30 Years in Search of the "Literate Brain"

- **Kenneth R. Pugh, PhD**
- Professor, University of Connecticut
- Associate Professor, Yale University School of Medicine
- Director of Research, Haskins Laboratories

A partial list of Collaborators (With Deep Gratitude!!!)

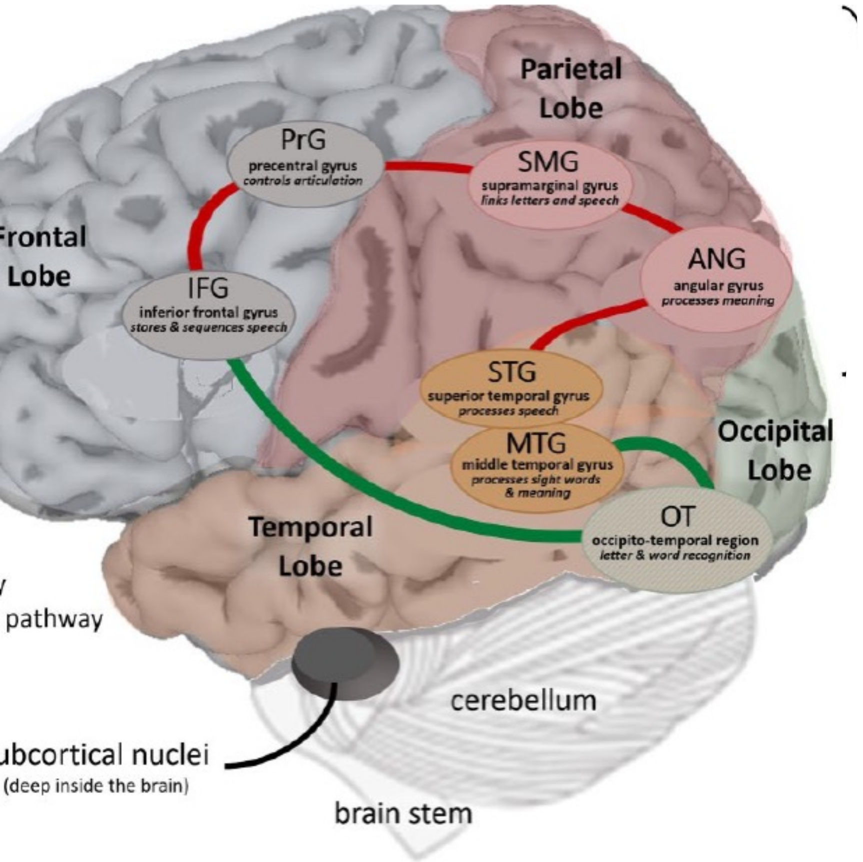
- **At Haskins Laboratories/Yale/UCONN and other partner institutions**:
- Al Liberman, Neil Johnson, Einar Mencl, Rebecca Sandak, Stephen Frost, Nicole Landi, Jon Preston, Leonard Katz, Jay Rueckl, Ram Frost, Fumiko Hoeft, Jim Magnuson, Donald Shankweiler, Elena Grigorenko, **Hollis Scarborough**, Laurie Cutting, Mark Seidenberg, Noam Siegelman, Jun Ren Lee, Ovid Tzeng, Daisy Hung, Nissan Kuo, Denise Wu, Carol Fowler, Michael Turvey, Philip Rubin, David Braze, Kaja Jasinska, Jeff Malins, Tian Hong, Mark Van Den Bunt, Devin Kearns, Vince Gracco, Augusto Buchweitz, Nabin Koirala, Ben Powers, Robin Morris, Maureen Lovett, Peggy McCardle, Jack Fletcher, Reid Lyon, Brett Miller, Peter Molfese, Daragh Sibley, Allison Austin, Lesley Jacobson, Todd Constable, Robert Fulbright, Doug Rothman, John Gore, Jason Zevin, Ludo Verhoeven, Heikki Lyytinen, Nandini Singh, Pekka Rasinnen, Hua Shu, Joy Hirsch, Roeland Hancock, Manuel Carrerias, Richard Aslin, Will Baker, Pat Roberts, Nancy Blair, John Russell.

The beginnings of my journey in search of understanding the mind…

My most important supporters!

Guiding Principles:
Speech, Language, Reading, and the Brain

- Speech is a **biological specialization** but written language is largely a cultural invention.
-
- Speech is mastered naturally in almost all people, without direct instruction.
- But reading is difficult and reading failure occurs in large numbers of children across all written languages. **Explicit instruction is essential.**
- No brain specialization for reading. Reading is, in some sense, an exercise in neuronal recycling (Dehaene, 2010).



