

Geometric Shape Scaling Factors for the Pediatric Brain Based on Morphometric Analysis

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ABSTRACT

More brain structure specific scaling factors are needed to create more accurate models of the pediatric population for injury prevention research. This study examines the internal structure of the brain using the common imaging modality of magnetic resonance imaging to collect data on subjects ranging in age from newborn to 21 years old. This data set was then analyzed using geometric morphometrics to quantify the shape change of the measured structures. From this analysis geometric scaling factors for each structure were determined. The accuracy of parametric models of the head will be improved by using these structure specific scaling factors.

INTRODUCTION

Injuries caused by motor vehicle crashes (MVCs) are the leading cause of death for children in the United States as well as the leading cause of head injury[1-3]. Head trauma also results in significant morbidity in the pediatric population and contributes to approximately 300,000 hospitalizations a year[4]. The focus of this study is the improvement of geometric scaling factors for the pediatric brain structures using a morphometric analysis. Geometric morphometrics has been used in the anthropology and comparative biology fields for some time to assess differences in fossils and across species[5]. This knowledge can be combined with medical imaging modalities to quantify shape changes[6]. The application for this knowledge is improving the predictive abilities of current finite element models. These models of the brain, such as the National Highway Traffic Safety Administration's (NHTSA's) SIMon model[7], have detailed representations of the structures within the brain but are the size and shape of an adult. Geometric scaling factors for these structures will allow for the adaptation of these models to a correct

pediatric size and shape. With more accurate finite element models the response of the pediatric skull and brain can be better predicted for improved countermeasure evaluation and design.

METHODS

The Magnetic Resonance (MR) imaging modality, instead of the more common Computed Tomography (CT) modality, was selected for this study because it better displays soft tissue. The individual structures in the brain studied were shown more clearly in these scans with clearer delineation between them. The scans used in this study were selected from a medical center's radiological database. A trained radiologist assisted in the collection and identification of the scans to ensure all subjects were grossly normal in their brain and skull anatomy. The individuals ranged in age from newborn to 21 years old and included males and females. The data set consisted of 58 individuals from the following age groups: newborn, three months, six months, one year, three years, six years, ten years, fifteen years, and twenty one years. There was limited availability of MR scans for children under one year. Normally a MR imaging procedure was reserved for children with conditions resulting in abnormal brain anatomy; therefore, there was some flexibility in the exact age of the child. This variation in age was accurately accounted for in the landmark data analysis by using the exact age of the child, correct to the day, in the data analysis steps.

Slice et al [5, 8] described a method to compare homologous points across individuals to assess shape differences. This method relies on identifiable landmarks on all individuals, such as points on bony structures, as the basis of comparison. The problem encountered with these "true" landmarks for the brainstem was that while they could be used to

determine basic relationships and general sizing of the structure, they failed to accurately describe the curvature. The basic height of the brainstem could be determined using the most anterior point of the brainstem at the level of the foramen magnum and the most anterior point on the cerebral peduncle. This measurement could provide scaling factors for this measurement; however, the effect of age on diameter of the brainstem for the majority of the structure could not be measured. Additionally, there is significant variability in the location of the point of intersection between the slices of the scan and the brainstem. This variability combined with the differing heights of individuals made first appearance type landmarks inconclusive because the points could not be reasonably argued to be homologous. Therefore, true landmarks were supplemented with the sliding landmark method described by Bookstein [6] and Gunz [9].

Sliding landmarks were created by developing a surface on the structure by placing an equal number of points on the structure of interest on all individuals in the data set. Then, these points are allowed to slide on planes tangent to the surface until a value described as bending energy is minimized. This concept of bending energy is based on drafting methods that used a thin plate metal spline to draw curves. By taking heights of the curve between points, the amount of energy needed to bend the spline into the shape of the curve is determined. Algebraic manipulations are performed resulting in a matrix equation that describes the tangent vectors (T) the points move along to minimize bending energy as described by equation 1.

$$T = -(U^T L_K^{-1} U)^{-1} U^T L_K^{-1} Y^0 \quad (\text{eq.1})$$

In equation 1, U is the matrix describing the x, y, and z directions each point would travel tangent to the curve described by the landmarks; the L term is the bending energy matrix; and the Y term is the initial position in x, y, and z coordinates of the landmarks. If the bending energy is minimized, the points on the curves are considered homologous structures. This step is effectively a statistical analysis of the data to determine the point locations that would be homologous across structures.

