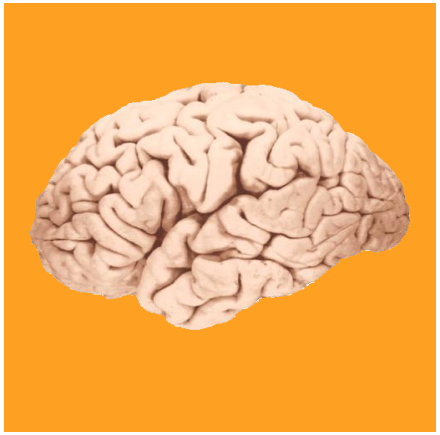
The typical and atypical reading brain:

How a neurobiological framework of reading development can inform educational practice and policy



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Overview

- Typical and atypical reading development and its neurobiology
- Remediating the atypical reading brain
- The 'Dyslexia Paradox'
- Early pre-markers of reading difficulties before reading onset
- Compensatory mechanisms, resiliency and protective factors
- Detecting children at risk for reading difficulties in infancy?
- Educational and Clinical Implications

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Timeline of typical reading development

Sound and Language Processing

Visual Processing

Phonological Processing

Letter Recognition

Grapheme-phoneme Mapping

Reading of single words

Reading sentences and connected text

Reading complex text

Reading Fluency

Reading Comprehension

Key predictors of reading ability before reading instruction starts:

- Phonological/Phonemic awareness
- Speech perception/production
- Syntax production and comprehension
- Receptive/expressive vocabulary
- Rapid automatized naming abilities
- Letter name knowledge
- Verbal short-term memory

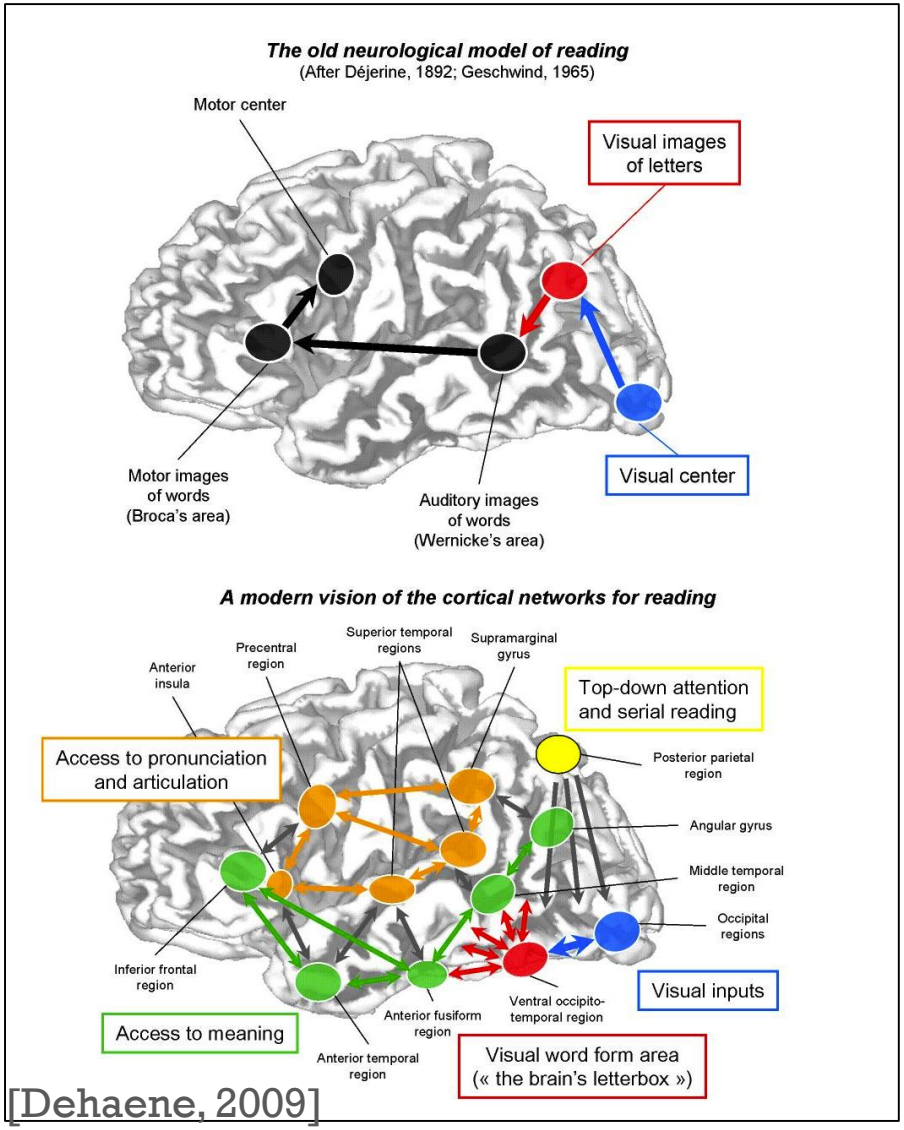
(e.g., Schatschneider et al., 2004; Georgiou et al., 2008; de Jong & van der Leij, 1999; Scarborough, 1998; Pennington & Lefly, 2001).

Home Literacy Environment (HLE)

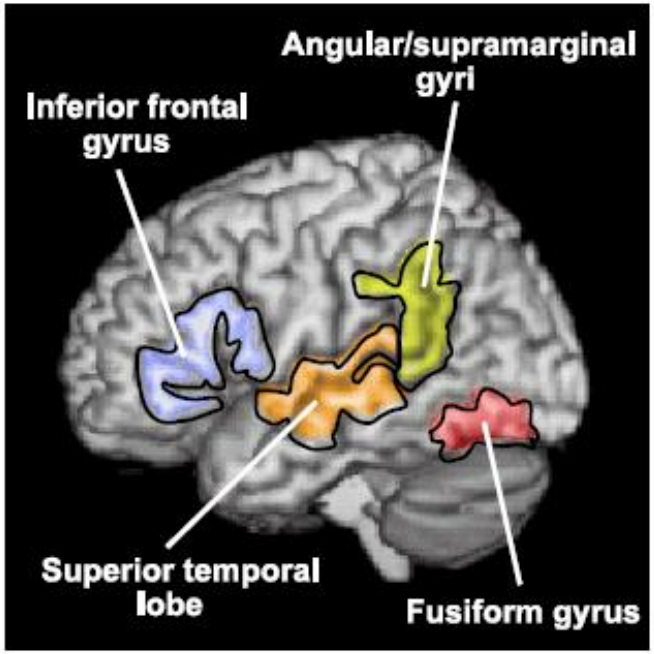
Aspects of HLE that are most predictive of future language and literacy skills include (e.g., Hamilton, 2013; Payne, Whitehurst, & Angell, 1994; Bus et al., 1995; Rodriguez et al., 2011):

- Age of onset of shared reading
- Frequency and quality of book reading
- Frequency of library visits
- Parental knowledge of storybook titles
- Parental mediating style during shared reading
- Parental language during shared reading
- …

The typical reading network with its key components



[Dehaene, 2009]

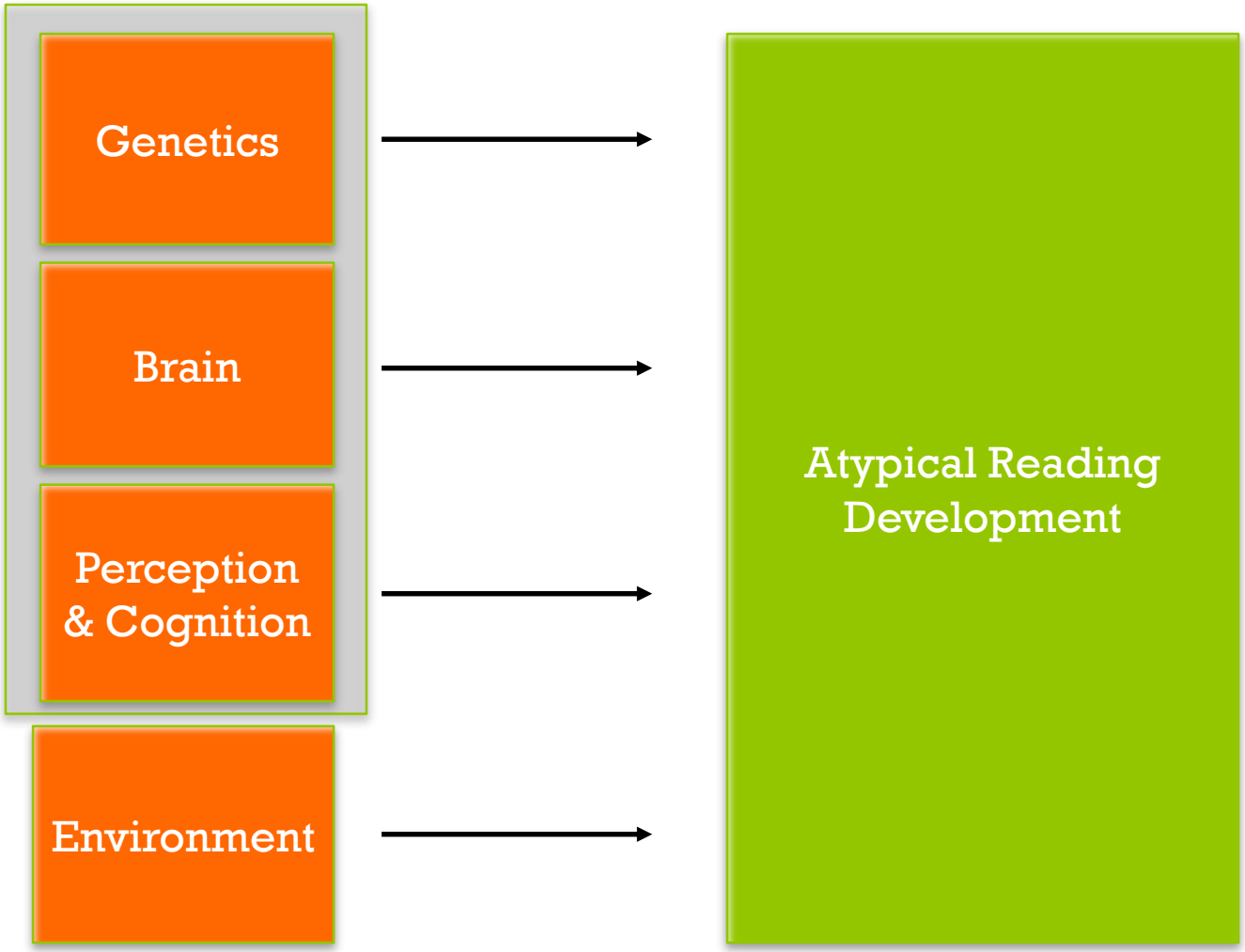


The development of basic reading skills is one of the primary goals of elementary education…but

- 66% of U.S. fourth graders are not reading at grade level
- Among students from low socio-economic backgrounds, 80% are reading below grade level

National Center for Education Statistics (2013). The Nation's Report Card: A First Look: 2013 Mathematics and Reading (NCES 2014-451). Institute of Education Sciences, U.S. Department of Education, Washington, D.C.

Factors contributing to atypical reading development



What is Developmental Dyslexia?

- Affects 10-12% of children.
- Specific learning disability characterized by
  - difficulties with speed and accuracy of word/text decoding
  - poor spelling and poor comprehension performance.
- Cognitive difficulties may further include
  - Speech perception
  - Accurate representation and manipulation of speech sounds
  - Verbal memory
  - Rapid automatized naming
  - Letter sound knowledge
- Cannot be explained by poor vision or hearing, lack of motivation or educational opportunities.
- Strong psychological and clinical implications that start long before reading failure
- Familial occurrences as well as twin studies strongly support a genetic basis for DD.

Genetics

- Studies of families with DD suggest that DD is strongly heritable, occurring in up to 68% of identical twins and up to 50% of individuals who have a first degree relative with DD [Finucci *et al.,* 1984; Volger *et al.,* 1985; Grigorenko, 2008).

- Several genes (e.g.; ROBO1, DCDC2, DYX1C1, KIAA0319) have been reported to be candidates for dyslexia susceptibility and it has been suggested that the majority of these genes plays a role in early brain development. [e.g.; Galaburda *et al*., 2006; Hannula-Jouppi *et al*., 2005; Meng *et al.,* 2005; Paracchini *et al*., 2006; Skiba *et al*., 2011].

- A tentative pathway between a genetic effect, developmental brain changes and perceptual/cognitive deficits in DD has been proposed based on studies in animal and humans (Galaburda et al., 2006).

