Intraindividual variability of the Eustachian tube function: a longitudinal study in a pressure chamber

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Abstract
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Introduction: The Eustachian tube (ET) is essential for fast and direct pressure equalisation between middle ear and ambient pressure. It is not yet known to what extent Eustachian tube function in healthy adults changes in a weekly periodicity due to internal and external factors. This question is particularly interesting with regard to scuba divers among whom there is a need to evaluate intraindividual ET function variability.
Methods: Continuous impedance measurement in a pressure chamber was performed three times at one-week intervals between measurements. Twenty healthy participants (40 ears) were enrolled. Using a monoplace hyperbaric chamber, individual subjects were exposed to a standardised pressure profile consisting of a 20 kPa decompression over 1 min, a 40 kPa compression over 2 min, and a 20 kPa decompression over 1 min. Measurements of Eustachian tube opening pressure (ETOP), opening duration (ETOD), and opening frequency (ETOF) were made. Intraindividual variability was assessed.
Results: Mean ETOD during compression (actively induced pressure equalisation) on the right side was 273.8 (SD 158.8) ms, 259.4 (157.7) ms, and 249.2 (154.1) ms (Chi-square 7.30, $P = 0.026$) across weeks 1–3. Mean ETOD for both sides was 265.6 (153.3) ms, 256.1 (154.6) ms, and 245.7 (147.8) ms (Chi-square 10.00, $P = 0.007$) across weeks 1–3. There were no other significant differences in ETOD, ETOP and ETOF across the three weekly measurements.
Conclusions: This longitudinal study suggests low week-to-week intraindividual variability of Eustachian tube function.

Introduction

The Eustachian tube (ET) is an anatomical connection between the middle ear and nasopharynx that can be subdivided into a medial cartilaginous and a lateral osseous section.[1,2] Physiologically, it has three commonly described main tasks: first, pressure equalisation between the middle ear and ambient pressure; second, protection against repercussion or pathogens from the nasopharynx; and finally, mucociliary clearance of middle ear secretions.[3,4] To balance pressure between the middle ear and the ambient pressure there slow gas exchange across the tympanic membrane as well as middle ear mucosa. In contrast, the ET periodically allows a fast and direct middle ear ventilation which is a fundamental prerequisite for pressure equalisation during flying and diving.[5] Under physiological conditions, pressure equalisation during decompression (ambient pressure decrease, e.g., airplane takeoff or diving ascent) normally happens spontaneously. During compression (ambient pressure increase, e.g., airplane landing or diving descent) pressure equalisation must be actively induced.[6]

The development of an exact, objective and sufficiently specific tool to measure the pressure equalisation function of the ET remains a challenge, even though a variety of assessments (e.g., impedance measurements, manometric, sonographic and endoscopic methods or tubomanometry) were established in recent years. Unfortunately, no single test appears to match the criteria to become a gold standard.[7] The combination of missing universal applicability as well as a lack of general informative value is the main problem in this process. On the one hand, a physiological test environment is required to obtain reliable data on ET function. On the other, most tests generate only short and non-dynamic information or use non-physiological pressure levels and/or pressure change rates.[8]

With this working group, a method was used to determine the pressure equilibration ET function involving the use of a pressure chamber. The combination of diagnostic impedance measurement and application of a defined pressure profile in a hypo- and hyperbaric pressure chamber allows a dynamic and objective analysis of ET function. Therefore, variables describing ET function were introduced and examined in healthy cohorts.[9,10] According to recent studies, the present method is also applicable if cohorts consist of patients with chronic Eustachian tube dysfunction (ETD).[11,12]

Unspecific symptoms overlapping with other middle and inner ear pathologies complicate a clear distinction of ETD. For this reason, a recent consensus agreed on the definition as being a "*syndrome with a constellation of signs and symptoms suggestive of dysfunction of the Eustachian tube*".[4] Typically, patients report symptoms like aural fullness, popping, discomfort or pain, among others.[13] Chronic ETD can lead to the development of tympanic membrane retraction and chronic otitis media with effusion, with or without cholesteatoma.[14–16] In general, ETD is presumed to have a prevalence of 0.9% among adults.[17,18] One study reported a prevalence of 4.6% among adults in the United States of America.[19] The development of new treatment strategies has amplified the need for patient selection through reliable ET function testing and objective outcome measurement to improve quality of care.[20]

