Creating A Population Specific Brain Atlas for Children with Chromosomal 8p Rearrangement

Indira Jaikaran[1], Jesslyn Lopez[1], Kaiti Syverson[2], Bina Maniar[2], Jacob Borello[2], Dr. Lauren Chaby[2] , Dr. Jennifer Legault-Wittmeyer[1]

[1]Department of Psychology, Neuroscience Program at Elizabethtown College

[2]Project 8p Foundation 501(c)(3), 787 Seventh Avenue – 31st Floor, New York, NY

Introduction

Chromosome 8p disorders are rare genetic conditions affecting ~1 in 10,000 children. Children with intellectual and developmental disorders such as Autism and ADHD may also present with chromosome 8p mutations. Mutations vary in type and can drastically impact brain development and function.

- Three major types of 8p mutations: Deletion-only, Duplication-only, and Inversion-duplication-deletion ("8p Genetics", 2023).
- These mutations can lead to broad and variable neurodevelopmental outcomes, depending on size, location, and type of structural change.

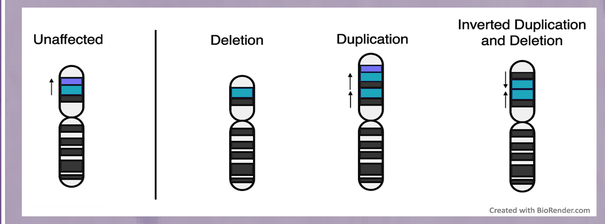


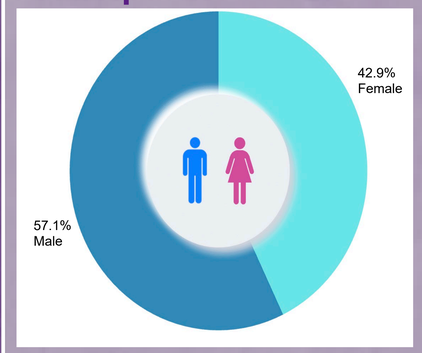
Figure 1: Variations of Chromosomal Mutations

The current study is part of a larger Chromosome 8p Natural History Study, which is a global, retrospective, and prospective natural history study designed to collect and analyze data on individuals diagnosed with or suspected of having Chromosome 8p rearrangements.

The use of standard MRI analysis pipelines is based on and focuses on neurotypical brain atlases which can introduce a significant bias when applied to atypical neurodevelopment. Therefore, recent research has highlighted the importance of population-specific atlases in neurodevelopmental research. For example, Queder et al. (2022) demonstrated that using Joint-Label Fusion (JLF) atlases in Down Syndrome research significantly improves the accuracy of regional brain volume measurements compared to standard templates.

The current study compares standard and population-specific frameworks to critically evaluate the differences in structural brain measurements, which can be used to inform brain-behavior relationships.

Participants



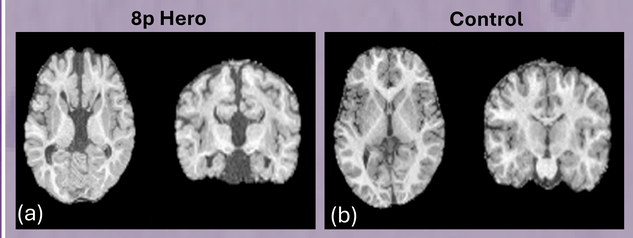
Sample consisted of 7 participants diagnosed with Chromosome 8p rearrangements, including 57.1% male and 42.9% female individuals. Participants ranged in age from 12 to 77 months, representing a diverse clinical cohort within the 8p community.

The protocol conducted by this study was approved by the Institutional Review Board (IRB approval number NB2448844-1), and Informed consent was obtained from all participants of their legal guardians prior to enrollment. Participants have the right to withdraw at any time. Data security and confidentiality measures are strictly adhered to in compliance with HIPPA and GDPR regulations. All the 8p heroes' MRIs were ethically collected over the course of clinical care.