To create the initial surface point clouds, the MR scans were individually imported into Amira (Mercury Computer Systems, Chelmsford, Massachusetts). For the MR images, sagittal and transverse scans of each individual were used and had to be co-registered since these scans of the same individual were taken at different times. This process is an automated process in the software and for this study the options "extensive direction" and "normalized mutual information" were selected. For each slice, the structure was outlined with multiple landmarks placed close to each other. Each landmark set started at the most anterior point on the mid-brain line. The mid-brain line was determined by

the position of the falx for the superior components and the division of the cerebellum for the inferior components. From this point, the outline of the structure was followed until it returned to the starting point. Below is a picture of a single slice of a cerebrum illustrating the datapoints selected to outline the structure.

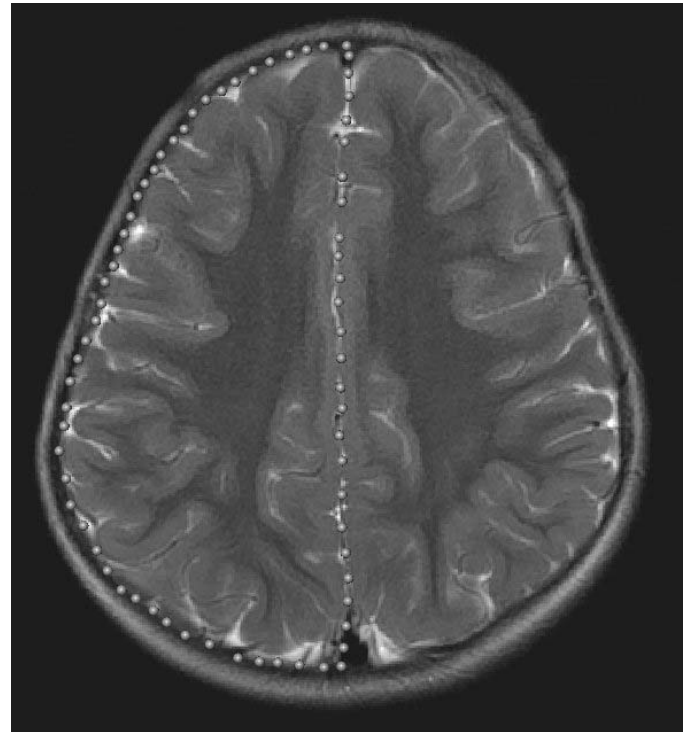


Figure 1- Sample Cerebrum Points

This process was repeated on each slice beginning on the first appearance and ending at the last appearance. Each slice was defined as a separate landmark set since there were different numbers of points selected on each slice. The same process was repeated using sagittal slices to capture the points superior and inferior to the first and last appearances on the transverse slices.

The problem with these data sets is that there were not an equal number of data points on each individual. This is a necessary requirement for the bending energy and Procrustes analysis; therefore, the next step was creating surfaces with the same number of points regardless of the number of points collected from the images. A function was written in Matlab (The MathWorks, Natick, Massachusetts) that created a curve from the data points selected on each slice. The data points were taken close together on the images to make this curve as accurate as possible. The next step was taking a user specified number of points from this curve. The program equally spaced these points along each curve defined by a landmark set. After creating evenly spaced points along the curve within a slice, equally spaced points were created in an orthogonal direction. As an example, on the transverse slices, the orthogonal direction was in the superior and inferior direction. The line defined in the orthogonal direction was the point of the same number for each transverse slice. For example, the first orthogonal line would go through point

one on transverse slice one then point one on transverse slice 2 and continue to point one on the last transverse slice. Once this curve was defined, the same process of equally spacing points based on a user input number of points desired for the curve was completed. After this Matlab program was complete, every individual had the brain structures of interest defined by an equal number of points. For this study, 290 landmark points were calculated for the brainstem and 340 points were calculated for the cerebellum and cerebrum for each individual according to this method.

