pure tone audiometry; NGL: normoxia at ground level; NHA: normoxia at high altitude; HHA: hypoxia at high altitude.

For the NHA and the HHA conditions, both altitude corrected and noncorrected data are reported in separated rows. Mean S_aO_2 levels are also indicated for all the three respiratory conditions. Significant statistical findings are reported at bottom and indicated with asterisks within the table.

* $P < 0.03$; ** $P < 0.001$.

Corrected Data

The ANOVA indicated a significant effect [$F(2,14) = 9.89$; $P < 0.002$] of the stimulus frequency, with different behavior of 2000 Hz with respect to both 1000 Hz ($P < 0.03$) and 4000 Hz ($P < 0.002$). The interaction between test condition and stimulus frequency did not reach the adopted criterion of significance [$F(4,28) = 2.29$; $P < 0.08$]. Thus planned comparisons were performed, which confirmed that threshold values at 2000 and 4000 Hz (i.e., where a mean threshold increase was observed from the NGL condition to the HHA one) were not significantly different [$F(1,7) = 4.21$, $P < 0.08$ and $F(1,7) = 4.11$ $P < 0.08$, respectively].

The statistical power of the analysis comparing NGL and HHA data was 0.103 at 1000 Hz, 0.223 at 2000 Hz, and 0.383 at 4000 Hz. At all frequencies, no significant differences between the NHA and the HHA conditions were observed for either noncorrected or corrected data. The different behavior of the mean audiometric thresholds during the three test conditions is outlined in **Fig. 1**, where a graphical representation of the noncorrected (Fig. 1A) and corrected (Fig. 1B) findings is shown.

DISCUSSION

In this study, the PTA of healthy normal adults was analyzed after 20 min of exposure to mild hypoxic conditions, in agreement with previous reports where the duration of exposure resulted in an important variable to detect significant auditory threshold changes.[4,14] The results showed a different behavior across octave test frequencies, with a specific significant threshold shift at 4000 Hz during hypobarism (both NHA and HHA condition), with respect to NGL recording, for the sole noncorrected data (Table I).

Interestingly, in both cases the presence of a significantly reduced hearing sensitivity at 4000 Hz during the high altitude exposure was not confirmed after the application of the correcting factor[12] secondary to the different performance at 15,000 ft of the TDH-39P earphone, as documented by the results of the corrected data under the same NHA and HHA conditions (Table I).

Such a finding outlines the crucial role of hypobarism per se in sound transmission and loudspeakers' performance at high altitude, and the absolute need of a recalibration of PTA data, whose effects can be clearly detected in Fig. 1, where the mean behavior observed for each frequency and test condition is indicated before (Fig. 1A) and after data recalibration (Fig. 1B). However, even for corrected data, the most evident PTA changes under hypoxia were observed at 4000 Hz, where the threshold increase, with respect to NGL recordings, was 8.7 dB HTL (i.e., a decrease of 4.2 dB with respect to noncalibrated data), not far from statistical significance ($P < 0.08$), although with a low statistical power (0.383).

