BA&Sc – Honours Cognitive Science
COGS 444 – Honours Research Project

Characterizing cerebellar growth in infants born pre-term or with congenital heart defects between 6 and 12 months of age

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Introduction

The cerebellum

Key Insights

- The cerebellum represents **10% of the total brain** size and weight.[1]
- The **most active period** of **cerebellar development** occurs during the **3rd trimester** of pregnancy and the first year of postnatal life.[1]
- The cerebellum is known to play a **key role** in **higher-order cognitive functions** and **emotional control**.
- **Atypical** cerebellar development is thought to be an underlying mechanism of many **neurodevelopmental disorders**.

Clinical population

Infants born Very Pre-Term (VPT)

- VPT infants are highly **vulnerable** to **cerebellar injury**.[1]
- Timing of preterm birth coincide with most active period of cerebellar development.[1]

Infants born with Congenital Heart Disease (CHD)

- Congenital heart disease is the **most common neonatal malformation,** and the most complex forms require **open heart surgery** during infancy to survive.
  → **Impaired cardiovascular circulation** during pregnancy observed in CHD infants could contribute to **altered cerebellar development**.[2]

- **BOTH** clinical populations are at **high risk** for **neurodevelopmental disorders**, such as:[3,4]
  - ADHD
  - Impaired executive functions

OBJECTIVES

This research project aims to quantify and compare cerebellar growth between 6-months and 12-months of age for infants born preterm and for infants with congenital heart disease, using quantitative MRI.

Table 1. Participant Characteristics

	VPT (N = 15)		CHD (N = 14)		*p* value
Participants present at both visits	6	(40.00%)	6	(42.86%)	-
Age at MRI (weeks)					
6-month visit (N_{vpt} =10, N_{chd} =12)	26.83	(±1.66)	28.19	(±1.12)	0.04
12-month visit (N_{vpt}=10, N_{chd}=9)	56.48	(±3.86)	5.18	(±2.17)	0.40
Sex					
Male	11	(73.33%)	8	(57.14%)	0.44
Female	4	(26.67%)	6	(42.86%)	
Gestational age at birth (weeks)	28.96	(±2.52)	39.31	(±1.81)	<0.001
Maternal Education					
Partial school completed	-		1	(7.14%)	
High school completed	2	(13.33%)	1	(7.14%)	
Cegep/College	4	(26.67%)	1	(7.14%)	0.49
Undergraduate degree	4	(26.67%)	5	(35.71%)	
Graduate degree	5	(33.33%)	6	(42.86%)	
Type of CHD					
Single ventricle	-		2	(14.29%)	
Tetralogy of Fallot			3	(21.43%)	
TGA			6	(42.85%)	
Other two ventricle			3	(21.43%)	
Participants presenting brain abnormality	4	(26.67%)	6	(42.86%)	
Abnormalities Likely Acquired in Origin	3	(20.00%)	4	(28.57%)	
Abnormalities Likely Developmental in Origin[a,b]	2	(13.33%)	2	(14.29%)	

[a] No qualifying criteria for Chiari I malformation.
[b] No sign of white matter injury

Methods

Participant selection criteria

Group

VPT
- ✓ Gestational age of <32 weeks

CHD: Congenital Heart Disease
- ✓ Gestational age ≥37 weeks
- ✓ Underwent open heart surgery during the first 3 months of postnatal life.

MRI age (in weeks) calculated

- ✓ Using the date of birth (DoB) for CHD.
- ✓ Using corrected age for VPT instead of DoB.

Exclusion criteria

- ⦸ No history of congenital infection, chromosomal anomaly, cerebral palsy, multi-organ dysmorphism, history of brain tumor or malformation, traumatic brain injury.

Data

Structural MRI

- ✓ High resolution T1 weighted images were acquired at 6 and 12 months of age using a 3.0 Tesla scanner and 32 channel head coils.

Segmentation using Infant FreeSurfer toolbox (ages 0-2) [5]

Pre-processing

1. Visual assessment of image quality
2. Resampling (FSL-flirt – *only* for images with voxel sizes other than 1 x 1 x 1 mm)
3. Bias Field Correction (N4ITK algorithm)

Manual correction done on all images for regions:

- ✓ Left and right cerebellar hemispheres (cerebellar cortex and cerebellar white matter)
- ✓ Left and right cerebral cortices
- ✓ Vermis

Figure 1.
3.0 Tesla MRI scanner at the McGill University Hospital Centre.

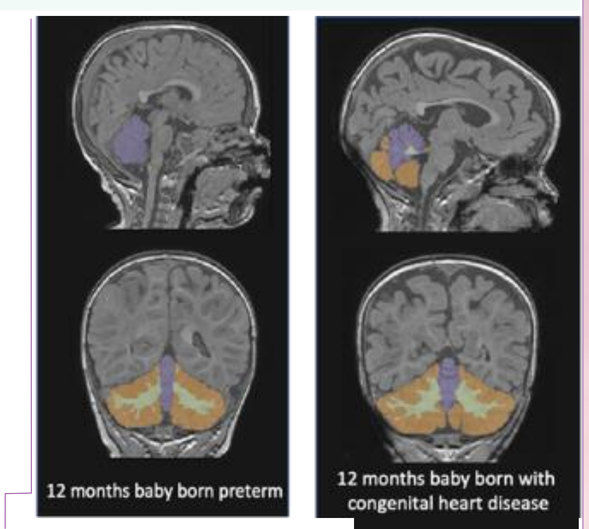


Figure 2. Cerebellar segmentation of a T1-MRI image collected at the 12-month visit with a VPT participant (left) and a CHD participant (right) using Infant FreeSurfer.[5]