The aim of this study was to characterise the intraindividual variability of ET function in healthy participants in a longitudinal study by using a continuous impedance measurement during pressure changes in a hypo- and hyperbaric pressure chamber. The impact of possible ET function-influencing factors such as nutrition, sport activity, hormonal status, nasal cycle, or mild subclinical infection on ET function has not yet been sufficiently characterised.[21–25] A further goal was to help classify ETD treatment outcome measurements in previous as well as in future studies, since periodic fluctuations of ET function may interfere with conclusions about treatment effects. As previous studies suggest that the ET opening pressure during decompression may be higher in patients with ETD and can be reduced by Eustachian tube balloon dilatation (ETBD), results of this study were compared with earlier studies.[10–12]

Methods

The study was approved by the local ethics committee of the University of Cologne medical faculty. Written and informed consent had been obtained from all participants. The study is in accordance with the latest version of the Declaration of Helsinki.

PARTICIPANTS

This prospective study included twenty healthy participants (40 ears). The mean age was 25.9 (SD 4.0) years, 60.0% were female and 40.0% male. All participants affirmed that no symptoms and/or signs of ET dysfunction were present on each date of measurement. None of the participants reported prior problems with pressure equalisation while flying or diving. A full ear, nose and throat examination including ear microscopy and endoscopy of the nose and epipharynx was conducted by an otorhinolaryngologist. The ability to perform a visible Valsalva maneuver on both ears was confirmed. Exclusion criteria were colds, any form of perforated tympanic membrane, symptoms and/or signs of active allergic rhinitis, severe septum deviation, adenoid hypertrophy, gastroesophageal reflux disease and pregnancy.

CONTINUOUS IMPEDANCE MEASUREMENT IN A HYPO- AND HYPERBARIC PRESSURE CHAMBER

A single person chamber (Haux Life Support, Karlsbad, Germany) was used to apply a defined pressure profile for ET function measurements with an interval of one week between sessions. The pressure profile has been utilised in previously published studies.[6,8–12] It consists of two decompression phases of one minute each and a compression phase of two minutes between them (see Figure 1A). For continuous measurement of tympanic impedance, a size-adjusted rubber earplug was fitted in the external ear canals on both sides. The earplug contains three channels: (1) a loudspeaker delivering a 226 Hz tone; (2) a microphone; and (3) a small tube for pressure equalisation between the chamber and the external ear canal (see Figure 2). ET function was measured by recording the reflection of the acoustic signal simultaneously with the controlled application of pressure change. The setup as a combination of pressure chamber and continuous tympanic impedance measurement allows an objective and dynamic measurement of the ET function separately for the left and right side. In this way generated curves (see example in Figure 1B) were subsequently analysed in a specific analysis program.

In case of a participant's discomfort due to any reason, measurements would have been stopped immediately. The pressure could have been manually equalised to the atmospheric pressure.

EUSTACHIAN TUBE FUNCTION IN DECOMPRESSION (PASSIVE OPENINGS) VS COMPRESSION (ACTIVELY INDUCED OPENINGS)

While participants were instructed to not induce any active pressure equalisation during phases of decompression, they were asked to actively equalise pressure either by Valsalva manoeuvre or by swallowing during compression. They were advised to perform the Valsalva manoeuvre or swallowing whenever a feeling of discomfort occurred. They were advised to not switch the chosen equalisation method for the compression phase between measurements.

Further and detailed ET function analysis was achieved by using the variables ET opening pressure (ETOP), ET opening duration (ETOD) and ET opening frequency (ETOF). All

Figure 1
A – Pressure/time profile of the chamber test runs; B – Example of the continuous impedance measurement (green curve); detailed analysis was performed with a tenfold magnification. L – left side; R – right side

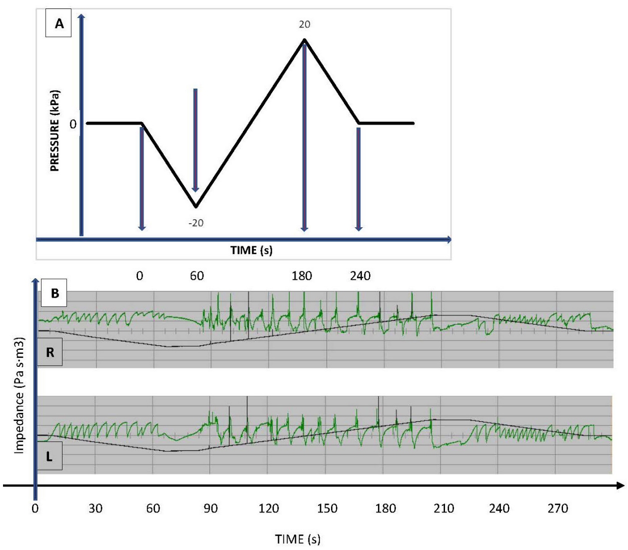


Figure 2
Setup of the ear plug arrangement inside the single person pressure chamber