Variant function in any number of genes involved in cortical development

↓

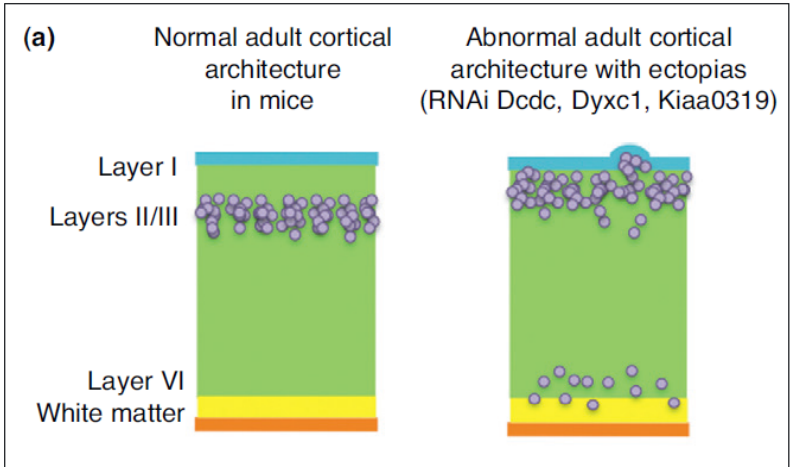
Subtle cortical malformation involving neuronal migration and/or axonal growth

↓

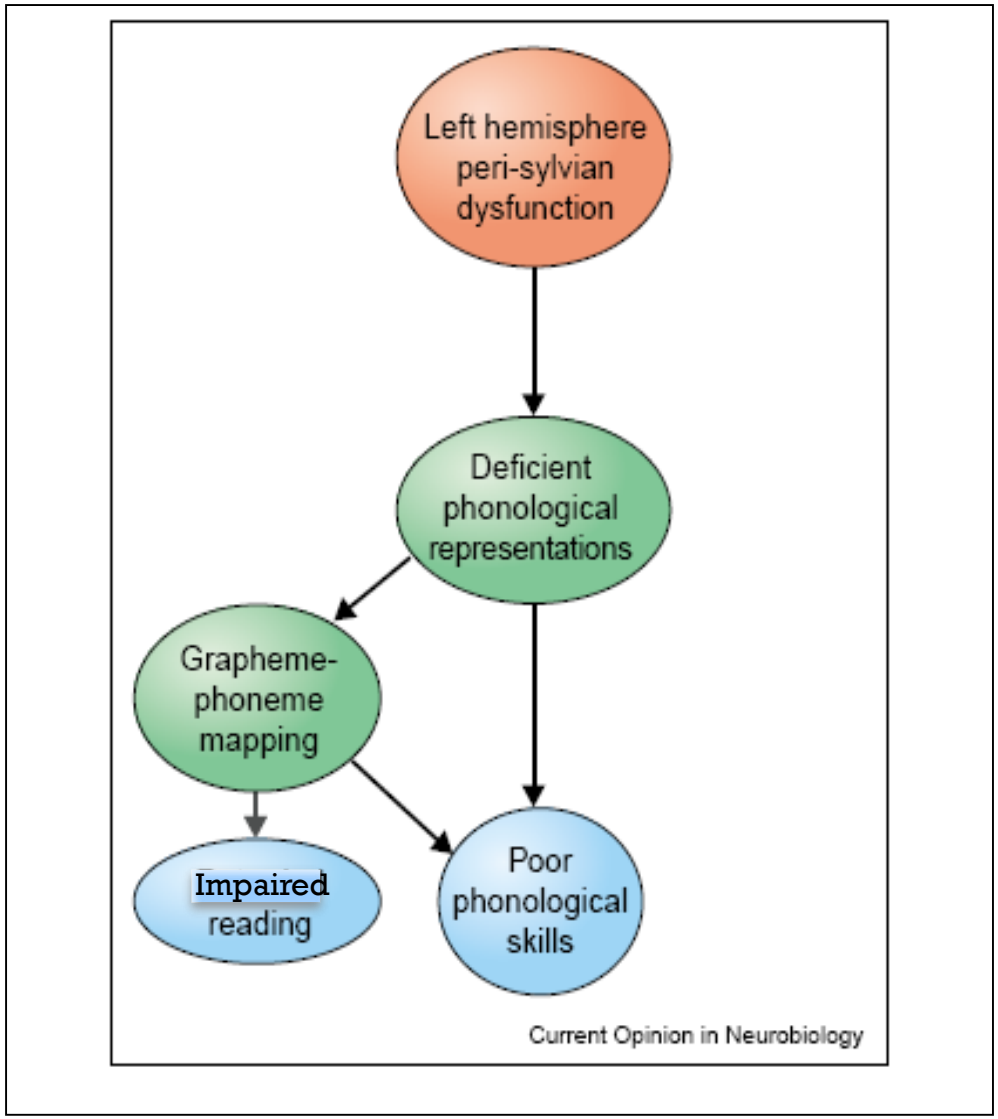
Atypical cortico-cortical circuits

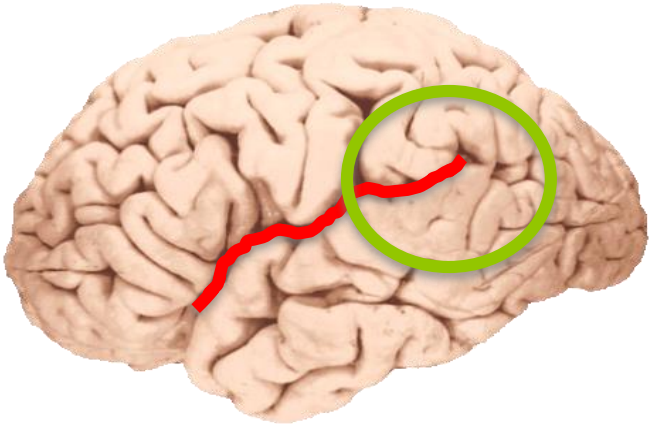
↓

Atypical sensorimotor, perceptual and cognitive processes critical for learning (to read)



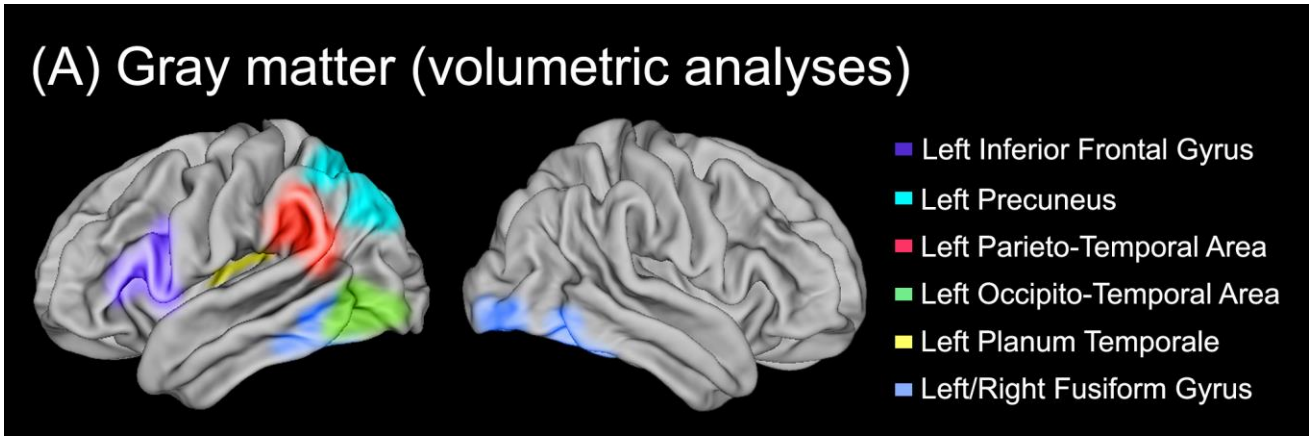
Giraud & Ramus, 2013





[after Ramus, 2003]

Structural and functional brain alterations in DD

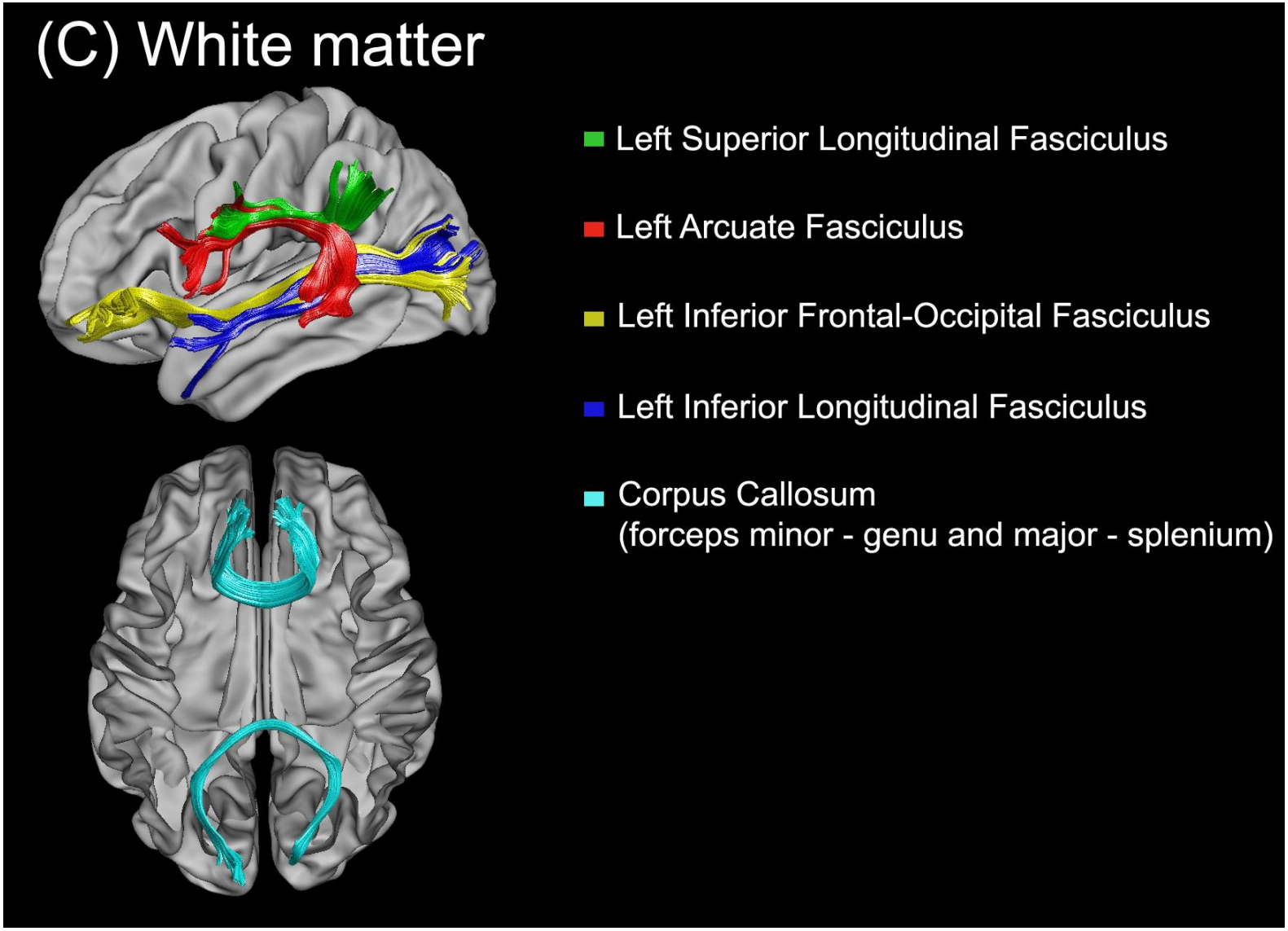


[e.g. see Meta-analyses: Richlan et al., 2013; Linkerdoerfer et al., 2012, Martin et al., 20015]

[e.g. see Meta-analyses: Richlan et al., 2011; Temple et al., 2002]

Ozernov-Palchik et al., under review

White matter alterations in DD



Ozernov-Palchik et al., under review

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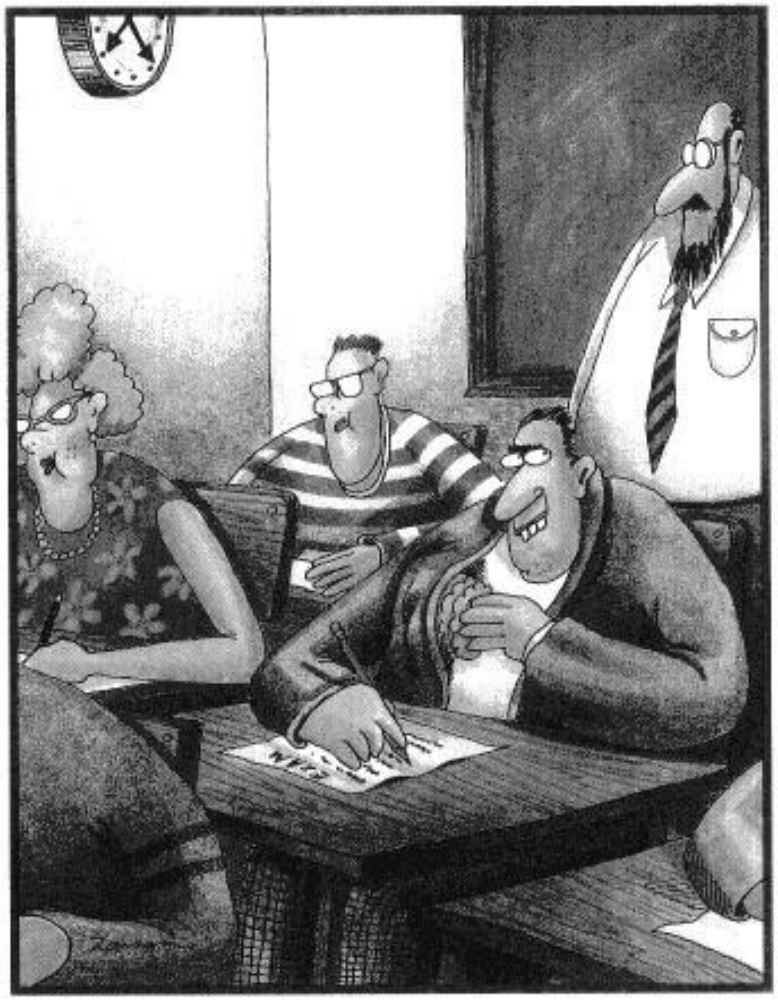
Brain Changes After Remediation



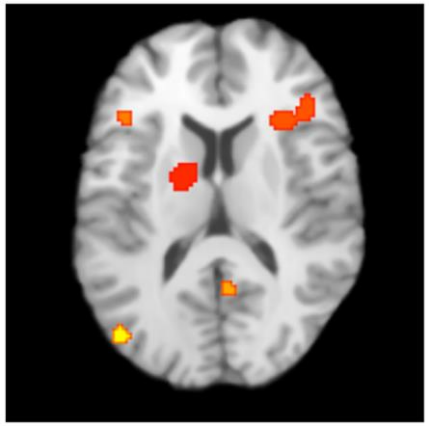
Midway through the exam, Allen pulls out a bigger brain.

