Infant Brain Structure Predicts Later Cognition:

Investigating Thalamocortical Connectivity

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T32 Journal Club Series

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Outline

- Background & Relevance
- Work from a Recent Study
- Our Published/Preliminary Data
- General Conclusions
- Future Directions

NIMH Strategic Plan - 2015

Strategy 2.1: Characterize the developmental trajectories of brain maturation and dimension of behavior to understand the roots of mental illnesses across diverse populations.

"Create a comprehensive, cross-lifespan map of trajectories of typical and atypical brain, cognitive, and behavioral development."

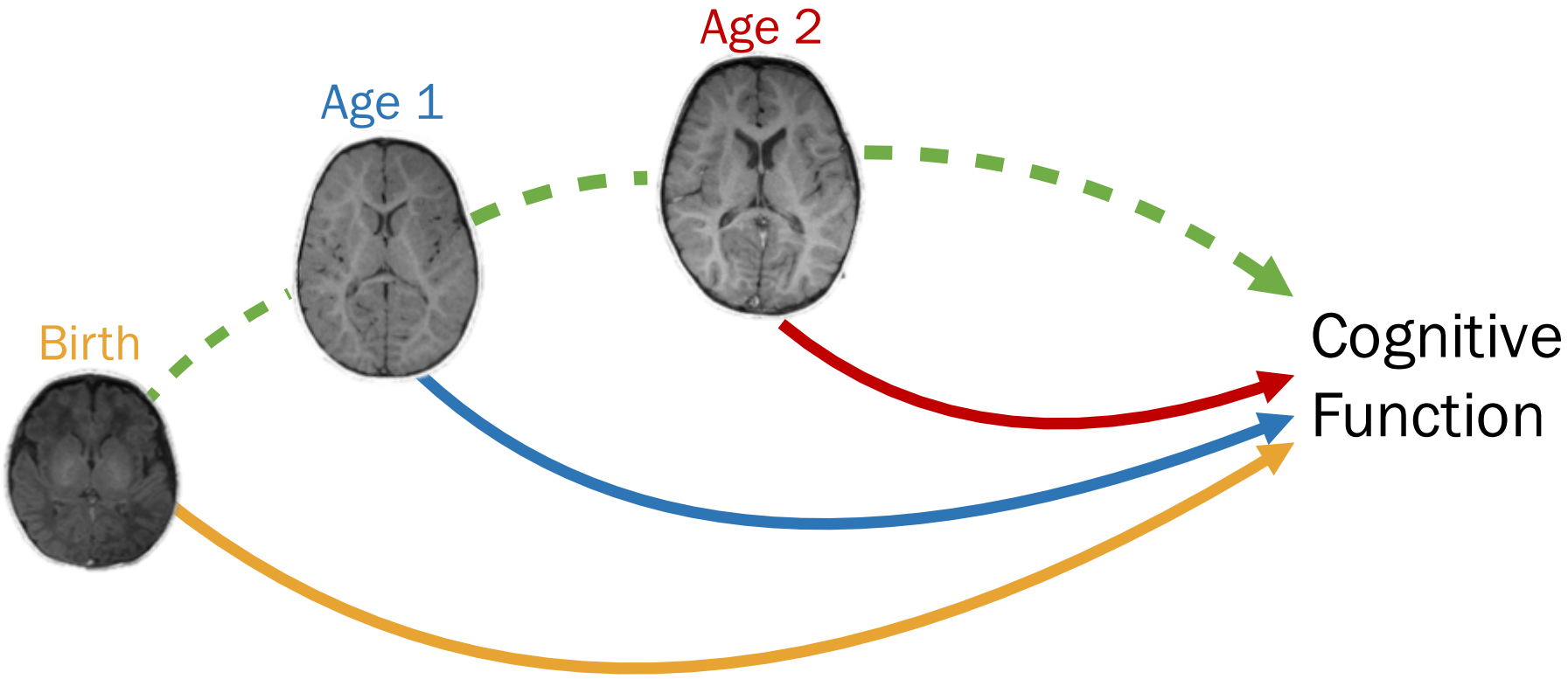
Cognition is related to Psychiatric Illness

- Higher general cognition in childhood, less psychological distress later in life
  (Gale, 2009)
- Cognitive function is predictive of mental health
  (Deary, 2012)
- Higher risk for psychiatric conditions associated with lower cognition
  (Gale 2008 & 2010, Zammit 2004, Frazier 2004, Trotta 2015, Tiihonen 2014)
  - SCZ, MDD, BPD, ADHD, ASD

