Language and Reading after Preterm Birth

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Learning Objectives:

By the conclusion of this talk, participants should be able to

- Describe the long-term outcomes of children born preterm in domains of language and reading
- Explain the role of one neurobiological factor, white matter microstructure, on long term outcomes
- Discuss the role of a social-environmental factor, child-directed speech, on long term outcomes
- Apply this information to clinical care of children born preterm

Outcomes of Preterms born VL/ELGA

- 20% have severe disability: cerebral palsy, intellectual disability, blindness or deafness
- About 50% have mild to moderate disabilities: subtle, discreet, and additive differences that contribute to challenges
- Intelligence quotient falls 10-15 points below matched peers
- Preterm behavioral phenotype
  - Poor attention
  - Weak executive function skills
  - Increased anxiety
  - Poor peer relations

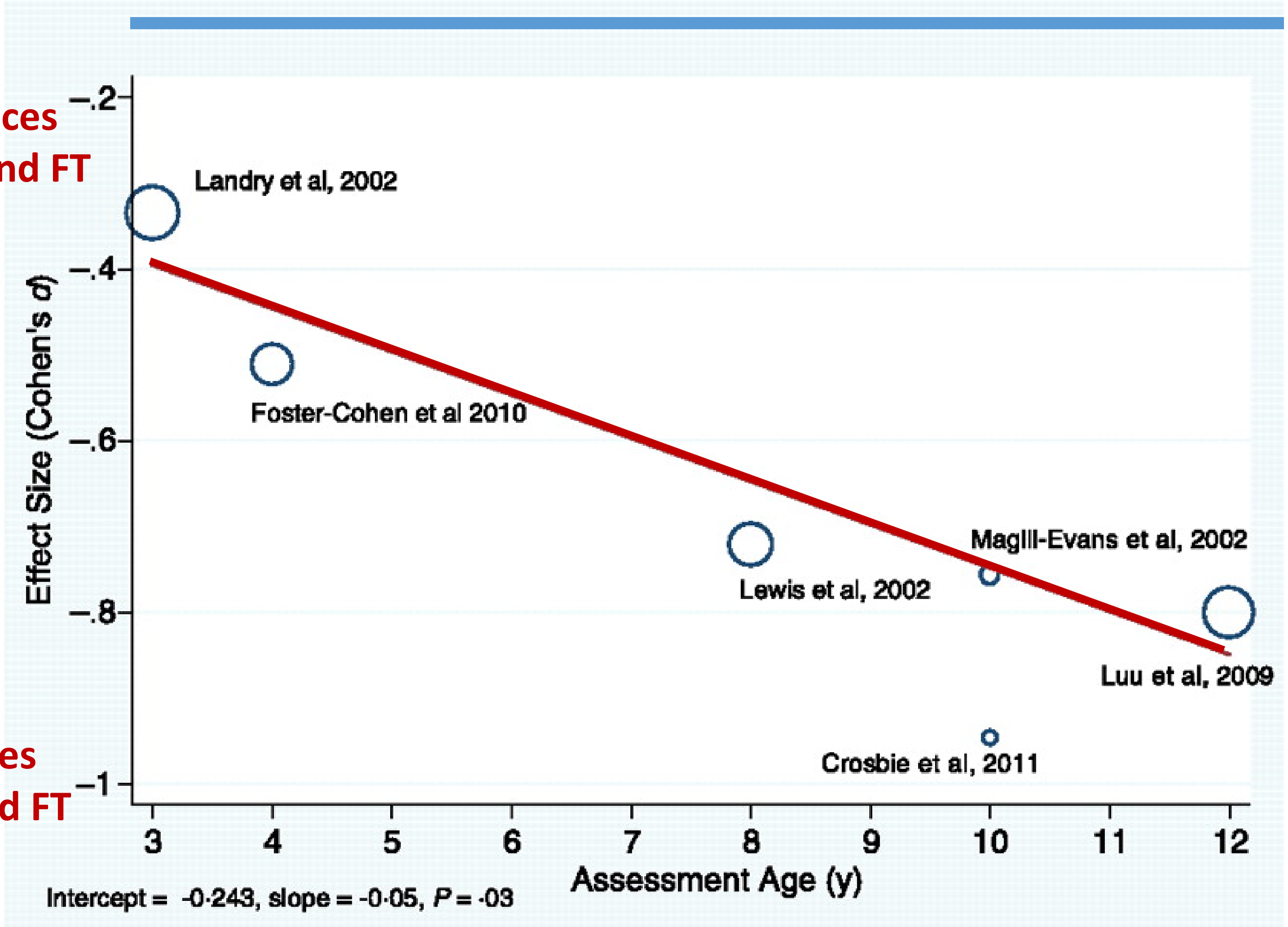
Language outcomes

- Results of two meta-analyses
  - Children born preterm score below children born at term on measures of language ability from age 3 to 12 years (Barre et al, 2007; van Noot vander Spek, et al, 2010)
  - Group differences persist even if children with severe disability are excluded (van Noot vander Spek, et al, 2010)

Complex language skills across childhood

Small differences between PT and FT

Large differences between PT and FT

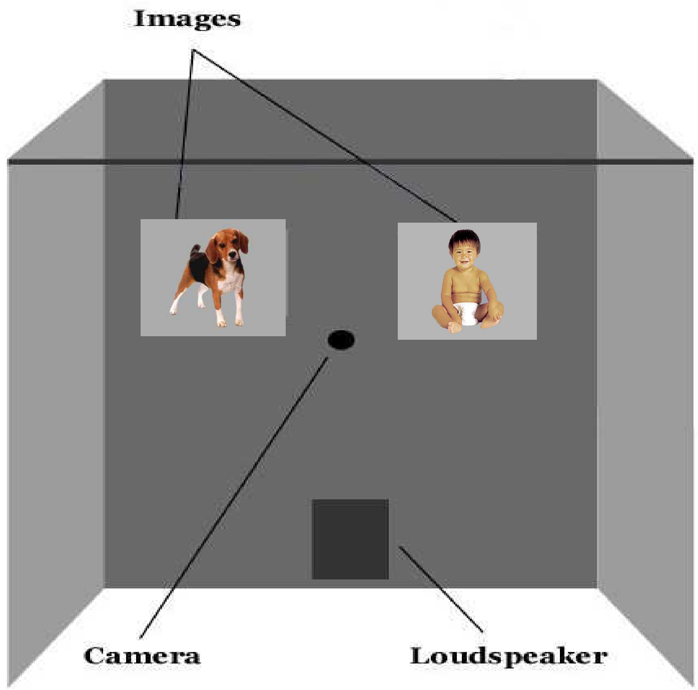


Van Noort van der Snoot et al, 20

Need for an Alternative Metric

- Standardized measures, such as Bayley Scales of Infant Development
  - Assess relative standing in comparison to a population
  - Measure accumulated knowledge
  - Do no reveal underlying neuropsychological abilities to explain standing
- **Looking While Listening (LWL) task**
  - Objective, simple assessment of language processing, appropriate for toddlers
  - Uses eye gaze to infer understanding
  - Generates measures that tap attention, verbal memory, and speed of processing

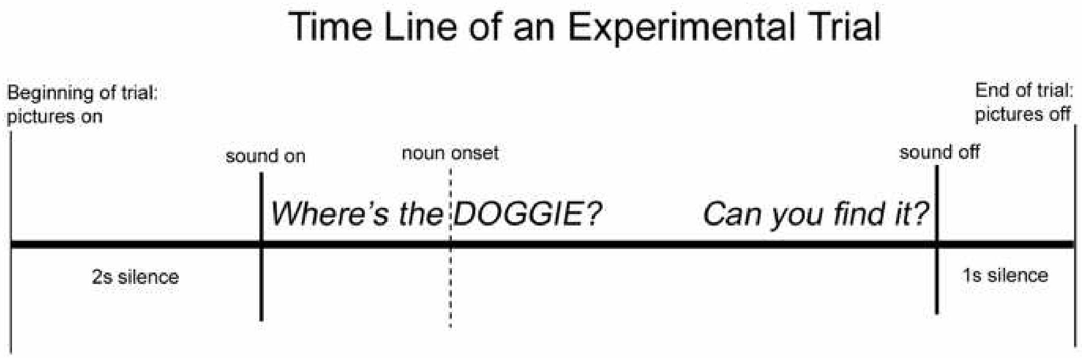
Procedures



“Where’s the Doggy? Can you see it?”

Fernald, et al. 1998; 2008

Coding



- Trained coders unaware of sentence or picture placement then analyze eye movements off-line, frame by frame, from the video
- After coding, links between gaze direction, auditory stimulus and visual stimuli are made automatically

Measures

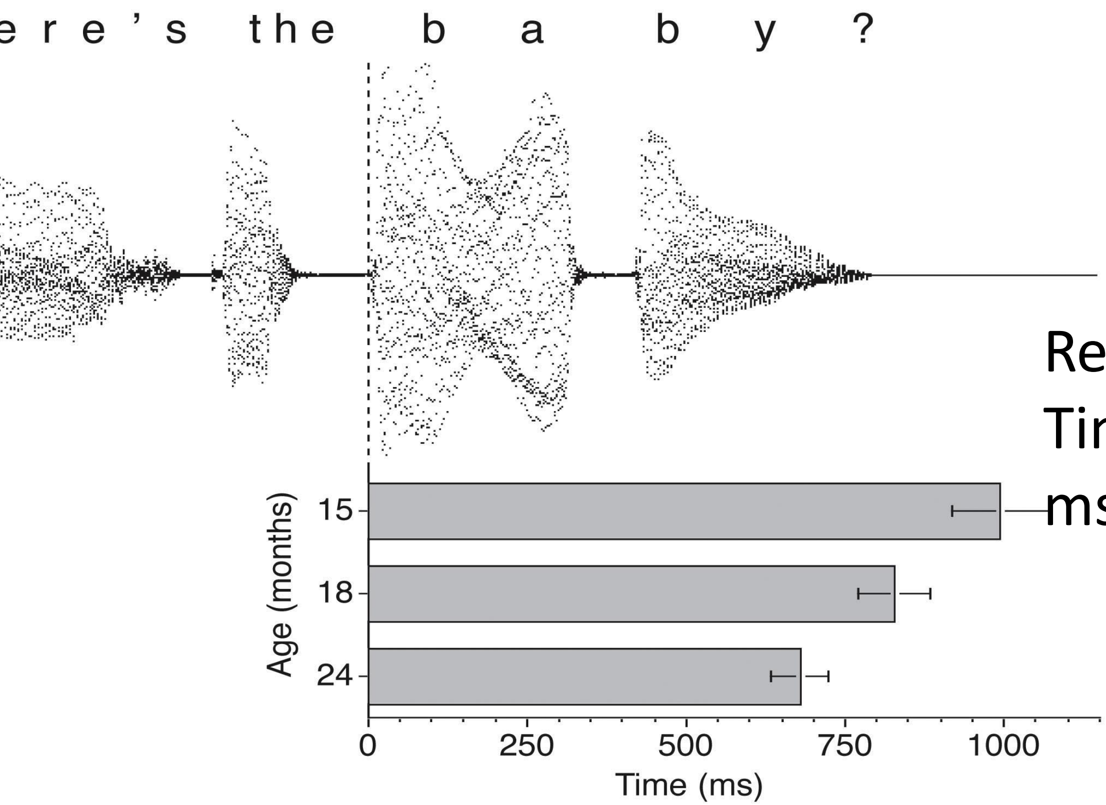
- Accuracy
  - Proportion of time looking at target
  - Index of word recognition
  - Taps into attention and verbal memory
- Reaction Time
  - Time in milli-seconds (msec) to shift eyes from incorrect picture (Distractor) to the correct picture (Target)
  - Assesses language processing speed

