Linking Language Development to Brain Structure in Children with Chromosome 8p Rearrangements

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Introduction

Chromosome 8p rearrangements affect around 1 in 10,000 children[1].

- Main types of 8p rearrangements: dup(8p), del(8p), invdupdel(8p)[2]
  - People with invdupdel(8p) tend to have the greatest number of and the most severe clinical manifestations.
- 8p syndrome can manifest in a wide variety of ways.
  - Some common manifestations are epilepsy, neurodevelopmental disorders such as autism, sensory processing disorders, and neurostructural differences[3].
  - Because of the limited volume of research done on the 8p population, the relationship between these differences in brain structure and perceived behavior is not yet known.

Language delays have also been found to be prevalent among people with chromosome 8p rearrangements (8p heroes). However, the neural basis of these delays is uncertain. This study aims to uncover one part of this issue by considering how elements of the physical structure of 8p heroes' brains correlate with their delays in achieving expressive language milestones. This study will help lay the foundation for a greater understanding of the links between brain structure and behavior in 8p heroes.

This study is part of the Chromosome 8p Natural History Study, which is a retrospective and prospective study with the purpose of collecting and analyzing data from 8p heroes and the long-term goal of finding treatments.

Participants

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 HIPAA and GDPR regulations. All the 8p heroes' MRIs were ethically collected over the course of clinical care.

Participant ID	MRI Age in Years	Sex	Primary_8p_Rearrangement
sub-03	1.08	Male	8p inverted duplication/deletion
sub-06	1.33	Female	8p inverted duplication/deletion
sub-08	6.75	Female	8p inverted duplication/deletion
sub-09	2.42	Female	8p deletion
sub-10	1.92	Female	8p inverted duplication/deletion
sub-11	3.17	Male	8p inverted duplication/deletion
sub-14	6.00	Female	8p inverted duplication/deletion
sub-16	1.00	Male	8p inverted duplication/deletion
sub-17	5.83	Female	8p inverted duplication/deletion
sub-18	0.00	Female	8p duplication
sub-19	2.58	Male	8p deletion
sub-15	12.08	Male	8p inverted duplication/deletion
sub-22	16.92	Female	8p trisomy
sub-21	1.08	Female	8p inverted duplication/deletion

Methods

- MRI from all 14 participants were preprocessed using FreeSurfer[6]
- Regions of interest (ROIs) included regions of the frontal and temporal lobes that are associated with expressive language development in young children.

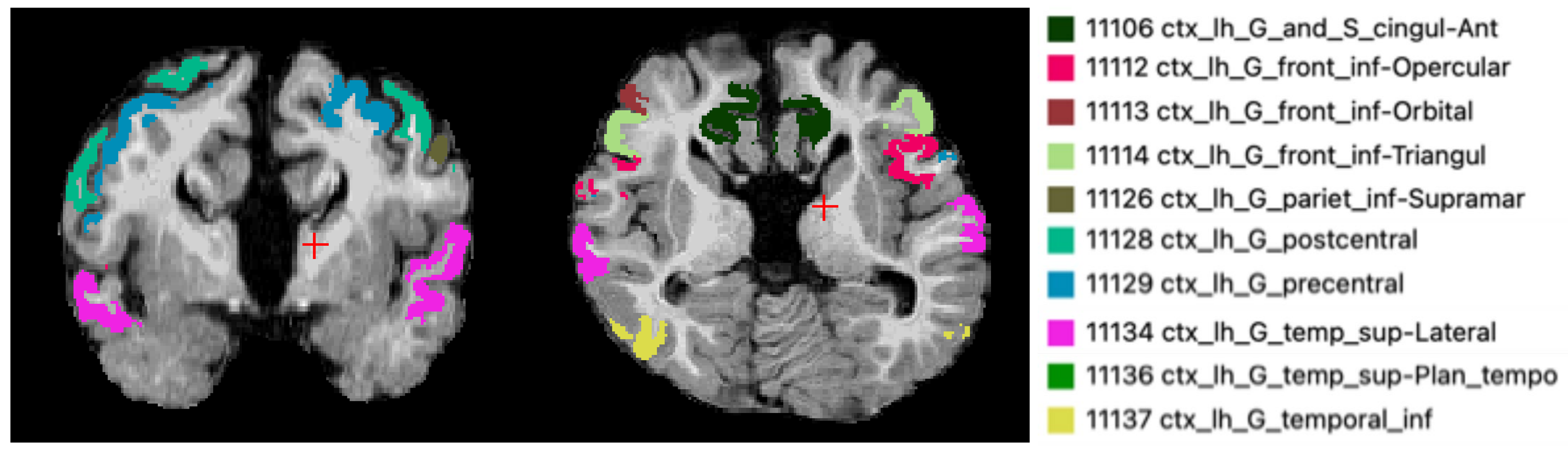

Figure 1. Language-related brain regions of interest (ROIs) selected from the Destrieux[4] atlas used in our study, projected on an 8p hero's MRI.