Neuroimaging of Reading Intervention: A Systematic Review and Activation Likelihood Estimate Meta-Analysis

Laura A. Barquero[1]*, Nicole Davis[1,2,3,4], Laurie E. Cutting[1,2,3,4,5]

Table 1. Participant groups and interventions.

Study	RD N	CT N	Age	Intervention	Dosage
Simos et al., 2002	8; 6 received Phono-Graphix, 2 received Lindamood Phonemic Sequencing	8	7–17 yrs	Phono-Graphix (Read America, Orlando FL) Lindamood Phonemic Sequencing (Lindamood-Bell, San Luis Obispo, CA)	80 hrs: 1-2 hr/day over 8 wk
Aylward et al., 2003	10	11	139.1 (9.8) months, 137.5 (7.9) months	Instruction in linguistic awareness, alphabetic principle, fluency, and reading comprehension	28 hrs: 2hr/day over 14 session days (3 wk)
Temple et al., 2003	20	12	8–12 yrs	Fast ForWord Language (Scientific Learning Corporation, Oakland, CA)	100 min/day, 5 days/wk, average 27.9 days
Eden et al., 2004	19 total; 9 received intervention	19	adults, RD 44.0 (9.4), CT 41.1 (9.7)	Multisensory instruction including sound awareness, letter-sound association, articulatory feedback administered by Lindamood-Bell Learning Corporation staff	3 hr/day, 8 wks, avg 112.5 hr total
Shaywitz et al., 2004	49 total; 37 received experimental intervention, 12 received community intervention	28	6.1 – 9.4 yrs; RD experimental 7.9 (0.5), RD community 8.1 (0.6), CT 8.0 (0.5)	Experimental intervention [127] included sound-symbol associations, blending, timed reading for fluency, oral reading, dictation	50 min/day for 8 months
Simos, et al., 2005	16; 13 responders, 3 non-responders	17	5.6–7.2 yrs at baseline (Low risk group 5.6–6.5, High risk group 6.0–7.2) 6.4–8.1 yrs at posttest (Low risk 6.4 – 7.5, High risk group 7.0 – 8.1)	Proactive Reading and Responsive Reading [128]	40 min/day, 5 day/wk for 8 months
Richards et al., 2006	18; 8 orthographic treatment, 10 morphological treatment	21	RD 130.8 months, CT 132.6 months	Instruction in alphabetic principle, composition, and either orthographic spelling treatment or morphological spelling treatment	28 hr total: 2 hr/day for 14 sessions over 3 wk
Hoeft et al., 2007	64 struggling readers (identified by teachers, many had scores in average range)	-	10.0 (1.09) yrs	Power4Kids Reading Initiative. Many participants received 1 of 4 interventions, but there was no significant effect of intervention on decoding scores.	about 6 months during school year
Richards et al., 2007	20; 11 phonological treatment, 9 nonphonological treatment	10 nonphonological treatment	RD phonological 137.7 (10.00) months, RD nonphonological 134.60 (11.10) months, CT 128.60 (8.00) months	Phonological treatment included explicit written language instruction using phonological working memory, phoneme-grapheme correspondences in spelling, and science report writing [129]. Nonphonological treatment included nonverbal virtual reality supported science problem solving [130]	24 hrs total—8 sessions over 2 wks with 3 hr/session
Simos, Fletcher, Sarkari, Billingsley-Marshall, et al., 2007	15	-	7–9 years	Phono-Graphix [131] and Read Naturally [132]	16 weeks total: 2 hr/day for 8 wks Phono-Graphix, 1 hr/day for 8 wks Read Naturally
Simos, Fletcher, Sarkari, Billingsley, et al., 2007	15; 8 responders, 7 nonresponders (same as Simos, et al., 2007 above)	10	7–9 years	Phono-Graphix [131] and Read Naturally [132]	16 weeks total: 2 hr/day for 8 wks Phono-Graphix, 1 hr/day for 8 wks Read Naturally
Meyler et al., 2008	23 (possible overlap with Hoeft, et al., 2007)	12	5th grade	Power4Kids project used four programs: Corrective Reading, Wilson Reading, Spell Read Phonological Auditory Training (PAT), Failure Free Reading	100 hrs total over 6 months
Odegard et al., 2008	12 total: 6 responders, 6 nonresponders	6	10 – 14 yrs	Take flight: A comprehensive intervention for students with dyslexia [133]	90 min/day, 4 days/wk for 2 school years
Richards & Berninger, 2008	18 (same as Richards et al., 2006)	21	RD 130.8 months, CT 132.6 months	Instruction in alphabetic principle, composition, and either orthographic spelling treatment or morphological spelling treatment	28 hrs total—14 sessions over 3 wks with 2hr/session;
Davis et al., 2011	10 total: 5 responders, 5 nonresponders	4	7.5 (0.43) yrs	Intervention consisted of sight word reading, letter sound practice, decoding practice, and reading for fluency.	45 min, 3 days/wk, 17 weeks
Farris et al., 2011	10 total: 5 responders, 5 nonresponders (same as Odegard et al., 2008)	5	10 – 14 yrs	Take flight: A comprehensive intervention for students with dyslexia [133]	90 min/day, 4 days/wk for 2 years
Hoeft et al., 2011	25	20	RD 14.0 (1.96) CT 11.0 (2.57)	*This study did not provide an intervention.* 11 participants received some form of intervention, but no differences were observed for intervention.	-
Rezaie et al., 2011a	20 total: 10 Adequate Responders (AR), 10 Inadequate Responders (IR)	20	Adequate Responders 158±7 months, Inadequate Responders 153±11 months, CT 151±11 months	Instruction included word study, fluency, vocabulary, comprehension [134]	45–50 min/day over 1 schoolyear
Rezaie et al., 2011b	27 total: 16 AR, 11 IR (possible overlap with Rezaie, et al., 2011a)	23	Adequate Responders 159±9 months, Inadequate Responders 156±16 months, CT 153±12 months	Instruction included word study, fluency, vocabulary, comprehension [134]	45–50 min/day over 1 schoolyear
Yamada et al., 2011	7 (at-risk)	7 (on-track)	At-risk 5.6 (0.2) yrs, On-track 5.7 (0.3) yrs	Early Reading Intervention [135]	30 min/day, 3 months
Gebauer Fink, Kargl et al., 2012	20 total (poor reading and spelling): 10 Treatment (TG), 10 Waiting Group (WG)	10	10–15 yrs, ($M = 11.80$; $SD = 1.58$)	Morpheus: a computer-aided morpheme-based spelling training in German [136]	Daily handwritten and computer homework, 1/wk instructor-guided courses for 2 hr, over 5 wks.
Bach et al., in press	6 poor readers (group classification made at follow-up)	11	Poor Readers 6.33±0.19 yr, Normal Readers 6.35±0.29 yr	Graphogame: a computerized training game teaching grapheme-phoneme correspondences in German [137–139]	321.5±124.3 min over 8 wk



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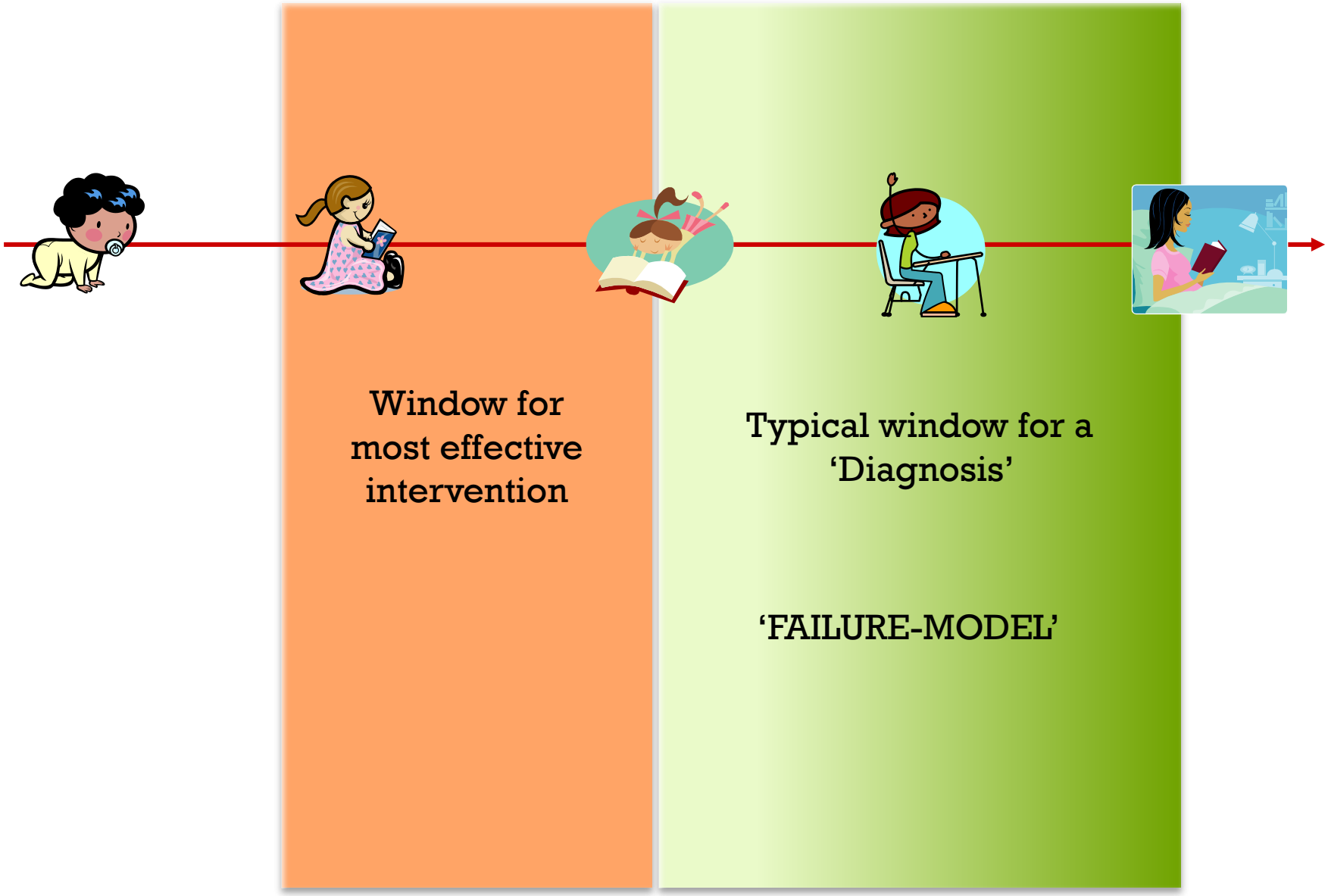
The dyslexia paradox



Early versus late intervention

- A meta-analysis comparing intervention studies offering at least 100 sessions, reported larger effect sizes in kindergarten/1st grade than in 2nd and 3rd grades (Wanzek & Vaughn, 2007) .
- When "at risk" beginning readers receive intensive instruction, 56% to 92% of at-risk children across six studies reached the range of average reading ability (Torgesen, 2004).
- Overall, converging research points to the importance of early and individualized interventions for at-risk students for improving the effectiveness of remediation (Denton & Vaughn, 2008; Connor et al., 2009; Shaywitz, Morris, & Shaywitz, 2008, Torgesen, et al., 1999; Flynn, Zheng, & Swanson, 2012; Vellutino et al., 1996; Morris, Lovett, Wolf et al., 2012; Morris et al., 1997).