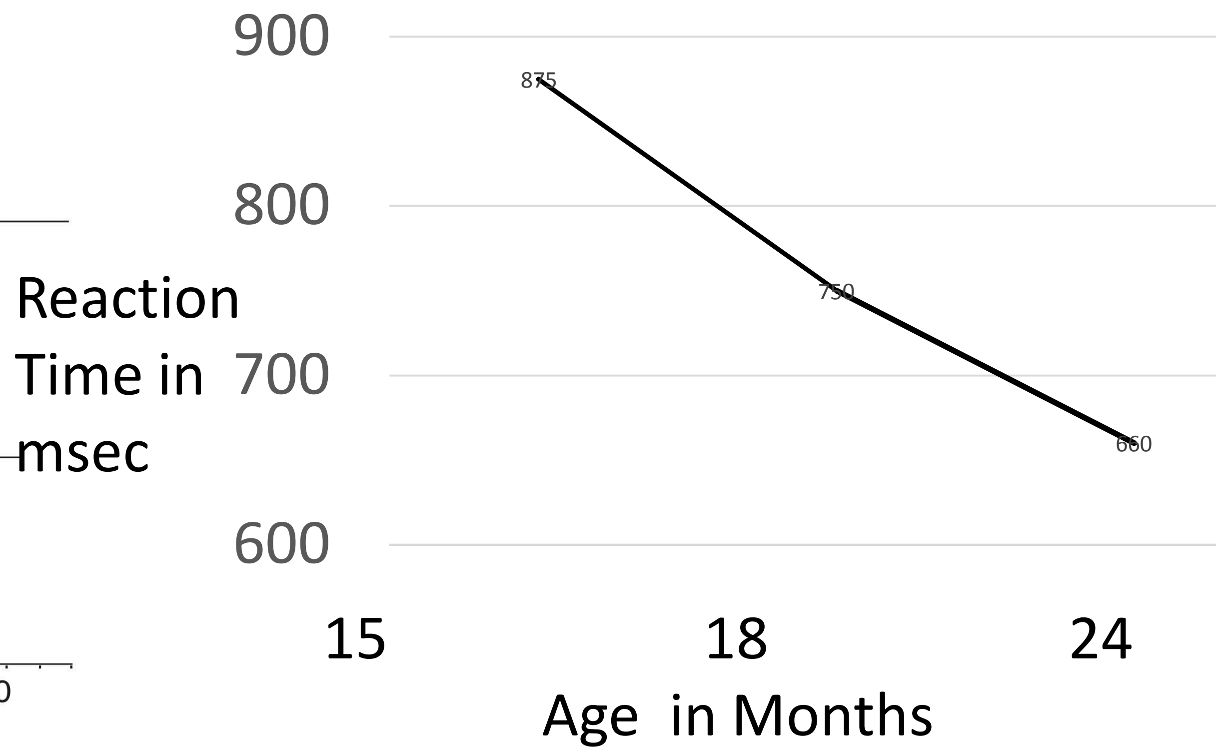
18 months: Distracter-to-Target shift

24 months: Distracter-to-Target shift

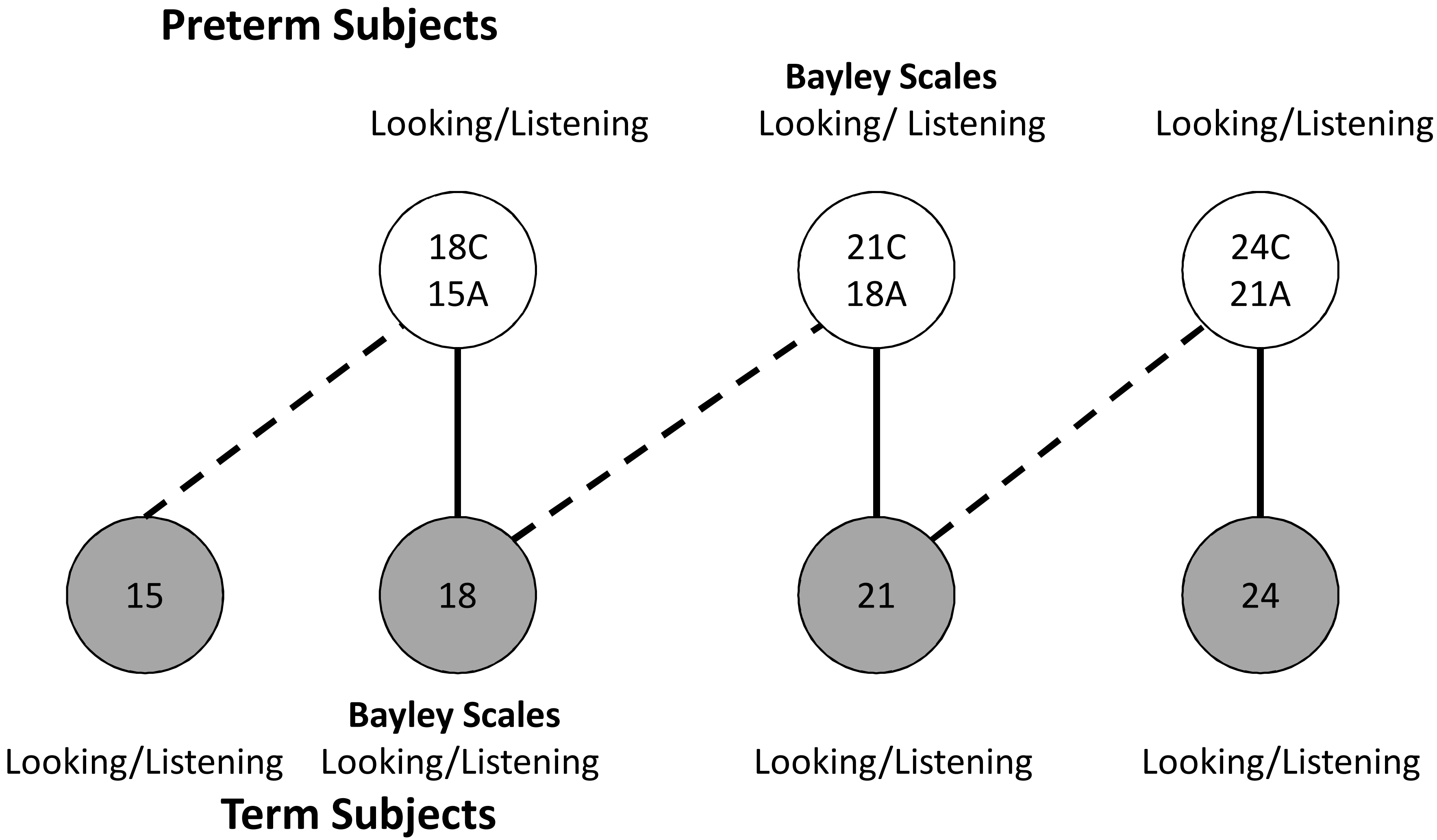
30 months: Distracter-to-Target shift

Reaction Time





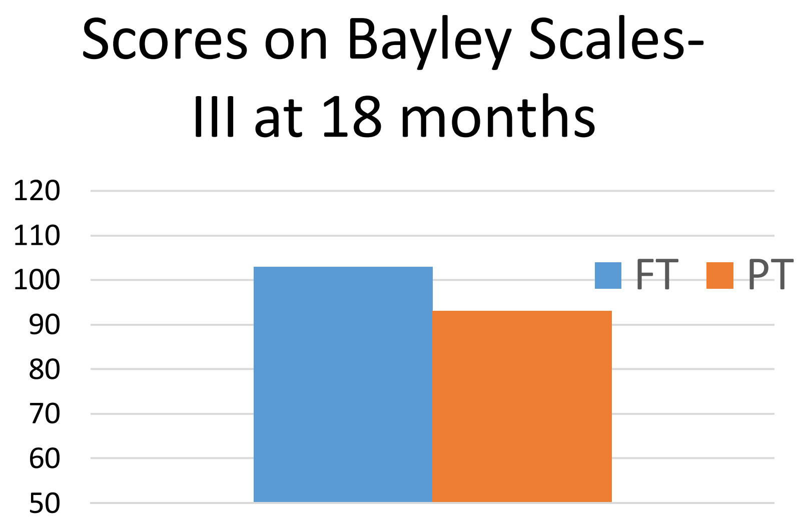
Looking While Listening Study Design



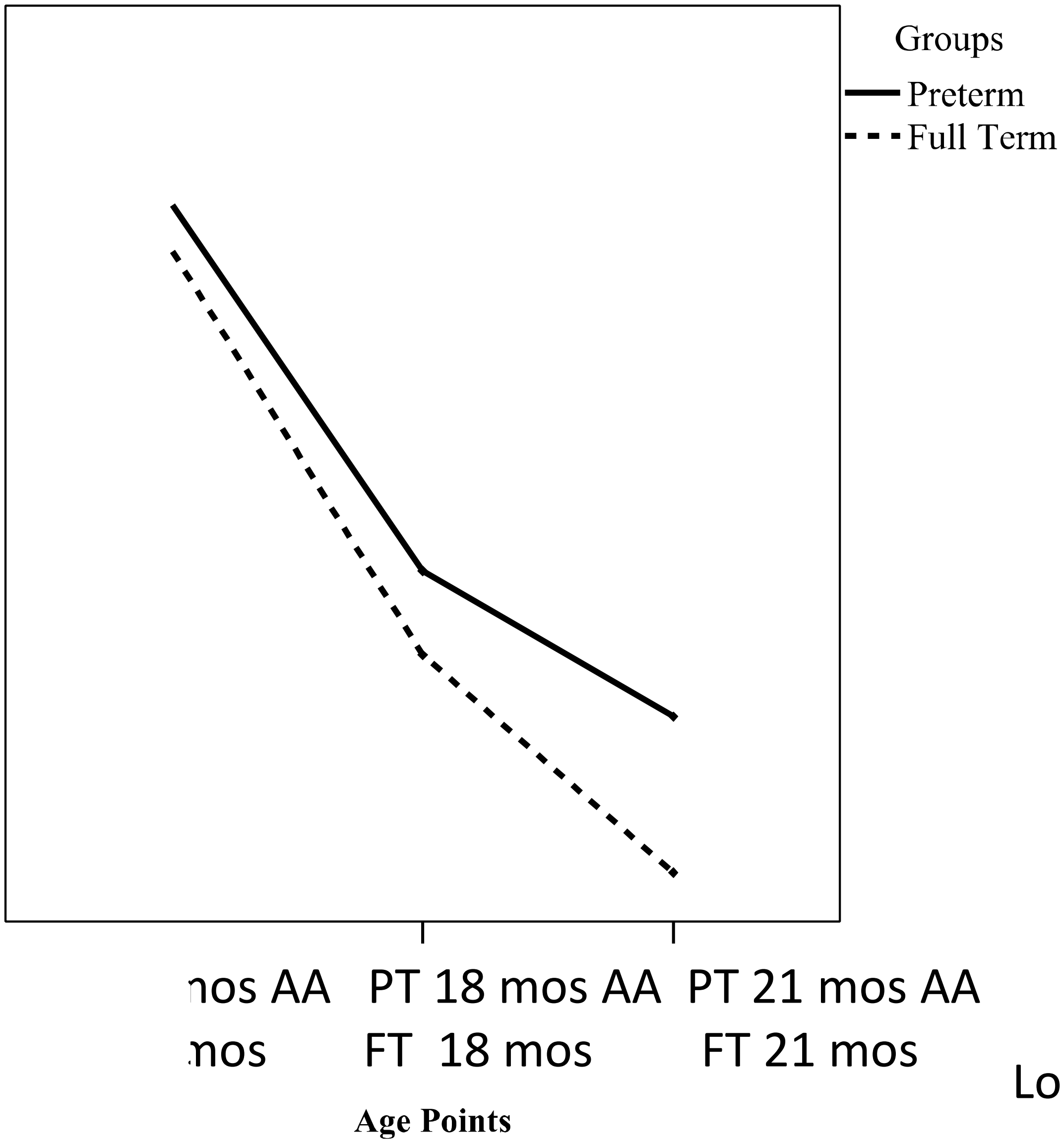
Loi et al, 2018

Study Sample

	Preterm (n = 44)	Full Term (n = 44)
Mean (SD) Gestational Age in weeks	29.7 (3.1)	39.9 (1.)
Mean (SD) Birth Weight in grams	1246 (302)	3500 (465)
% male	54.5	54.5
Hollingshead Index (HI: out of 66)	58.2	59.5