- Expressive language measures were extracted from a larger dataset of developmental milestones:
  - Age at first syllable produced
  - Age at first word produced
  - Age at first combination of words
  - Age at first sentence
- Linear regression analyses were performed in Jamovi[5] to find relationships between each brain region and each language measure.
- Limitations
  - Small sample size
  - Missing responses from several participants

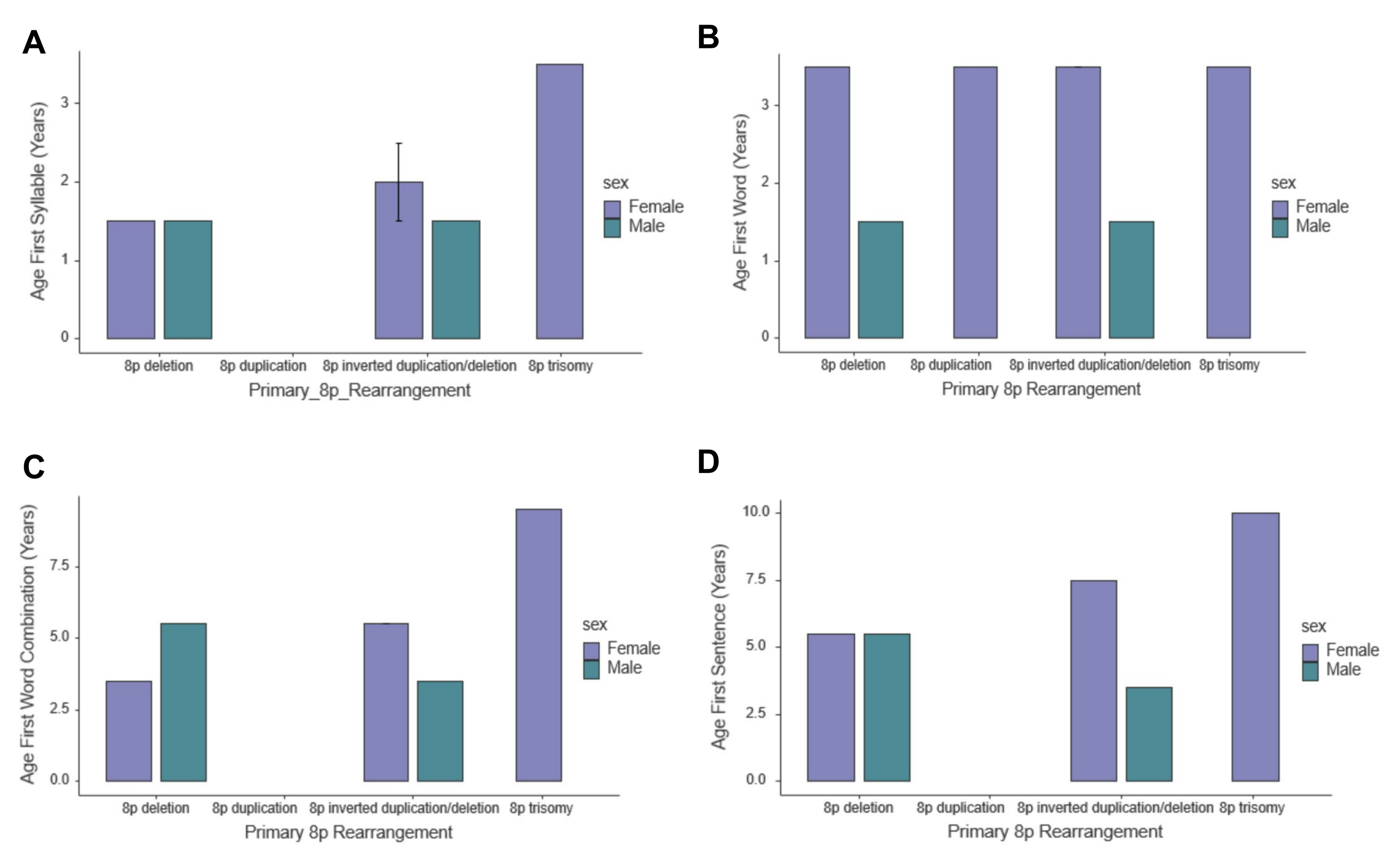

Figure 2. Age at First Syllable (A), Word (B), Word Combination (C) and Sentence (D) production shown across sex and 8p rearrangements.

