# Association between volumes of preterm brain structures, neurodevelopmental outcomes and neonatal morbidities

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## Introduction

- Premature infants are prone to have impaired neurodevelopmental outcomes due to the injury or underdevelopment of brain
- However, impaired neurodevelopmental outcomes may be present without any brain lesions
- Association between neonatal morbidities and the volume of segmental brain structures have not been fully understood yet

## Method

- Retrospective cohort study (from January 2007 to December 2019)
- Seoul National University Children's Hospital (SNUCH) NICU
- Inclusion
  - SNUCH NICU inborn preterm infants less than GA 29 weeks
  - With brain MRI at term equivalent age (TEA-MRI)
  - With Bayley scales of infant development 3rd edition (Bayley-III) at CA 18-24mo
- Exclusion
  - Congenital anomaly
  - Significant brain injuries on TEA-MRI (e.g. IVH ≥ Gr 3, cerebellar hemorrhage, PVL)
  - Unanalyzable MRI in Infant Freesurfer
- Adjusted for GA, PMA at TEA-MRI in multivariate regression analysis

## Result

### Study Population

Total 158 preterm infants

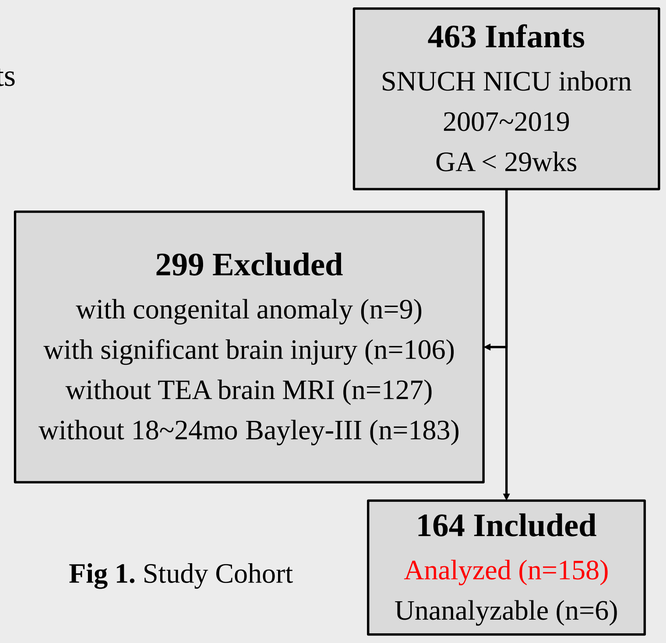



**Fig 1.** Study Cohort

### Segmental Brain Volume Evaluation

Using Infant Freesurfer

- Volume of each brain structures was obtained (e.g. estimated total intracranial volume, lateral ventricle, cerebellum cortex, thalamus, caudate, putamen, pallidum, 3rd ventricle, 4th ventricle, hippocampus, amygdala, accumbens, ventral diencephalon, vermis, pons, medulla, cortex volume, cerebral white matter volume, subcortical gray matter volume, supratentorial volume, etc.)
- Each volume of brain region was measured in milliliters (mL)

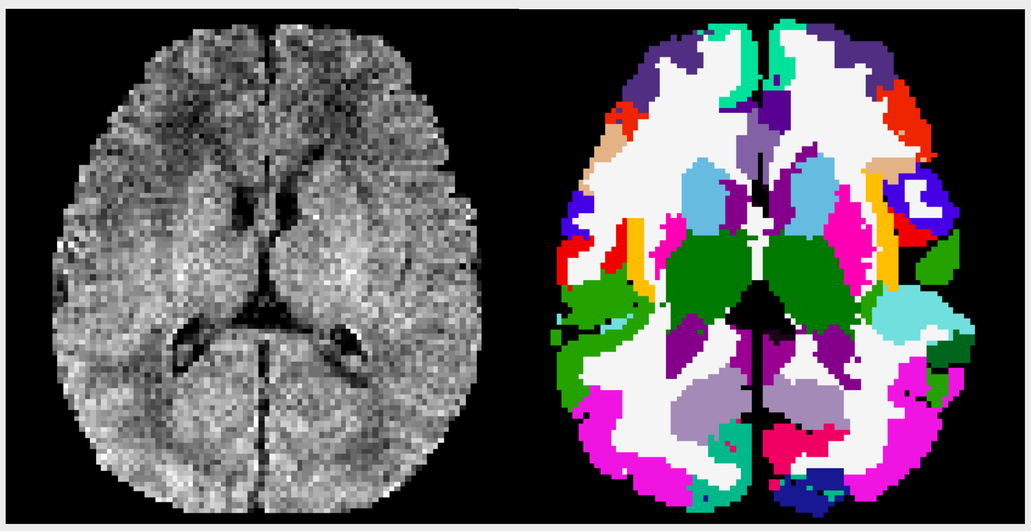


**Fig 2.** Segmental Brain Volume Evaluation by Infant Freesurfer

### Neurodevelopmental Outcomes

Based on BSID-III performed at CA 18-24mo

- Definition of NDI:
  - cognitive or language or motor scale less than 70 at BSID-III
  - Presence of unilateral or bilateral hearing loss, blindness, or cerebral palsy