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The Boston Longitudinal Dyslexia Study (BOLD)

Early Identification
children at-risk

'Diagnosis'
Dyslexia/
Reading difficulty

Preschool

Kindergarten

3rd grade

Middle School

- Functional MRI
- Structural MRI
-Behavioral tests
-Psychophysics
-Questionaires
-DNA

Follow up:
-prior to first grade
-prior to second grade
-prior to third grade

- Pre-readers (Word ID <5), reading instruction within next year.
- To date 165 children are enrolled longitudinally

Psychometric Measures:

- Clinical Evaluation Language Fundamentals –Preschool 2
- Comprehensive Test Of Phonological Processing
- Grammar And Phonology Screening Test
- York Assessment for Reading for Comprehension
- Rapid Automatized Naming and Rapid Alternating Stimulus Test
- Kaufman Brief Intelligence Test 2
- Year 2: Word reading (timed/untimed), passage comprehension, fluency, spelling, letter knowledge

Psychophysics Measures:

- RAP (tones and environmental sounds)
- Rise Time perception

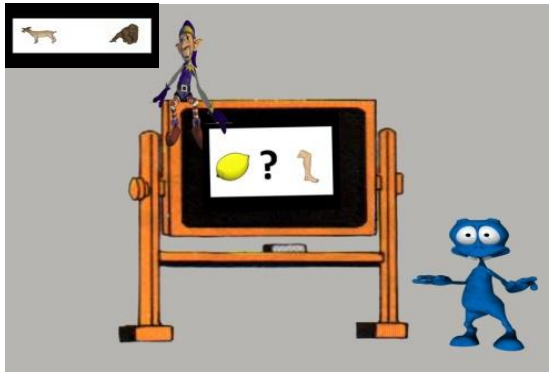
Questionaires :

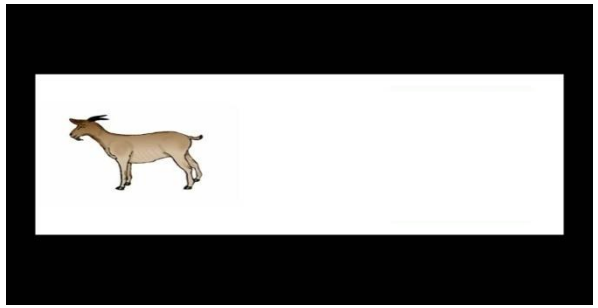
- Development
- Home literacy
- SES

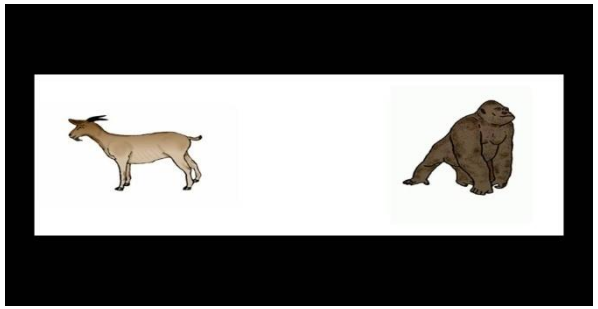
Tasks within MRI scanner :

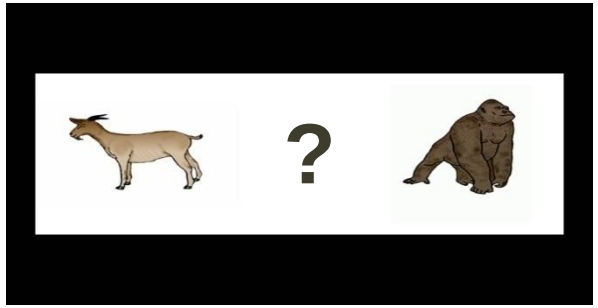
- Phonological Processing
- Rapid auditory processing
- Executive functioning
- Reading Fluency

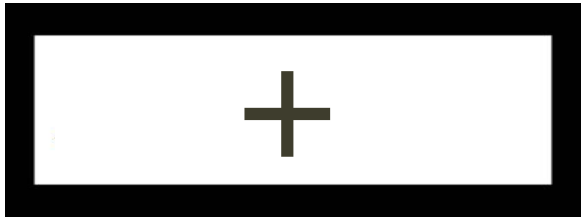
Structural brain differences (gray matter, DTI)



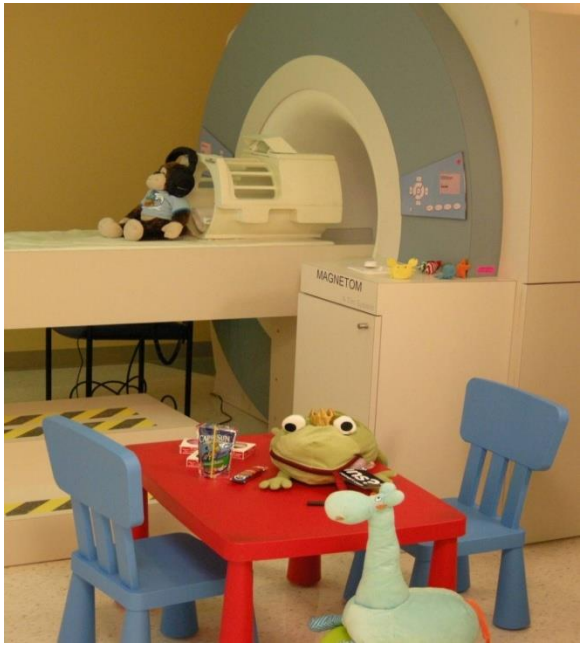








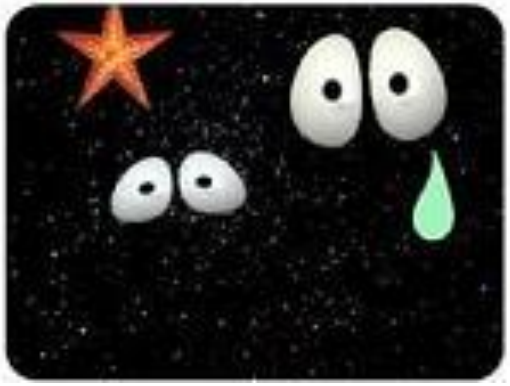
Control task:
Voice matching

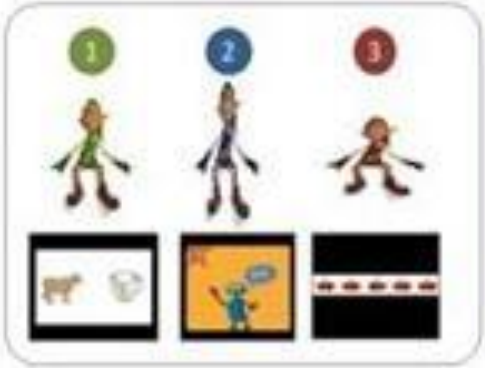


[Raschle *et al.*, 2009; Raschle *et al.*, 2012]






1
2
3

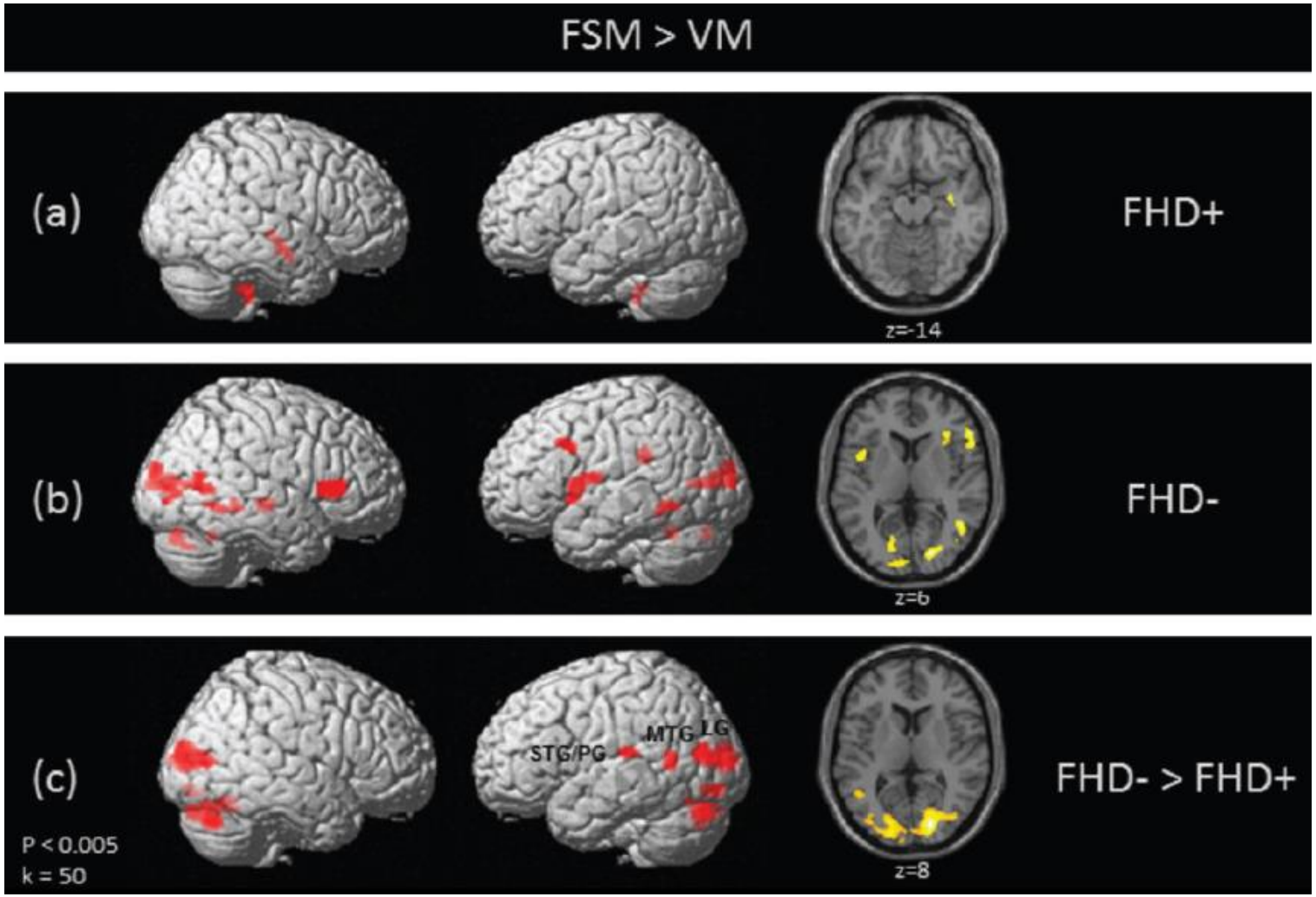
Can you help them?

YEAR 1 (prereading status)	YEAR 2 (beginning readers)	YEAR 3/4 (readers)
Significant differences in:	*Significant differences in:*	*Significant differences in:*
Expressive and receptive language/content	Expressive language/ Language content	Core and receptive Language
Phonological processing	Phonological processing	
Rapid automatized naming	Rapid automatized naming	Rapid automatized naming
	Letter knowledge	
	Single word reading (timed/untimed)	Single word reading (timed/untimed)
	Passage comprehension	Passage comprehension
	Spelling	Spelling
		Reading Fluency
Rapid auditory Processing		
all $p<0.05$	*all $p<0.05$*	*all $p<0.05$*

No differences in
IQ, age, Home Literacy, SES

Functional characteristics of developmental dyslexia in left-hemispheric posterior brain regions predate reading onset

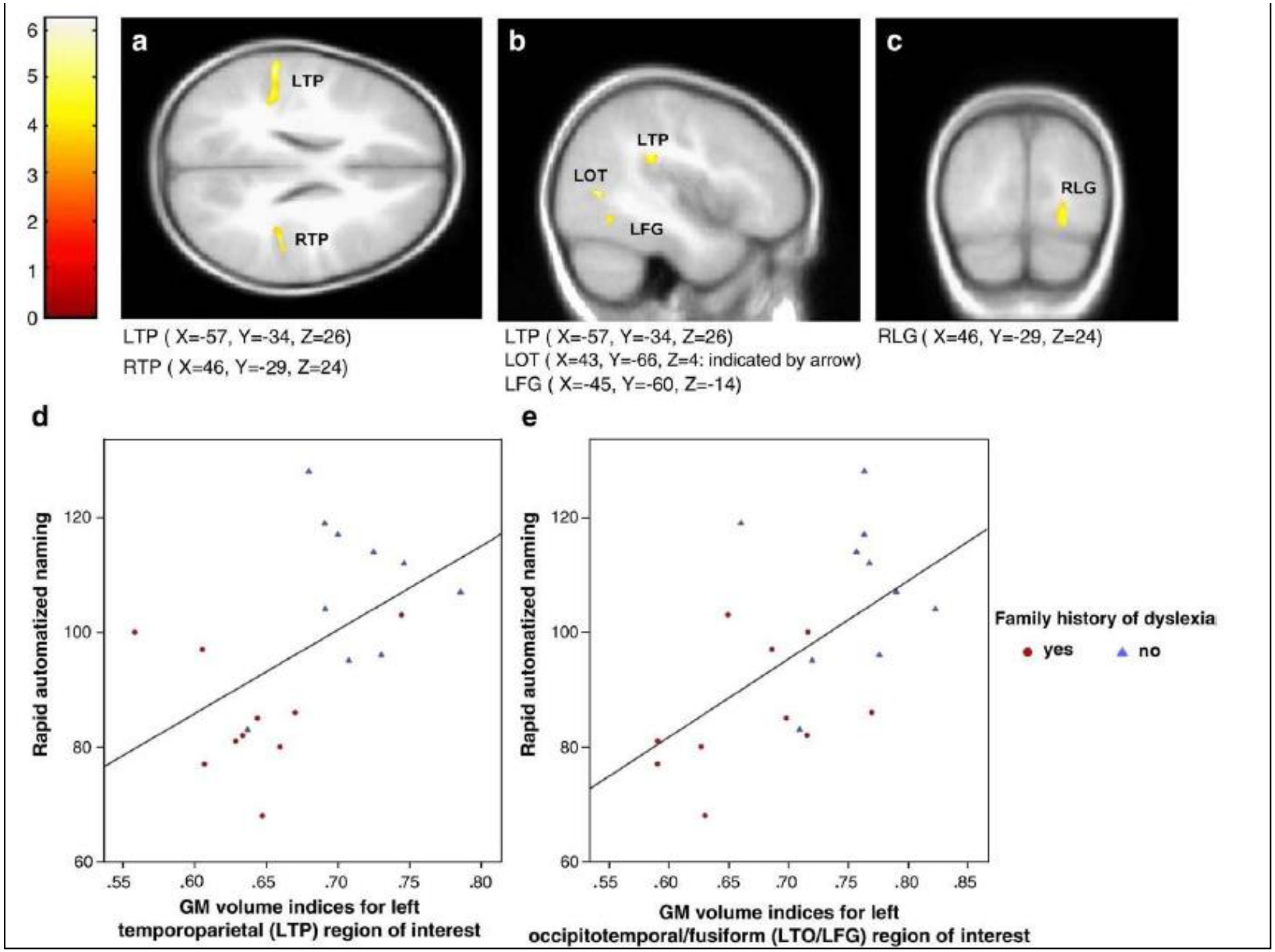
Nora Maria Raschle[a,b], Jennifer Zuk[a], and Nadine Gaab[a,b,c,1]



[Raschle *et al.*, PNAS 2012]

Structural brain alterations associated with dyslexia predate reading onset

Nora Maria Raschle, Maria Chang, Nadine Gaab *



[Raschle *et al.*, Neuroimage 2010]

ORIGINAL ARTICLE

Atypical Sulcal Pattern in Children with Developmental Dyslexia and At-Risk Kindergarteners

Kiho Im[1,4], Nora Maria Raschle[2,4,6], Sara Ashley Smith[2], P. Ellen Grant[1,3,4], and Nadine Gaab[2,4,5]

- Sulcal pattern (global pattern of arrangement, number and size of sulcal segments) has been hypothesized to relate to optimal organization of cortical function and white matter connectivity (Van Essen, 1997; Klyachko and Stevens, 2003; O'Leary et al., 2007; Fischl et al., 2008).

