Abnormal Corpus Callosum Morphology in Congenital Hypothyroidism

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Disclosure

I have nothing to disclose
Corpus Callosum

- Largest white matter (WM) tract in brain
- Transfers information between hemispheres
- Needed for many functions (e.g., bimanual coordination, social communication, complex reasoning)
Corpus Callosum

Corpus Callosum Abnormalities


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Corpus Callosum Abnormalities

fetal alcohol syndrome

Turner syndrome

ADHD

prematurity

autism
Corpus Callosum Abnormalities

- Down syndrome
- Williams syndrome
- 22q11.2 syndrome
Thyroid hormone is essential for corpus callosum development


Thyroid hormone is essential for corpus callosum development

Corpus Callosum Development

- Undergoes major development in gestation and postnatally
  - period of exuberant axonal growth
    - bidirectional & inside-out pattern
    - anterior before posterior
Corpus Callosum Development

- Undergoes major development in gestation and postnatally
  - period of exuberant axonal growth
  - exuberant axonal pruning
  - myelination
Corpus Callosum Development

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Is corpus callosum development affected in congenital hypothyroidism (CH)?
Experience a circumscribed period of thyroid hormone deficiency

- reflects etiology, severity of hypothyroidism at diagnosis, treatment factors (age, dose)
3 Research Questions

1. Is corpus callosum morphometry and morphology affected in congenital hypothyroidism (CH)?

2. Are corpus callosum abnormalities associated with disease severity and treatment?

3. Are effects correlated with (suboptimal) outcome?
Sample: CH

- N=41
- 9 to 16 yrs (mean=12.4 yrs)
- 11 athyrosis, 21 ectopic, 6 dyshormonogenes, 3 unknown
- Median Rx onset=13 days
- Median TSH@diagnosis=311 mU/L
- Mean T4@diagnosis=53.9±36.2 nmol/l
Sample: Controls

- 42 youth matched with CH for:
  - age (mean=12.0 yrs)
  - sex
  - socioeconomic status
Procedures

- Day 1: 4-hour neuropsychological evaluation
- Day 2: 1-hour MRI scan in 1.5 Tesla magnet
  - 7-min axial T1 FSPGR sequence (TR/TE=10.3/4.2 ms, inversion time=400 ms, flip angle = 20°, slice thickness = 1.5mm)
- Corpus callosum manually traced and measured using Analyze 9.0
Quantitative Approach

Quantitative Approach

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Qualitative Approach

- Curvature ($\delta$)
- Droop ($\varepsilon$)
- Peak ($\alpha$)

Qualitative Approach

- Shape ("bulbosity") of genu (A/B) and splenium (C/D)
CH have smaller genus
CH have narrower genus
CH show abnormal shape

- Flatter corpus callosum, \( p<0.001 \)
- Less droop in splenium, \( p=0.017 \)
- No difference in peak of genu
CH show “more bulbous” genus
CH show normal spleniums
Question 2: Is CC Morphometry Associated with Early Disease Factors?

- No effect of TSH or T4 levels at diagnosis, age of treatment onset, starting dose LT4
- Genu smaller in athyrosis & dyshormonogenesis vs ectopic etiology
Question 3: Is CC size associated with specific abilities?

Genu & anterior midbody size highly correlated with IQ
In Summary

- Youth with CH show:
  - Reduced size and width of CC genu
  - Less curvature, abnormal orientation of splenium, more bulbous genu
- More severe CH at diagnosis associated with reduced size of genu
- Reduced size of certain CC regions predictive of specific cognitive weaknesses
Conclusion

- Despite the current optimal care of congenital hypothyroidism, persisting residual cognitive deficits may still arise from corpus callosum abnormalities associated with early thyroid hormone insufficiency.
Thank You