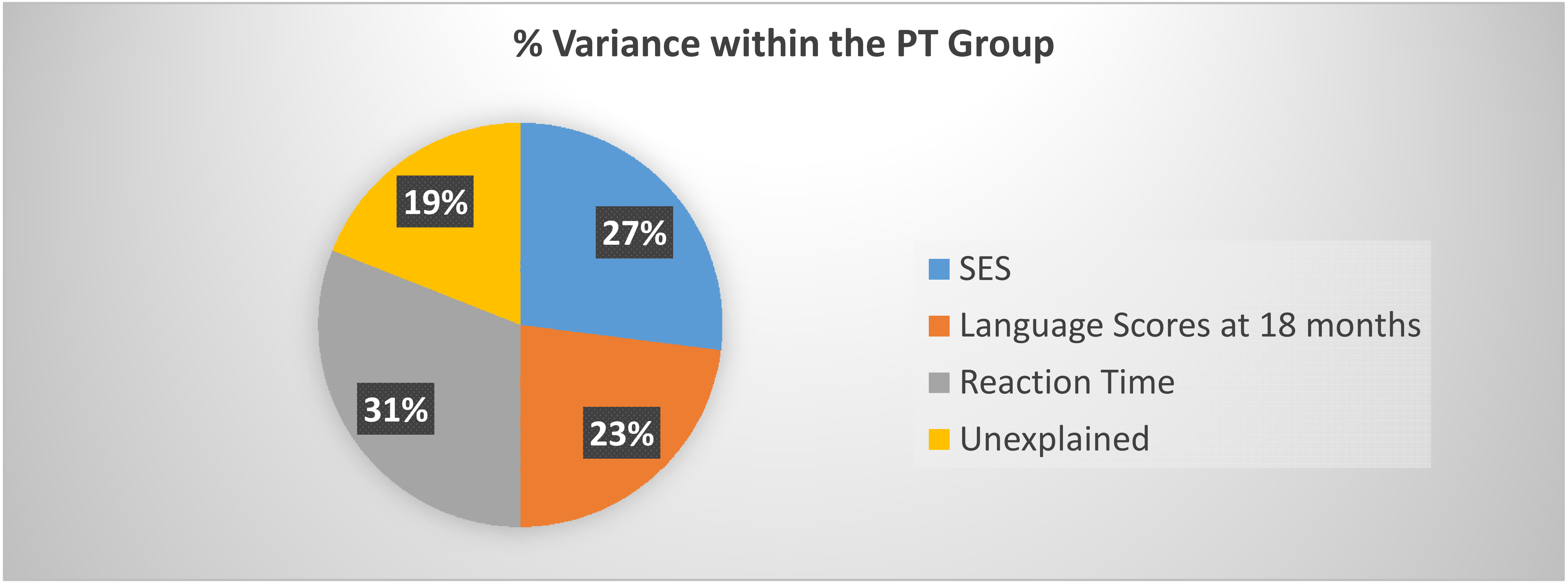


Results



Loi et al, 2018

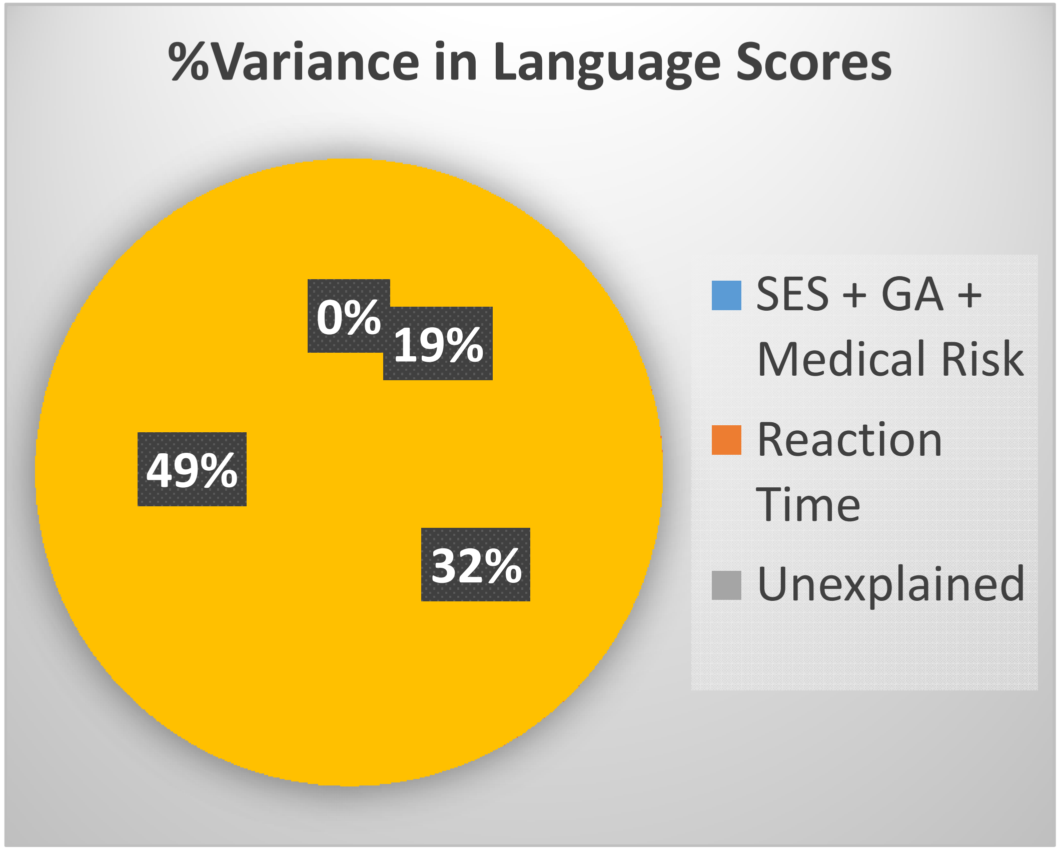
Predicting Receptive Vocabulary at 36 mos

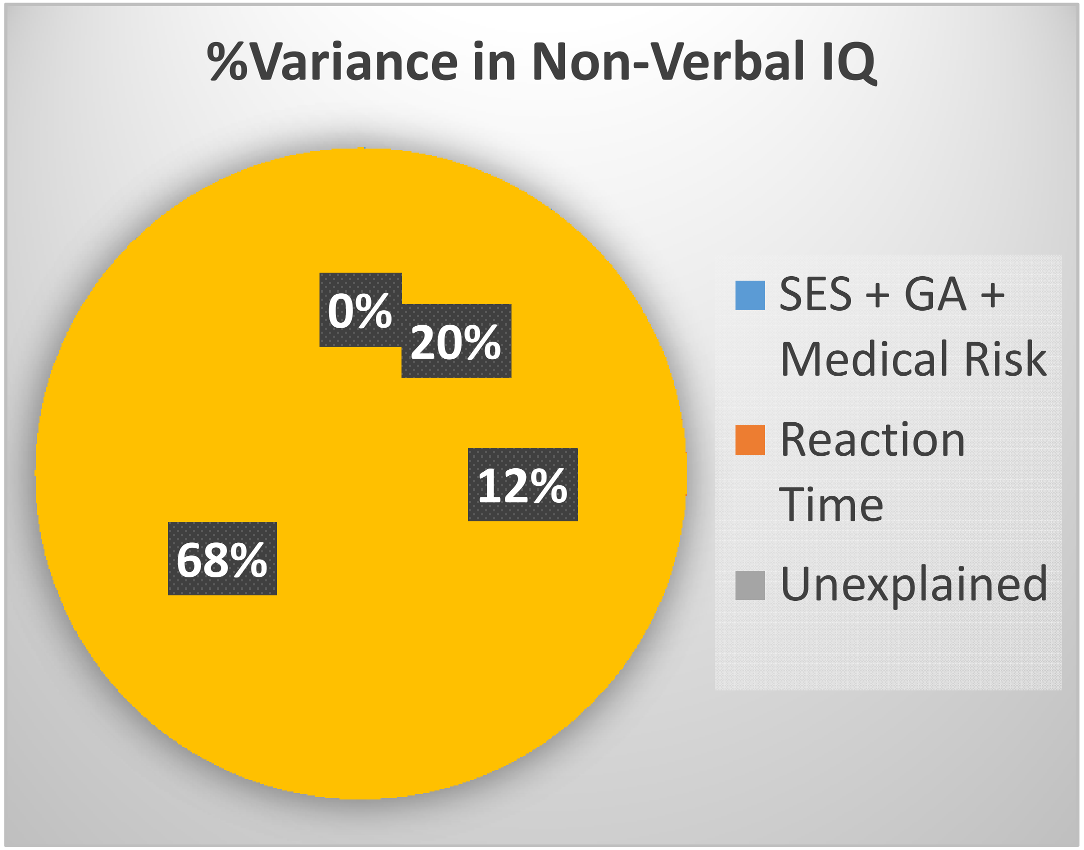


Reaction Time at 18 months of age accounted more variance in Receptive Vocabulary Scores at 36 months of age than results of the Bayley Scales plus the MacArthur Bates Communicative Development Inventory.

Marchman et al, 2015

Predicting Scores at 54 months in PT group





Reaction Time at 18 months of age accounted for variance in a standard language measure and a measure of non-verbal IQ at 54 months. Test scores did not contribute to variance in non-verbal IQ

Marchman et al, 2017

Summary

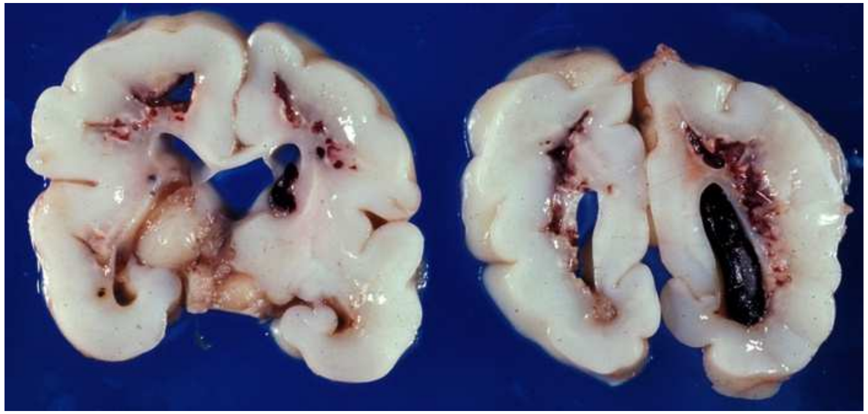
- PT children scored below FT children on standardized measures
- PT children had **slower Reaction Time** than FT children at 18 and 21 months
- Reaction Time at 18 months **predicted language scores** at 36 and 54 months
- Reaction Time at 18 months **predicted predicts non-verbal IQ** at 54 months, other language measures do not
- Slow speed of processing reflects limited cognitive resources that set PT children up for different developmental trajectories, persistent differences

What may account for slower reaction times in preterm children?