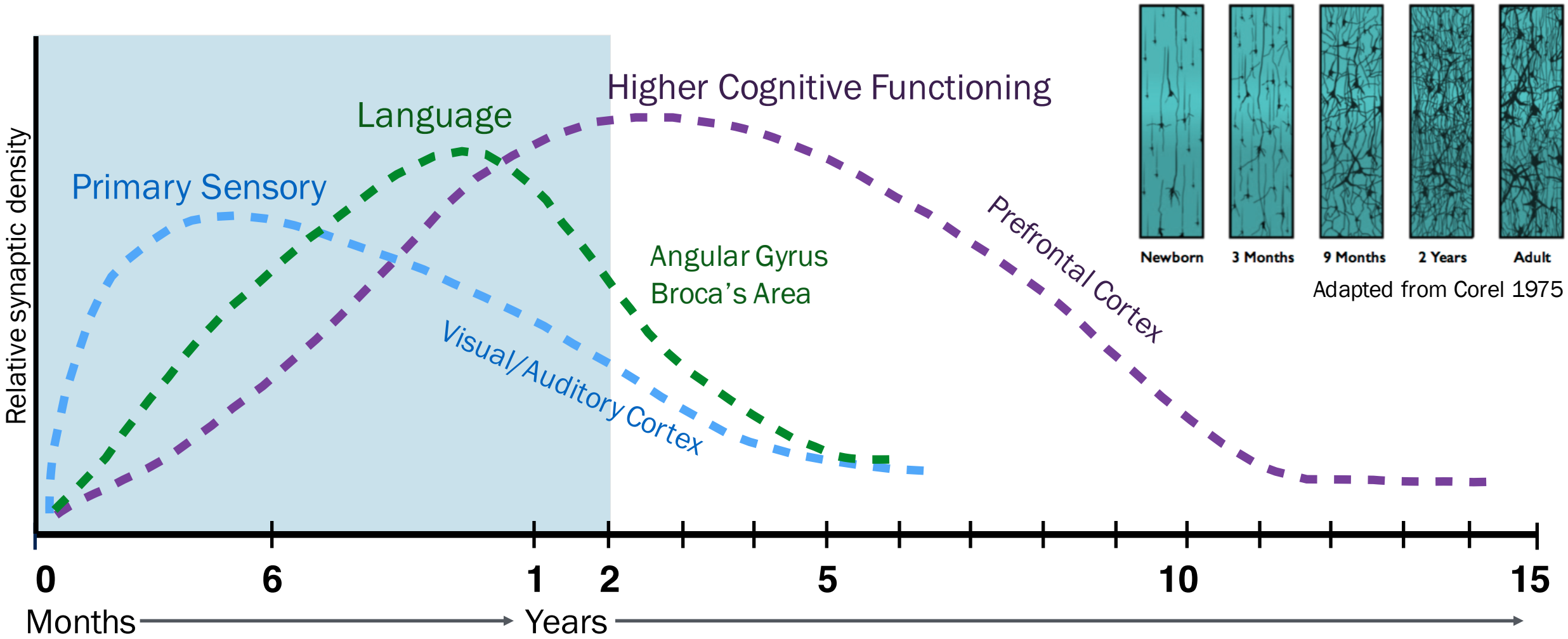
Understanding neural foundations for cognition is critical to understanding neurodevelopmental disorders.

My Thesis Project Goal

Understand the relationship between structural brain maturation and cognitive development in early life.



Critical Period in Brain Development



Adapted from Corel 1975

Adapted from Nelson 2001 (Data from Huttenlocher 1979,1990,1999)

Critical Period in Cognitive Development

Limited motor skills for feeding	Grasping objects, reaching, standing	Walking	Sensorimotor	
Cooing	Word Comprehension	50-200 Word Vocabulary	Language	
Secondary reactions to environment	Searching for hidden objects	Imitation of adult behaviors	Higher Cognition	

Birth — 2 years

Paper

Thalamocortical Connectivity Predicts Cognition in Children Born Preterm

Gareth Ball[1,†], Libuse Pazderova[2,†], Andrew Chew[1], Nora Tusor[1], Nazakat Merchant[1], Tomoki Arichi[1], Joanna M. Allsop[1], Frances M. Cowan[2], A. David Edwards[1], and Serena J. Counsell[1]

