Research Article

A Pilot Study to Investigate the Relationship Between Interaural Differences in Temporal Bone Anatomy and Normal Variations in Caloric Asymmetry

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Purpose: This study assesses interaural differences in temporal bone anatomy in subjects with normal caloric findings.

Method: Eligible patients included those referred to the Duke University Medical Center otology clinic complaining of dizziness, with a head computed tomography scan and caloric stimulation results within normal ranges (inter-ear difference $\leq 10\%$ or $< 25\%$ unilateral weakness). Three-dimensional reconstructions of computed tomography scans in 11 patients were used to calculate the surface area and volume of lateral semicircular canals (LSCCs), mastoid airspaces, mastoid bones, and internal auditory canal diameter and circumference. Percent differences in interaural temporal bone anatomy (i.e., left-to-right asymmetry) were analyzed and correlated with warm caloric inter-ear difference (WCD) and clinically indicated caloric predictor asymmetry.

Results: A multivariate model predicting WCD from 9 interaural anatomic variables demonstrated a Pearson's coefficient of 0.999. A similarly constructed model of the clinically indicated caloric predictor demonstrated a Pearson's coefficient of 0.999. The univariate correlation was strongest for WCD versus Proctor internal auditory canal diameter ($r = 0.476$; $p = .139$) and WCD versus lateral semicircular canal surface-area-to-volume ratio ($r = -0.474$; $p = .141$).

Conclusions: This pilot study provides multivariate models that predict caloric asymmetry in subjects without vestibular pathologic findings per caloric testing, based on interaural differences across variables of the temporal bone anatomy.

Supplemental Material: <https://doi.org/10.23641/asha.5895988>

Caloric stimulation is the gold standard in identifying vestibular pathology, with a sensitivity and specificity of 46% and 75%, respectively (Dros et al., 2010; Tusa, 2010). Caloric testing is most often prompted by symptoms of vertigo, for which the lifetime prevalence is 7% (Lempert & Neuhauser, 2009). Testing is performed by infusing warm or cold water into the external auditory canal, eliciting nystagmus with saccades toward the ipsilateral or the contralateral ear, respectively (Fitzgerald

& Hallpike, 1942). Caloric output is then measured in terms of the peak maximum slow phase velocity of the nystagmus; output values from one ear are compared to those of the other side (Baloh & Furman, 1989; Baloh, Sills, & Honrubia, 1977).

The mechanism of caloric stimulation can be divided into three phases: (a) the transfer of heat from the external auditory canal to the inner ear organs, (b) the generation of a neurologic impulse within the inner ear organs, and (c) impulse modulation and vestibulo-ocular reflex production via central nervous system pathways, ultimately measured by the frequency of nystagmus. Understanding the role of heat transfer and how it may be influenced by variations in interaural differences in temporal bone anatomy is an essential first step toward understanding the mechanism of caloric stimulation testing.

The mechanistic step of heat transfer is dependent on temporal bone anatomy. A majority of studies describing heat transfer across the temporal bone have not used caloric output (i.e., nystagmus) as an end point, focusing instead

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Editor: Sumitrajit Dhar

Associate Editor: Owen Murnane

Received April 27, 2016

Revision received August 25, 2016

Accepted September 29, 2017

https://doi.org/10.1044/2017_AJA-16-0048

Disclosure: The authors have declared that no competing interests existed at the time of publication.

on identifying the mechanistic components of heat flow. Barany (1906) first proposed that the initial heat transfer phase occurs via conduction through the temporal bone. Subsequent studies refined this theory, culminating in the Feldmann, Huttenbrink, and Delank (1991) study, demonstrating that heat transfer occurs as some combination of radiation, convection, and conduction through the temporal bone and mastoid air spaces (Feldmann, Huttenbrink, & Delank, 1991; Harrington, 1969; Hood, 1973; O'Neill, 1987, 1995; Pau, Sievert, Just, & Wild, 2001; Young, 1972; Zangemeister & Bock, 1979). Although such studies have better defined the complexity of heat transfer, they provide little insight into its integration into the greater caloric mechanism. Caloric output is usually the information that dictates clinical decision making.

To date, very few studies have explored the relationship between interaural differences in temporal bone anatomy and caloric stimulation (O'Neill, Calhoun, Francis, Chui, & Hayward, 1987; Proctor, 1982). These studies did not identify a significant anatomic correlation to caloric output. Since temporal bone anatomy can now be investigated with greater precision using advanced technological methods to generate anatomically accurate three-dimensional reconstruction of the temporal anatomy from subject-specific computed tomography (CT) scans, further investigation aimed at investigating this relationship is necessary.

