Linking Brain Structure with Longitudinal Measures in 8p Heroes and Controls

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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. There are three major types of 8p mutations:
  - Deletion-only, Duplication-only, and Inversion-duplication-deletion [1].
- These mutations can lead to broad and variable neurodevelopmental outcomes, depending on size, location, and type of structural change. This can include agenesis of the corpus callosum, sensory processing disorders, epilepsy, and more [2].

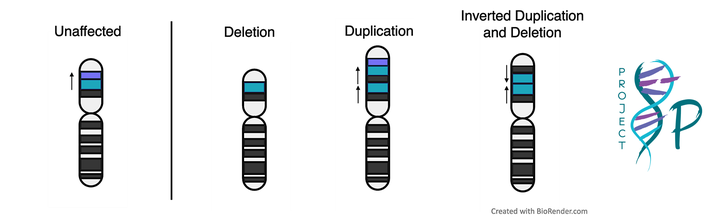

Figure 1. Variations of the Chromosomal 8p mutation that can occur

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.

Epilepsy in 8p:

Many individuals with Chromosome 8p abnormalities often present with epilepsy. In our previous studies, structural brain alterations in 8p heroes were associated with epilepsy and seizure severity, including:

- Enlarged Ventricles
- Decreased Left Hemisphere Hippocampal Volumes

In our current study, we aim to look at how these regions change over time in 8p Heroes versus children without chromosomal rearrangements.

Participants

Group	Mean Age in Months at Scan (SD)	# of Participants	# and Sex of Participants
8p Heroes	32.2 (27.6)	13	6 (M) 7 (F)
Controls	31.8 (25.9)	16	7 (M) 9 (F)

The study protocol was approved by an Institutional Review Board (IRB approval number NB200051), and informed consent is obtained from all participants or their legal guardians prior to enrollment. Participants have the right to withdraw at any time, and data security and confidentiality measures are strictly adhered to in compliance with HIPAA and GDPR regulations. Participant MRIs were collected over the course of their clinical care.

The control participant data were acquired from three open science data sets [3, 4, 5]: https://openneuro.org/datasets/ds006169/versions/1.0.1, https://osf.io/y9jcv, https://openneuro.org/datasets/ds005450/versions/1.0.0

8p Heroes

Brain Visualizations:

The following structural MRI images demonstrate the comparison and the neurodevelopmental differences between an 8p Hero and a control subject at the same age and the regions of interest examined in this study.

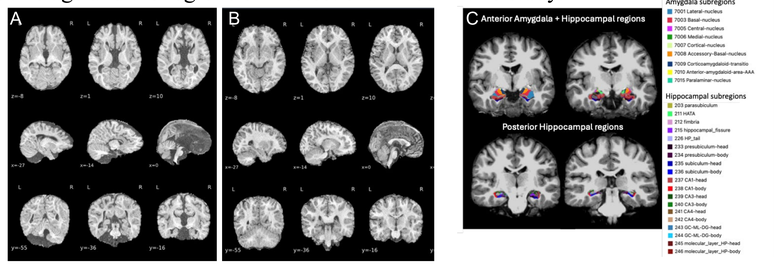

Figure 2. Data visualization of A) one 8p subject (sub-03) and B) a control participant for sub-03 and C) regions of interests included in all subjects, shown here on an 8p hero using hippocampal and amygdala subfield atlases [6, 7].

Methods & Results

Our Approach:

Statistical analyses were conducted through Jamovi [8]. Linear mixed effects models were run on various key regions of interest with main fixed effects being:

- Age, Group, and Age x Group Interaction

Measures were controlled by sex and estimated total intracranial volume (eTIV). We applied False Discovery Rate (FDR) corrections to correct for multiple comparisons.