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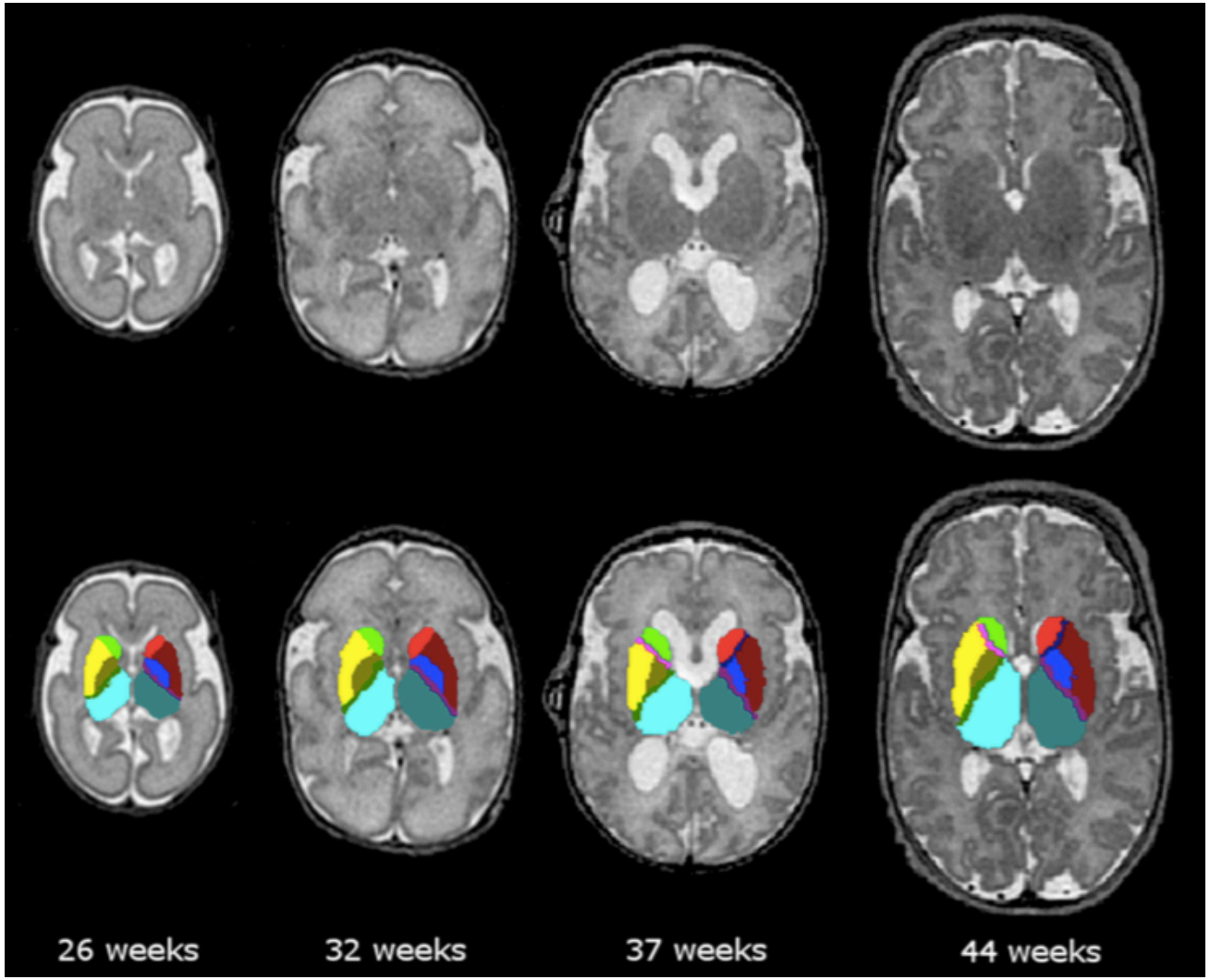
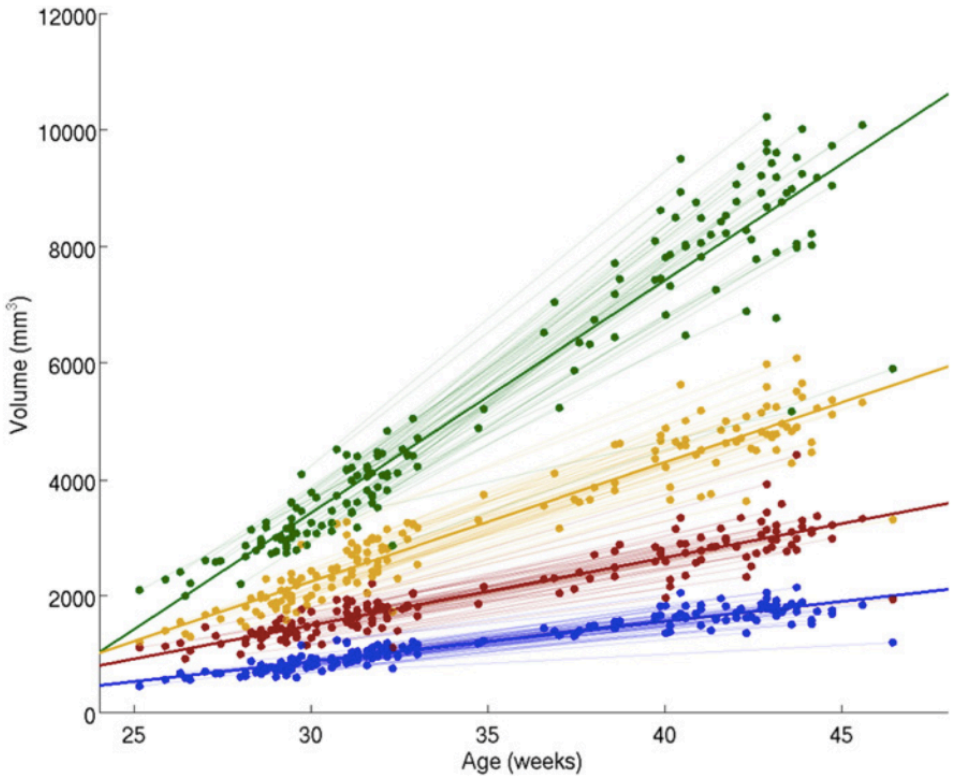
Thalamic Growth in Early Life