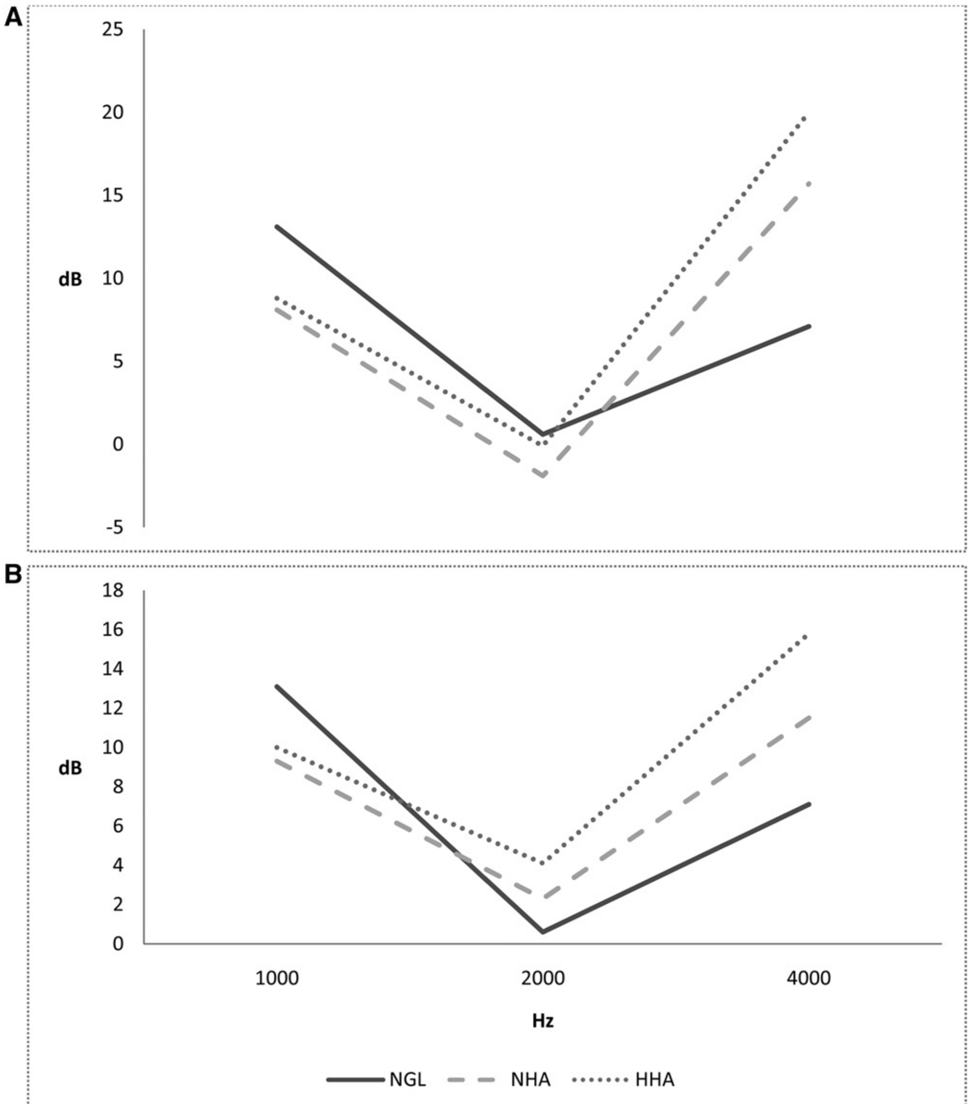

Fig. 1. Mean threshold behavior at 1000, 2000, and 4000 Hz under the three experimental test conditions for both A) noncorrected and B) corrected data.

a frequency band on word recognition.[19] Accordingly, Burkett and Perrin recorded a small and not significant reduction of speech discrimination score (from 97.5 to 90.5%) between the ground level and 15,000 ft recording.[3]

Therefore, based on the sole PTA data, only minor effects should be expected on the individual's capability of word recognition. On the other hand, due to possible derangements of the central acoustic pathways and related cognitive performance, other factors affecting speech communication and consequent cognitive tasks cannot be ruled out under hypoxia, despite a substantially unaltered air conducted PTA, which has "limited value for diagnostic purposes and is insufficient to make valid judgements regarding the site of a lesion."[27]

Past literature findings under similar hypoxic conditions showed electrophysiological derangements following acoustic stimuli, especially for cognitive tasks, indicating the cortex as the area most sensitive to hypoxic stress.[9,10,26] Such findings were substantially confirmed in the animal model, where very severe levels of experimental hypoxia can be reached.[20,21] Moreover, cognitive performance following acoustic stimulation was impaired in previous studies on working memory and verbal learning.[15,17]

Moreover, due to the low number of individuals analyzed in this study, a type II statistical error (i.e., a falsely negative outcome) cannot be ruled out, although previous literature findings, along with our present data, globally support the hypothesis that only small PTA changes (limited to high frequencies), if any, can be expected under experimental hypobaric hypoxia.[3,16] This is in agreement with a previous report from Carlile et al., where an ABR latency increase under normobaric hypoxia was observed in six subjects for S_aO_2 levels ranging from 75 to 85% (vs. a mean value of 75% in the present research).[4] Those authors interpreted these findings as a change in sensitivity of about 5 dB, which is very similar to the mean increase of 6.1 dB within the 2000–4000 Hz frequency range (i.e., the most active in the genesis of the ABR[25]) detected in our study.

From a practical point of view, a frequency impairment at frequencies higher than 3300 Hz evokes a reduction of speech intelligibility lower than 10% due to the reduced impact of such

Three main aspects characterized the method used in the present study: 1) the PTA sensitization with the use of 1-dB intensity steps; 2) the prolonged exposure to hypoxia; and 3) the adoption of a recalibration table aiming at compensating for the different performance of earphones at high altitudes. To our knowledge, in recent times, air conducted PTA has been investigated by a very few authors under acute hypobaric conditions.[3,16] In the case of Burkett and Perrin's study,[3] eight individuals were exposed for 5 min to 15,000 ft (i.e., to the same simulated altitude that we used) and to 20,000 ft. In their case, 5-dB intensity steps were administered with a TDH-39 earphone (i.e., identical to ours) without performing any stimulus recalibration at altitude. At 15,000 ft, a better threshold at 2000 Hz at the right ear was observed (substantially in agreement with our noncorrected data at the same frequency), while only minor and no significant changes were observed at the other tested frequencies. This finding was probably related to the particular performance under hypobarism of the TDH-39 earphone at such a frequency.[12]

Research having a more similar methodological approach with respect to ours was conducted by McAnally et al., who also considered the problem of the stimulus recalibration at altitude.[16] From a technical point of view, they used a lower simulated altitude (i.e., 3700 m, corresponding to 12,000 ft, and producing S_aO_2 values higher than 80%), along with an earphone having an electric impedance much higher than the TDH-39 (and so probably a different behavior when exposed to environmental pressure changes). In their study, a significant mean increase of the auditory threshold of 2.57 dB under hypobaric hypoxia was detected at 1000, 8000, 12,000, and 16,000 Hz (i.e., without testing 2000 and 4000 Hz, as in our case), while no frequency-related differences were observed. In this case, different research targets and methodological aspects can explain the discrepancies between the two studies, although a mild hearing impairment was observed in both reports.

In conclusion, all these studies substantially confirm a mild auditory system sensitivity to those levels of hypoxia that can be safely reached in humans for research purposes, especially when the higher frequencies of the standard PTA range are analyzed after sufficiently prolonged durations of exposure. A recalibration of air conducted stimuli is essential in the analysis of data recorded within a hypobaric environment, especially when mild audiometric variations are observed.

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