Once the bending energy was minimized, the points could be considered homologous. The shape differences were then quantified using a general Procrustes analysis then a regression analysis. The Procrustes analysis translated, scaled and rotated the landmark data set to remove size differences and align them to a common centroid and orientation[8]. This manipulation of the dataset was performed using the general Procrustes analysis as described by equation 2.

$$r(X_2 - 1t)H = X_1 + E \quad (\text{eq.2})$$

In this equation r is the matrix that scales the landmark set through an isometric dilation or compression about the centroid; X_1 and X_2 are the compared individuals; t is the matrix that translates the two datasets to a common centroid; H is the rotation of the point set; and E is the shape difference between the two individuals. This equation was iteratively run for all individuals until the changes were no longer significant. At this point a linear and quadratic regression analysis was performed to determine the relationship between age and point location. To assess the statistical significance of the changes, a permutation statistical test was used. The permutation test assesses if a predicted landmark configuration better matches the actual landmark configuration than a random combination of age and landmark location. It is important to note that in shape analysis the individual data points have no meaning except as a part of the shape description.

The end state of this study was the calculation of initial geometric scaling factors for the brainstem. To calculate these values, the 21 year old age group was considered the base age because current models have the size and shape of an adult. The maximum height, length, and width of the structure were measured for each predicted shape based on age. The scaling factors are basic ratios that relate the measured length of the target age to the measured length of the same dimension of a 21 year old.

RESULTS

Each structure was separately analyzed. The brainstem was analyzed first and a method of using the general Procrustes analysis with and without scaling was tested.

BRAINSTEM - The general Procrustes analysis was completed using two methods for the brainstem. One method isolated shape change by including the scaling step of the analysis and the second method did not include scaling. By not scaling the data, the regression performed assessed the change in shape and size as a function of age.

The first method which included scaling resulted in age describing 83% of the shape change in the brainstem using a linear regression and 87% of the shape change in the brainstem using a quadratic regression. To assess the statistical significance, permutation tests with 100,000 iterations were performed with resulting p-values of 0.1745 for a linear regression and 0.1331 for a quadratic regression. Below are the resulting permutation graphs from these procedures.

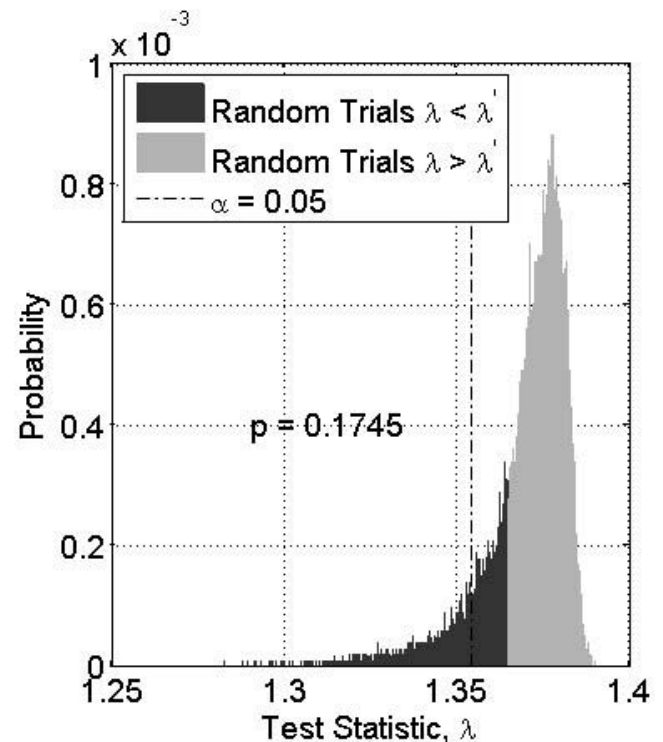


Figure 2- Permutation graph for a linear regression of brainstem points, with scaling