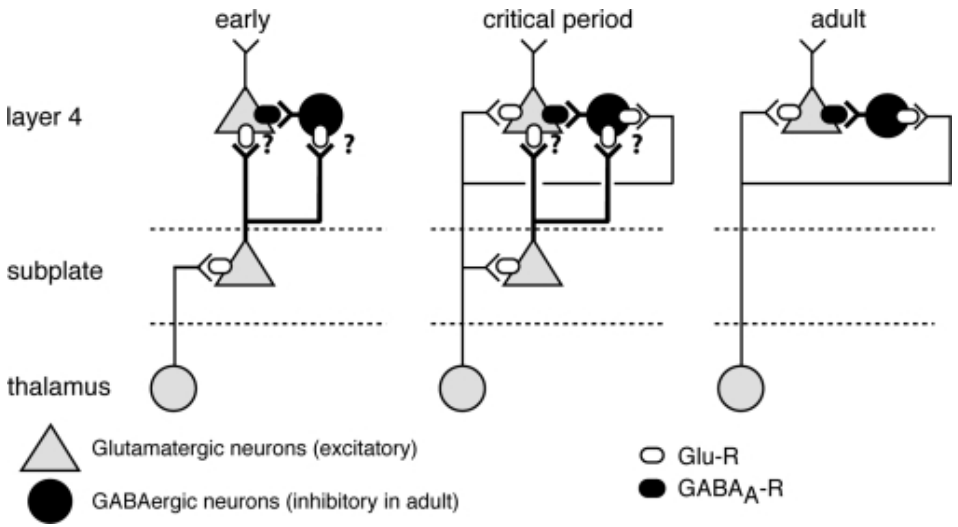




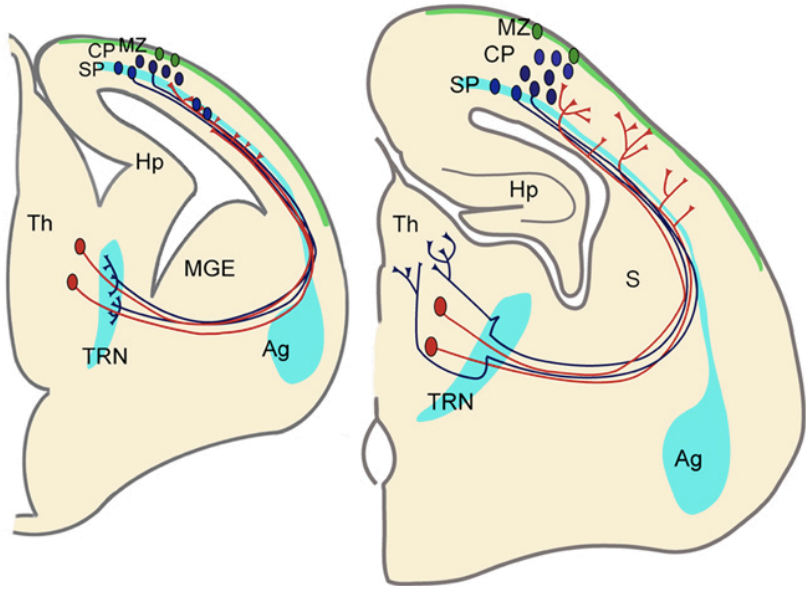
Young 2015

Early Thalamocortical Connectivity

- Time between preterm and term birth is critical for thalamocortical connections
- Damage during critical period could impact cortical and thalamic development and the white matter connections between them.



Kanold 2009



Montiel 2011

Subject Sample

Table 1 Infant characteristics

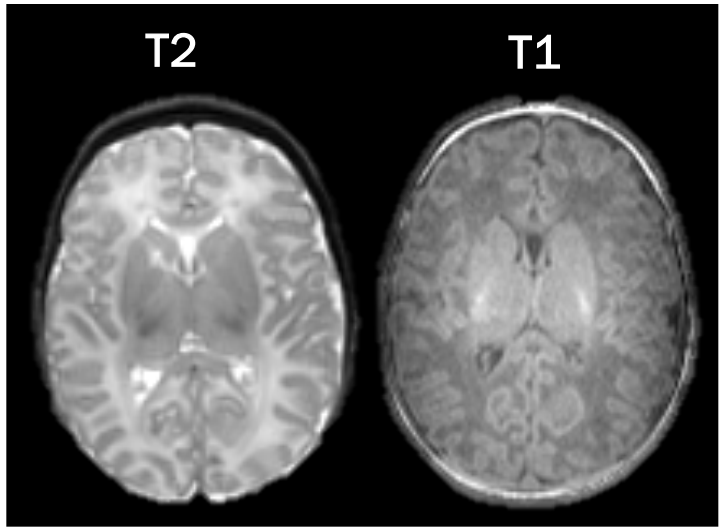
Characteristic	Value
Median (range) GA at birth (weeks)	29^{+5} (25^{+5}–34^{+4})
Median (range) birthweight (grams)	1210 (560–2280)
Male, no (%)	25 (44%)
Small for gestational age[a], no (%)	10 (17%)
Chronic lung disease[b], no (%)	9 (15%)
Received a full course of antenatal steroids, no (%)	44 (77%)
Culture positive post-natal sepsis, no (%)	7 (12%)
Mean (± SD) parental SES	2.4 (±1.4)

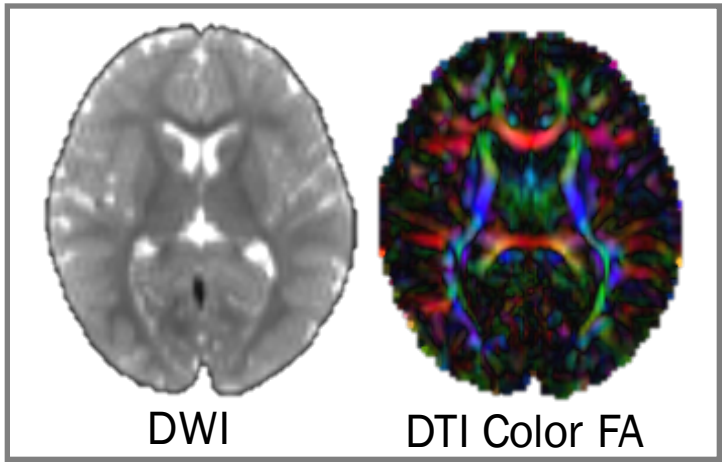
[a]Defined as <10th percentile.