Advancing the current understanding of the relationship between interaural differences in temporal bone anatomy and caloric stimulation output would be especially useful in clinical situations where clinically significant unilateral caloric weakness (> 25% caloric asymmetry) is present. Caloric testing is often either repeated or ignored when unilateral caloric weakness is demonstrated (Jacobson, 1993). The degree to which interaural differences in temporal bone anatomy may cause unilateral caloric weakness remains unknown. Quantifying the relationship between interaural anatomic differences and unilateral caloric weakness may help determine the applicability of calorimetry in cases of significant temporal bone asymmetry, both in the context of "normal" and "abnormal" caloric findings. The aim of this report is to provide a preliminary description of interaural differences in temporal bone anatomy in subjects with normal caloric testing. This pilot study may serve as a basis for comparison with the results of future studies that include subjects with clinically abnormal caloric testing in the setting of both "normal" and "abnormal" temporal bone symmetry.

Materials and Methods

Subjects

This is a retrospective study approved by the Duke University Health System Institutional Review Board. A search was conducted of the Duke University Medical Center medical records for patients who had undergone both a standard-of-care CT scan and caloric testing between

July 1, 2010 and February 1, 2015. Inclusion criteria included (a) clinically "normal" caloric findings: monothermal warm caloric (inter-ear difference, IED) $\leq 10\%$ or bithermal caloric (unilateral weakness, UW) $< 25\%$ (Jongkees & Philipszoon, 1963) and (b) no evidence of aberrant or altered temporal bone anatomy on CT scan in patients ranging from 18 to 89 years of age. Exclusion criteria included (a) abnormal vestibular testing results and (b) abnormal findings or inadequate resolution on CT. In addition, 22 temporal bones across 11 subjects meeting the study criteria were identified and analyzed.

Calorimetry

Caloric testing was conducted as part of a videonystagmography test also including ocular motility and positional testing. For the caloric test, patients were placed in a supine position with the head elevated 30° . Warm caloric irrigations were performed using water heated to 44°C , and each ear was irrigated for a fixed duration of 30 s (ATMOS MedizinTechnik Variotherm Plus). Our laboratory first conducts the caloric exam using a monothermal warm screening test and IED using the formula in Barber, Wright, and Demanuele (1971). Based on the results from Murnane, Akin, Lynn, and Cyr (2009), a 10% cutoff point for the monothermal warm screening yields a false-negative rate of 1%. In cases where the monothermal warm irrigations resulted in an IED of $\leq 10\%$, testing was terminated, and monothermal response was recorded (see Table 1). If the IED was $> 10\%$, then cool irrigations were completed at 30°C and UW was calculated using Jongkees' formula with a normal cutoff of $< 25\%$ (Jongkees & Philipszoon, 1963). Immediately after irrigation had begun, caloric responses were recorded for 2 min using the Neuro Kinetics Vest 7.1 and I-Portal eye tracking system.

Table 1. Subject inclusion criteria by monothermal (inter-ear difference, IED) and bithermal (unilateral weakness, UW) caloric testing are displayed for all subjects, with corresponding warm caloric difference (WCD) and clinically indicated caloric predictor (CICP) values used in subsequent analysis.

Subject	IED $\leq 10\%$	UW $< 25\%$	WCD	CICP
	% (Y/N)	% (Y/N)	(%)	(%)
S1	19.2 (N)	19.5 (Y)	38.3	39.0
S2	0.0 (Y)	N/A	0.0	0.0
S4	5.6 (Y)	N/A	11.1	11.1
S6	0.0 (Y)	N/A	0.0	0.0
S8	2.4 (Y)	N/A	4.9	4.9
S13	33.3 (N)	9.7 (Y)	66.7	19.4
S14	0.0 (Y)	5.3 (Y) ^a	0.0	10.5
S16	10.0 (Y)	N/A	20.0	20.0
S17	16.7 (N)	9.1 (Y)	33.3	18.2
S19	21.4 (N)	16.3 (Y)	42.9	32.6
S21	7.1 (Y)	N/A	14.3	14.3

^aFor S14, bithermal caloric output was calculated in clinic despite an IED of $< 10\%$ and subsequently used to calculate CICP.