three variables were calculated for decompression and compression separately as previously published.[9–12,26] The ETOP during decompression (passive pressure equalisation) was defined as the pressure difference between the initial pressure and first ET opening. Similarly, ETOP during compression (actively induced pressure equalisation) was calculated as the mean of pressure differences between minimum and maximum impedance during pressure increase. The time interval between ET opening (maximum impedance) and ET closing (minimum impedance) represented ETOD during decompression. The mean of time intervals between ET opening (maximum impedance) and ET closing (minimum impedance) was calculated to determine ETOD during compression. In contrast to phases of decompression, ETOP during compression is influenced by the participant's personal perception, as it depends on the individual decision to induce pressure equalisation. Therefore, all actively induced openings were analysed individually and afterwards an average value was calculated to represent the variable.

Since preliminary studies have shown that ETOP during decompression is the most important variable to represent Eustachian tube function, we have compared our findings with results from previous studies.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS Statistics version 26 (IBM Corporation, Armonk, NY, USA). Data are presented as mean standard deviation (SD). Initially, the Shapiro-Wilk and Kolmogorov-Smirnov tests were used to determine whether the resulting values of the three repetitive measurements follow a normal distribution. Depending on the results, either a one-way analysis of variance (ANOVA) for repeated measurements or a Friedman test was performed to detect possible differences between measurements. To exclude a proportional bias, a final linear regression was carried out. To compare the results of ETOP during decompression with recent publications, an additional ANOVA was performed.[10–12] Null hypotheses were tested with a significance level set at $P < 0.05$.

Results

The means (SD) of all ET function-reflecting variables for each measurement are presented in Table 1. The results are shown for the right, left and the mean for both sides, respectively. Except for the ETOD during compression (actively induced pressure equalisation) on the right side and the mean for both sides, there were no significant differences calculated for variables between measurements I–III.

Linear regression revealed no evidence for any proportional bias. For ETOD, a non-parametric Friedman test of differences among repeated measurements rendered a Chi-square value of 7.30 (right) and 10.00 (mean of both sides), which was significant ($P = 0.026$ for the right side and $P = 0.007$ for the mean of both sides). Dunn-Bonferroni-adjusted post-hoc analysis revealed that measurement I and III differ from each other ($z = 2.69$, $P_{adjusted} = 0.022$ for the right side and $z = 3.16$, $P_{adjusted} = 0.005$ for the mean of both sides).

As an ANOVA appears to be quite robust against violations of the assumption of normal distribution, it was also performed

Table 1
Eustachian tube function measurements in the pressure chamber; all data are mean (standard deviation); B – both sides; ETOD – Eustachian tube opening duration; ETOF – Eustachian tube opening frequency; ETOP – Eustachian tube opening pressure (ETOP); L – left side; R – right side

Parameter	Measurement I			Measurement II			Measurement III		
	R	L	B	R	L	B	R	L	B
Pressure decrease (passive pressure equalisation)									
ETOP (kPa)	2.65 (1.08)	2.55 (0.96)	2.6 (0.95)	2.82 (1.05)	2.61 (0.90)	2.72 (0.92)	2.67 (0.97)	2.60 (0.87)	2.63 (0.89)
ETOD (ms)	806.5 (323.2)	781.0 (374.6)	793.8 (331.6)	828.8 (351.9)	752.5 (372.)	790.6 (343.2)	813.8 (342.3)	799.5 (356.1)	806.6 (337.0)
ETOF (min^{-1})	7.7 (5.0)	8.0 (5.0)	7.9 (4.7)	7.5 (6.0)	7.9 (6.2)	7.7 (5.8)	7.6 (5.5)	8.3 (5.7)	7.9 (5.3)
Pressure increase (actively induced pressure equalisation)									
ETOP (kPa)	2.90 (1.46)	2.97 (1.63)	2.94 (1.55)	2.98 (1.57)	3.11 (1.70)	3.04 (1.63)	2.87 (1.50)	2.96 (1.66)	2.92 (1.58)
ETOD (ms)	273.8 (158.8)	257.5 (153.7)	265.6 (153.3)	259.4 (157.7)	252.8 (155.7)	256.1 (154.6)	249.2 (154.1)	242.3 (143.7)	245.7 (147.8)
ETOF (min^{-1})	5.3 (2.8)	5.5 (2.9)	5.4 (2.8)	5.9 (3.2)	5.8 (3.3)	5.9 (3.2)	6.1 (3.4)	6.1 (3.5)	6.1 (3.4)