[b]Defined as requirement for supplementary oxygen at 36 weeks PMA.

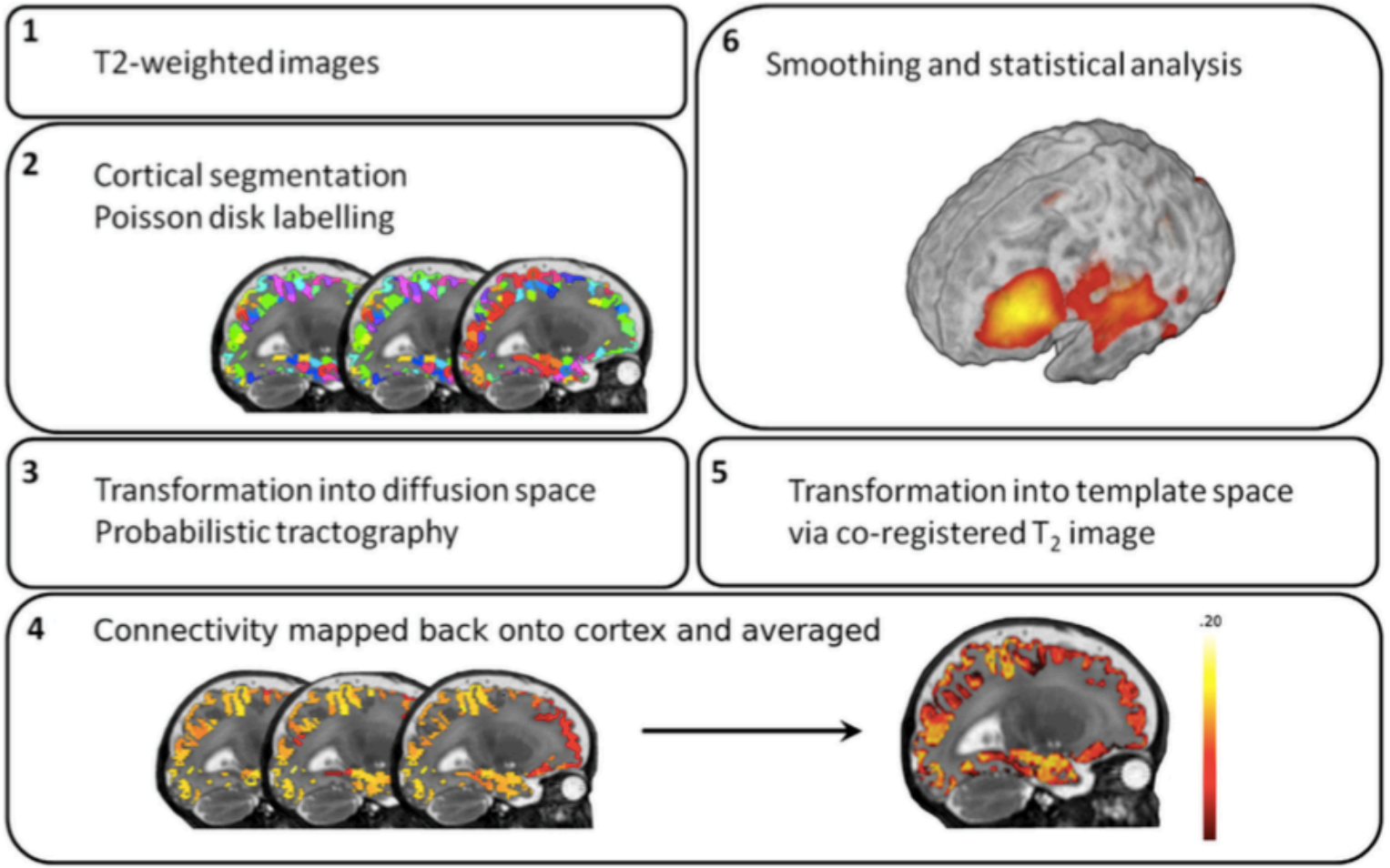
MR Imaging

- 3T Scanner
- T1 & T2w MRI
- 32 direction diffusion MRI
- Sedated in NICU



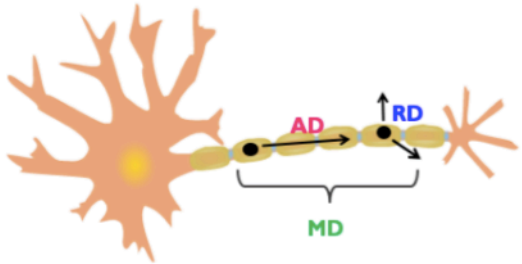


Assessment of Thalamocortical Connectivity & Gray Matter Diffusivity



Ball 2013

Voxel-wise measures of mean diffusivity (MD) in the cortex and thalamus



AD = Axial Diffusion
Diffusion along the principle direction

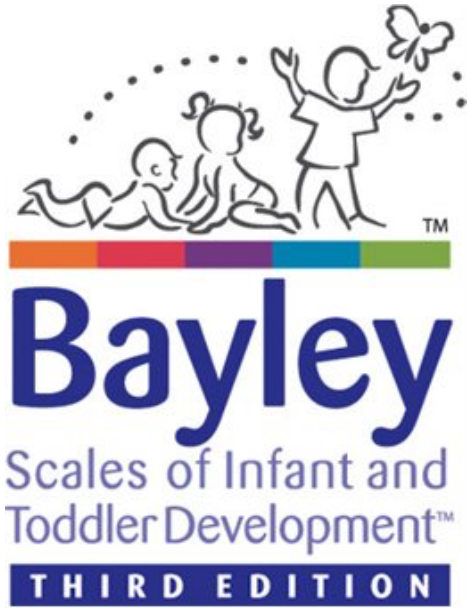
RD = Radial Diffusion
Diffusion along the orthogonal direction