To confirm normal vestibular function as determined by normal caloric findings during videonystagmography testing, patients included in this study were also required to exhibit no evidence of vestibular pathology during ocular motility and positional testing. Ocular motility examination measured horizontal and vertical gaze stability, horizontal smooth pursuit, horizontal saccade, and horizontal optokinetic subsystem function. Positional testing was performed to rule out nystagmus and benign paroxysmal positional vertigo.

3D Anatomic Reconstruction

The methodology of three-dimensional (3D) anatomic reconstruction used in the present study has been reported to be accurate to the hundredth of a millimeter (Calloway et al., 2013). Furthermore, the accuracy of our 3D reconstructions in this study was verified to be accurate to the hundredth of a millimeter, by comparing tympanic membrane (TM) reconstructions to CT scan measurements as shown in Figure 1.

Temporal bone CT scans were obtained using a Siemens SOMATOM Definition Flash machine. The 11 scans in this study had 123 slices on average (range = 56–193) with a section thickness of 0.6 mm, 512 × 512 matrix, rotation time of 1 s, and exposure time of 1825 ms. Patients were in the head-first supine position with a 0 gantry tilt. DICOM (Digital Imaging and Communications in Medicine) images had 512 rows, 631 columns, and a pixel spacing of 0.176 × 0.176 mm.

DICOM images for each head CT scan were imported into image analysis software Avizo 8.1 standard (FEI Visualization Sciences Group, Burlington, MA) and de-identified. Moreover, 3D reconstructions of the temporal bone anatomy were created in Avizo, and the following parameters were computed: mastoid airspace and bone volume (V), mastoid airspace and bone surface area (SA), and mastoid airspace and bone surface-area-to-volume ratio (SA:V); lateral semicircular canal (LSCC) V, LSCC SA,

LSCC SA:V, and LSCC-to-TM distance; and internal auditory canal (IAC) diameter and circumference using two separate protocols for IAC measurement (Proctor, 1982; Stimmer, Niedermeyer, Kehl, & Rummeny, 2015). This process is visually depicted in Figure 2. The resultant 16 anatomic parameters were divided into four groups based on location: LSCCs, IAC, mastoid airspace, and mastoid bone dimensions. The anatomic parameters selected for analysis were chosen based on previous studies linking anatomy to the mechanism of heat transfer, while emphasizing prior significant correlation (Feldmann et al., 1991; Harrington, 1969; Hood, 1973; O'Neill, 1987; Proctor, 1982; Young, 1972; Zangemeister & Bock, 1979). All variables were quantified through Avizo with the exception of IAC measurements, which were quantified using the computer-aided design software package ICEM-CFD 14.5 (ANSYS, Canonsburg, PA). In cases where circumferences could not be determined in ICEM-CFD, circumferences were derived from the following hydraulic diameter formula:

$$DH = \frac{4A}{P}, \quad (1)$$

where DH is the hydraulic diameter of an irregular channel, A is the cross-sectional area, and P is the perimeter of the cross section.

Interaural Differences

All interaural differences pertaining to temporal bone anatomy were calculated using the following equation:

$$X(\%) = \left| \frac{L - R}{0.5(L + R)} \right| \times 100, \quad (2)$$

where X is the percent interaural difference for a given anatomic variable of interest (e.g., mastoid airspace, mastoid bone, and LSCC), L is the left-sided anatomic measurement (mm), and R is the right-sided anatomic measurement (mm).

The same formula for X was used to calculate warm caloric IED (WCD), where L is left ear warm and R is right ear warm, such that $WCD = 2IED$. Similarly, the clinically indicated caloric predictor (CICP) was calculated as follows: For subjects with $IED \leq 10\%$, $CICP = WCD$, and for subjects with $IED > 10\%$, CICP is equal to a variant of X where $L = LW + LC$ (LW is left ear warm; LC is left ear cool) and $R = RW + RC$ (RW is right ear warm; RC is right ear cool). Notice that

$$CICP = \begin{cases} 2IED, & \text{for subjects with } IED \leq 10\% \\ 2UW, & \text{for subjects with } IED > 10\% \text{ and } UW < 25\% \end{cases} \quad (3)$$

(Table 1).

Our rationale for computing WCD and CICP rather than using the standard IED and UW in this work is to be consistent with the formula for X used in calculating interaural differences in temporal bone anatomic variables.

Figure 1. The accuracy of three-dimensional reconstructions was confirmed by identical measurements of maximum tympanic membrane diameter (8.06 mm) between computed tomography scans (A and B) and reconstructions (C) that were created using medical imaging software Avizo 8.1 standard (FEI Visualization Sciences Group, Burlington, MA) and measured using software package ICEM-CFD 14.5 (ANSYS, Canonsburg, PA).