- Individuals with DD may undergo atypical sulcal development. Moreover, global sulcal pattern is determined during prenatal development and may therefore better reflect genetic brain development (Rakic, 2004; Kostovic and Vasung, 2009).

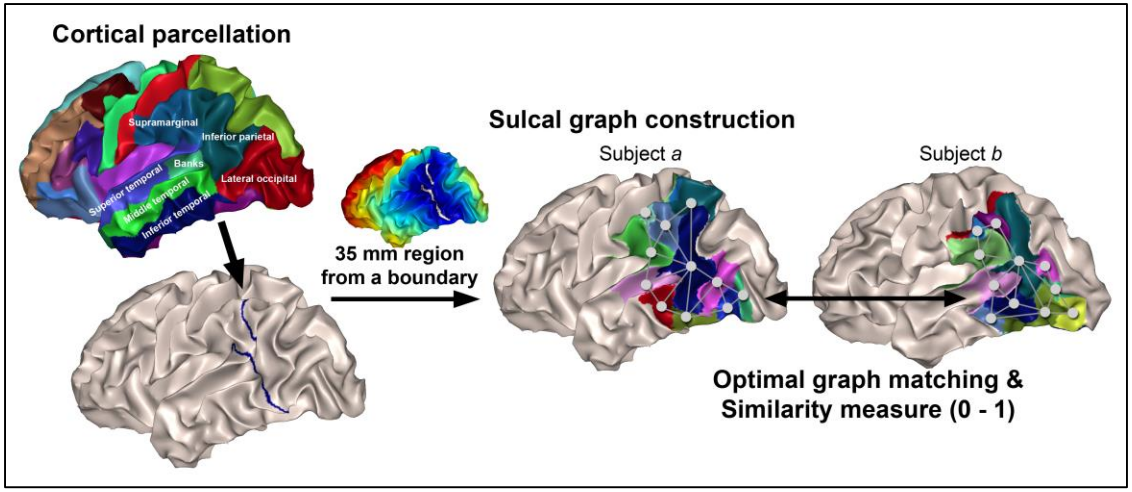
[Im *et al.*, Cerebral Cortex 2015]

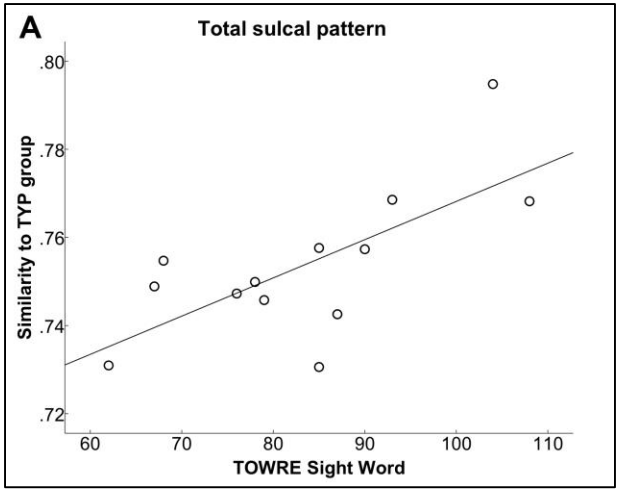
Four groups:
1. Beginning readers FHD-
2. Beginning readers FHD+

3. Developmental Dyslexia
4. Typical developing children

- The pattern of sulcal basin area in the left parieto-temporal and occipito-temporal regions was significantly atypical in children with DD compared to controls.

- Significantly atypical sulcal area pattern was also confirmed in kindergarteners with a familial risk of DD compared to controls.





Im *et al.*, in 2015

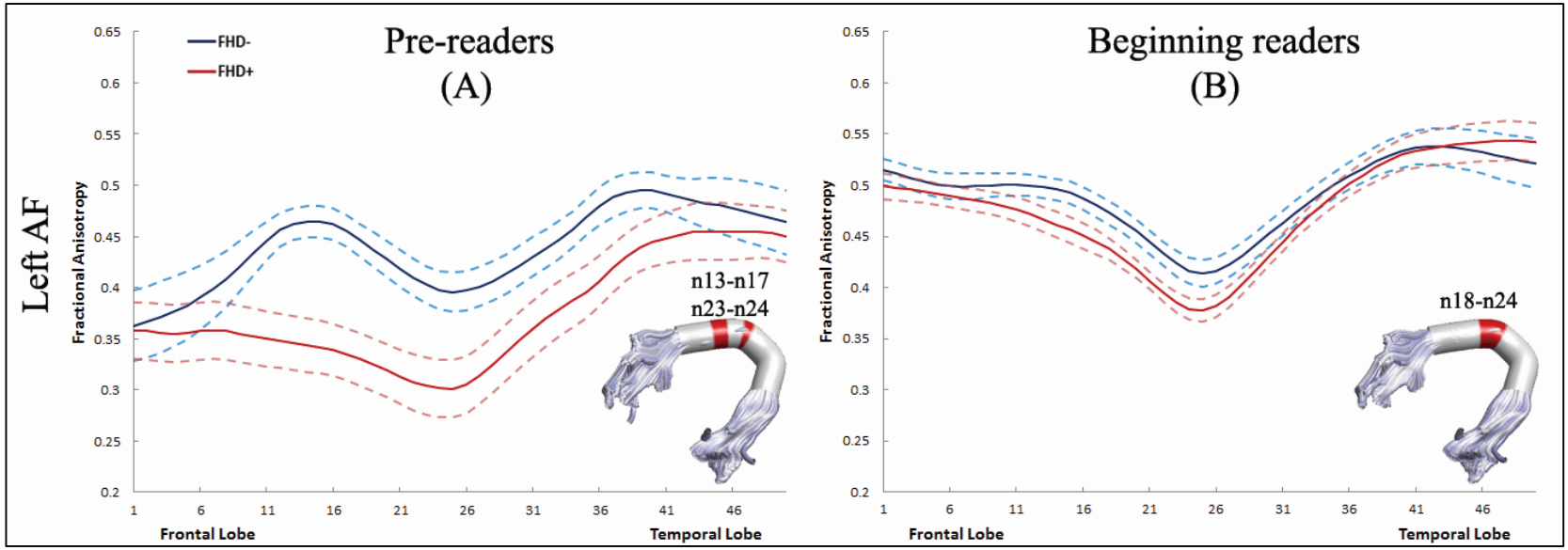
Development of tract-specific white matter pathways during early reading development in pre-readers at familial risk for dyslexia

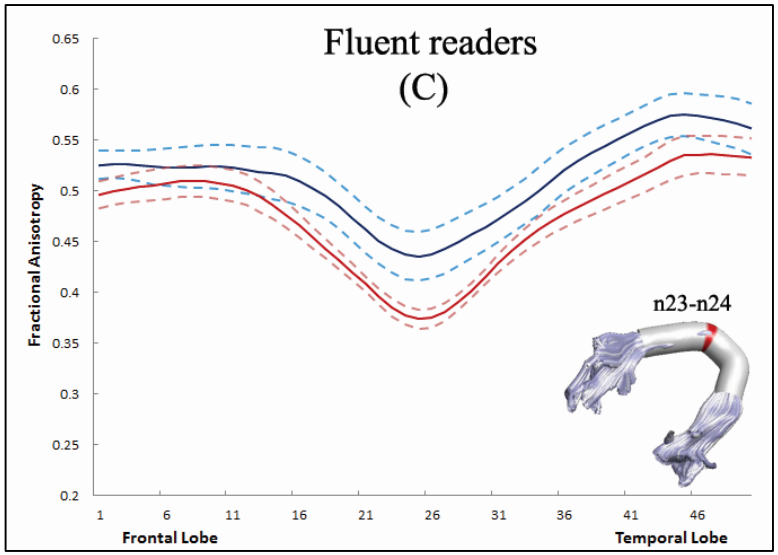
Yingying Wang [1, 2], Meaghan Mauer [1], Talia Raney [1], Barbara Peysakhovich [1], Bryce Becker [1], Danielle Sliva [1], Nadine Gaab [1, 2, 3]

- 78 healthy, native English-speaking children (45 FHD+, 33 FHD-)
- Among them, 45 children (23 FHD+ and 22 FHD-) had at least two scans and composed a longitudinal cohort.
- Three time points: re-reading, beginning reading, fluent reading

[Wang *et al.*, in revision]

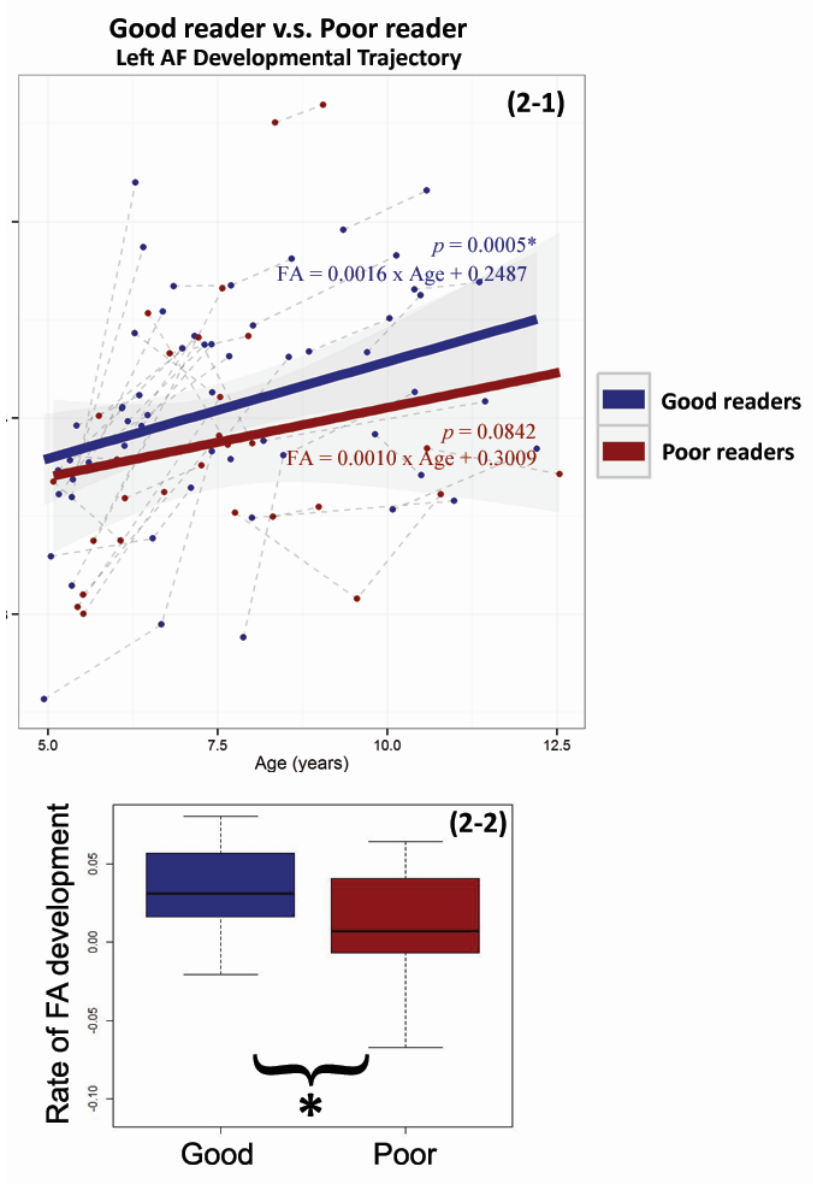
Cross-sectional results (n = 78): Arcuate Faciculus





