International Journal of Pediatric Otorhinolaryngology 84 (2016) 110–115

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

# Craniofacial shape in children with and without a positive otitis media history

Allison P. Gremba [a,*], Seth M. Weinberg [b], J. Douglas Swarts [c], Margaretha L. Casselbrant [c]

[a] Department of Anthropology, University of Pittsburgh Dietrich School of Arts and Sciences, United States
[b] Center for Craniofacial and Dental Genetics, Department of Oral Biology, School of Dental Medicine, University of Pittsburgh, United States
[c] Department of Otolaryngology, University of Pittsburgh School of Medicine, United States

ARTICLE INFO

*Article history:*
Received 23 December 2015
Received in revised form 12 February 2016
Accepted 27 February 2016
Available online 5 March 2016

*Keywords:*
Craniofacial shape
Geometric morphometrics
Otitis media
Children

ABSTRACT

*Objectives:* Past studies using traditional morphometric approaches have reported a handful of differences in craniofacial dimensions between individuals with and without otitis media (OM). In this study, a geometric morphometry (GM) approach was used to determine if craniofacial shape is different among children with no history of OM and a history of recurrent acute OM (RAOM) at two different ages.
*Methods:* Nineteen standard landmarks were identified on lateral cephalometric radiographs from 79 children (41 Control, 38 RAOM) at 4 years and 52 children (27 Control, 25 RAOM) at 6 years of age. Following Procrustes superimposition of the landmark coordinate data, comparisons of group differences in overall size and shape were performed. Discriminant function analysis and principal component analysis were used to determine which, if any, aspects of shape variation distinguished RAOM from Control groups.
*Results:* At 4 years of age, craniofacial size and shape were significantly different between RAOM and Control groups ($p < 0.05$). Shape differences were evident in the relative positions of the mandible, cranial base, external acoustic meatus, sphenoid and palate. Those shape differences were not found in the 6-year old group.
*Conclusions:* At 4 years of age, the RAOM and Control groups have distinct craniofacial morphologies, but by 6 years of age these differences have largely disappeared. This is consistent with the clinical observation that excess RAOM risk resolves around 6 years of age and the hypothesis that this resolution is partially a result of age-related craniofacial changes.


## 1. Introduction

Otitis media (OM), an inflammation of the middle ear (ME) mucosa, is most prevalent in the pediatric population but also occurs in adolescents and adults [1]. Usually, OM onset is closely associated with the signs and symptoms of a viral upper respiratory infection [2]. Localized symptoms and signs of ME mucosal infection may signal extant OM, called acute OM (AOM), or may not, called OM with effusion (OME). While most OM episodes are self-limited, the mucosal inflammation can persist from months to years in a subset of affected children, a form of the disease called chronic OME (COME). In addition, some children experience frequent AOM recurrences (RAOM). COME and RAOM are difficult to manage conditions accompanied by complications such as hearing losses and balance disturbances that contribute to childhood morbidity [1].

There is an extensive literature describing the characteristic traits, behaviors, environments and conditions that may increase a child's risk for RAOM or COME. For example, past studies reported a high heritability for both COME and RAOM [3,4], and the risks for those expressions are increased by behaviors and environments that promote upper-respiratory virus infections [5], comorbidities such as nasal allergy, frequent colds, and gastro-esophageal reflux disease [2,6–9], and craniofacial dysmorphologies such as cleft palate [10,11]. Regarding the latter category of risk modifiers, more subtle craniofacial variants reflected in "head shape" [12–16],

*Abbreviations:* AOM, acute otitis media; COME, chronic otitis media with effusion; DFA, discriminant function analysis; ET, Eustachian tube; ETD, Eustachian tube dysfunction; ETF, Eustachian tube function; GM, geometric morphometry; ME, middle ear; OM, otitis media; OME, otitis media with effusion; PC, principal component; PCA, principal components analysis; RAOM, recurrent acute otitis media.

* Corresponding author at: University of Pittsburgh, Department of Anthropology, 3302 WWPH, Pittsburgh, PA 15260, United States. Tel.: +1 412 728 2455.
*E-mail address:* apc22@pitt.edu (A.P. Gremba).

http://dx.doi.org/10.1016/j.ijporl.2016.02.029
0165-5876/

cranial base width, length and flexion angle [16–20], facial proportions [15–18], maxillary-mandibular interactions [21–26], and nasopharyngeal volume [27–31] have been reported to characterize children and adults with RAOM or COME.

Common to all of these morphological OM risk modifiers is their potential to disturb the functional anatomy and geometry of the Eustachian tube (ET) system resulting in ET dysfunction (ETD) [19,32,33]. The ET, a usually closed biological tube extending along the cranial base between the middle ear and nasopharynx, actively opens during swallowing and yawning to equalize middle ear and ambient pressures [34]. Clinical studies and animal experiments convincingly show that an inefficient ET opening mechanism, i.e. ETD, plays a causal role in the pathogenesis of OM, its persistence as COME and its recurrence as RAOM [35–39].