MD = Mean Diffusion
Average diffusion

Cognitive Assessments

- Bayley Scales of Infant and Toddler Development III
  - Sensorimotor
  - Exploration
  - Object relatedness
  - Concept formation
  - Memory

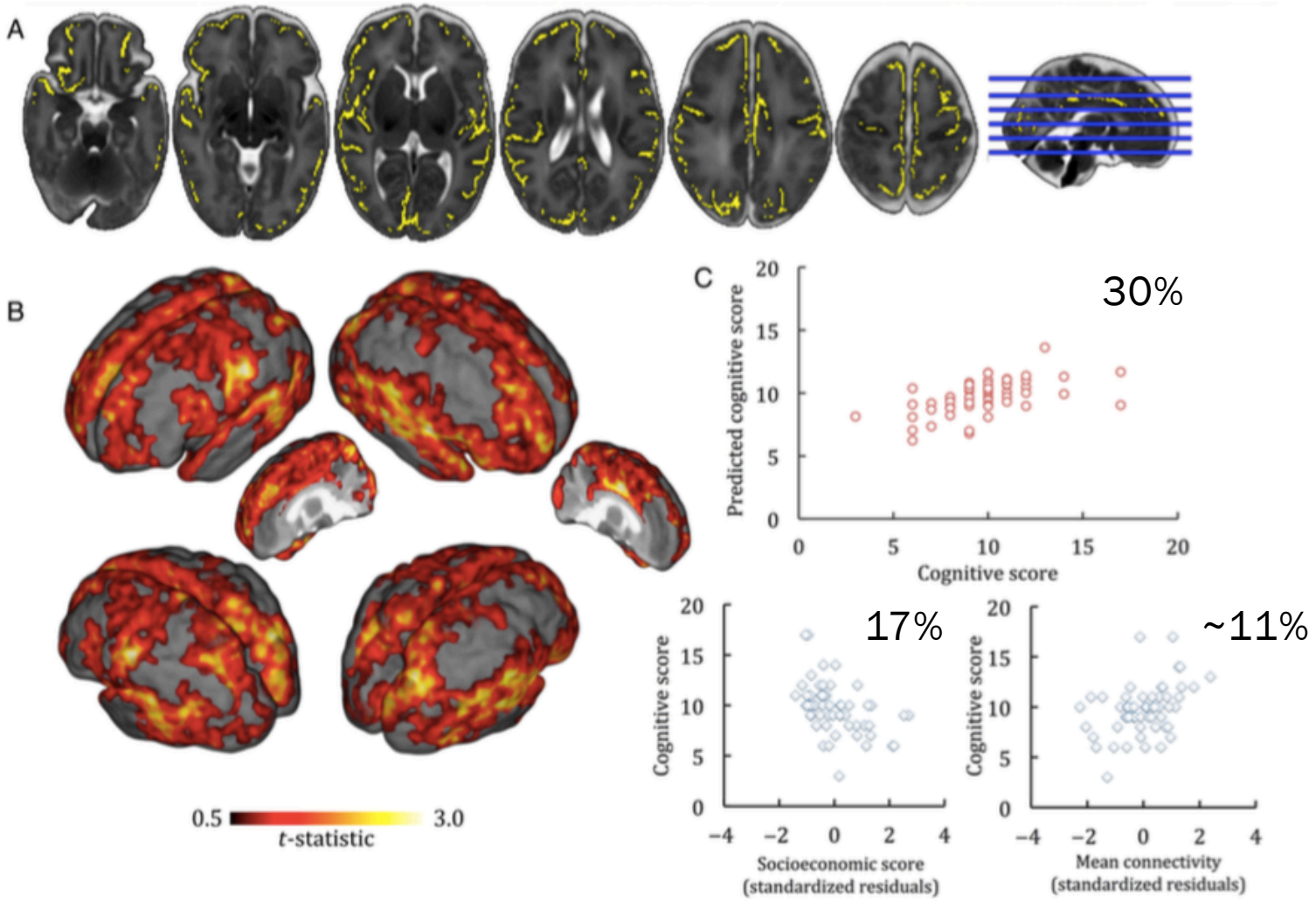
- Mean composite of 98 (+/- 14)



Statistical Analyses

- Voxel wise analyses of thalamo-cortical connectivity and gray matter diffusivity
- Linear Regression to assess relationship between connectivity and cognitive scores
  - Correcting for: GA at birth, age at scan, and SES.