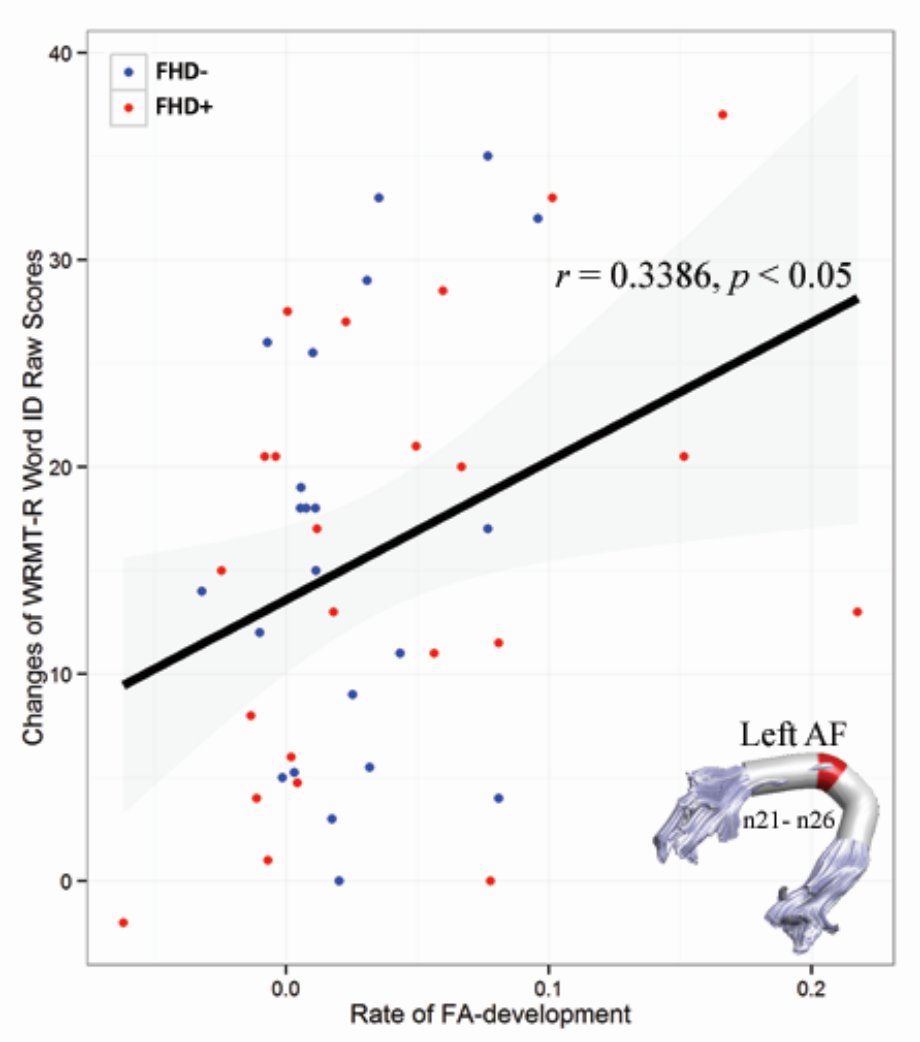
[Wang *et al.*, in revision]

Longitudinal Analysis: Development rate of the AF (n=45)



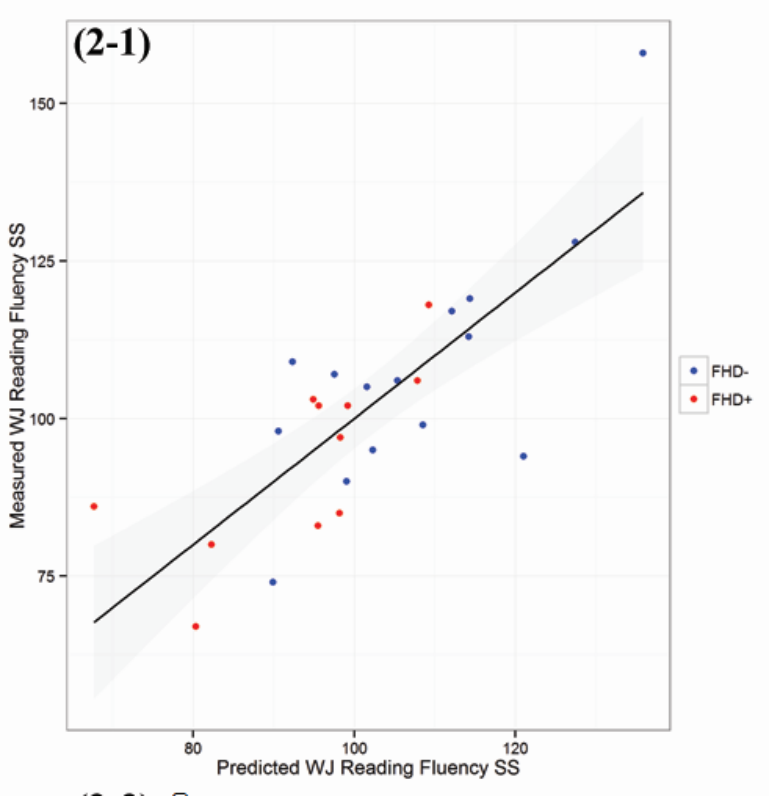
Wang *et al.*, in revision

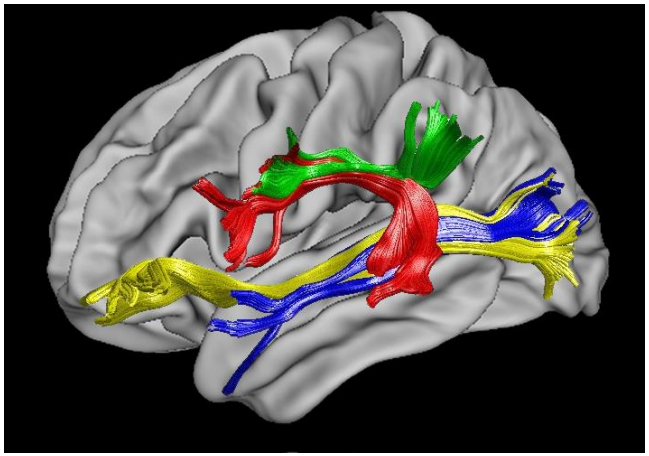
Linking FA development and individual differences in reading development



Wang *et al.*, in revision

Predicting reading fluency





Outcome measure: WJ-III Reading Fluency (R^2 =0.62); $p<0.0003$
FA-development rate of left SLF (contributing 27% of R^2),
RAN Objects (contributing 31% of R^2),
KBIT-2 Nonverbal IQ standard scores (contributing 19% of R^2)
Familial risk (contributing 23% of R^2).

Wang *et al.*, in revision

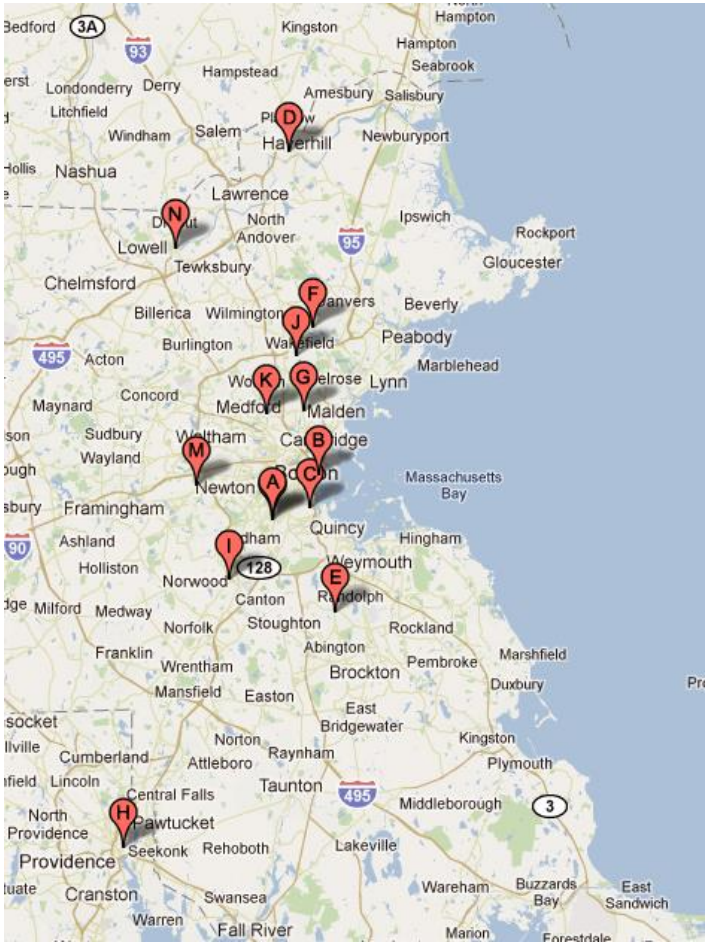
The READ Study

(Researching Early Attributes of Dyslexia)

- Screening of 1,433 children in 21 'partner' schools in New England in 2011, 2012 and 2013. Highly diverse sample in terms of SES, race/ethnicity, and school type.
- Invited children with and without risk for dyslexia to participate in a follow-up study including brain imaging with MRI and EEG (n =180 for EEG and n=160 for MRI).
- Following these children to see which measures from kindergarten best predict reading ability at the end of 1st and 2nd grade.

READ at a Glance

- 21 schools: inner-city charter schools, private, suburban district-run schools, and Archdiocese schools
- Free/reduced lunch eligibility from 0% to 80%
- Ethnically diverse student population (49% minority)
- Teacher professional developments and parent presentations conducted in all schools
- Brain awareness days conducted in various schools



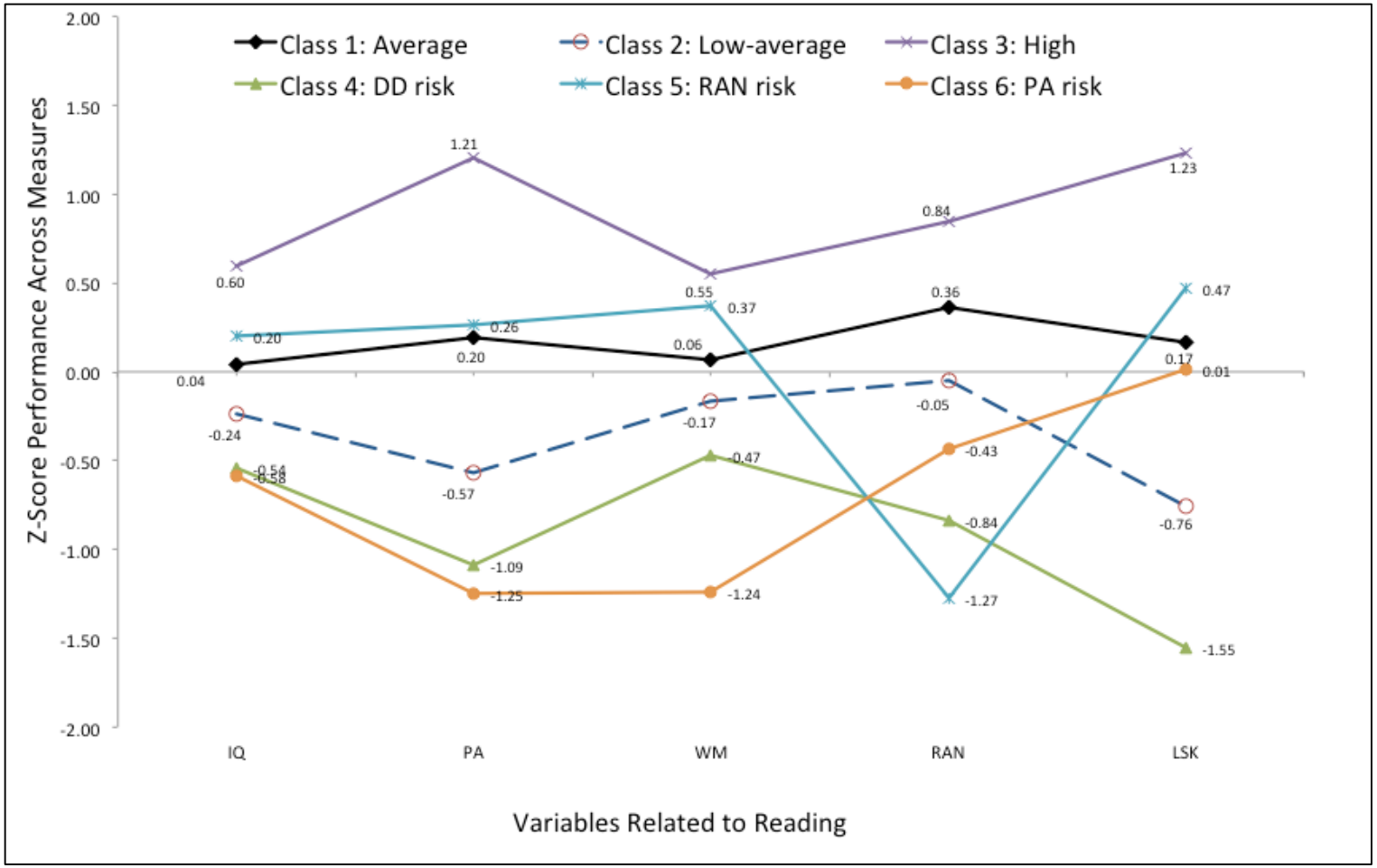
"We very much enjoyed everything you and your staff provided. You are warm and professional and certainly put your subjects at ease…It's exciting to see such cutting-edge research from the inside out!" (Parent, Wheeler School)

"…They were excellent presenters. The students had a wonderful time and were very engaged in the activities." (Teacher, Lowell Elementary)

"Your whole team was terrific in making the afternoons lots of fun and educational" (Parent, Hosmer Elementary)

