Biology 152

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Are cervical vertebral sizes different in Trisomy 21? A developmental comparative pilot study

Alexis Schroeder, Courtney Miller, and Houri K. Vorperian

Vocal Tract Development Lab, Waisman Center, University of Wisconsin - Madison

I. OBJECTIVE:

Individuals with Down syndrome (DS), who are born with an extra copy of chromosome 21 (Trisomy 21), experience high rates of cervical spine (C-spine) abnormalities. This developmental pilot study quantitatively compares the C-spine areas, using computed tomography (CT) images in the midsagittal plane, from individuals with Trisomy 21 against the C-spine area growth trends of typically developing individuals.

II. INTRODUCTION:

The C-spine, which consists of the first seven cervical vertebrae (C1-C7), plays a central role in head mobility, skull stability, and protection of the spinal cord. Due to the vital role the C-spine plays, complications and instability can be harmful, and even deadly.

Individuals with DS (Trisomy 21) experience higher rates of C-spine abnormalities and instabilities [1, 4, 5] including, but not limited to: atlantoaxial instability, occipitocervical instability, widened anterior atlanto-odontoid distance, and cervical spondylosis.

The higher rates of instability in individuals with DS has been attributed to C-spine birth defects, loosening of the transverse ligaments, misshapen condyles, and reduced muscle tension [3, 10]. However, to our knowledge, there is no research to date, to determine if developmental differences of the C-spine could also contribute to understanding these spinal complications.

Additionally, understanding the development of the C-spine in individuals with DS is necessary because the C-spine serves as the skeletal framework of the vocal tract (VT; oral and pharyngeal cavities used during speech production). The VT dysmorphology in speakers with DS is believed to contribute to the reduced speech intelligibility or speech clarity that is a typical and often a lifelong problem in speakers with DS is [6, 11, 12].

Finally, quantifying C-spine development is necessary to better understand the shorter stature in individuals with DS, which has been attributed to skeletal developmental delays [2] and decreased pubertal growth rate in DS [8,9]. It is only recently that researchers in the Vocal Tract Development Lab (Waisman Center, UW-Madison) have started quantifying the development of the C-spine in typically developing individuals.

The purpose of this developmental pilot study is to compare areas of the C2-C7 cervical vertebral bodies in DS, in the midsagittal plane, to the typically developing (TD) male and female growth trends. We hypothesize that the C-spine areas will be smaller and growth during puberty will be decreased in DS as compared to TD. Such information will help understand how the C-spine in individuals with DS develops to help guide future research and potential treatment plans.

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III. METHODS:

Imaging studies: Using the Vocal Tract Development Lab imaging database, 10 CT scans from 7 individuals with DS (4 females and 3 males) ages 1-19 years were used for data collection using the following procedures.

Procedures:

1. Landmarking: Using CT scans, 3D landmarks were placed on the corners of the vertebral bodies in the midsaggital plane using the sagittal (X), coronal (Y) and axial (Z) views to guide accurate landmark placement on C2-C7 (unless C5, C6 and C7 were cutoff from view). As seen in Figure 1, three landmarks were placed on C2, and 4 were placed on C3-C7; and used to calculate the area of each C-spine after the following pre-processing steps (2-to-4).

Figure 1: CT midsagittal view of the C-spine (C2-C7). The landmarks (red dots) are placed on the corners of the vertebral bodies in the midsagittal plane.

2. Best Fit Plane: The least square best fit plane was found for the 3D landmarks of each vertebra. See Figure 2, blue plane.

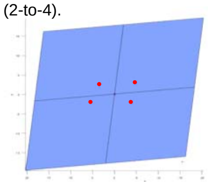


Figure 2: The blue plane shows the least square best fit plane for the four corner landmarks.

3. Plane Rotation: The best fit plane was rotated until all x-coordinates were the same, resulting in a vertical plane in 2D. See Figure 3.

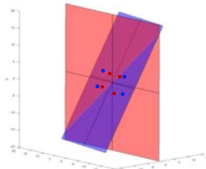


Figure 3: The blue plane with the red landmarks is the same as Figure 4. The red plane with the blue landmarks depicts the rotation of the best fit plane to a vertical position removing the third dimension of the plane. The landmarks maintain a constant distance from the plane throughout the rotation.

4. Point Rotation: All points were rotated onto the best fit plane while maintaining the distance from each landmark to the centroid, creating a 2D polygon representing the midsagittal vertebra. See Figure 4.

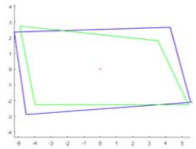


Figure 4: The blue polygon depicts the shape made after the points were rotated onto the best fit plane while maintaining constant distance from the centroid. The green polygon shows the shape that would have been made if the points were moved onto the plane, without maintaining constant distance from the centroid.