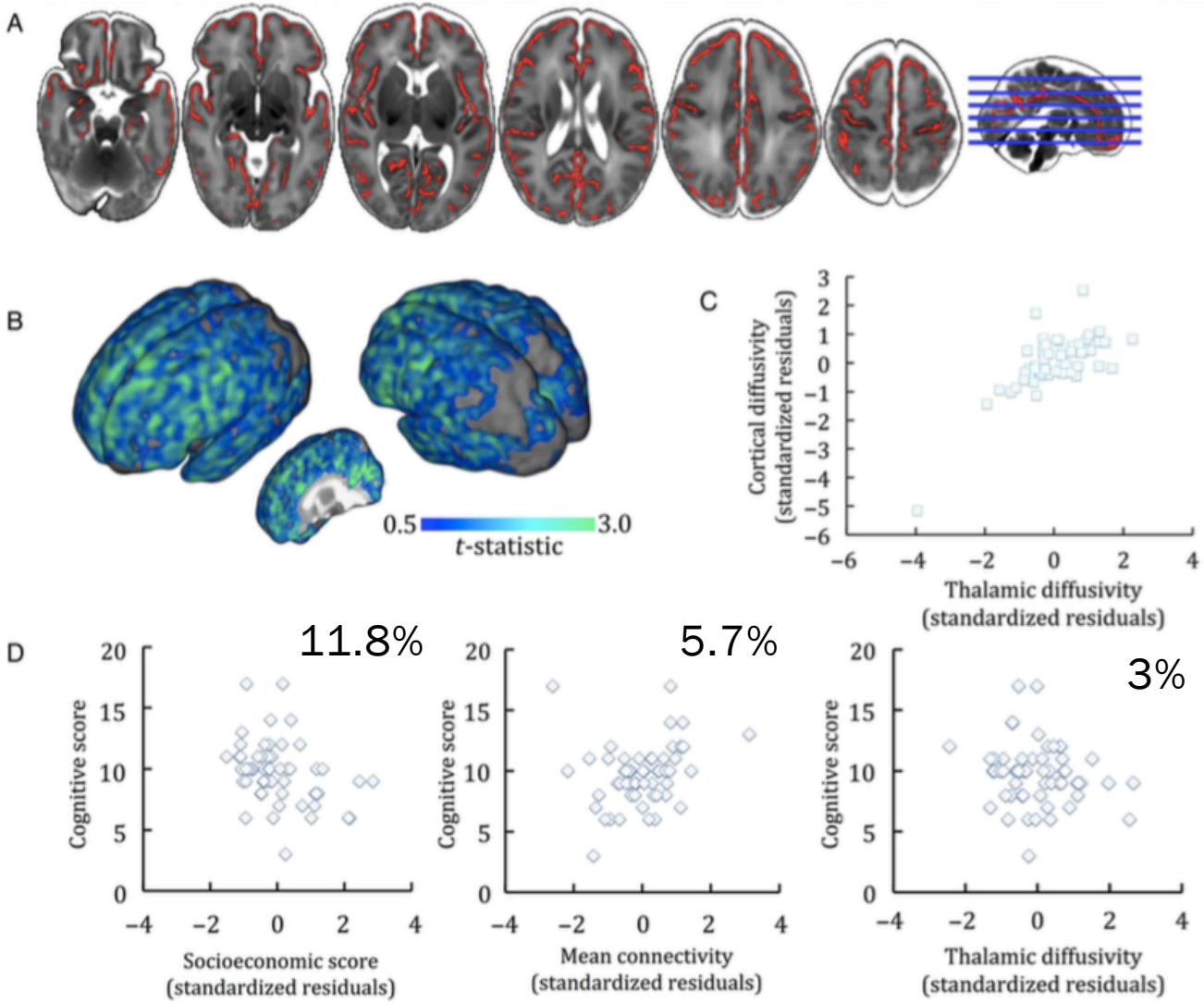
Thalamocortical Connectivity and Cognition



Cognitive scores were significantly **positively correlated** with thalmocortical connectivity in many regions on the cortex

Parental socioeconomic score was the single largest predictor of ability

Gray Matter Mean Diffusivity and Cognition



Cognitive scores were significantly **negatively correlated** with mean diffusivity in the thalamus and cortex

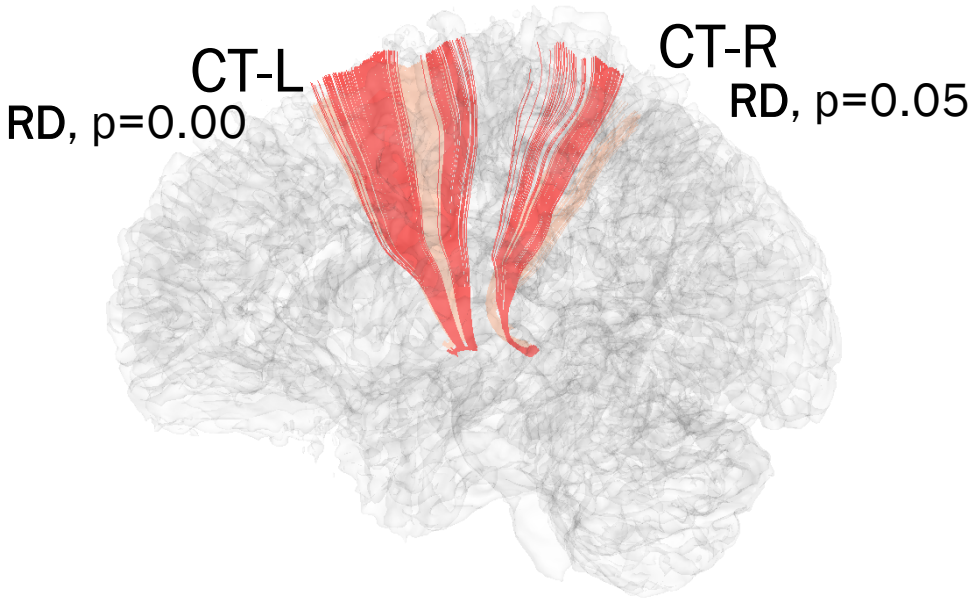
Parental socioeconomic score was the single largest predictor of ability