Six Distinct Cognitive Profiles of Early Reading

Ozernov-Palchik et al., submitted

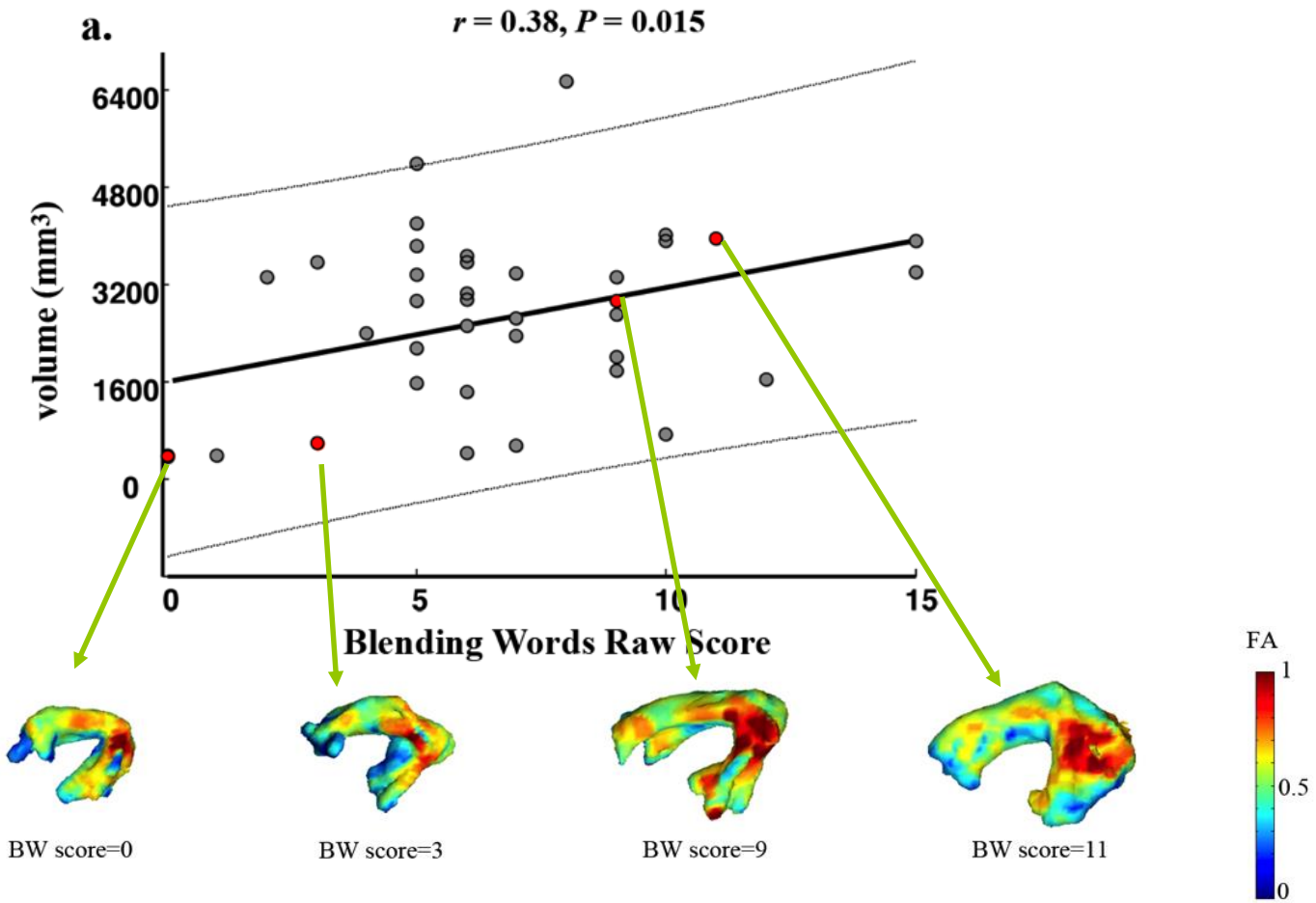


Latent Profile analysis model for the Identification of Reading Subgroups: PA-phonological awareness, WM-working memory, RAN-rapid automatized naming, LSK-letter sound knowledge [n = 1,215 children].

Tracking the Roots of Reading Ability: White Matter Volume and Integrity Correlate with Phonological Awareness in Prereading and Early-Reading Kindergarten Children

Zeynep M. Saygin,[1*] Elizabeth S. Norton,[1*] David E. Osher,[1] Sara D. Beach,[1] Abigail B. Cyr,[1] Ola Ozernov-Palchik,[3] Anastasia Yendiki,[4] Bruce Fischl,[2,4] Nadine Gaab,[3] and John D.E. Gabrieli[1]

The Journal of Neuroscience, August 14, 2013 • 33(33):13251–13258 • 13251



Overview

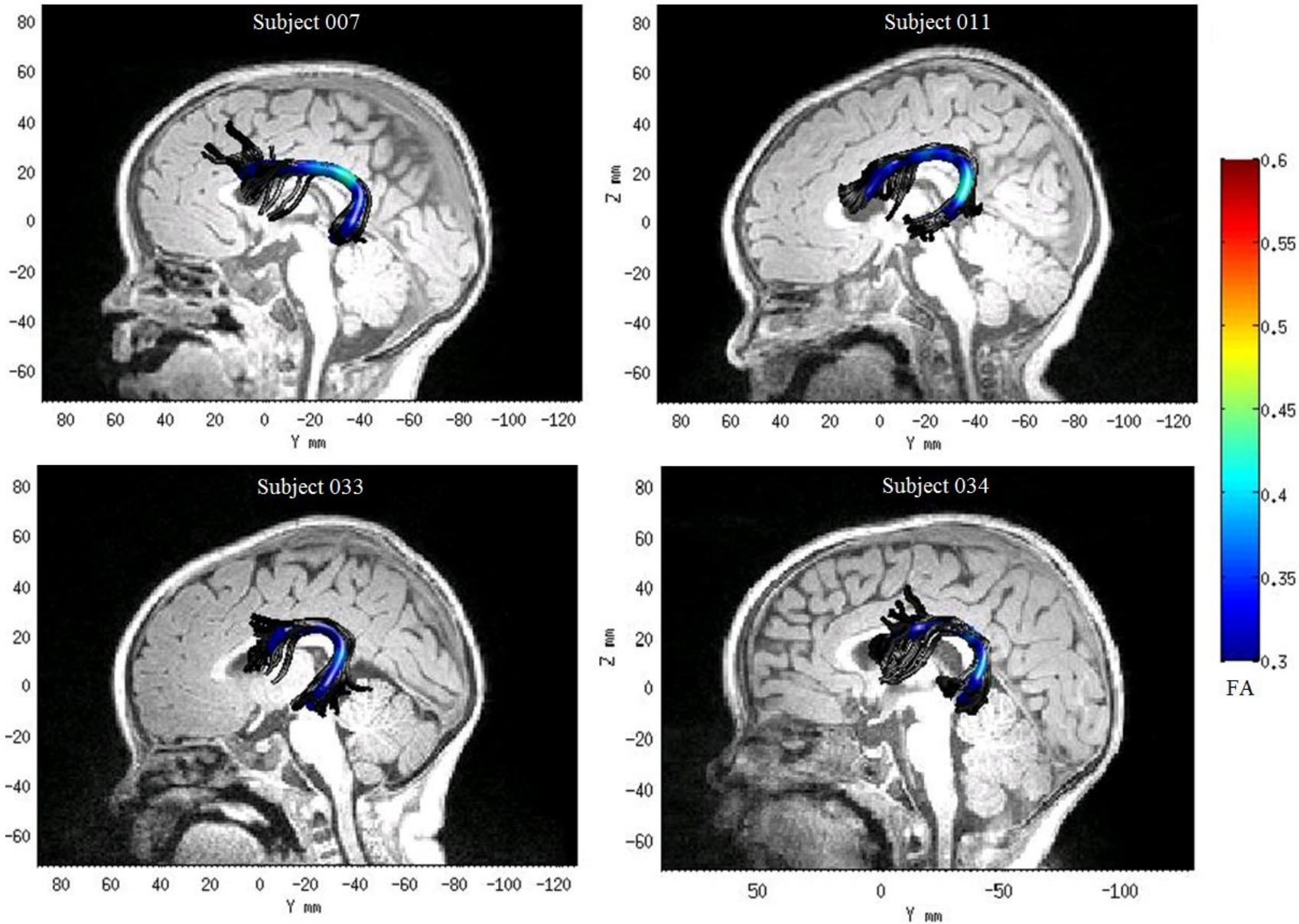
- Typical and atypical reading development and its neurobiology
- Remediating the atypical reading brain
- The 'Dyslexia Paradox'
- Early pre-markers of reading difficulties before reading onset
- Compensatory mechanisms, resiliency and protective factors
- Detecting children at risk for reading difficulties in infancy?
- Educational and Clinical Implications

Demographics

	FHD-	FHD+	T-test 2-tailed
N	18	14	
Age (days)	297.78 ± 99.13	332.64 ± 117.91	$p > .100$
Expressive Mullen T-score	48.67 ± 4.77	47.90 ± 10.87	$p > .100$

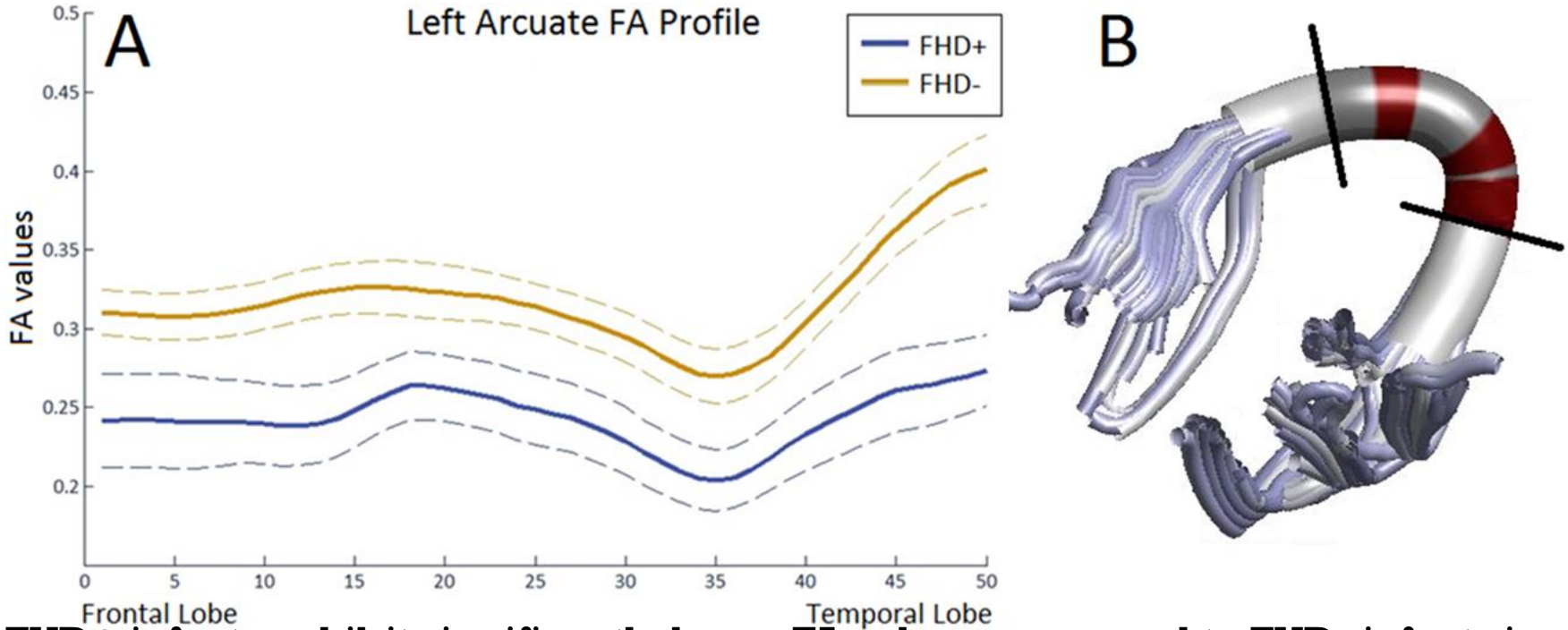
Langer *et al.*, in press

AFQ


Subject 007
Subject 011
Subject 033
Subject 034
Z mm
Y mm
FA
0.6
0.55
0.5
0.45
0.4
0.35
0.3

White Matter Alterations in Infants at Risk for Developmental Dyslexia

Nicolas Langer[1,3,†], Barbara Peysakhovich[1,†], Jennifer Zuk[1,3], Marie Drottar[2], Danielle D. Sliva[1,2], Sara Smith[1], Bryce L. C. Becker[1], P. Ellen Grant[2,3] and Nadine Gaab[1,3,4]



FHD+ infants exhibit significantly lower FA values compared to FHD- infants in red regions (all $p < 0.02$, controlled for multiple comparisons)