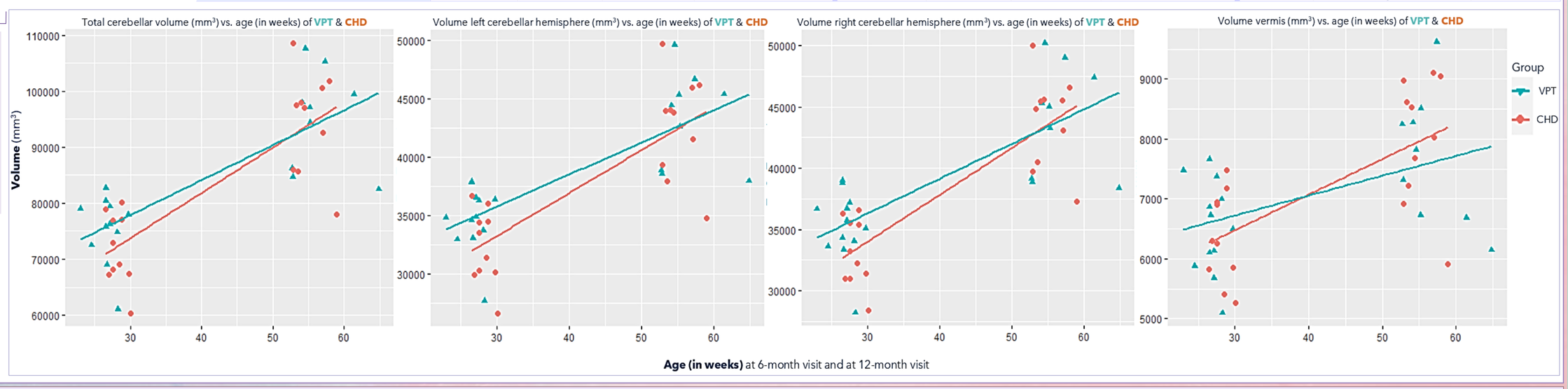
Results

Table 2. Cerebellar volumes at 6 months and 12 months of age, and percentage volume gain between visits for infant groups VPT & CHD; Significance was established at $p < 0.05$.

	6-month visit				12-month visit				Volumetric differences			
	Mean volume (mm3)		t-test	Adjusted for MRI_AGE + TBV	Mean volume (mm3)		t-test	Adjusted for MRI_AGE + TBV	Visit (6-months vs 12-months)		Group (VPT vs CHD)	
	CHD	VPT	p-values	p-values	CHD	VPT	p-values	p-values	CHD	VPT	6-months	12-months
Total cerebellum	71832.0	75449.5	0.18	0.62	94585.4	95031.4	0.92	0.73	-31.68	-25.95	-4.79	-0.47
Left cerebellar hemisphere	32386	34733.5	0.08	0.24	42733.0	43272.1	0.78	0.60	-31.95	-24.58	-6.76	-1.25
Right cerebellar hemisphere	33116.5	35229.6	0.10	0.37	43850.8	44055.8	0.92	0.78	-32.41	-25.05	-6.02	-0.47
Vermis	6340.1	6539.0	0.55	0.90	8001.6	7703.6	0.56	0.76	-26.21	-17.81	-3.04	3.87
Total brain	690282.9	710240.6	0.43	-	823391.6	812452.1	0.67	-	-19.28	-14.39	-2.81	1.35

- Legend: CHD, Infant participants born with congenital heart disease, VPT, Infant participants born pre-term; TBV, Total brain volume (cerebral hemispheres + cerebellar hemispheres + vermis+ brainstem, but excluding all ventricles).

Figure 3: Cerebellar growth trajectories from 6 months to 12 months of age for infant participant groups **VPT** & **CHD**



- Legend: CHD, Infant participants born with congenital heart disease; VPT, Infant participants born pre-term.

Overview

No significant differences observed between cerebellar volumes for VPT & CHD infant participants at both visits (6- and 12- months of age) in all regions of interest (total brain volume, total cerebellar volume, left and right cerebellar hemispheres, and vermis).

Conclusion

Based on a preliminary analysis conducted on a partial sample:

- Our results suggest that there is **no significant difference** in cerebellar **volumes** over the second half of the first year of life (6 and 12 months of age) between infants born VPT, and those born with CHD.
- Further analysis should focus on potential **group difference** in the **cerebellar volumetric gain** between the 6 & 12 month visit in each group.
  →To do so, the number of **participants present at both visits** must be **increased** (participant recruitment is currently ongoing).
- Further studies should focus on **comparing** the cerebellar growth trajectory **between these two** clinical populations **and healthy term-born** infants.
  →To determine if the observed cerebellar developments in these two clinical populations are altered or follow a typical trajectory.
- The next step of this project would be to look at the possible **association** between these **cerebellar growth** trajectories and the **neurodevelopmental assessments** (cognitive, language and motor performance) at the **12-month visit**.

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