## Result

**Table 1.** Demographic and BSID-III scores

| | No NDI (n=144) | NDI (n=14) | p value |
|---|---|---|---|
| **GA (week)** | 26.6 ± 1.4 | 26.0 ± 1.7 | 0.129 |
| **Birthweight (gram)** | 855.2 ± 202.9 | 855.3 ± 338.9 | 0.999 |
| **C-sec** | 80 (55.6%) | 10 (71.4%) | 0.388 |
| **Female** | 74 (51.4%) | 6 (42.9%) | 0.742 |
| **1 min Apgar score** | 3.5 ± 1.8 | 2.5 ± 1.7 | 0.041 |
| **5 min Apgar score** | 6.0 ± 1.7 | 5.0 ± 1.7 | 0.035 |
| **Bayley-III cognitive score** | 97.3 ± 12.8 | 79.6 ± 17.8 | <0.001 |
| **Bayley-III language score** | 93.7 ± 14.6 | 76.7 ± 16.9 | <0.001 |
| **Bayley-III motor score** | 95.6 ± 9.8 | 76.6 ± 14.8 | <0.001 |
| **RDS** | 102 (70.8%) | 12 (85.7%) | 0.382 |
| **PDA operation** | 41 (28.5%) | 4 (28.6%) | 1.000 |
| **ROP operation** | 42 (29.2%) | 7 (50.0%) | 0.191 |
| **NEC operation** | 12 (8.3%) | 2 (14.3%) | 0.798 |

**Table 2.** Brain volume analysis

| | No NDI (n=144) | NDI (n=14) | p value |
|---|---|---|---|
| **PMA (week) at MRI** | 37.2 ± 1.7 | 36.9 ± 1.5 | 0.456 |
| **Weight (gram) at MRI** | 2269.7 ± 414.8 | 2185.0 ± 328.6 | 0.460 |
| **Head circumference (cm) at MRI** | 31.2 ± 1.7 | 30.7 ± 1.8 | 0.357 |
| **Lateral ventricle (mL)** | 6.4 ± 18.2 | 19.9 ± 55.7 | 0.384 |
| **3rd Ventricle (mL)** | 0.2 ± 0.1 | 0.2 ± 0.1 | 0.383 |
| **4th Ventricle (mL)** | 0.2 ± 0.1 | 0.2 ± 0.1 | 0.584 |
| **Midbrain (mL)** | 1.7 ± 0.2 | 1.5 ± 0.2 | 0.016 |
| **Pons (mL)** | 1.8 ± 0.3 | 1.6 ± 0.3 | 0.128 |
| **Medulla (mL)** | 0.7 ± 0.2 | 0.8 ± 0.2 | 0.252 |
| **Vermis (mL)** | 1.6 ± 0.5 | 1.3 ± 0.3 | 0.075 |
| **Cerebellum (mL)** | 14.9 ± 3.3 | 14.1 ± 3.4 | 0.369 |
| **Thalamus (mL)** | 8.4 ± 1.0 | 7.9 ± 1.9 | 0.318 |
| **Caudate (mL)** | 3.0 ± 0.6 | 2.6 ± 0.7 | 0.062 |
| **Putamen (mL)** | 3.7 ± 0.7 | 3.6 ± 1.0 | 0.782 |
| **Pallidum (mL)** | 2.0 ± 0.4 | 1.9 ± 0.6 | 0.896 |
| **Hippocampus (mL)** | 2.0 ± 0.3 | 1.9 ± 0.3 | 0.217 |
| **Amygdala (mL)** | 1.0 ± 0.2 | 1.0 ± 0.2 | 0.502 |
| **Accumbens (mL)** | 0.5 ± 0.1 | 0.5 ± 0.1 | 0.344 |
| **Ventral diencephalon (mL)** | 1.7 ± 0.3 | 1.7 ± 0.4 | 0.629 |
| **Subcortical gray matter (mL)** | 22.4 ± 2.9 | 21.3 ± 5.0 | 0.407 |
| **Cerebral white matter (mL)** | 96.7 ± 12.3 | 92.3 ± 17.9 | 0.384 |
| **Cerebral cortex (mL)** | 104.7 ± 16.1 | 99.1 ± 16.4 | 0.216 |
| **Total gray matter (mL)** | 139.5 ± 20.3 | 132.2 ± 23.0 | 0.203 |
| **Supratentorium (mL)** | 229.1 ± 29.4 | 218.0 ± 37.3 | 0.187 |
| **Total intracranial volume (mL)** | 261.7 ± 37.8 | 254.0 ± 43.6 | 0.476 |

### Multivariate Regression Analysis of Brain Volume and Neurodevelopment

- **Neurodevelopmental impairment** (< 70 on BSID-III) was associated with **smaller midbrain volume** (aOR 0.804, 95% CI 0.647-0.998)

### Multivariate Regression Analysis of Brain Volume and Neonatal Morbidities

- **RDS** was associated with **smaller volume** of
  - **Medulla** (aOR 0.593, 95% CI 0.387-0.908)
  - **Ventral diencephalon** (aOR 0.730, 95% CI 0.572-0.932)
  - **Putamen** (aOR 0.874, 95% CI 0.788-0.969)
- **PDA requiring operation** was associated with **smaller volume** of
  - **Pons** (aOR 0.727, 95% CI 0.594-0.889)
  - **Vermis** (aOR 0.766, 95% CI 0.646-0.907)
- **ROP requiring operation** was associated with **smaller volume** of
  - **Pons** (aOR 0.729, 95% CI 0.600-0.886)
- **NEC requiring operation** was associated with **smaller volume** of
  - **Pons** (aOR 0.751, 95% CI 0.661-0.854)
  - **Vermis** (aOR 0.832, 95% CI 0.745-0.930)
  - **Cerebellum** (aOR 0.974, 95% CI 0.960-0.989)

## Conclusion

Among preterm infants without significant brain injuries, a smaller volume of the midbrain was associated with impaired neurodevelopment. RDS, PDA requiring operation, ROP requiring operation, and NEC requiring operation were associated with reduced segmental volumes of the brain in preterm infants.