At present, a causal relationship between craniofacial morphology and excess OM risk remains hypothetical. Most past studies examining that relationship were designed as general surveys of a large number of constructed linear and angular craniofacial measures with "risk factors" that discriminate between control and disease groups identified using pairwise tests. The drawbacks of this methodology are the inability to separate size from shape and its susceptibility to false identifications of significant measures due to the multiple comparisons problem. In addition, the panel of craniofacial dimensions examined is not consistent across studies and only a few studies provided sufficient information to characterize the OM phenotypes (no OM, COME, RAOM, chronic suppurative OM) being compared, though the risk modifiers are expected to be phenotype specific. Consequently, the identified panel of (candidate) morphological risk modifiers is extremely broad with few replicated members across studies. Often, as for example with cranial shape, identified associations with OM are not reproduced across studies even when the specific morphology is well characterized (e.g. the cephalic index) [13].

The current study was designed to explore the validity of the structure-function hypothesis using methods that avoid many of the methodological criticisms listed above. Specifically, the formal mathematical techniques of geometric morphometry [40,41] (GM) were used to reconstruct and mathematically describe complex representations of craniofacial shape based on a set of standard landmarks identified on lateral cephalometric X-rays. The landmarks chosen capture previously identified regions that discriminate between affected and unaffected children. Our basic hypotheses are: (1) craniofacial shape is different in children with a well-documented history of RAOM when compared with unaffected Controls, and (2) these shape differences involve components of the cranial base and palate. The comparison was performed at two age points (4 and 6 years) in order to test the additional hypothesis that these shape differences will decrease with advancing age so as to correspond with the clinically observed reduction in RAOM risk around 6 years of age [42].

## 2. Methods

The materials analyzed in this report derive from an ongoing, NIH-funded, longitudinal study designed to characterize the changes in craniofacial anatomy, ET function (ETF) and OM prevalence in young children enrolled at 3 years of age and followed through 8 years of age. Study participants were recruited from the general Pittsburgh area by targeted advertisement. As part of this study, data on craniofacial morphology (via anthropometry, dental casts, cephalometric X-rays and MRI scans) are collected at standardized time intervals. Further, detailed data are routinely collected on ETF, middle ear status (otomicroscopy, tympanometry) and episodes of OM, RAOM and COME. Upon entry to the study, the enrolled children are assigned to 1 of 3 groups (Control, COME or RAOM) based on a history provided by the parent and review of personal physician and, when available, hospital records. The criteria for Control included no significant history of OM (no COME or RAOM episodes) and no history of receiving tympanostomy tubes. Children were classified as RAOM if they had 3 or more episodes of AOM in one year or 5 or more episodes of ME effusion, at least 2 AOM, by study entry or tympanostomy tubes inserted for RAOM during the year prior to study enrollment with or without intervening episodes of OME. Children were classified as COME if they did not have RAOM, but had 3 or more consecutive months of middle ear effusion bilaterally, 6 consecutive months of effusion if unilateral or 3 or more episodes of OME lasting for at least 2 months with at least one episode of OME or tympanostomy tubes insertion in the year prior to entry [13]. Children were excluded from study participation if presenting with cleft palate, other craniofacial anomalies, syndromes predisposing to OM, or orthodontic treatment, cholesteatoma or ear surgery other than tympanostomy tube insertion. The study was approved by the University of Pittsburgh Institutional Review Board (IRB).

The present study compared the Control and RAOM groups; the COME group and other subgroup sample sizes were too small to be included in the comparison. At 4 years of age, data for a total of 41 Control and 38 RAOM children were available. At 6 years, the currently available sample is 27 Control and 25 RAOM children. The sample demographics are presented in Table 1. There were no significant differences between the Control and RAOM group in terms of the age, sex or racial distribution ($p > 0.05$). Lateral cephalometric images were recorded using standard clinical procedures from the enrolled children in the two groups at ages 4 and 6 years. Using the tpsDig2 program [43], 19 standard cephalometric landmarks (Table 2), were identified on each image (Fig. 1) by the first author and those identifications were repeated after at least 2-weeks. The first author was blinded to the child's group assignment during both landmarking sessions. There were no significant differences in landmark coordinates between the two sessions (intra-class correlation coefficient >0.99 for each landmark). The $X$ and $Y$ coordinates for two measures of each landmark on all images were averaged and imported into the program MorphoJ v1.05f for GM analysis [40,44,45].

Shape comparisons were done separately for each age group (4 and 6 year). The first step in the analysis was a Procrustes superimposition of the raw landmark coordinates to center, rotate and scale the landmark configurations [46]. This iterative process allows multiple homologous shapes (e.g. from different

**Table 1**
Demographic characteristics for the groups and subgroups.

| Age group | OM group | *N* | Avg. age | Sex | | Race | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Male | Female | White | Black | Native American | Not reported |
| 4 years[a] | Control | 41 | 4.2 | 22 | 19 | 29 | 6 | 1 | 5 |
| | RAOM | 38 | 4.1 | 19 | 19 | 25 | 7 | 1 | 5 |
| 6 years[a] | Control | 27 | 6.3 | 13 | 14 | 18 | 5 | 0 | 4 |
| | RAOM | 25 | 6.2 | 14 | 11 | 14 | 5 | 1 | 5 |

[a] No significant differences in mean age or in the sex or race distribution between control and rAOM (all $p > 0.05$).