Figure 2. Three-dimensional reconstruction of temporal computed tomography scans via Avizo 8.1 standard (FEI Visualization Sciences Group, Burlington, MA) was used to analyze the dimensions of (A) mastoid bone and airspaces, (B) lateral semicircular canals and tympanic membrane, and (C) internal auditory canal. WCD = warm caloric inter-ear differences; P = Proctor; S = Stimmer.

Furthermore, univariate analysis using the conventional caloric output formula yields identical statistical output (Supplemental Material S1; Supplemental Material S2).

Data Analysis

Temporal bone anatomy was correlated to warm caloric stimulation findings by plotting interaural anatomic differences to inter-ear warm caloric percent differences and calculating the respective Pearson's correlation coefficients (r) and p values. This was done in two ways: (a) developing a multivariate regression model consisting of several temporal bone anatomic parameters and (b) fitting univariate regression lines for each temporal bone anatomic parameter. All analyses were performed using JMP pro 11 (SAS Institute Inc., Cary, NC).

Results

Warm Caloric Versus Temporal Bone Anatomy: Multivariate Approach

Three multivariate regression models consisting of interaural differences in temporal bone anatomic parameters were developed to predict percent inter-ear WCD (see Table 1).

Model 1. In this model, the following IAC anatomic parameters were used to predict WCD: Proctor IAC

circumference (x_1), Stimmer IAC circumference (x_2), Proctor IAC diameter (x_3), and Stimmer IAC diameter (x_4). Model 1 is of the following form:

$$PredCal = |21.059 + 1.024x_1 - 2.216x_2 + 0.676x_3 - 1.134x_4|, \quad (4)$$

where *PredCal* is predicted caloric response. Table 2 shows the predicted value of Model 1 for each subject and the

Table 2. Comparison of multivariate regression model predictions of interaural difference (in percent) in warm caloric inter-ear differences (WCD) versus actual measurements of WCD.

Subject	Model prediction of WCD			Actual WCD
	Model 1	Model 2	Model 3	
S1	24.147	31.208	36.624	38.298
S2	1.843	13.957	1.516	0.000
S4	23.226	30.446	11.507	11.111
S6	14.844	16.825	1.635	0.000
S8	18.163	8.481	5.418	4.878
S13	51.193	51.568	66.928	66.667
S14	13.878	1.278	0.700	0.000
S16	5.449	32.265	20.772	20.000
S17	13.663	18.441	32.388	33.333
S19	52.622	32.643	43.675	42.857
S21	16.087	5.682	14.937	14.286

corresponding actual value. As demonstrated in Figure 3, the correlation between Model 1 and warm caloric response was $r = 0.778$.

Model 2. This model consists of the following temporal bone anatomic parameters that are unrelated to IAC: mastoid airspace volume (y_1), mastoid airspace surface area (y_2), LSCC volume (y_3), LSCC surface area (y_4), LSCC–TM distance (y_5), mastoid bone volume (y_6), and mastoid bone surface area (y_7). The regression equation for Model 2 is defined as follows:

$$\text{PredCal} = |-41.888 - 2.922y_1 + 3.643y_2 - 0.569y_3 + 1.498y_4 + 4.100y_5 + 2.537y_6 + 3.838y_7|, \quad (5)$$

where *PredCal* is Model 2 predicted WCD response. Table 2 also shows the predicted values of Model 2 and

Figure 3. Multivariate models are shown for (Model 1) internal auditory canal parameters, (Model 2) temporal bone anatomic parameters unrelated to the internal auditory canal, and (Model 3) a combined model of all measured anatomic parameters, all with respect to warm caloric inter-ear differences (WCD).

the corresponding actual WCD values for all subjects. The correlation between Model 2 and warm caloric response was $r = 0.813$ (see Figure 3).

Model 3. Model 3 comprises both computed IAC and temporal bone anatomic parameters: Proctor IAC circumference (z_1), Stimmer IAC circumference (z_2), Proctor IAC diameter (z_3), and Stimmer IAC diameter (z_4), mastoid airspace surface area (z_5), LSCC volume (z_6), LSCC surface area (z_7), LSCC–TM distance (z_8), and mastoid bone surface area (z_9). The regression equation for Model 3 is defined as follows:

$$\text{PredCal} = |3.493 + 2.656z_1 - 2.055z_2 + 0.933z_3 - 1.221z_4 - 0.514z_5 - 0.142z_6 - 1.606z_7 - 0.091z_8 + 4.440z_9|, \quad (6)$$

where *PredCal* is predicted caloric response by Model 3. A comparison of the Model 3 predicted values of WCD versus subjects' actual WCD is presented in Table 2. In addition, Model 3 had an almost perfect correlation with warm caloric response ($r = 0.999$; see Figure 3).