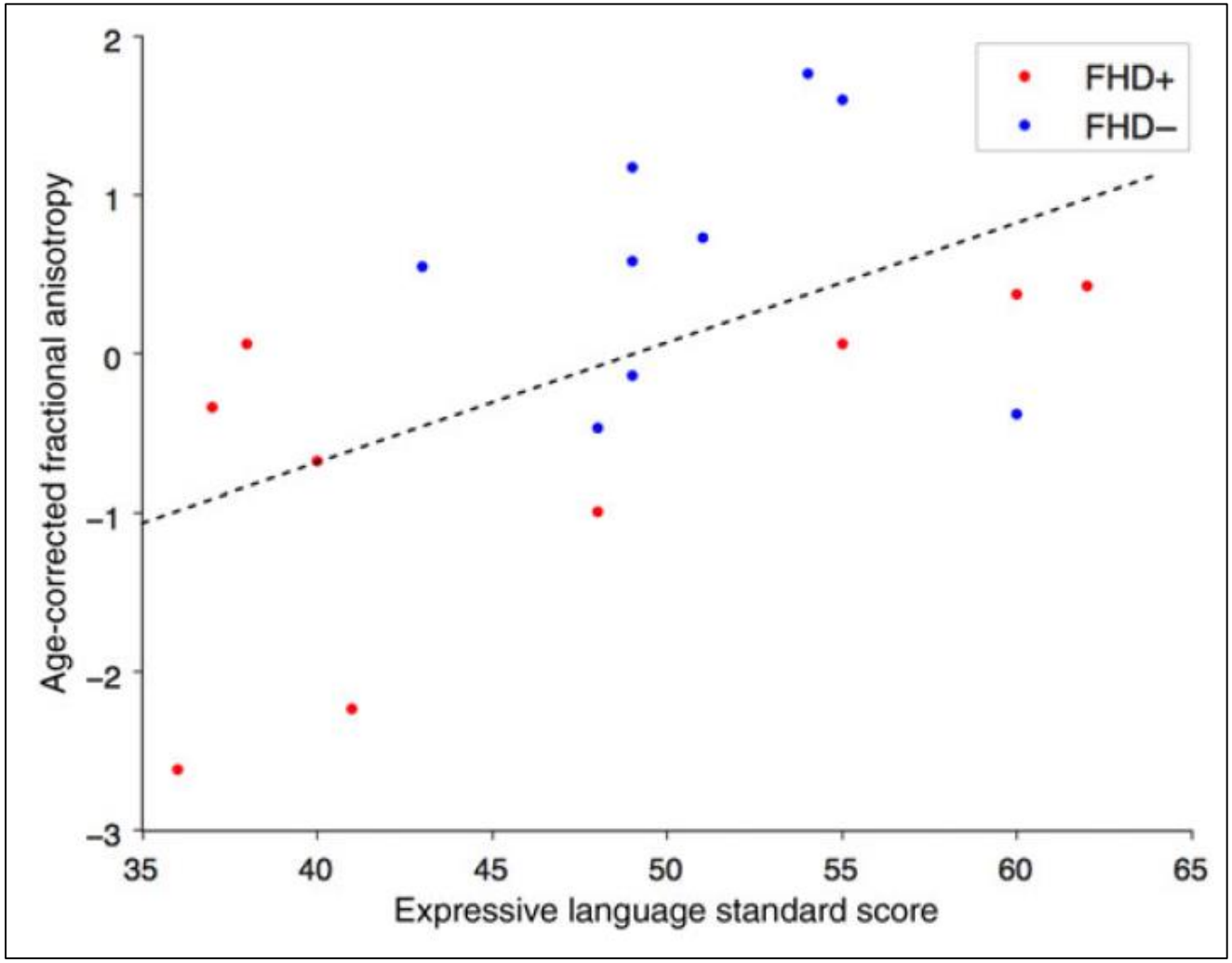
Multivariate pattern analysis (MVPA):

MVPA (using FA at each node of the left AF as input) was performed to determine whether FA can distinguish FHD+ and FHD- infants

- 82% prediction accuracy ($p = 0.001$)

Langer *et al.*, in press

FA values correlate with 'expressive language Scores'

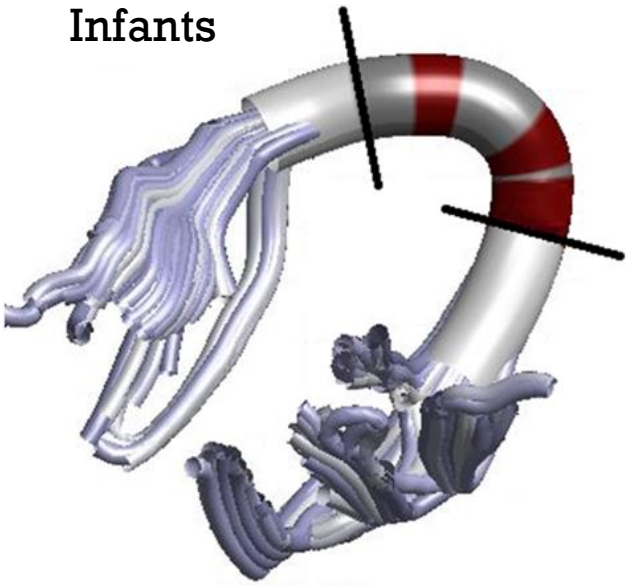


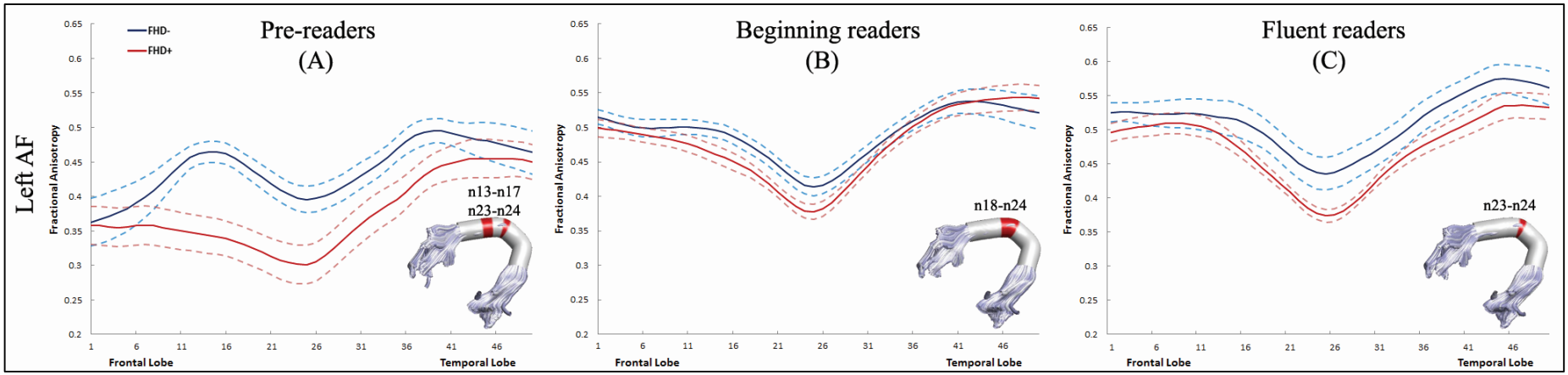
Langer *et al.*, in press

R = 0.481
p = 0.037

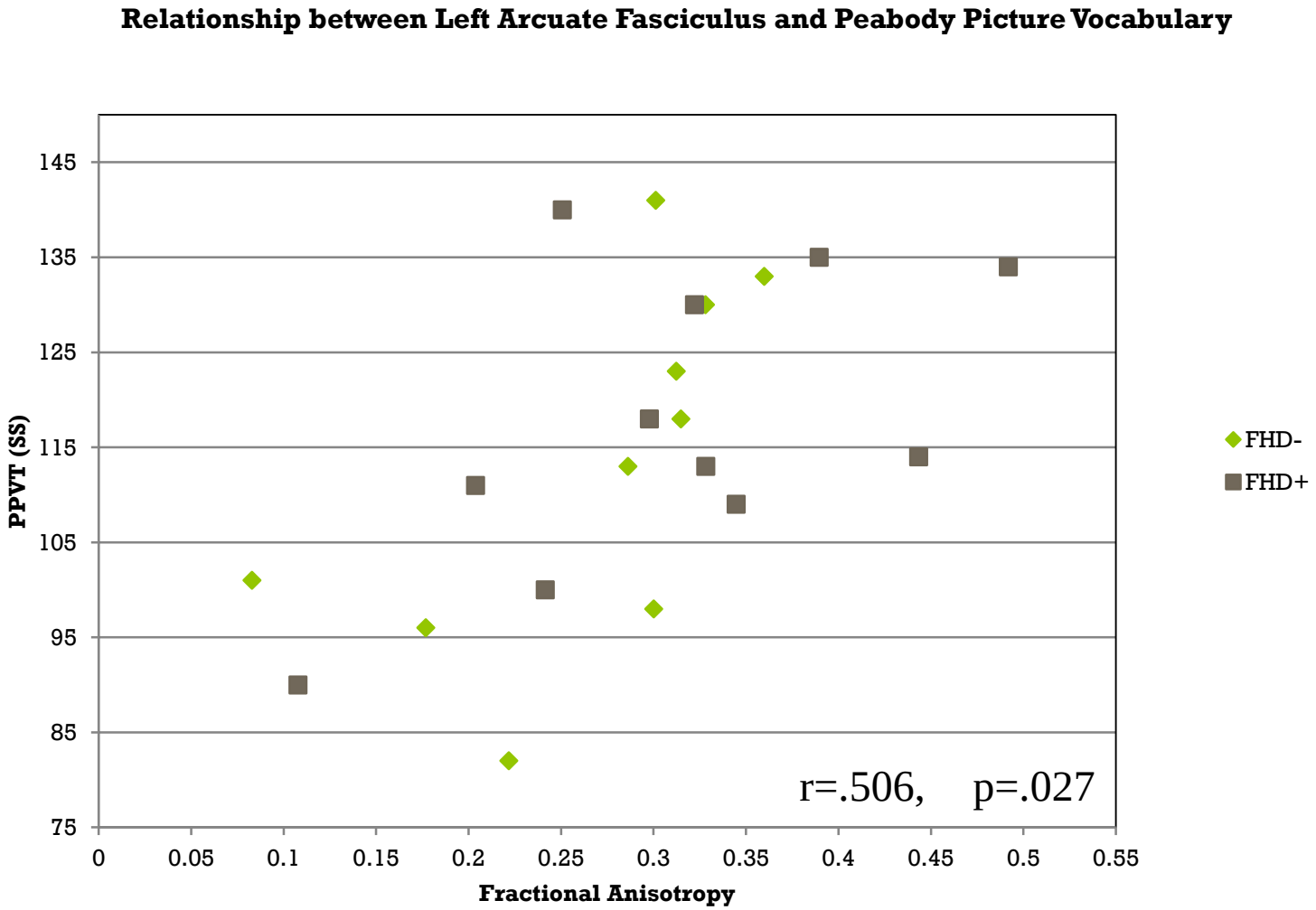
Atypical development of AF from infancy to late elementary school

Infants





FA in infancy correlates with language measures at age 4



Figuccio *et al.*, in preparation

Overview

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Educational and clinical implications

- Early identification may reduce the clinical, psychological and social implications of DD.
- Understanding the complex etiology of specific learning disabilities and their co-occurrences will be essential to underpin the training of teachers, school psychologists, and clinicians, so that they can reliably recognize and optimize the learning contexts for individual learners→ personalized medicine/education (Butterworth & Kovas, 2013)
- Development and implementation of early and customized remediation programs (who should get which intervention) → Subtyping and early customized remediation
- Informing (early) diagnostic guidelines
- Changes in educational policies (early IEPs; design and implementation of customized curriculums for children at-risk).
- Evaluation and improvement of existing remediation programs will likely prove cost-efficient as programs are made more effective.
- Improved psycho-social development (reduced child stress, parental stress, improved overall family dynamic).

Grand Challenges…

Develop an understanding of how individual differences in brain development interact with formal education

Adapt learning pathways to individual needs

Butterworth & Kovas, 2013

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Sandra/Joseph Jacobson, Wayne State
Gennaro Chierchia, Harvard University
Maryanne Wolf, Tufts University
Paulo Andrade, São Paulo
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Autism Excellence Center

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Xi Yu (Postdoc)
Elizabeth Norton (former Post-doc READ)
Nora Raschle (former Postdoc)
Nicolas Langer (former Postdoc)
Jennifer Zuk (Graduate student, HST)
Michael Figuccio (Graduate student, BU)
Ola Ozranov-Palchik (Graduate student, Tufts)
Bryce Becker (former Project Coordinator)
Meaghan Maurer (Project Coordinator, BOLD + Infants)
Talia Raney (RA, BOLD, Infants)
Danielle Sliva (former Data Coordinator, BOLD + Infants)
Barbara Peysakhovich (former RA)
Sara Smith (former RA)
Sara Beach (RA, READ)
Zeynep Saygin (READ)
MRI Team, Children's Hospital Boston & MIT

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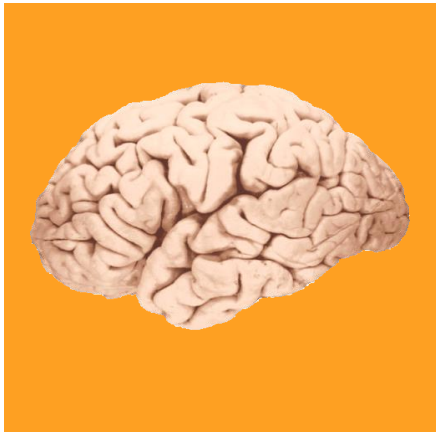
  - ACE: (1R01MH100028-04)
  - FASD (1UO1AA023503-01)
- Harvard Catalyst (Infants)
- Melinda and Bill Gates Foundation
- Harvard Mind/Brain/behavior Faculty Award
- Charles H. Hood Foundation (BOLD)
- Grammy Foundation
- William Randolph Hearst Foundation (Infants)
- Children's Hospital Boston Pilot Award (BOLD)
- Developmental Medicine Center Young investigator Award
- Victory Foundation

The typical and atypical reading brain:

How a neurobiological framework of reading development can inform educational practice and policy



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