Methods & Results

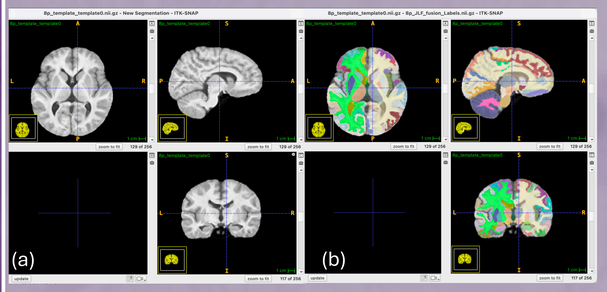
Brain Visualizations

The following sMRI images show the comparison of brain atlases without segmentations or edits between an 8p hero (a) and an age and sex-matched control subject (b). There is clear neurodevelopmental differences in the brain formation in each scan.



8p Brain Atlases and templates

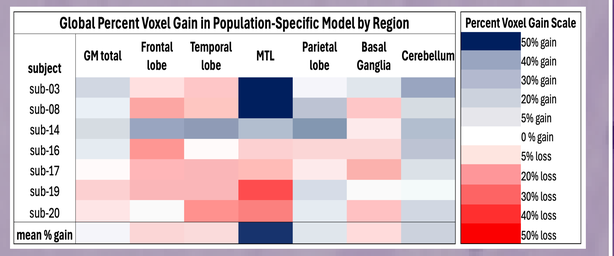
The sMRI images (a) shows the averaged 8p Brain template and (b) the applied Desikan Killiany atlas which were developed using Advanced Normalization Tools. These were created to detect and identify consistent structural markers that differ among the 8p heroes atlas segmentations.



All MRI data were preprocessed in Freesurfer (Reuter et al., 2010). The 8p population specific brain template and atlases were generated using Advanced Normalization Tools (Avants et al., 2009). It was also edited and analyzed manually through ITK-SNAP to provide comparisons to the different templates (Yushkevich et al., 2006).

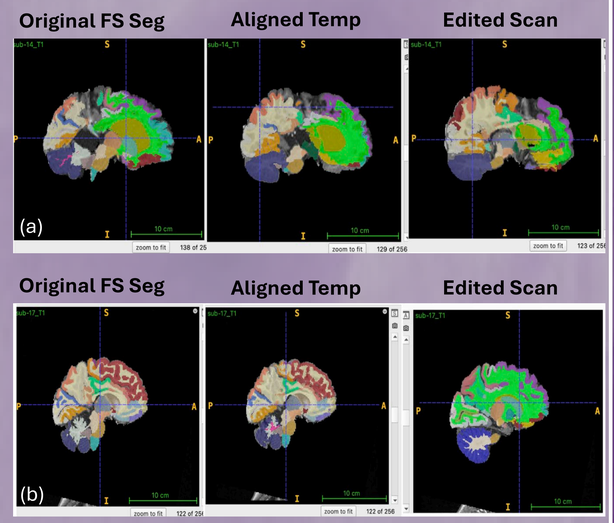
Heatmap of Global Percent Voxel Gain

Heat map shows the global percent voxel gain (blue) or loss (red) across specific brain regions for the individual subjects (sub 03- sub 20).



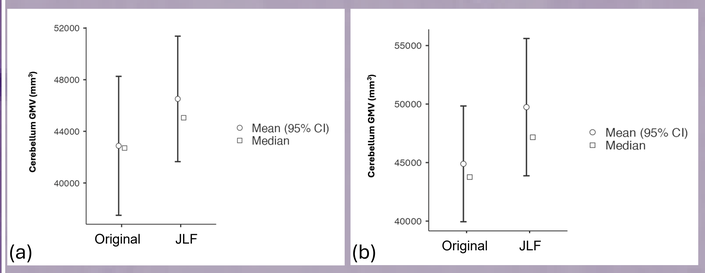
Brain Segmentations of 8p Heros

Structural MRI scans (a/b) from two distinct subjects are based on neurotypical brains and may introduce bias when applied to atypical neurodevelopment. We compare standard and population-specific frameworks to evaluate differences in structural measurements and brain-behavior relationships.



Statistical Analysis

A series of paired-sampled t-tests were conducted in Jamovi to compare regional brain volumes between the original automated segmentation and the Joint-Label Fusion (JLF) reconstruction method.



These plots illustrate the mean voxel volumes for the (a) Left and (b) Right Cerebellum. JLF (right) significantly increased captured volume compared to original FS (left) in both hemispheres (Left: $p = 0.009$; Right: $p = 0.034$). Tighter confidence intervals in the JLF group indicate increased segmentation precision.