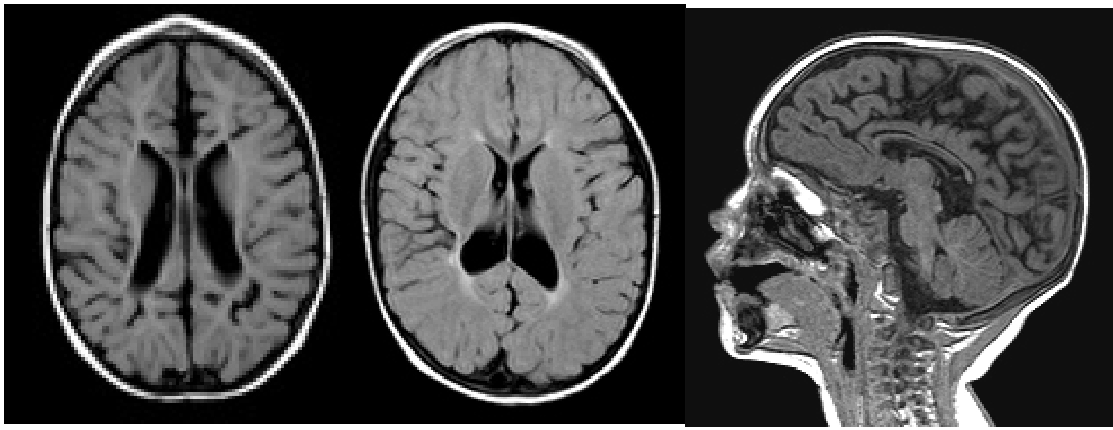
White matter

- Bundles of myelinated axons
- Connect distal brain regions
- Injured after preterm birth

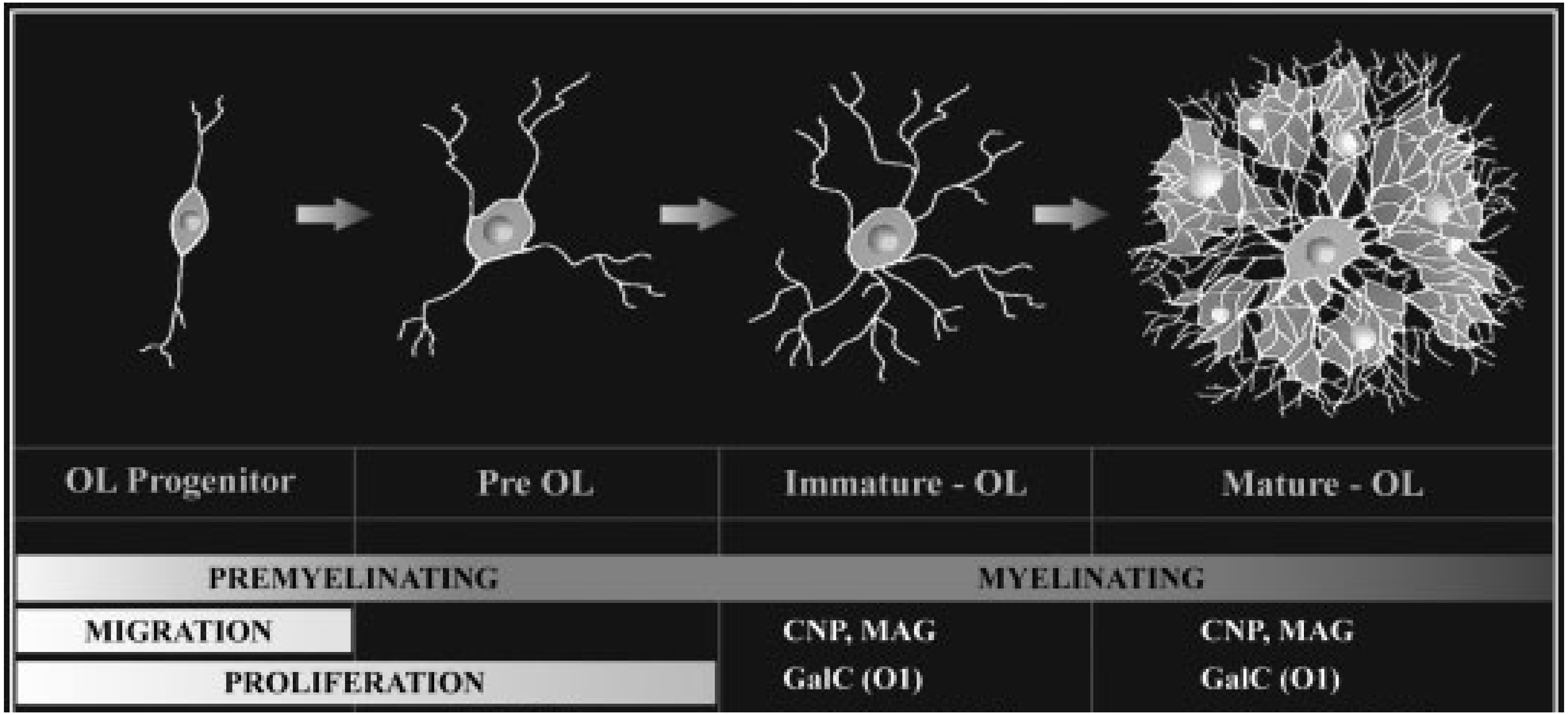
Cystic Periventricular Leukomalacia



Non-cystic white matter injury



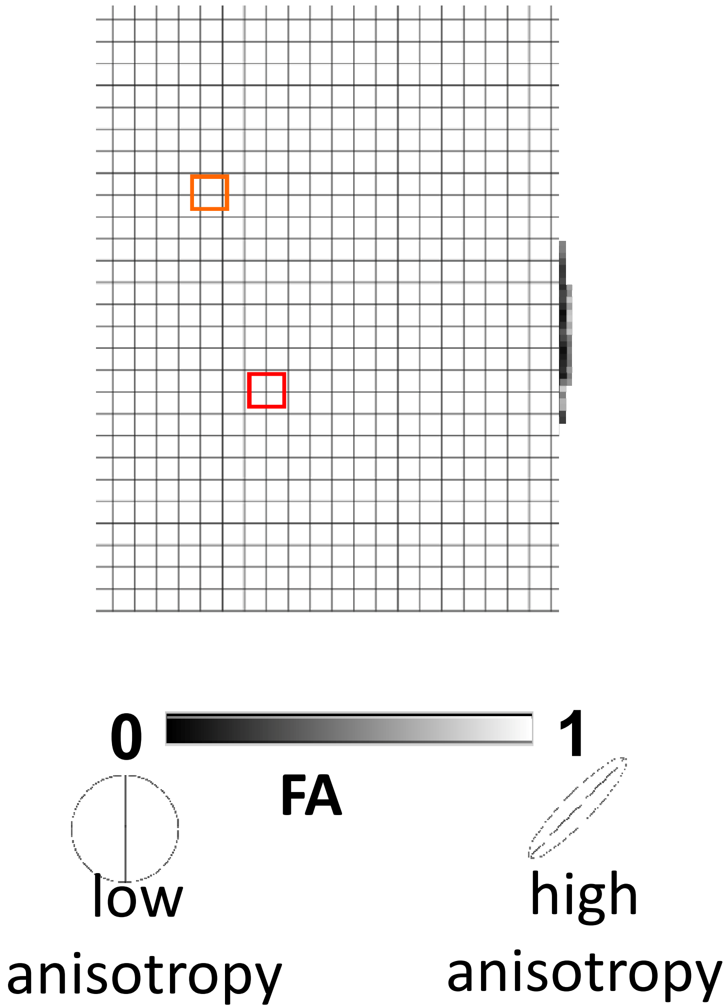
Vulnerability of Oligodendrocytes (Ols)

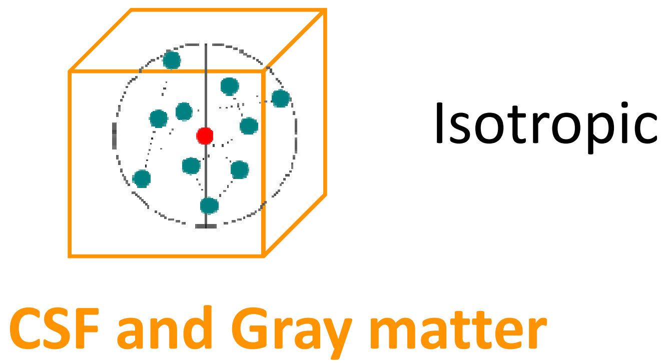


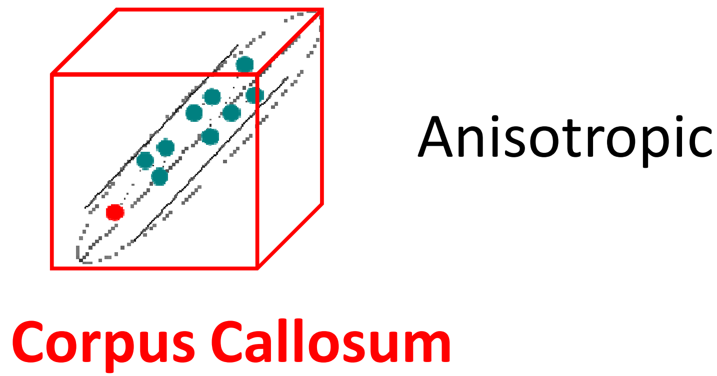
24 weeks ➔ 33 weeks ➔

Assessing White Matter: Diffusion MRI

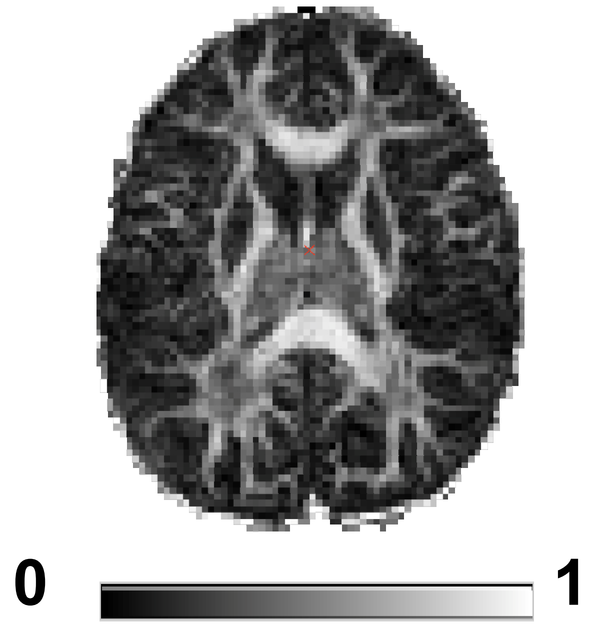
Tensor Model of Water Diffusion







White Matter Microstructure



LOW FA

Axon diameter

HIGH FA

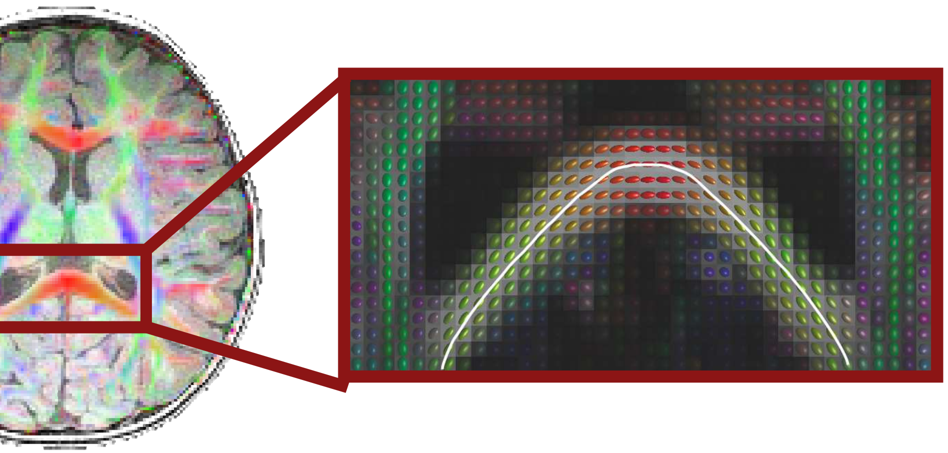
Myelin content

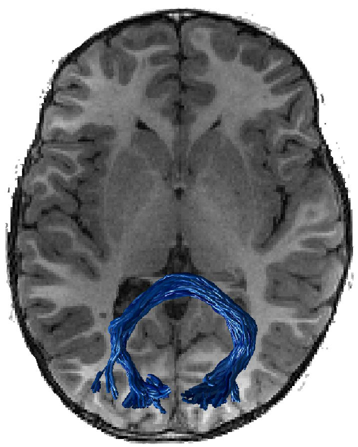
Axon density

Fiber coherence

maging White Matter: Diffusion MRI

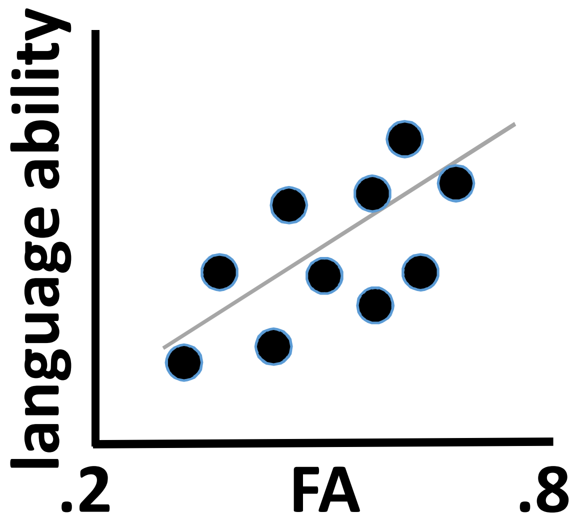
Tract Identification





Measure of Tract Structure

Behavior-Structure Associations



Precursors of language outcomes

- **Objective:** To determine whether white matter microstructure, measured on near-term equivalent age dMRI, would be associated with language scores at 18-24 months corrected age in PT children.
- **Hypothesis:** FA within selected white matter pathways would correlate with Bayley language scores