CICP

Two multivariate regression models consisting of interaural differences in temporal bone anatomic parameters were developed to model CICP (see Table 1).

Model 4. Model 4 applies the anatomic variables from Model 3 in the estimation of CICP. IAC and temporal bone anatomic parameters, namely, Proctor IAC circumference (z_1), Stimmer IAC circumference (z_2), Proctor IAC diameter (z_3), Stimmer IAC diameter (z_4), mastoid airspace surface area (z_5), LSCC volume (z_6), LSCC surface area (z_7), LSCC–TM distance (z_8), and mastoid bone surface area (z_9), were included. The regression equation for Model 4 is defined as follows:

$$\text{PredCal} = |-20.498 - 0.676z_1 + 1.063z_2 + 0.905z_3 - 0.357z_4 + 0.516z_5 - 0.710z_6 + 0.2906z_7 + 1.150z_8 + 2.774z_9|, \quad (7)$$

where *PredCal* is predicted CICP response by Model 4. A comparison of the Model 4 predicted values of CICP response versus subjects' actual CICP responses are presented in Table 3. The correlation between Model 4 and CICP was $r = 0.986$ (see Figure 4).

Model 5. In this model, which was optimized to determine the CICP, the following IAC anatomic parameters were used to predict unilateral caloric weakness: Proctor IAC circumference (x_1), Stimmer IAC circumference (x_2), Proctor IAC diameter (x_3), Stimmer IAC diameter (x_4), LSCC volume (x_5), mastoid airspace surface area to volume (x_6), LSCC–TIM distance (x_7), and mastoid bone

Table 3. Comparison of multivariate regression model predictions of interaural difference (in percent) in clinically indicated caloric predictor (CICP; bithermal unilateral caloric weakness or warm caloric inter-ear difference) versus actual measurements of CICP.

Subject	Model prediction of CICP		Actual CICP
	Model 4	Model 5	
S1	35.070	38.911	38.961
S2	3.509	0.454	0.000
S4	12.020	11.082	11.111
S6	3.785	0.364	0.000
S8	6.123	5.200	4.878
S13	19.939	18.754	19.355
S14	8.899	10.981	10.526
S16	21.788	19.946	20.000
S17	15.987	18.116	18.182
S19	34.430	32.903	32.558
S21	15.791	14.043	14.286

surface area to volume (x_8). Model 5 is of the following form:

$$\begin{aligned} \text{PredCal} = & |-5.999 + 0.076z_1 + 0.602z_2 + 0.500z_3 \\ & + 1.297z_4 - 1.039z_5 + 1.589z_6 \\ & + 1.106z_7 + 0.024z_8|, \end{aligned} \quad (8)$$

where *PredCal* is predicted caloric response. Table 3 shows the predicted value of Model 5 for each subject and the corresponding actual value. As demonstrated in Figure 4, the correlation between Model 5 and CICP response was $r = 0.999$.

Warm Caloric Versus Temporal Bone Anatomy: Univariate Approach

Scatter plots and fitted linear regression lines of warm caloric IED (WCD; in percent) against interaural differences (in percent) in each temporal bone anatomic parameter are presented in Figures 5–7. Correlations between WCD and interaural differences in temporal bone anatomy were not statistically significant in all anatomic parameters investigated at $\alpha = 0.05$. Correlation was strongest for WCD versus Proctor IAC diameter ($r = 0.476$; $p = .139$) and WCD versus LSCC SA:V ($r = -0.474$; $p = .141$). Fitted regression lines showed an upward trend between WCD and Proctor IAC diameter and a downward trend between WCD and LSCC SA:V. Correlations of interaural differences in temporal bone anatomic parameters and WCD were lowest at Proctor IAC circumference ($r = 0.007$; $p = .984$) and mastoid bone volume ($r = 0.051$; $p = .438$). In a recently published work by our group comparing absolute anatomic measurements and warm caloric response for each unilateral ear on the same cohort of subjects as in the present study, Patki, Ronen, Kaylie, Frank-Ito, and Piker (2016) reported that associations between warm caloric output and temporal bone anatomy were strongest at mastoid airspace volumes ($R^2 = 0.24$), followed by mastoid airspace SA:V ($R^2 = 0.22$). Although not reported in Patki et al. (2016), correlations between warm caloric output and mastoid airspace

Figure 4. Multivariate models are shown for the clinically indicated caloric predictor (CICP) using the optimized anatomic parameters for warm caloric inter-ear differences (Model 4) and an independently optimized model for the CICP (Model 5).

volumes ($p = .02$) and between warm caloric output and mastoid airspace SA:V ($p = .03$) were statistically significant.