Figure 3
The mean and standard deviation of all ET function variables for each measurement (I, II and III) during compression (A–C) and decompression (D–F); aETOD – actively induced Eustachian tube opening duration; aETOF – actively induced Eustachian tube opening frequency; aETOP – actively induced Eustachian tube opening pressure; pETOD – passive Eustachian tube opening duration; pETOF – passive Eustachian tube opening frequency; pETOP – passive Eustachian tube opening pressure

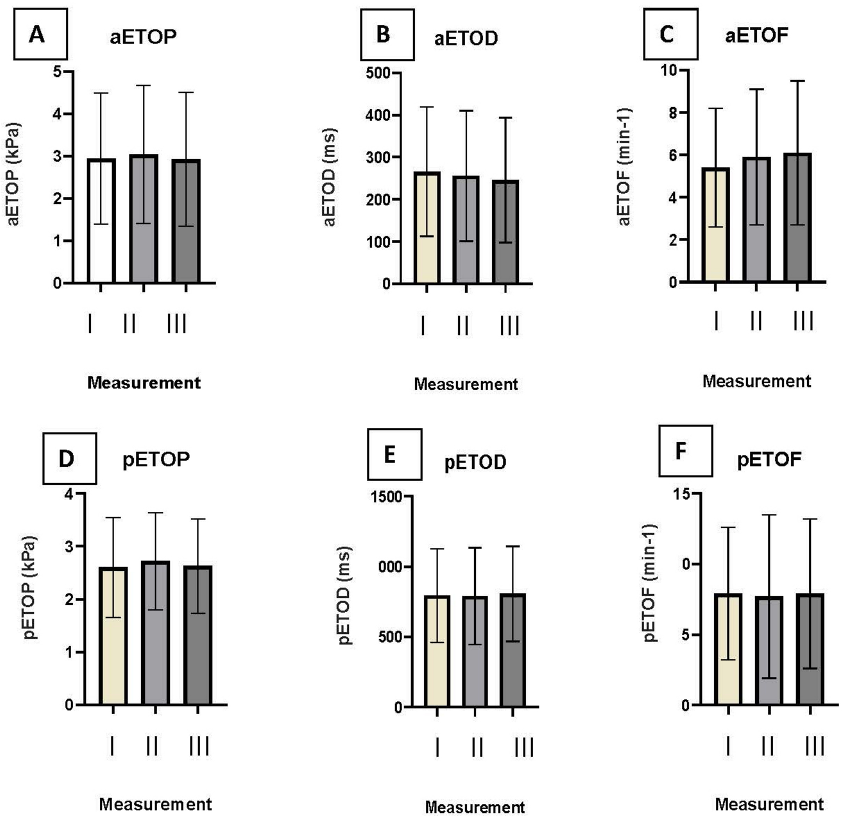
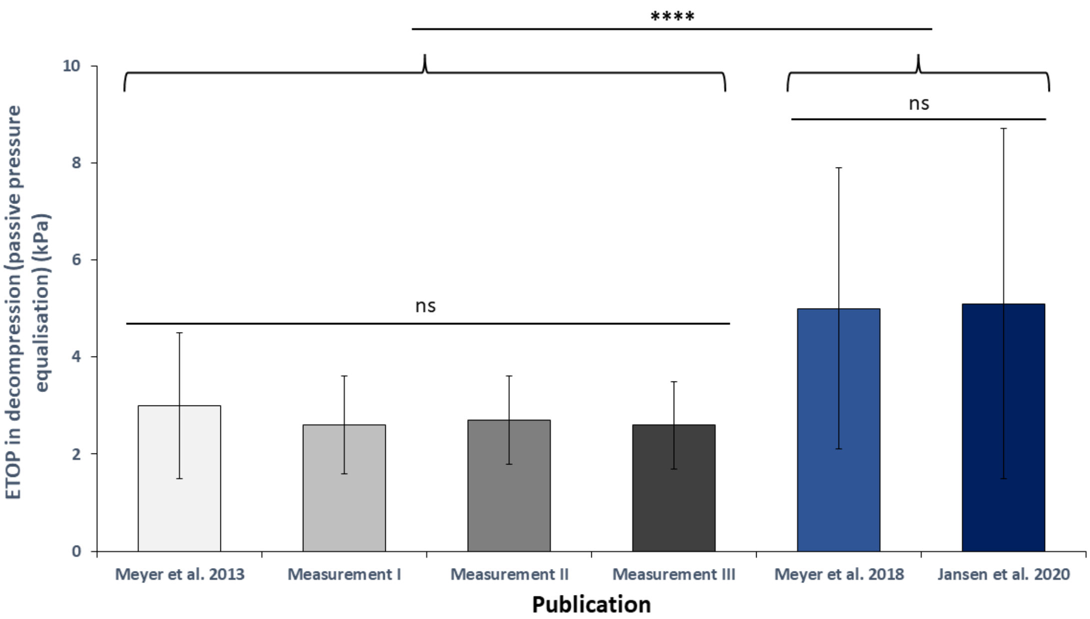