Dubner et al, 2019

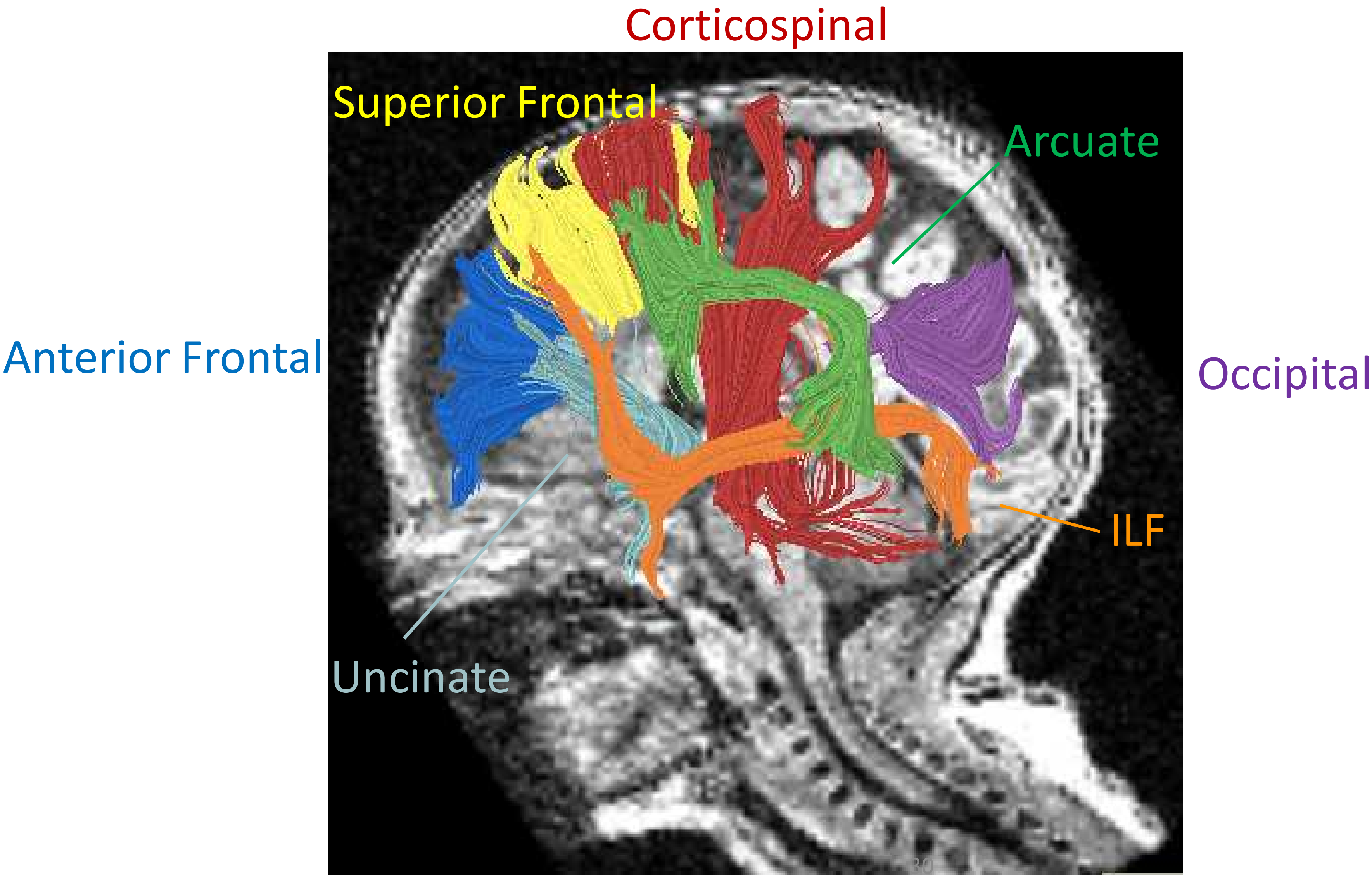
Methods

- 102 PT children recruited from LPCH NICU
- 48 participants with dMRI and Bayley Scales of Infant Development – III at 18-27 months corrected age
- Pearson correlations were used to assess relations between tract FA and Language outcomes.

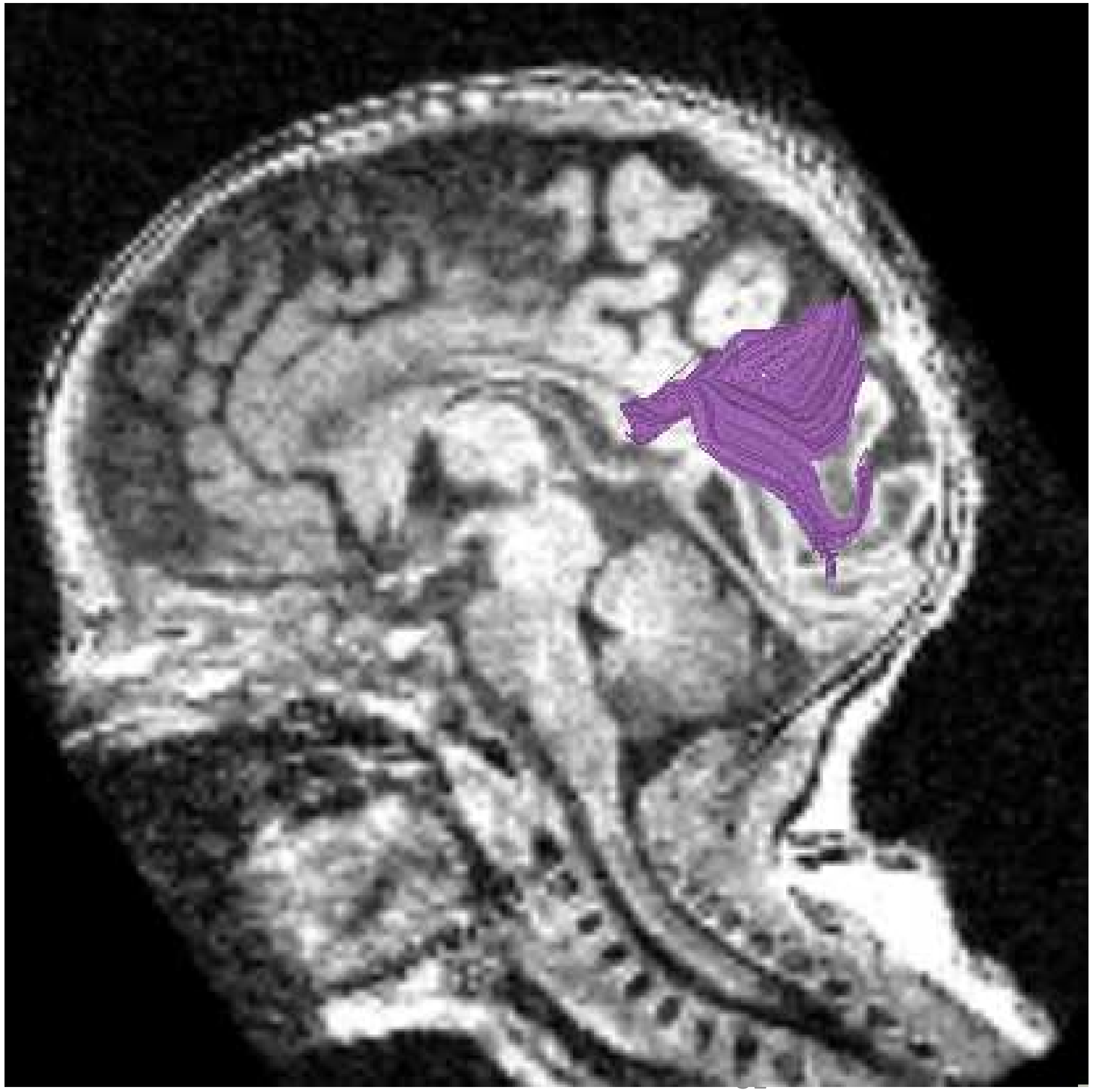
Results

Bayley Scales of Infant Development III	N = 48
	Mean (sd)
Cognitive Composite	97.1 (12.7)
Language Composite	**88.4 (17.2)**
Expressive Scaled Score	**8.2 (3.5)**
Receptive Scaled Score	**8.4 (3.4)**
Motor Composite	94.4 (11.8)
Gross Motor Scaled Score	8.4 (2.4)
Fine Motor Scaled Score	10.0 (2.8)

Fiber Tracts Assessed

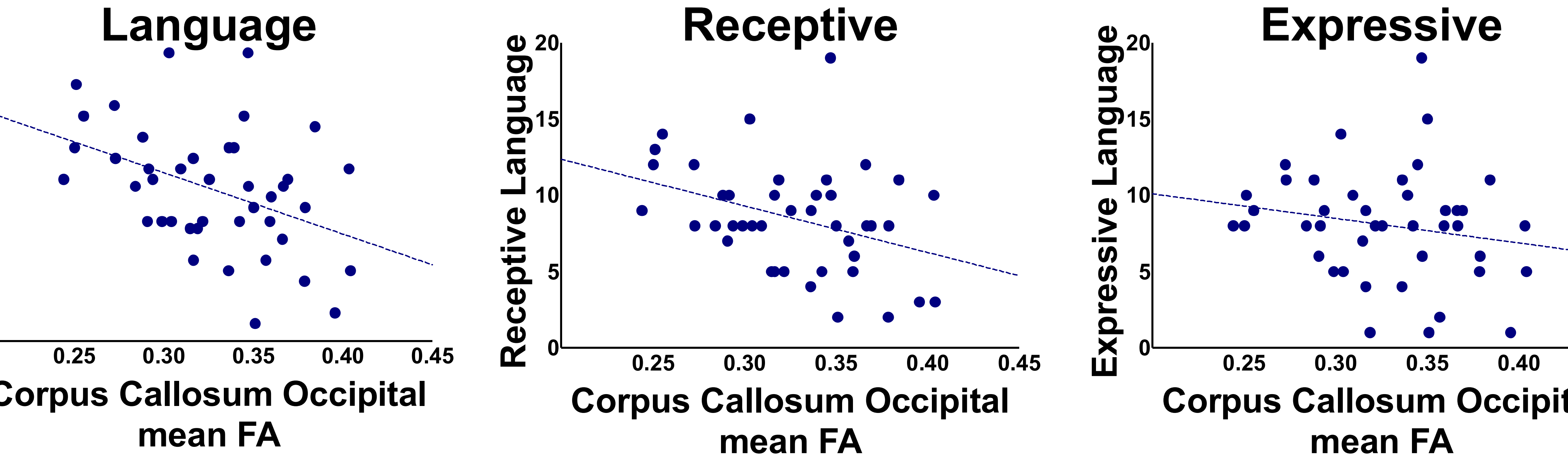


Associations Found



Occipital

Corpus Callosum–Language Correlations



r = -0.42, p = 0.005

r = -0.37, p = 0.016

r = -0.187, p = 0.24

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Children's Health | Lucile Packard
Children's Hospital
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Summary