Conclusions

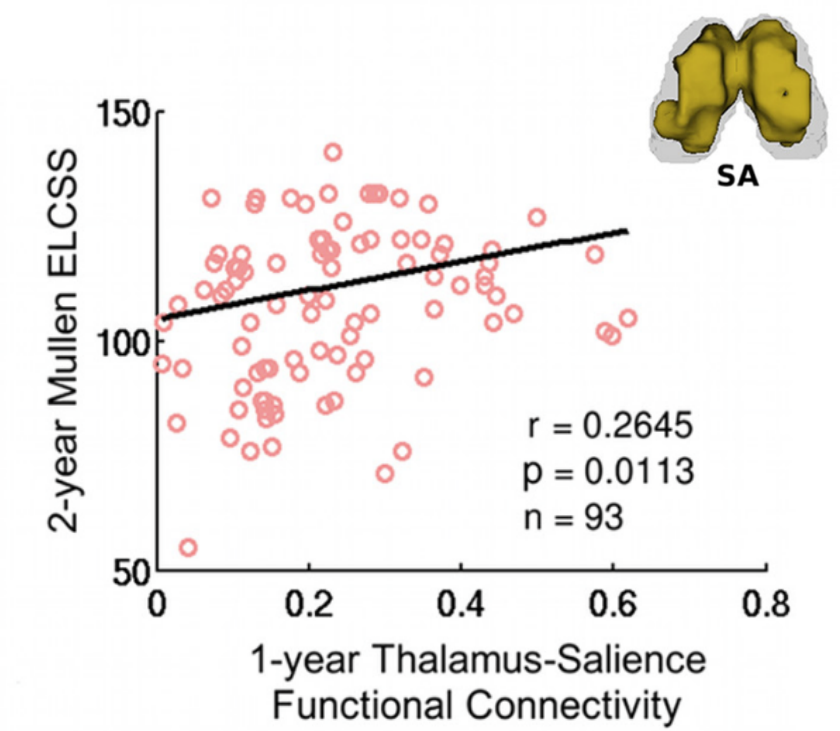
- Foundational thalamocortical connectivity important for cognitive outcomes
- Socioeconomic status is a large predictor of outcome

Relation to our Work

DTI Tractography and Functional Connectivity reveal the important role of thalamocortical connectivity for early cognition.



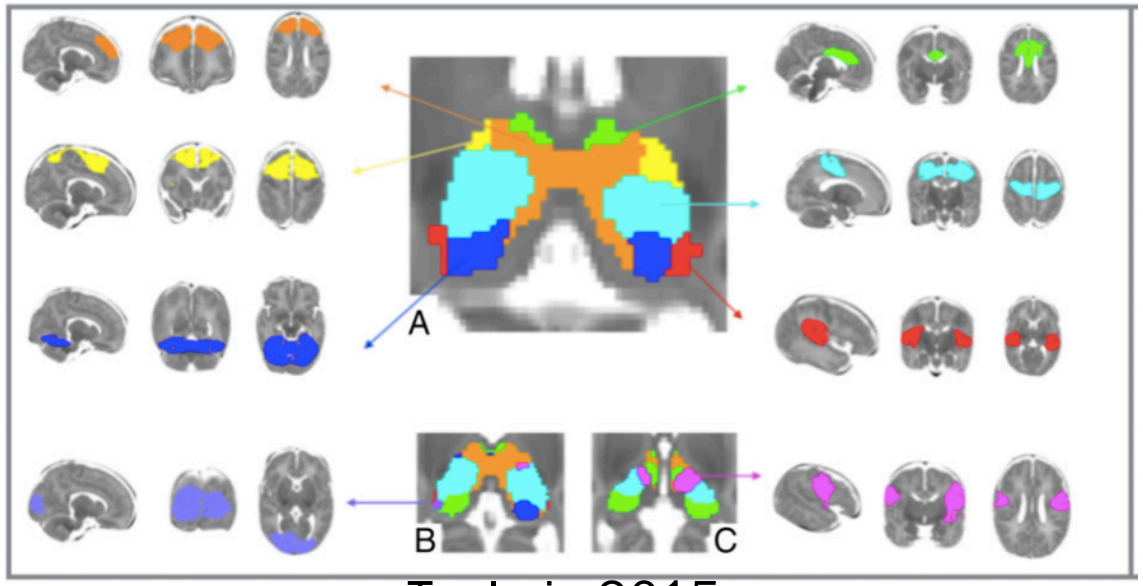
1 year MSEL composite is related to global RD in 1 year olds.



Alcuater 2014

Future Directions

- Classify the development of WM connectivity between thalamus and cortex in relation to cognition
- Subdivide thalamic nuclei
- Relate findings to postmortem research of subplate development in mid – late gestation



Toulmin 2015