Statistical Analysis Results

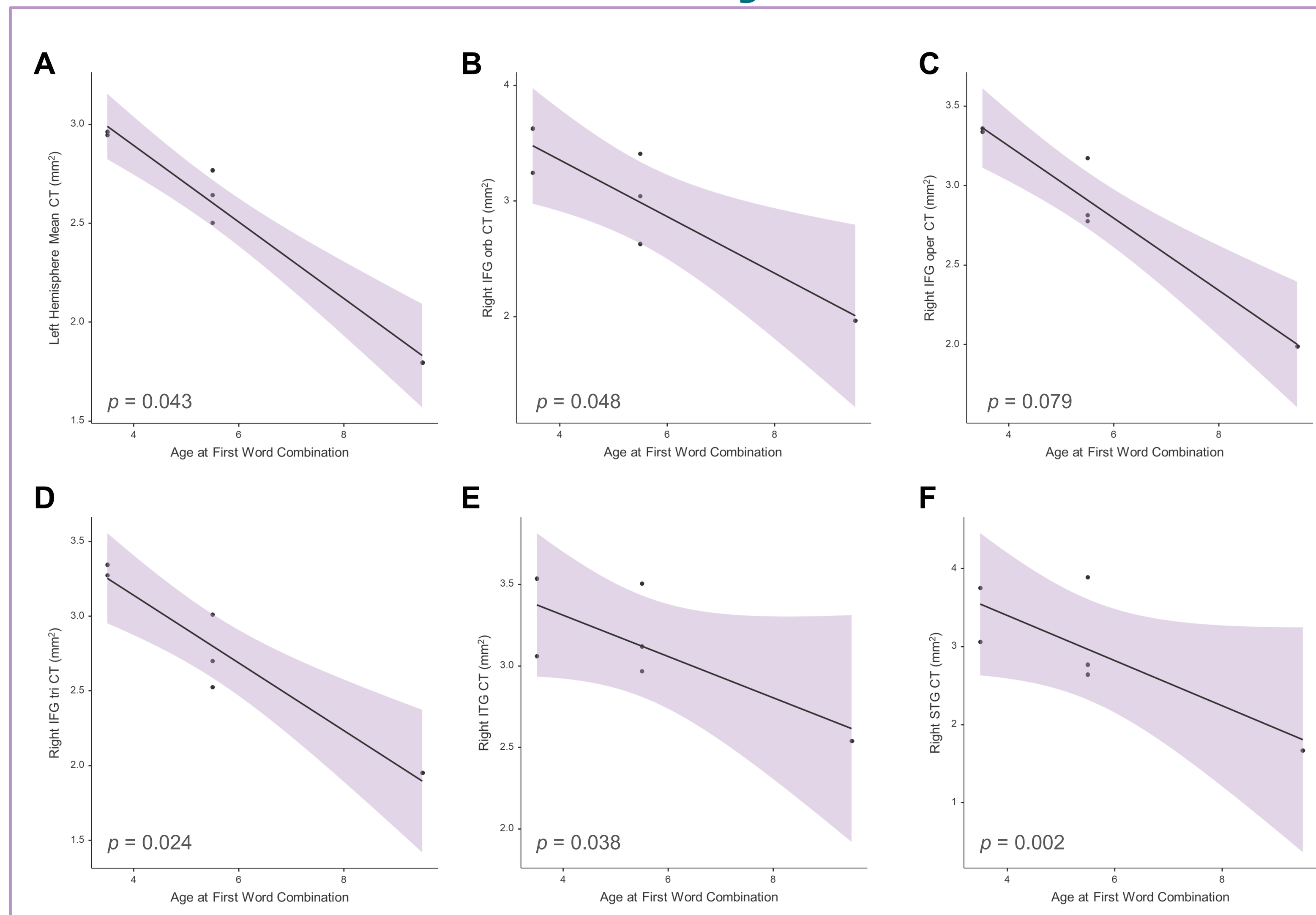

Figure 3. Age at First Word Combination was negatively correlated with regions in the left hemisphere (A), right inferior frontal gyrus (B-D), right inferior temporal gyrus (E), and right superior temporal gyrus (F).

- We found a significant negative correlation between cortical thickness in the brain and the age at first word combination
  - Right Inferior frontal gyrus (IFG), inferior temporal gyrus (ITG), and superior temporal gyrus (STG)
  - Left hemisphere overall cortical thickness
- Children who produced their first word combinations later (delay) showed less CT in these regions

Future Directions

- Increase sample size to improve statistical power
- Examine whether right hemisphere homologues compensate for atypical development of the left hemisphere language network
- Examine the involvement of language-related white-matter tracts in language delays

Acknowledgements

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