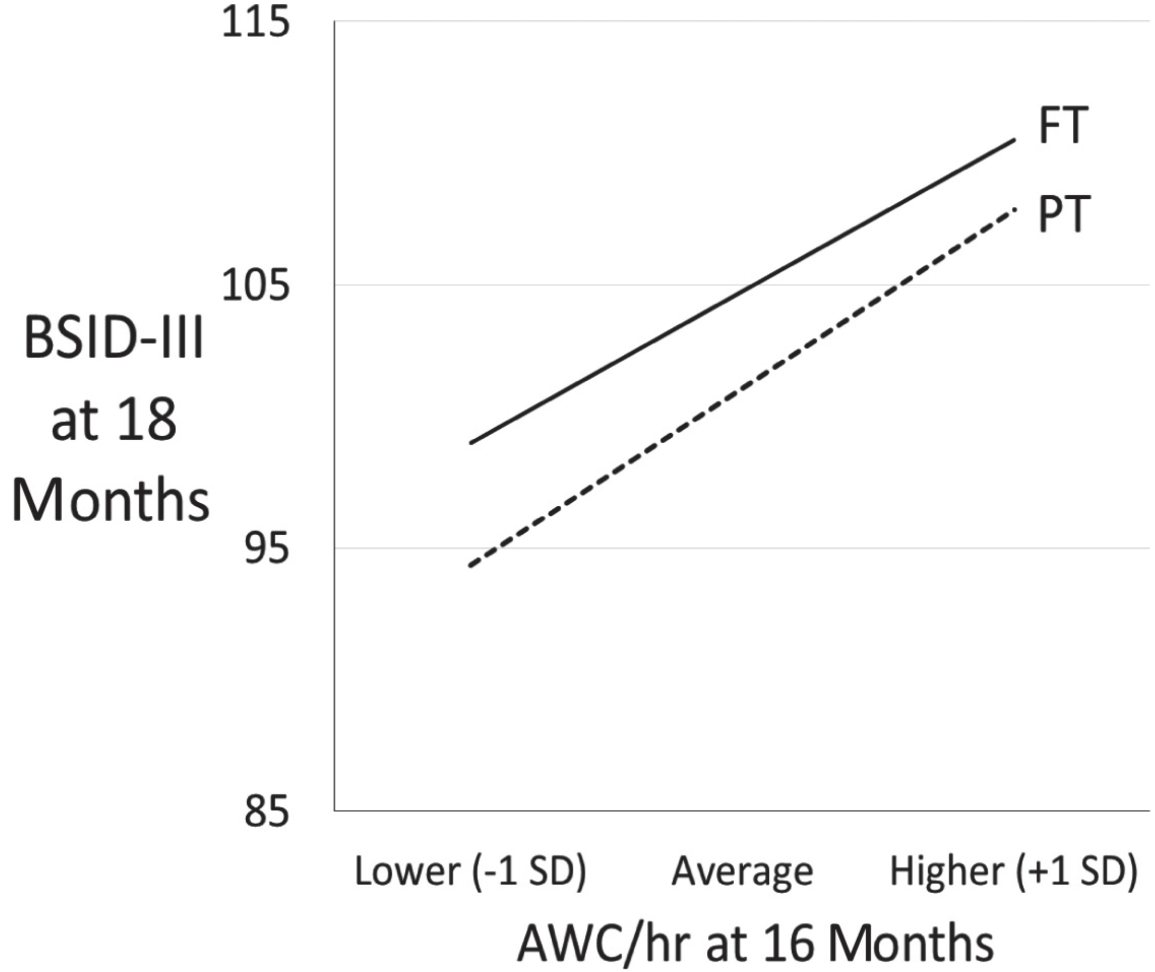
- We identified and **tracted white matter pathways** in preterm children at near term adjusted age
- Found an **association of mean tract FA of the occipital segment** of the corpus callosum and later language scores
- Why this location?
  - Region of high white matter vulnerability to hypoxia, ischemia and inflammation
  - Brain connections required for early language learning may be more extensive than those associated with developed language skills
- Why this negative association?
  - Feature associated with language may be axonal diameter or crossing fibers, not myelin

Social-Environmental contributions

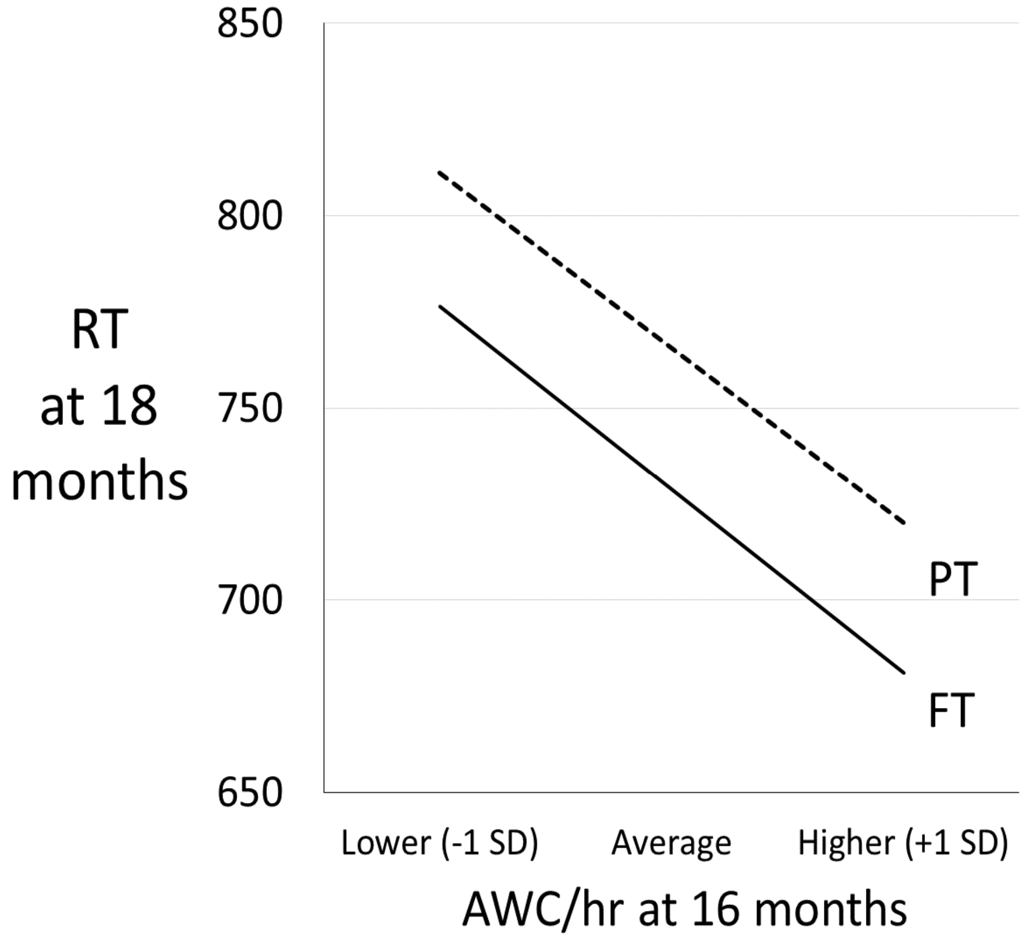
- Socioeconomic status associated with language outcomes
- Aim of the study: to determine if amount of child-directed speech in the home was associated with outcomes
- Method: LENA™ all day long recordings

- Measure: Adult Word Count/hour (AWC)during waking hours wearing the device

Results: Adult Word Count (AWC) at age 15 mos and Bayley Scales-III Scores at 18 months



Results: Adult Word Count (AWC)at age 15 mos and Reaction Time at 18 months



Sample: FT n=56
PT n=41

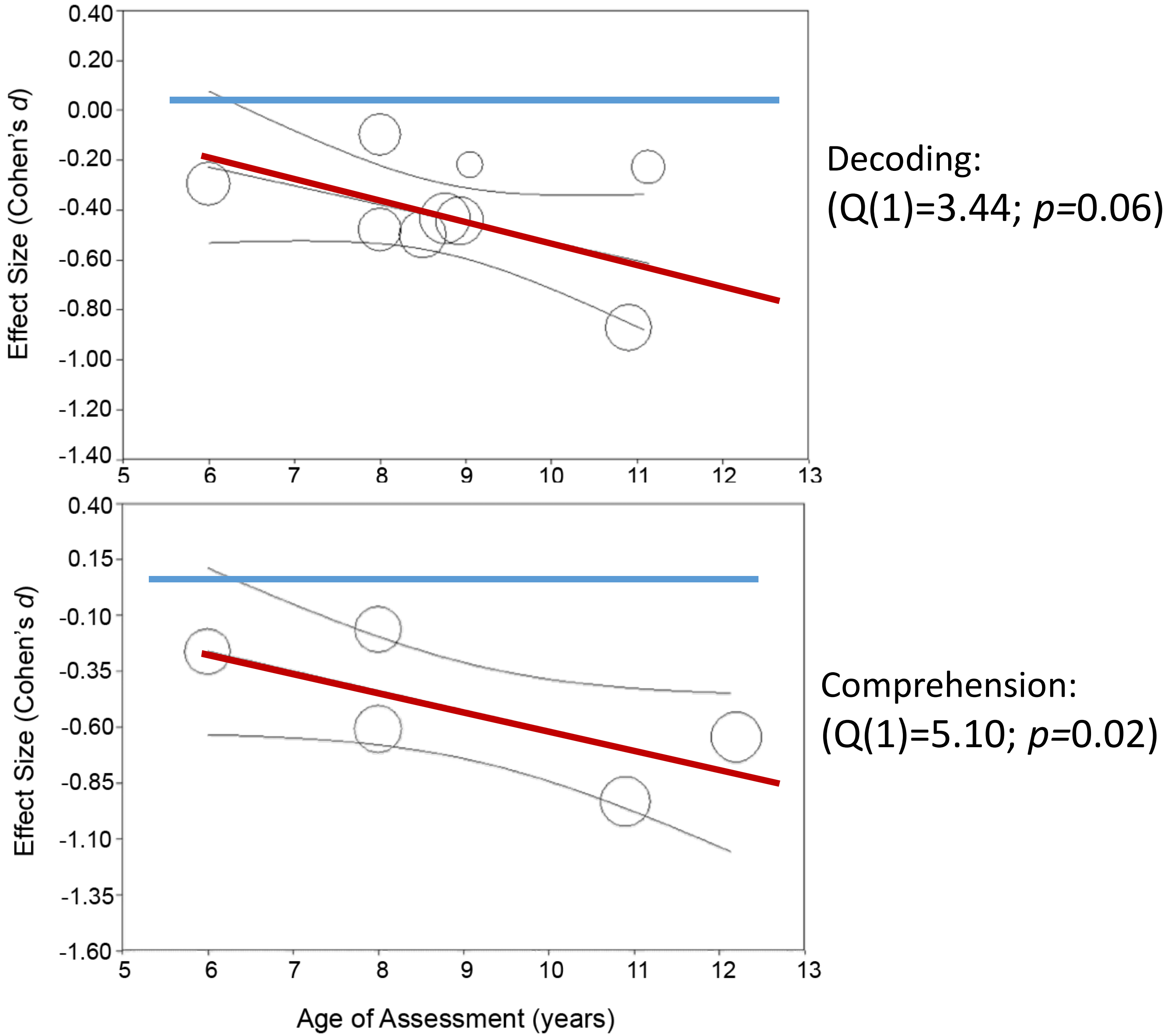
Adams et al, 2018

Summary

- **Quantity of child-directed speech**, measured from day-long recordings in the home, was associated with language **test scores**
- **Quantity of child-directed speech** also contributed to **reaction time** of the Looking-While-Listening Task
- Socio-environmental factors contribute to neuropsychological resources that then contribute to later language learning