Main Effect of Age

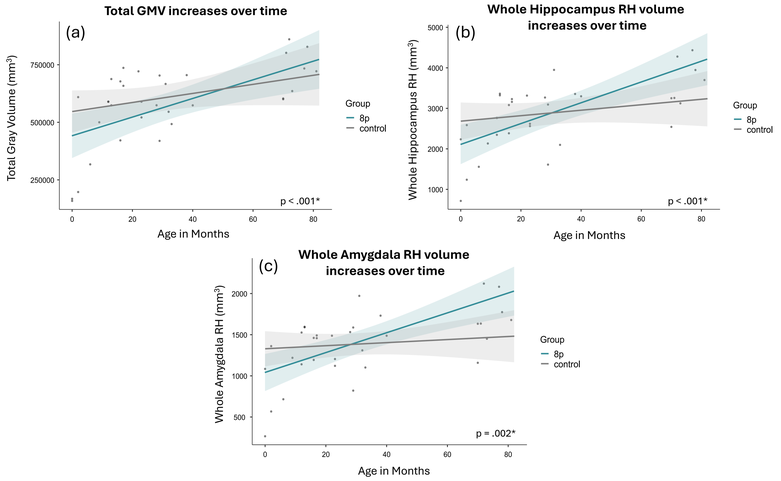

Figure 3. Data visualizations of linear mixed effects models correlating age in months to gray matter volume (mm^3) illustrating the main effect of age in (a) total gray matter volume, (b) whole hippocampus RH, and (c) whole amygdala RH. * Survives FDR Correction.

Age x Group Interaction

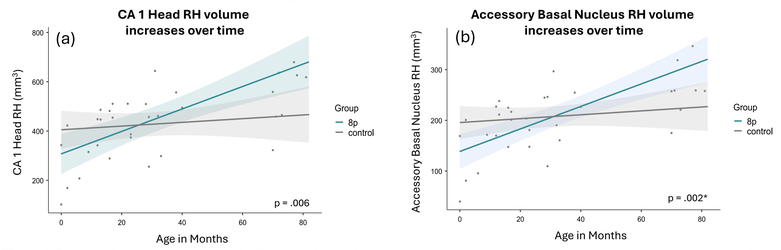

Figure 4. Data visualizations of linear mixed effects models correlating age in months and group to gray matter volume (mm^3) illustrating the age x group interaction in the (a) CA 1 Head RH, and the (b) Accessory Basal Nucleus RH. * Survives FDR Correction.

Results Cont.

Main Effect of Group

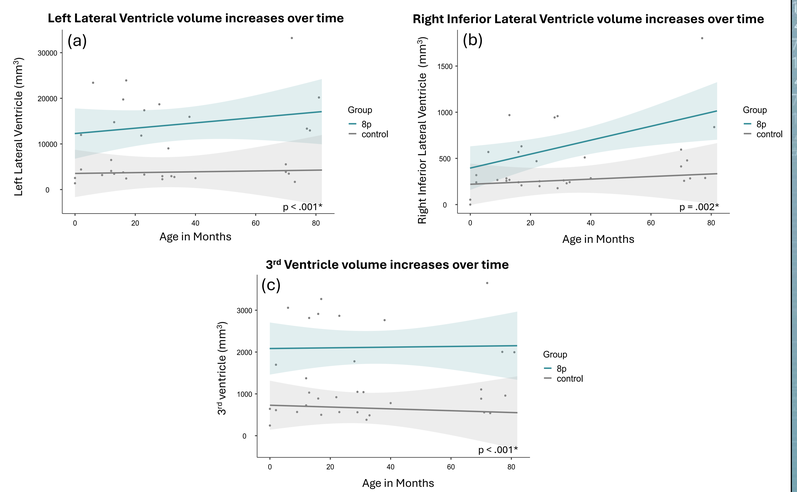

Figure 5. Data visualizations of linear mixed effects models correlating age in months to gray matter volume (mm^3) illustrating the main effect of group in the (a) CA 1 Head RH, and the (b) Accessory Basal Nucleus RH. * Survives FDR Correction.

Discussion

Age: Significant increase in hippocampal and gray matter regions aligns with expected patterns of pediatric maturation for both groups, confirming that age is a critical factor to account for when building an accurate 8p brain atlas.

Group: There were pronounced differences found in ventricular volumes, establishing enlarged ventricles as an important structural biomarker that distinguishes 8p heroes from controls.

Age × Group Interaction: Significant increases in brain volume localized to the amygdala and hippocampus indicate that the 8p brain follows a unique growth trajectory.

References and Acknowledgements

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