Comparison of Group Average and Individual Differences in Brain Morphometry in Williams Syndrome

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Introduction

Williams Syndrome (WS) is a rare genetic disorder caused by the deletion of approximately 25 genes in the 7q11.23 region of the genome, which produce several important proteins, like elastin, responsible for cardiovascular and physical characteristics associated with Williams Syndrome. Subjects with WS have low to moderate intellectual disability, and they have deficits in visuospatial ability with relatively preserved language abilities. Previous studies primarily resorted to laborious manual or automatic tracing of each individual 3D image volume to study the shape characteristics of certain neuroanatomical structures in the WS population [1-3]. An alternative is to use automatic methods to register volumes to each other and to generate group averages. These averages, if representative of the population as a whole, can then be used to identify morphological differences between normal and abnormal brains. In this study, we create group averages, and we demonstrate that morphological differences observed in the group averages are similar to the differences observed when measurements are made on each individual image volume.

Methods

Twelve subjects with Williams Syndrome (7 males and 5 females, 22.3±4.1 years old) and twelve age and gender matched typically-developing (TD) subjects (7 males and 5 females, 22.8±5.3 years old) were recruited for this study. The anatomical images were acquired with a 3T Philips Achieva MRI scanner with matrix size of 256*256*170 and isotropic voxels of 1mm^3. A rigid-body registration technique [4] was used to align all twenty-four volumes onto one TD volume. For each group, we generated a volume with average intensity and shape using the average atlas model proposed by Guimond et al [5]. This is an iterative technique, which starts with one of the volumes as an example and converges toward a virtual volume representative of the group as a whole. Images were registered non-rigidly to each other using an automatic intensity-based registration algorithm developed at our institution [6]. Brains were also extracted automatically from each image volume. This was done by applying a pre-defined brain mask to each of the averages and then deforming these masks using a transformation that registers the averages to each volume. Mid-axial views of both averages are shown in Figure 1. Surface renderings of the cortical surfaces are shown in Figure 2. Brain volumes and shape parameters, e.g. the midline length and bending angle as defined in [1], for the corpus callosum on mid-sagittal images, were computed using the skeleton extraction method of [7]. This was done for each of the subjects in the two groups as well as for the two averages. Furthermore, the CC shapes were analyzed along the contour using shape analysis theory and geodesic paths as described in [8].

Results

Figure 1 shows the axial views of the WS (left) and TD (right) averages. The WS average brain is narrower than the TD average brain, especially in the parietal and occipital lobes (after inspection through all slices), which could be linked with the visual-spatial deficits in WS. Figure 2 shows 3D renderings of the cortical surfaces of the two averages. The posterior end of the central sulcus in the left hemisphere does not bend as much and is farther from the inter-hemisphere fissure in the WS average than in the TD average. This agrees well with other findings based on measurements performed on individual brains [2, 3]. Figure 3 shows that the WS group has a substantially smaller (p=0.0003) brain volume, a shorter CC midline length (p=0.0005), and a larger CC bending angle (p=0.001) compared with the TD group. The means of all individuals (blue solid circles) are very close to the group average parameters (red solid circles). The ratio of WS/TD in each of these measurements agrees well with those in [1], where semi-automatic tracing was employed. Figure 4 shows the difference between the CC contours of the WS (red) and the TD (blue) averages. The bottom portion of the figure shows the geodesic difference between the shapes. The largest differences are observed in the genu and splenium sections. The similar results were obtained when all the contours were used.

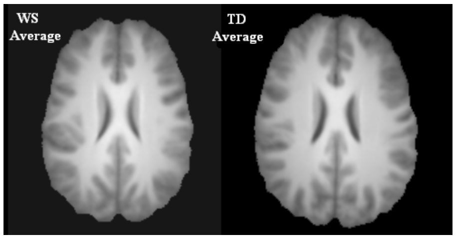

Fig.1.The WS and TD averages. The WS average is narrower than the TD average.

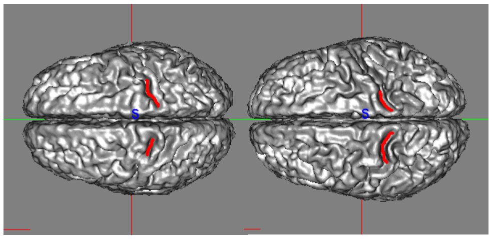

Fig.2. The 3D rendering of WS (left) and TD (right) averages. The red lines trace the central sulcus in each hemisphere.

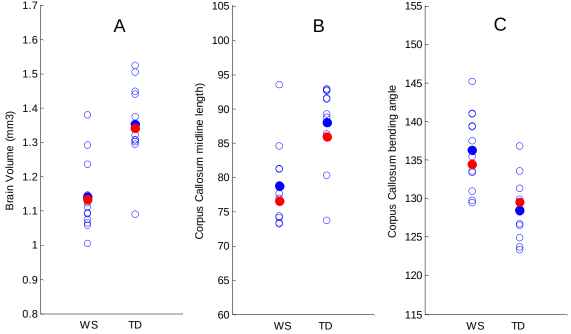

Fig.3. Comparisons between individuals and averages between WS and TD in A (brain volume), B (CC midline length), and C (CC bending angle). The red solid circles are for the averages, the blue solid circles are for the individual means.

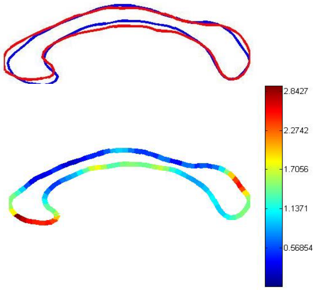

Fig.4. The upper: CC contour in WS (red) and TD (blue) average. The bottom: shape differences between the two contours, color coded with the geodesic path differences.

Conclusion

The study we have performed confirms that comparing measurements between the group averages is a valid approach for comparing group characteristics, and provides valid information similar to comparing measurements obtained manually from individual brains. For instance, differences in the central sulcus shape can be obtained by tracing them on the two average atlases rather than on each individual volume. The same is true for the CC. Comparing shape parameters obtained from contours delineated on individual volumes and those computed from the two averages leads to the same conclusions. Shape analysis based on group averages agrees well with shape analysis of individual volumes, but is fully automatic and so it can be used as a faster and more efficient technique to identify morphological differences between populations.

Acknowledgement

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