Reading in children born preterm

- Previous meta-analyses have shown that children born preterm score below peers on global reading measures
- Simple view conceptualizes two partially dissociable skills – decoding and comprehension
- Do preterm children differ in both components of reading? (Kovachy et al, 2015)


0.40
0.20
0.00
-0.20
-0.40
-0.60
-0.80
-1.00
-1.20
-1.40
Effect Size (Cohen's d)
5
6
7
8
9
10
11
12
13
Decoding:
(Q(1)=3.44; p=0.06)
0.40
0.15
-0.10
-0.35
-0.60
-0.85
-1.10
-1.35
-1.60
Effect Size (Cohen's d)
5
6
7
8
9
10
11
12
13
Comprehension:
(Q(1)=5.10; p=0.02)
Age of Assessment (years)

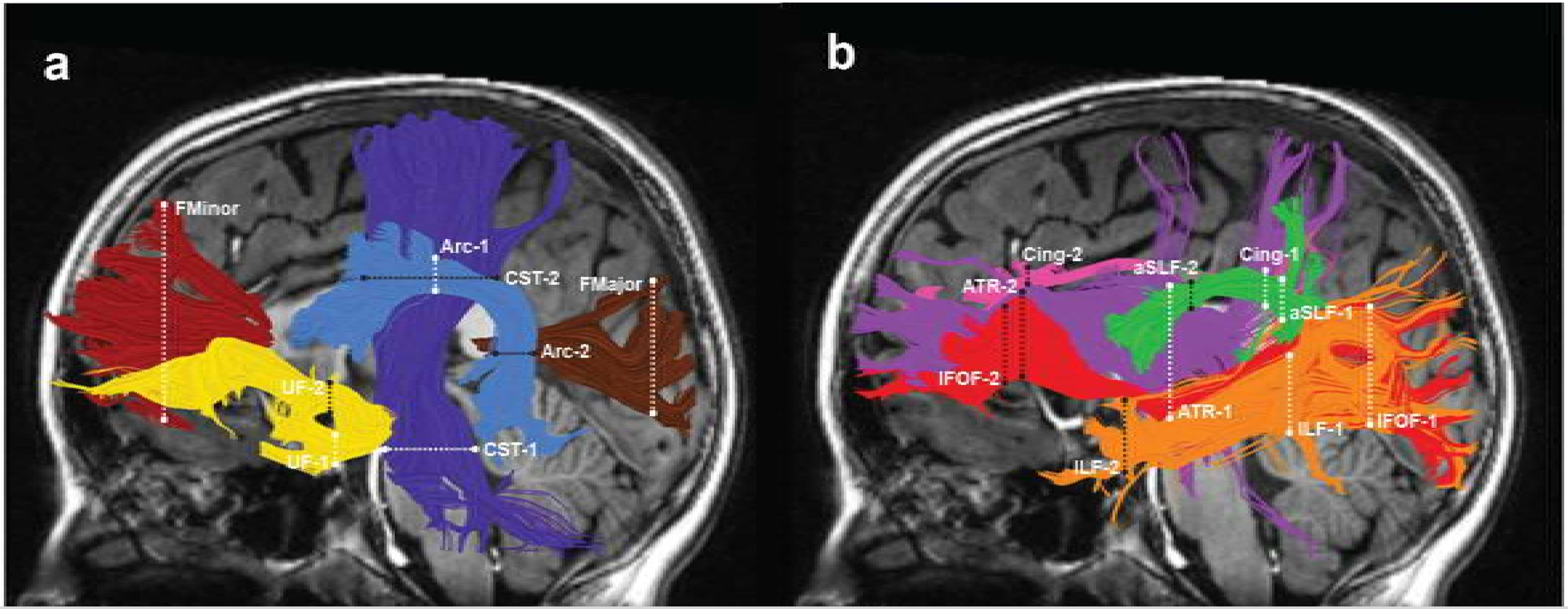
White matter associations with reading skill

- **Objective:** To determine whether white matter microstructure metrics measured in childhood would be associated with reading in PT children
- **Hypothesis:** FA would correlate with reading scores in white matter regions known to be associated with language and reading

Results: Reading outcomes

	Full Term (n = 19) M ± (SD) or n (%)	Preterm (n = 26) M ± (SD) or n (%)	t or X^2
Age	12.90 ± 2.16	12.80 (2.27)	0.149
Gestational Age	39.17 ± 1.13	28.17 ± 2.23	21.59**
Birth Weight, g	3154 ± 407	1159 ± 427	15.90**
Reading			
Decoding	106.7 (10.0)	105.3 (13.4)	0.402
Comprehension	108.1 (14.0)	102.5(12.7)	1.400

White matter pathways



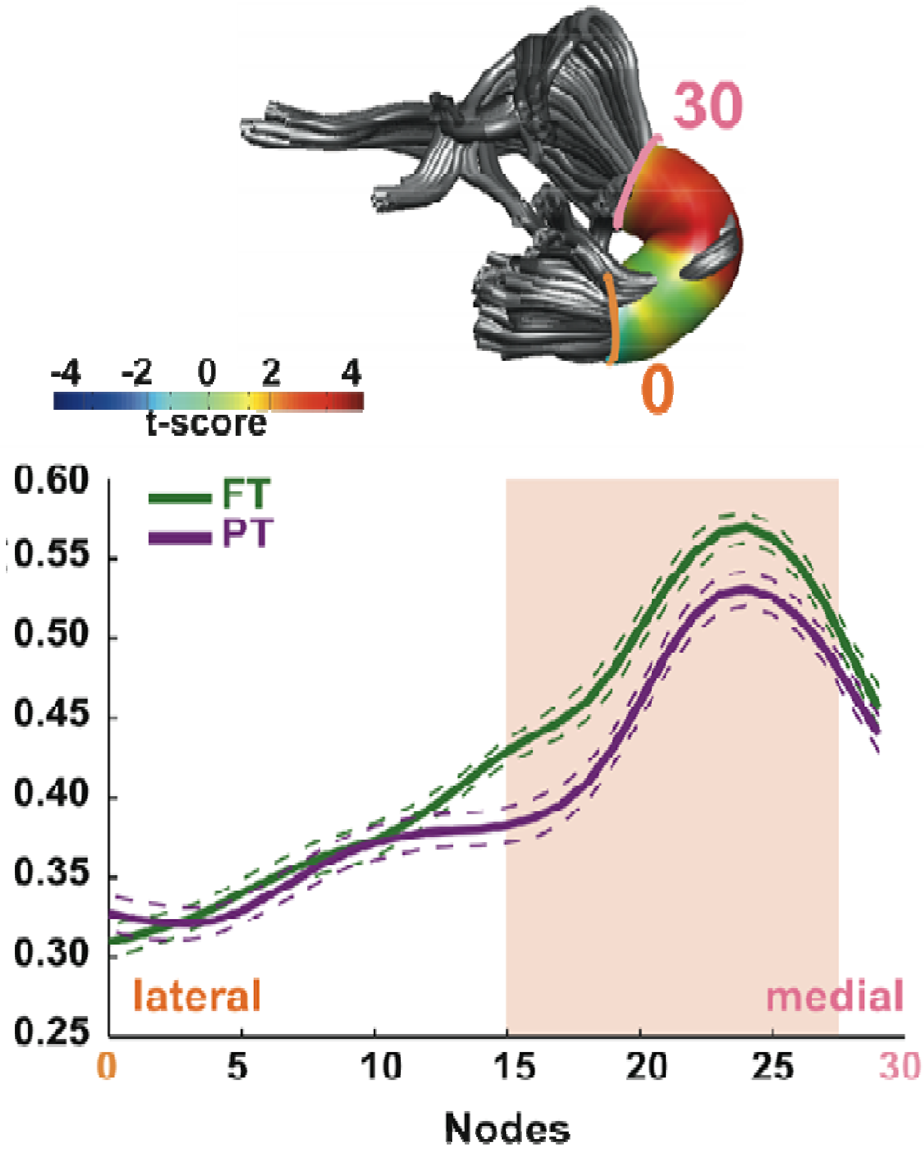
a

Forceps Major (Fmajor)
Forceps Minor (Fminor)
Uncinate Fasciculus (UF)
Arcuate (Arc)
Corticospinal Tract (CST)

b

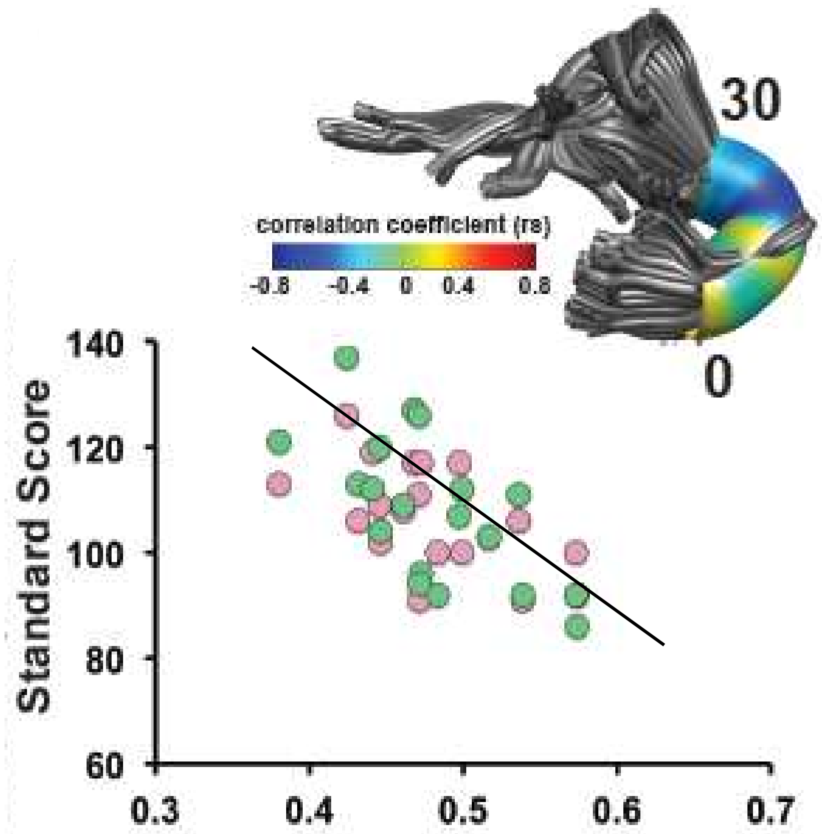
Anterior Thalamic Radiation (ATR)
Inferior Fronto-Occipital Fasciculus (IFOF)
Anterior Superior Longitudinal Fasciculus (aSLF)
Inferior Longitudinal Fasciculus (ILF)
Cingulate (Cing)