5. Calculations and Plotting: The polygon area was calculated and these areas were plotted onto the sex-specific TD growth trends recently established in the Vocal Tract Development Lab (based on 130 TD CT scans; 46 females and 84 males)[6].

Figure 5

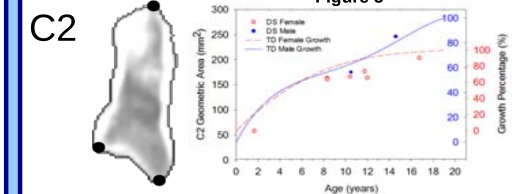


Figure 6

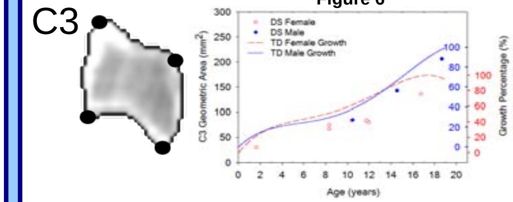


Figure 7

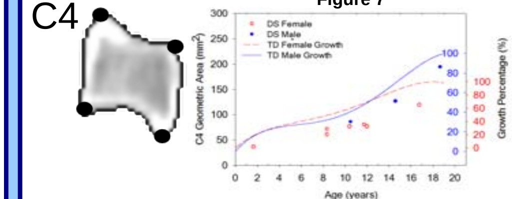


Figure 8

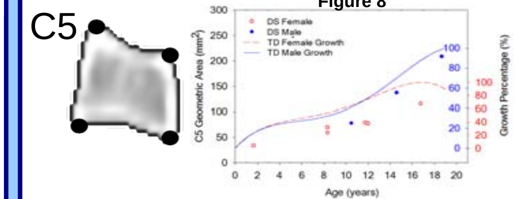


Figure 9

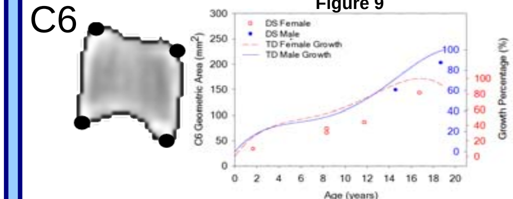
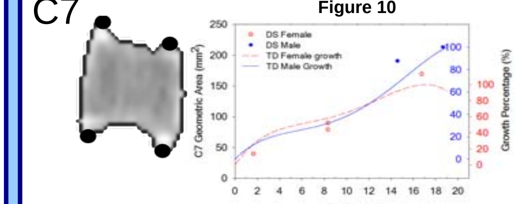


Figure 10



Figures 7-12: DS vertebral areas are plotted on the TD growth trends. Blue, filled circles represent male DS areas and red, unfilled circles represent female DS areas. The dashed, red line represents growth trends for TD females and the solid, blue line represents growth trends for TD males.

IV. RESULTS:

-The C-spine areas in individuals with DS predominately fell below the TD growth trends in C2-C6, however the DS C7 areas were closer to the TD trend line. See Figures 5 to 10.

- All female DS C2 areas fell below the TD growth trend, while the male DS C2 areas crossed the TD growth trend. Female DS vertebrae had little growth from age 8-12 years. See Figure 5.

- The males DS C3-C6 areas were consistently below the TD growth trends; while this was also the case for the female DS C3-C6 areas, the difference in areas appear to increase from the TD growth trend during the course of development. Additionally, like C2, lack of substantial growth occurs in female DS vertebrae from age 8-12 years, suggestive of developmental delay. See Figures 6-8.

-The male DS C7 areas were above the TD growth trend line, while female C7 areas crossed the TD growth trend. Compared to C2-C6, all DS C7 areas appear to correspond with the TD growth trend line. See Figure 10.

V. DISCUSSION:

-Overall, the DS C-spine areas fell below the TD growth trends, supporting the hypothesis that the C-spine of male and female individuals with DS are smaller than the TD C-spine growth trends.

-The lack of substantial growth that occurs in females with DS from age 8-12 years is consistent with previous research reporting decreased pubertal growth rates in individuals with DS [9].

-Males DS C-spine areas seem to follow the TD growth trend more closely, however more data is needed to evaluate further.

-Many of the C-spine problems associated with DS occur in the upper C-spine (C1-C3). Therefore it is noteworthy that C7 areas, which is the furthest cervical vertebra from the C1-C3 problem areas, closely follows the TD growth trend. This observation suggests that the functional instability of the upper C-spine may be correlated with decreased vertebrae size.

-Overall, findings from this pilot study suggest that there appears to be developmental delay in C-spine development in DS; however, additional research with more data is indicated.

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