Temporal Bone Confidence Interval Estimation

Descriptive statistics (average and standard deviation) alongside 95% confidence interval estimates for each of the 16 interaural anatomic differences (in percent) in temporal bone anatomic parameters are presented in Table 4. The average ($\pm SD$) percent interaural difference in Proctor IAC diameter across all 11 subjects was 25.76 ± 21.66 (LCL² = 11.21; UCL³ = 40.31), while the Stimmer IAC diameter was 9.57 ± 6.33 (LCL = 5.32; UCL = 13.83). The average interaural difference in mastoid airspace surface area was 17.70 ± 14.10 (LCL = 8.23; UCL = 27.18), the mastoid airspace volume was 25.71 ± 24.34 (LCL = 9.35; UCL = 42.06), and mastoid airspace SA:V was 11.59 ± 9.65 (LCL = 5.11; UCL = 18.08). Interaural differences in mastoid bone surface area, volume, and mastoid bone SA:V were 6.75 ± 3.49 (LCL = 4.22; UCL = 13.84), 9.03 ± 7.16 (LCL = 4.21; UCL = 13.84), and 6.52 ± 6.06 (LCL = 2.44; UCL = 10.59),

¹SD = standard deviation

²LCL = 95% lower confidence limit

³UCL = 95% upper confidence limit

Figure 5. Interaural differences in internal auditory canal measurements, using measurement protocols from Proctor, 1982 (P), and Stimmer et al., 2015 (S), to measure diameter (D), circumference (C), and the difference between D and C ($|P-S|_x$) are shown with respect to warm caloric inter-ear differences (WCD).

respectively. Interaural differences in LSCC surface area, volume, and mastoid bone SA:V were 14.47 ± 11.69 (LCL = 6.62; UCL = 22.33), 32.70 ± 21.08 (LCL = 18.54; UCL = 46.87), and 11.59 ± 9.65 (LCL = 5.11; UCL = 18.08), respectively. The average interaural difference in LSCC–TM distance was 5.30 ± 3.97 (LCL = 2.63; UCL = 7.96). In addition, the average percent inter-ear warm caloric difference across all anatomic parameters was 21.04 ± 21.77 with LCL = 6.41 and UCL = 25.67.

Averages ($\pm SD$) from absolute computed values with confidence intervals for each anatomic parameter across 22 temporal bones in 11 subjects are presented in Table 5. The average Proctor IAC diameter was 5.18 ± 1.51 mm (LCL = 4.51 mm; UCL = 5.85 mm), while the Stimmer IAC diameter was 4.37 ± 1.22 mm (LCL = 3.83 mm; UCL = 4.91 mm). The average mastoid airspace surface

area was $7,907 \pm 3,838$ mm² (LCL = 6,206 mm²; UCL = 9,609 mm²), the mastoid airspace volume was $5,395 \pm 3,079$ mm³ (LCL = 4,030 mm³; UCL = 6,761 mm³), and mastoid airspace SA:V was 1.55 ± 0.29 mm⁻¹ (LCL = 1.42 mm⁻¹; UCL = 1.68 mm⁻¹). The mastoid bone surface area, volume, and mastoid bone SA:V were $13,733 \pm 1,603$ mm² (LCL = 13,022 mm²; UCL = 14,444 mm²), $21,484 \pm 3,921$ mm³ (LCL = 19,746 mm³; UCL = 23,223 mm³), and 0.66 ± 0.14 mm⁻¹ (LCL = 0.60 mm⁻¹; UCL = 0.72 mm⁻¹), respectively. The LSCC surface area, volume, and mastoid bone SA:V were 64.21 ± 11.04 mm² (LCL = 59.31 mm²; UCL = 69.10 mm²), 11.84 ± 4.97 mm³ (LCL = 9.64 mm³; UCL = 14.04 mm³), and 5.87 ± 1.45 mm⁻¹ (LCL = 5.23 mm⁻¹; UCL = 6.52 mm⁻¹), respectively. The mean LSCC–TM distance was 9.85 ± 0.69 mm (LCL = 9.54 mm; UCL = 10.16 mm).