Figure 2: A Volumetric Comparison of Original vs. JLF Cerebellum Segmentations

Results Cont.

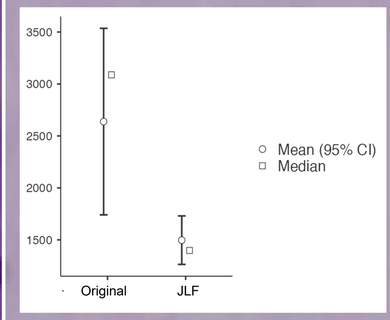


Figure 3: A Volumetric Comparison of Original vs. JLF Right Temporal Pole Segmentations ($p = 0.032$)

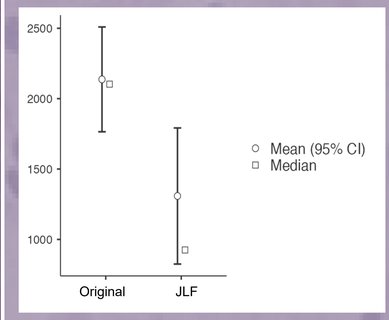


Figure 4: Volumetric Comparison of Original vs. JLF Left rostral anterior cingulate cortex Segmentations ($p = 0.036$)

Conclusions

The most significant findings within the study shows that aligning the MRI images to the template improves segmentations for certain regions.

- Regions in the cerebellum and medial temporal lobe were more accurately reconstructed than the original Freesurfer scan when compared.

Once additional data is collected, the study will focus on making more templates that are specific to chromosomal arrangements like Invdupdel, duplication, and deletions in more specific age ranges (e.g. newborns- child etc.) to further increase accuracy.

Acknowledgments

This research was supported by funding from Project 8p Foundation. We, along with the Project 8p Foundation, also express our deepest gratitude to the 8p heroes, caregivers, and families in the Project 8p community for their contributions, including the donation of biosamples and their valuable time. Their support was necessary to generate the datasets on chromosome 8p disorders essential to this research. We also thank Elizabethtown College and Megan Spiegelberg for her help on the project.

References

- Avants, B. B., Tustison, N., & Song, G. (2009). Advanced normalization tools (ANTS). *Insight j*, *2*(365), 1-35.
- Desikan, R. S., Ségonne, F., Fischl, B., Quinn, B. T., Dickerson, B. C., Blacker, D., ... & Killiany, R. J. (2006). An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *Neuroimage*, *31*(3), 968-980.
- Project 8p Foundation. (2023). 8p Genetics. Project8p.org. Retrieved April 16, 2025, from https://project8p.org/8p-genetics/
- Queder, N., Phelan, M. J., Taylor, L., Tustison, N., Doran, E., Hom, C., ... & Zhang, F. (2022). Joint-label fusion brain atlases for dementia research in Down syndrome. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 14(1), e12324. https://doi.org/10.1002/dad2.12324
- Reuter, M., Rosas, H. D., & Fischl, B. (2010). Highly accurate inverse consistent registration: a robust approach. Neuroimage, 53(4), 1181-1196. https://doi.org/10.1016/j.neuroimage.2010.07.020
- The jamovi project (2025). jamovi (Version 2.6) [Computer Software]. Retrieved from https://www.jamovi.org
- Vibert, R., Mignot, C., Keren, B., Chantot-Bastaraud, S., Portnoï, M.-F., Nouguès, M.-C., Moutard, M.-L., Faudet, A., Whalen, S., Haye, D., Garel, C., Chatron, N., Rossi, M., Vincent-Delorme, C., Boute, O., Delobel, B., Andrieux, J., Devillard, F., Coutton, C., … Heide, S. (2022). Neurodevelopmental phenotype in 36 new patients with 8p inverted duplication–deletion: Genotype–phenotype correlation for anomalies of the corpus callosum. *Clinical Genetics*, *101*(3), 307–316. https://doi.org/10.1111/cge.14096
- Yushkevich, P. A., Piven, J., Hazlett, H. C., Smith, R. G., Ho, S., Gee, J. C., & Gerig, G. (2006). User-guided 3D active contour segmentation of anatomical structures: significantly improved efficiency and reliability. *Neuroimage*, *31*(3), 1116-1128. https://doi.org/10.1016/j.neuroimage.2006.01.015