Piloting A New Method For Measuring Cerebellar Volume in Children with Neurodevelopmental Disorders

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Chromosome 22q11.2 Deletion

- Chromosome 22q11.2 deletion syndrome (22q11.2DS) includes DiGeorge and Velocardiofacial (VCFS) syndromes.
- Occurs in between 1:2000 and 1:4000 live births via a deletion of 3Mb pairs on the long (q) arm at the 11.2 band of one copy of chromosome 22.
- Complex neurodevelopmental disorder with atypical brain development, socioemotional, medical, and cognitive symptoms with 25-30% developing schizophrenia.
- Developmental neurocorrelates of this risk is under intense investigation using a variety of brain imaging methods.

Overview and Purpose

- Fully-automated computer methods of measuring regional brain differences in children with complex neurodevelopment disorders (NDDs) are subject to systematic error.
- Software and anatomical atlases are often based on typically-developing children's brains, but structural differences in NDDs can be dramatic, leading to further measurement error.
- Humans are more accurate but much slower and fatigable.
- We investigated size differences in putamen volumes between children with 22q11.2DS and those who are typically developing (TD) from MRI anatomical brain scans.

Participants

- Boys and girls ages 7 to 16 years in two groups.
- 22q11.2DS: n = 8: 5 male and 3 female: Mean age = 12.19, SD = 3.00
- TD: n = 2: 1 male and 1 female: Mean age = 12.56, SD = 5.01

Hypothesis

- Children with 22q11.2DS will have smaller cerebellum compared typically-developing controls.

Brain Imaging Method

- T1-weighted high-resolution 3D anatomical magnetic resonance images were acquired using a 3.0T Siemens Trio scanner with Echospeed gradients and a Siemens 8-channel whole head coil.
- Imaging parameters: TR = 2.17 s, TE = 4.82 ms, flip angle = 7°, NEX = 1, 192 slices, 128 x 128 acquisition matrix, FOV = 256, sagittal acquisition with 1 mm^3 voxels, 5 min 4sec duration.

Cerebellum Volume Measures

- The cerebellum was manually outlined on each MR image slice and blinded to diagnosis.
- For all steps of this process, Mango (Research Imaging Institute, U of Texas) was used for region-of-interest parcellation and volume calculations.

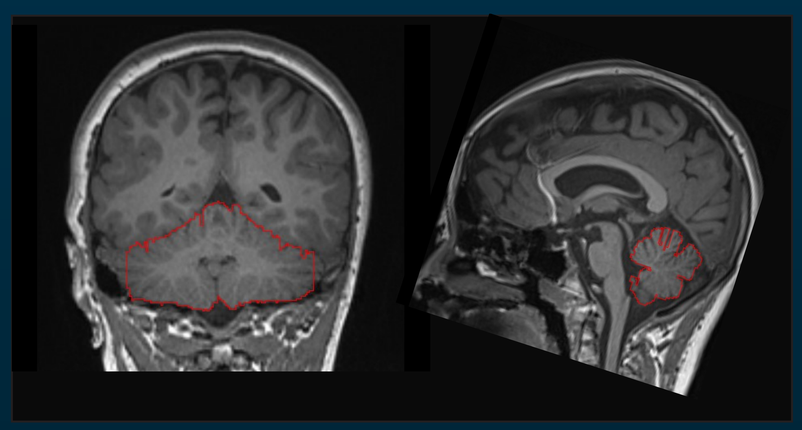

Figure 1. — (above, left to right) High-resolution T1-weighted MRI coronal and sagittal images showing single slices with cerebellum outlined in red.

- T1-weighted whole brain images were imported into Mango (Research Imaging Institute, U of Texas).
- Cerebellum volume was calculated via manual slice by slice tracings of the cerebellum in native space in the sagittal and coronal planes.
- Segmentation starts at the mid-sagittal region image slice progressing laterally in the left and then right hemispheres.
- The cerebellum is traced along the dorsal, caudal and ventral cortical surfaces of the cerebellum.
- The 4th ventricle serves as a boundary along cerebellar lobules I and II (dorsally) and X (ventrally) relative to the 4th ventricle.

Preliminary Results

- As expected, in this very preliminary analysis, mean total cerebellar volume in the 22q11.2DS group (M = 117651.5 mm^3, SD = 8369.2) appears to be smaller compared to the TD group (M = 139279.5 mm^3, SD = 17607.67). Given the small unequal groups, statistical analysis is not justified.
- Cerebellum appears to be smaller, bilaterally as well in the 22q11.2DS group versus the TD group.

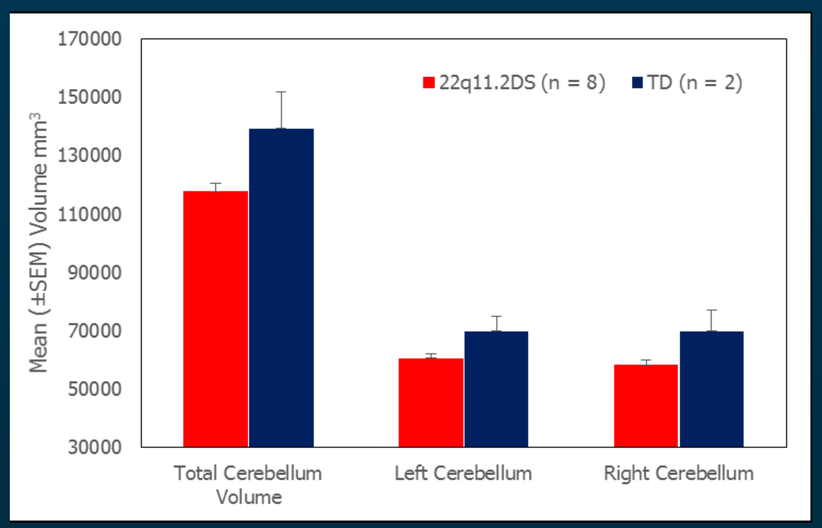

Figure 2. — Group means (±SEM) total, left and right cerebellum volumes by group.

Summary and Next Steps

- Preliminary data suggests that the cerebellum in children with 22q11.2DS is smaller than typically developing children; however, we have 20 more brains to process in this ongoing study.
- Next, we will compare these semi-automated methods to fully automated voxel-based morphometry methods and then again using the *spatially unbiased atlas template of the cerebellum* developed by Diedrichsen (2006).

References

Andreasen, N.C., & Pierson, R. (2008). The role of the cerebellum in schizophrenia. *Biological Psychiatry, 64*, 81-88.

Bish, J.P., Pendyal, A., Ding, L., Ferrante, H., Nguyen, V., McDonald-McGinn, D., . . .& Simon, T. J. (2006). Specific cerebellar reductions in children with chromosome 22q11. 2 deletion syndrome. *Neuroscience Letters, 399*, 245-248.

Diedrichsen, J. (2006). A spatially unbiased atlas template of the human cerebellum. *Neuroimage, 33*, 127-138.

Lancaster J.L., McKay D.R., Cykowski M.D., Martinez, M.J., Tan, X., Valaparla, S., Zhang, Y., & Fox, P.T. (2011). Automated analysis of fundamental features of brain structures. *Neuroinformatics*, 371-80.

Lancaster J.L., Cykowski M.D., McKay D.R,. Kochunov P.V., Fox P.T., Rogers W., Toga A.W., Zilles K., Amunts K., & Mazziotta, J. (2010). Anatomical Global Spatial Normalization. *Neuroinformatics, 8*, 171–182.

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