Figure 6. Inter-aural differences in volume (V), surface area (SA), and surface area-to-volume ratio (SA:V) for mastoid bone and mastoid airspaces are demonstrated with respect to warm caloric inter-ear differences (WCD).

Discussion

Temporal bone anatomy has been linked to heat transfer, the first step of the caloric mechanism (Buchman et al., 2004; Feldmann et al., 1991; Kondoh et al., 2009; Pau et al., 2001). Studies have reported that greater heat transfer occurs in the setting of smaller mastoid volumes and larger mastoid airspaces SA:V (Feldmann et al., 1991; Harrington, 1969). The present study investigates associations between interaural differences in temporal bone anatomy and magnitude of caloric asymmetry in subjects with normal caloric test results. Since the validity of the caloric test relies on the assumption that the temporal bone anatomy is either symmetrical in both ears or, if assessing vestibular function post-operatively, unchanged, it is important to understand this relationship. To our knowledge, this study is the first to investigate the role of interaural differences in temporal bone anatomy on inter-ear caloric differences by comparing caloric response against 16 anatomic parameter

values using both multivariate and univariate regression methods.

In this pilot study, we successfully developed multivariate regression models based on IAC and temporal bone anatomic parameters that can predict almost 100% of the variabilities in interaural differences in both warm caloric responses and CICP responses ($r = 0.999$, see Figure 3; $r = 0.999$, see Figure 4). Our pilot results suggest that the complexity of normal caloric asymmetry outcomes cannot be adequately described by a single anatomic parameter, but rather by a combination of anatomic parameters. Notice that interaural differences in mastoid airspace volume and mastoid bone volume were not included in Model 3, while the addition of either or both variables will increase the correlation coefficient to 1.0 from 0.999, the benefit of including either or both variables is less than overly complicating Model 3 equation. The variables included in all multivariate models were selected post hoc based on their

Figure 7. Interaural differences in volume (V), surface area (SA), surface-area-to-volume ratio (SA:V), and distance to the tympanic membrane (TM) of the lateral semicircular canal (LSCC) are demonstrated with respect to warm caloric inter-ear differences (WCD).

statistic significance as part of a hypothesis-generating data set of “normal” subjects to be applied toward the study of subjects with either vestibular dysfunction or alteration of the temporal bone.

The degree of interaural difference in temporal anatomy demonstrated in Table 4 is consistent with those of related studies, as a previous report evaluating the interaural anatomic variation in 48 normal subjects, using a 512×512 matrix resulting in 0.18×0.18 mm pixilation

as was performed in this report, demonstrated interaural differences averaging 13% (range = 9%–20%) across six temporal bone anatomic parameters (Sepahdari & Mong, 2013). Although such reconstructions are not perfect estimates of anatomic dimensions, a report of 3D reconstructions for 14 subjects with slightly poorer scan resolution than the above or present studies found mean error for labyrinth, ossicles, and auditory canal measurements to be below 0.5 mm (Noble, Dawant, Warren, & Labadie, 2009).

Table 4. Interaural differences of anatomic parameters.

Anatomic parameter	M (%)	SD (%)	LCL (%)	UCL (%)
Proctor IAC diameter	25.76	21.66	11.21	40.31
Proctor IAC circumference	11.03	8.74	5.16	16.90
Stimmer IAC diameter	9.57	6.33	5.32	13.83
Stimmer IAC circumference	8.06	7.55	2.99	13.13
[Proctor _{Circum} – Stimmer _{Circum}]	108.82	100.55	41.27	176.36
[Proctor _{Diam} – Stimmer _{Diam}]	125.97	64.19	82.85	169.10
LSCC volume	32.70	21.08	18.54	46.87
LSCC surface area	14.47	11.69	6.62	22.33
LSCC SA:V	19.64	11.82	11.70	27.57
LSCC-to-TM distance	5.30	3.97	2.63	7.96
Mastoid airspace volume	25.71	24.34	9.35	42.06
Mastoid airspace surface area	17.70	14.10	8.23	27.18
Mastoid airspace SA:V	11.59	9.65	5.11	18.08
Mastoid bone volume	9.03	7.16	4.22	13.84
Mastoid bone surface area	6.75	3.49	4.40	9.09
Mastoid bone SA:V	6.52	6.06	2.44	10.59

Note. LCL = 95% lower confidence limit; UCL = 95% upper confidence limit; IAC = internal auditory canal; LSCC = lateral semicircular canal; SA:V = surface-area-to-volume ratio; TM = tympanic membrane.