Uncinate fasciculus

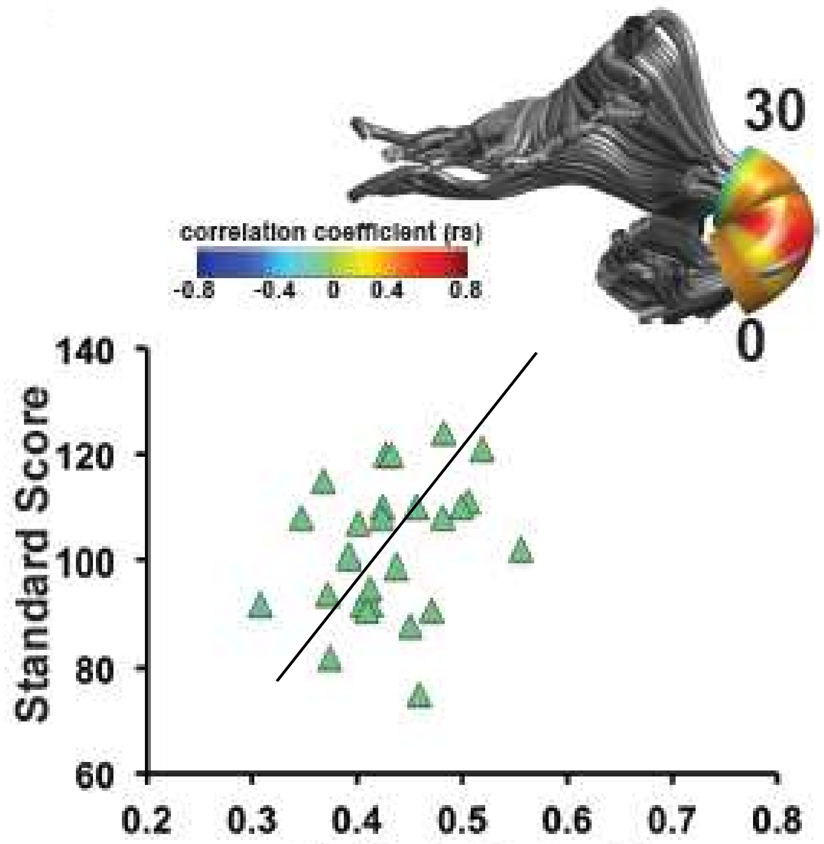


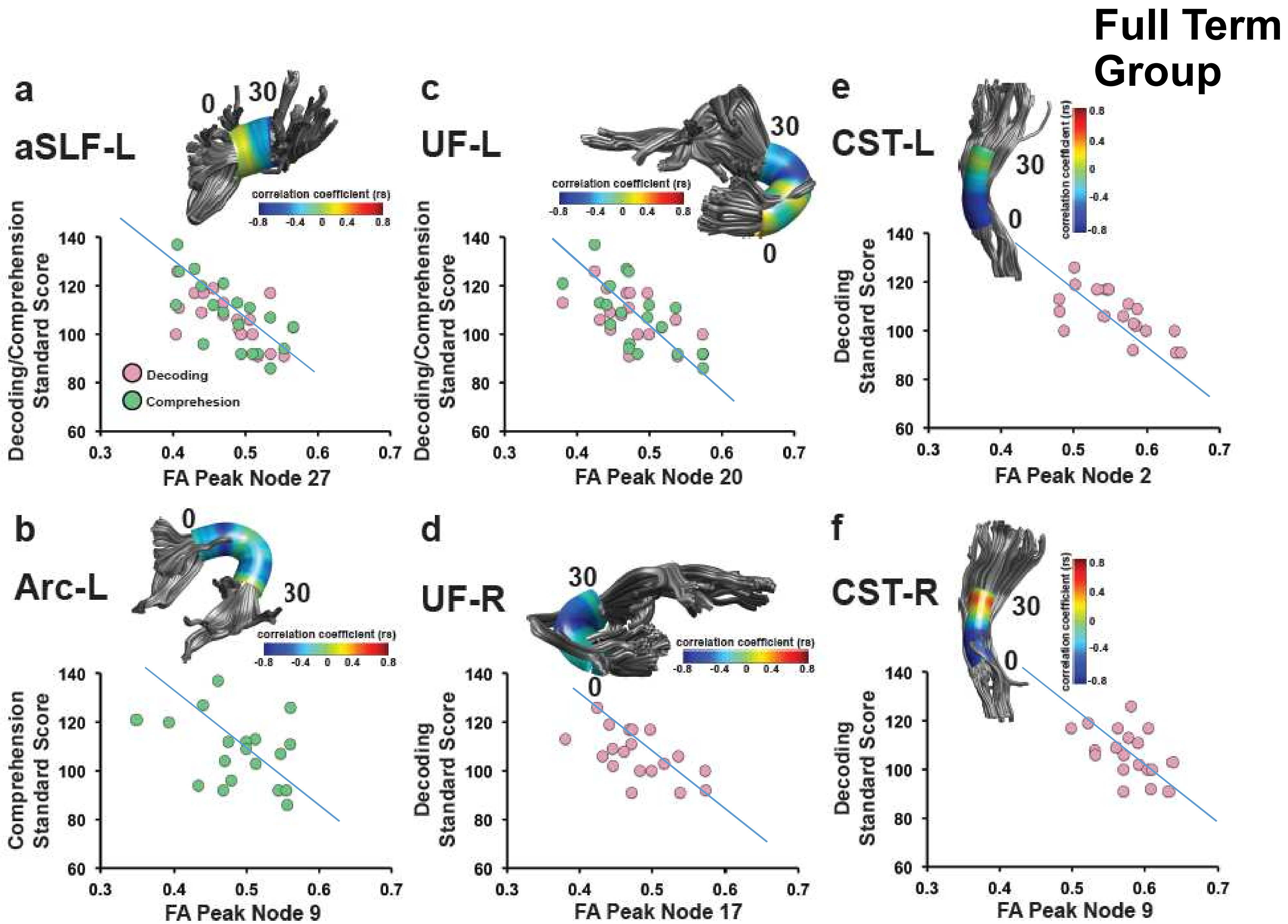
Uncinate

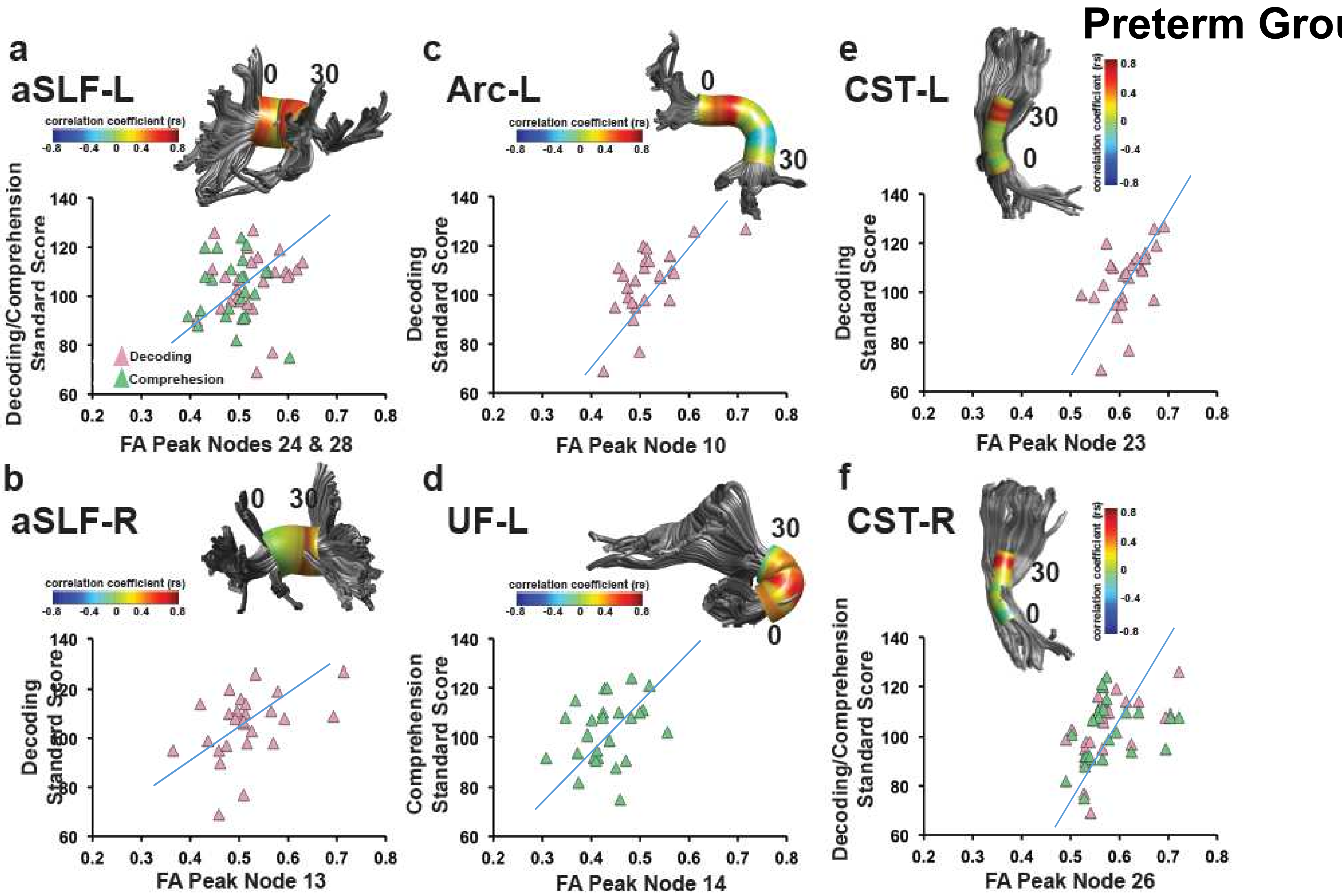
Full term children



Preterm children




Full Term Group
a
aSLF-L
0
30
correlation coefficient (rs)
-0.8 -0.4 0 0.4 0.8
Decoding/Comprehension Standard Score
140 120 100 80 60
Decoding
Comprehesion
0.3 0.4 0.5 0.6 0.7
FA Peak Node 27
b
Arc-L
0
30
correlation coefficient (rs)
-0.8 -0.4 0 0.4 0.8
Comprehension Standard Score
FA Peak Node 9
c
UF-L
30
0
correlation coefficient (rs)
Decoding/Comprehension Standard Score
FA Peak Node 20
d
UF-R
30
0
correlation coefficient (rs)
Decoding Standard Score
FA Peak Node 17
e
CST-L
30
0
correlation coefficient (rs)
Decoding Standard Score
FA Peak Node 2
f
CST-R
30
0
correlation coefficient (rs)
Decoding Standard Score
FA Peak Node 9



Preterm Grou
a
aSLF-L
0
30
correlation coefficient (rs)
-0.8 -0.4 0 0.4 0.8
Decoding/Comprehension Standard Score
140 120 100 80 60
Decoding
Comprehesion
0.2 0.3 0.4 0.5 0.6 0.7 0.8
FA Peak Nodes 24 & 28
c
Arc-L
0
30
correlation coefficient (rs)
-0.8 -0.4 0 0.4 0.8
Decoding Standard Score
140 120 100 80 60
0.2 0.3 0.4 0.5 0.6 0.7 0.8
FA Peak Node 10
e
CST-L
30
0
correlation coefficient (rs)
0.8 0.4 0 -0.4 -0.8
Decoding Standard Score
140 120 100 80 60
0.2 0.3 0.4 0.5 0.6 0.7 0.8
FA Peak Node 23
b
aSLF-R
0
30
correlation coefficient (rs)
-0.8 -0.4 0 0.4 0.8
Decoding Standard Score
140 120 100 80 60
0.2 0.3 0.4 0.5 0.6 0.7 0.8
FA Peak Node 13
d
UF-L
30
0
correlation coefficient (rs)
-0.8 -0.4 0 0.4 0.8
Comprehension Standard Score
140 120 100 80 60
0.2 0.3 0.4 0.5 0.6 0.7 0.8
FA Peak Node 14
f
CST-R
30
0
correlation coefficient (rs)
0.8 0.4 0 -0.4 -0.8
Decoding/Comprehension Standard Score
140 120 100 80 60
0.2 0.3 0.4 0.5 0.6 0.7 0.8
FA Peak Node 26

Summary

- Children born PT learn to read and function below age-matched peers
- FA of the white matter pathways associated with reading account for individual differences in reading scores
- Direction of association different in PT and FT groups
- Negative association in FT may relate to axonal size or tract coherence
- Positive associations in PT may relate to myelin content

Clinical implications

Systematic follow-up of PT childre

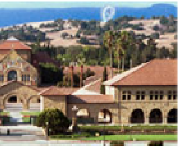
- Monitor development in children born PT to school age
- Focus on complex language and reading comprehension
- Also assess other components of the PT phenotype
- For children showing difficulties, get them help in kindergarten/first grade when interventions are most effective
- For children who fail to respond to intervention, consider compensation and by-pass strategies, such as audiobooks

Future directions

- Study opportunities to get children off to a good start: Increase language exposure in the NICU
- Test whether increased exposure to language can prevent or mitigate delays in language during preschool years
- Assess if improvements in language reduce reading difficulties
- Assess whether improved outcomes result in changes in white matter microstructure

Thanks to my team and funders



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