Figure 4

Comparison of mean and standard deviation ETOP during decompression (passive pressure equalisation) for healthy cohorts (Meyer, et al. 2013,[10] and present study measurements I-III), and cohorts consisting of patients with chronic ETD (Meyer, et al. 2018, Jansen, et al. 2020);[11,12] ****ETOP during decompression is significantly higher statistically in patients with chronic ETD than in healthy participants ($P < 0.0001$). ns – non-significant



and did not confirm a statistically significant difference between measurements for ETOD during compression (actively induced pressure equalisation; $F(2, 117) = 0.171$, $P = 0.843$).[27] Figure 3 gives a detailed overview.

As shown in Figure 4, an ANOVA revealed no significant differences among only healthy cohorts (measurement I-III) or among cohorts consisting only of patients with chronic ETD.[10–12] However, the ETOP during decompression (passive pressure equalisation) is significantly higher in subjects with chronic ETD than in healthy subjects ($P < 0.0001$).

Discussion

Diving results in large ambient pressure changes and there is a need for a properly functioning Eustachian tube. Probably every diver knows that there are better and worse days in terms of middle ear pressure compensation, even if the cause is not always known. Certainly, the hormonal cycle, nutritional status and colds involving the nose and nasopharynx play an important role. It would be interesting to determine whether Eustachian tube function shows differences at different times normal subjects. The test procedure used here was evaluated in preliminary studies as very reliable and dependable.[26] To our knowledge, this is the first longitudinal, dynamic and pressure chamber-based study aiming at identifying possible intraindividual ET function fluctuations in a weekly periodicity among healthy participants.

An initial question to be discussed is why ETOD during compression (actively induced pressure equalisation) differs on the right side between measurements I and III but not on the left side. If there was intraindividual variability shown for both sides, respectively, it would strongly suggest periodical fluctuations of ETOD. Considering the inconsistent results between both sides, other possible explanations are measurement inaccuracy or statistical imprecision. This hypothesis is also supported by the fact that no difference between both sides was detected for ETOF and ETOP during compression.

As stated by Tysome and Sudhoff, there is a need to enhance ET function measurement to improve the evaluation of new diagnostic approaches and therapeutic strategies for ETD.[28] For the same reasons, it is also essential to detect possible fluctuations in healthy participants. Otherwise, effects measured at a single point in time effects would be difficult to interpret due to natural range of variation in ET function. This study is a major step in the right direction, as it provides evidence that possible ET function fluctuation due to unmeasured natural factors is negligibly small in pressure chamber-based measurements. In addition, the study offers the advantage that pressure change relevant to diving can be simulated under standardised conditions, in contrast to studies in water, where a measurement under standardised conditions seems almost impossible.

Finally, there are certain limitations of this study. The interpretation of ET function-reflecting variables during compression (actively induced pressure equalisation) continues to be challenging, as the Valsalva manoeuvre is performed heterogeneously among people.[9–12] On the other hand, on an intraindividual level the analysed curves were, subjectively speaking, strikingly similar. Apart from that, observed differences between healthy participants and patients with ETD need to be confirmed in larger cohorts and related to different subgroups. Furthermore, an interval of one or two weeks was chosen in the study. This means, for instance, that it cannot be ruled out that monthly or annual changes may occur. In addition, the individual factors influencing Eustachian tube function were not queried and analysed. For example, in further studies hormone status, weight and hydration level can be additionally examined and correlated. As pressure chamber-based measurements are not widely used, it is also essential to link the knowledge gained and findings obtained with other, more commonly available methods.

Conclusions

This study shows that in three consecutive weekly repeated measurements no relevant variations in Eustachian tube function could be detected. In fit and well subjects there was no significant week to week fluctuation in ET functions tested through continuous impedance measurements in a pressure chamber.

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