Table 5. Absolute measurements of temporal bone anatomy.

Anatomic parameter	M	SD	LCL	UCL
Proctor IAC diameter	5.18 mm	1.51	4.51	5.85
Proctor IAC circumference	16.46 mm	4.01	14.68	18.24
Stimmer IAC diameter	4.37 mm	1.22	3.83	4.91
Stimmer IAC circumference	15.39 mm	4.27	13.49	17.28
$ Proctor_{Circum} - Stimmer_{Circum} $	1.14 mm	0.84	0.76	1.51
$ Proctor_{Diam} - Stimmer_{Diam} $	0.88 mm	1.13	0.38	1.38
LSCC volume	11.84 mm ³	4.97	9.64	14.04
LSCC surface area	64.21 mm ²	11.04	59.31	69.10
LSCC SA:V	5.87 mm ⁻¹	1.45	5.23	6.52
LSCC-to-TM distance	9.85 mm	0.69	9.54	10.16
Mastoid airspace volume	5,395.00 mm ³	3,079.00	4,030.00	6,761.00
Mastoid airspace surface area	7,907.00 mm ²	3,838.00	6,206.00	9,609.00
Mastoid airspace SA:V	1.55 mm ⁻¹	0.29	1.42	1.68
Mastoid bone volume	21,484.00 mm ³	3,921.00	19,746.00	23,223.00
Mastoid bone surface area	13,733.00 mm ²	1,603.00	13,022.00	14,444.00
Mastoid bone SA:V	0.66 mm ⁻¹	0.14	0.60	0.72

Note. LCL = 95% lower confidence limit; UCL = 95% upper confidence limit; IAC = internal auditory canal; LSCC = lateral semicircular canal; SA:V = surface-area-to-volume ratio; TM = tympanic membrane.

Clinical Significance

Despite gaps in its current mechanistic understanding, the caloric stimulation test remains the gold standard in helping clinicians determine the presence of vestibular disease (Dros et al., 2010; Tusa, 2010). This study suggests that, for subjects with “normal” caloric findings and without altered temporal anatomy, combined differences in interaural temporal bone anatomy may dictate caloric output, although the correlation does not hold true across individual interaural anatomic differences. This information may be particularly valuable for future reports of subjects with and without vestibular symptoms following changes in temporal anatomy, as commonly result from operations for infections of the mastoid bone, otosclerosis, TM perforations, and cochlear implants. Post-operative changes in temporal anatomy and the resultant mechanisms that may contribute to vestibular dysfunction in such patients are not well known (Buchman et al., 2004).

Limitations and Future Direction

Clinically “normal” caloric testing, even when alongside ocular motility and positional studies, is not synonymous with normal vestibular function. Caloric testing predominantly measures horizontal canal function, notably excluding the vertical canals and otoliths. The sample size was limited ($n = 11$) because temporal CT scans necessary for reconstruction are not commonly obtained for subjects found to not exhibit vestibular pathology. In addition, the current methodology for 3D reconstruction of the temporal bone anatomy is time consuming and can be cumbersome in patients with low-resolution CT images. Approximately 88 man-hours were required to create 3D models of 22 temporal bones used in the present study. Future directions aimed at strengthening preliminary findings in this study include continued identification of patients with head CT scan and caloric stimulation, which is necessary for

increasing the statistical power of our analyses. In addition, a prospective study including nonsymptomatic patients would increase the external validity of our findings.

Conclusion

In summary, this retrospective pilot study of the relationship between temporal bone anatomy and caloric output in subjects with clinically normal caloric testing and unmodified temporal anatomy showed that combined interaural anatomic differences correspond to the degree of observed IEDs in monothermal and bithermal caloric output. These findings may serve as a basis of comparison for future studies evaluating vestibular subjects with altered temporal bone anatomy and with clinically “abnormal” caloric findings.

Acknowledgments

Research reported in this article was supported by the National Institute on Deafness and Other Communication Disorders of the National Institutes of Health under Grant 5T32DC013018-03 and by the National Center for Advancing Translational Sciences of the National Institutes of Health under Grant TL1TR001117 (awarded to David Carpenter). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors thank Aniruddha Patki and Ofri Ronen for their contributions to this work and give special thanks to ANSYS, Paolo Maccarini, and Murali Kadiramangalam (ANSYS Global Academic Program Director) for support. All authors gave final approval for publication.

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