Outline: Language, Reading, and the Brain

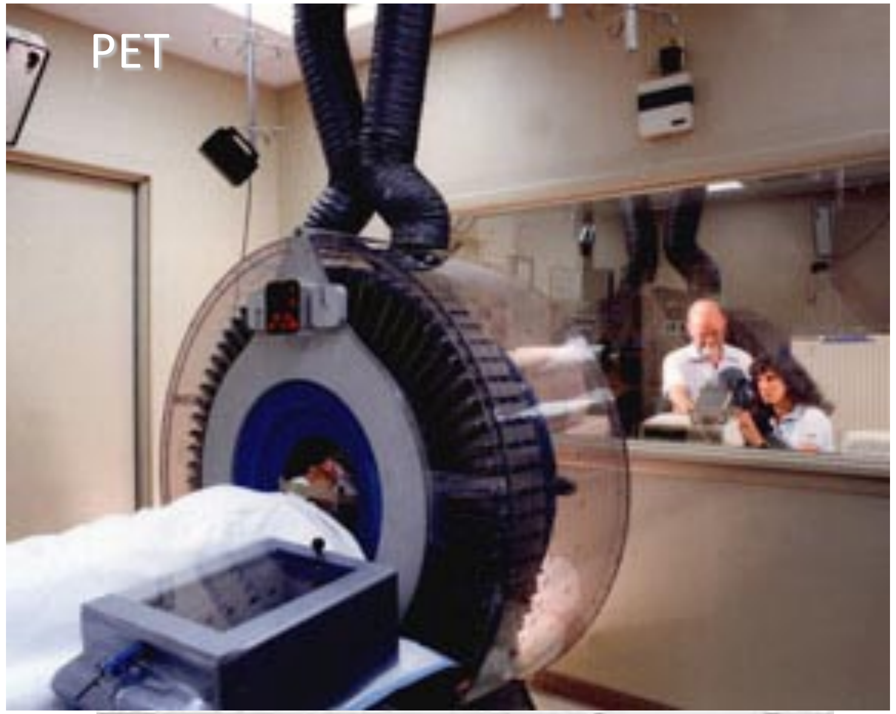
- Three major questions for this presentation:

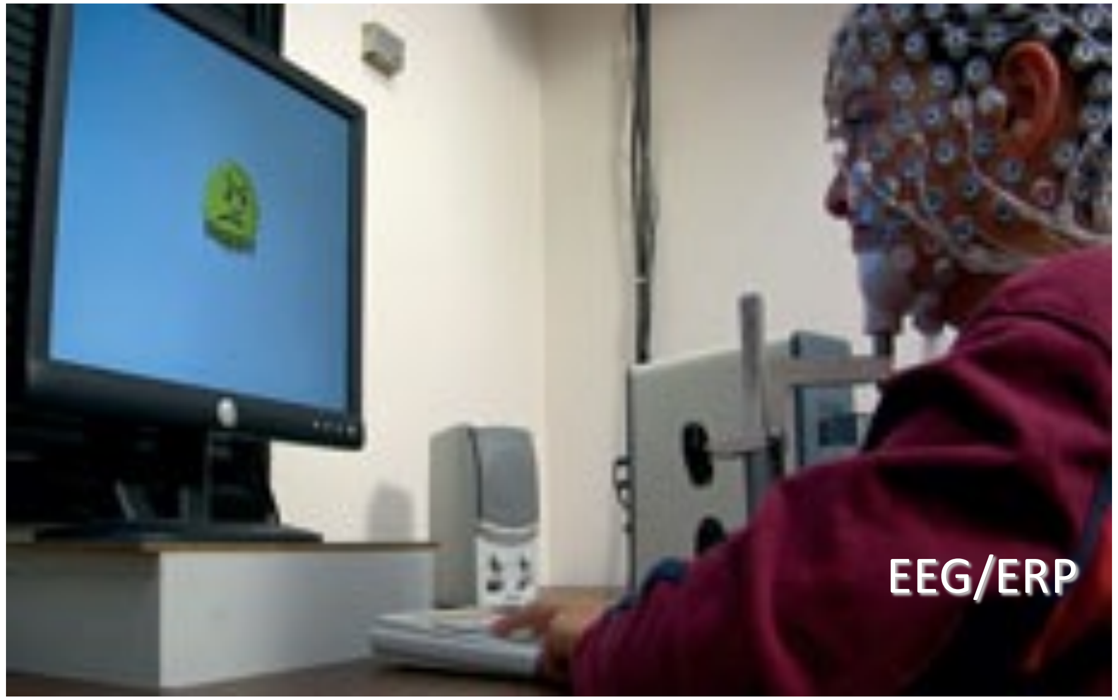
- 1) How do typically developing learners build a neurocircuitry for reading?

- 2) How (and why) does this neurodevelopmental trajectory differ in atypically developing learners?

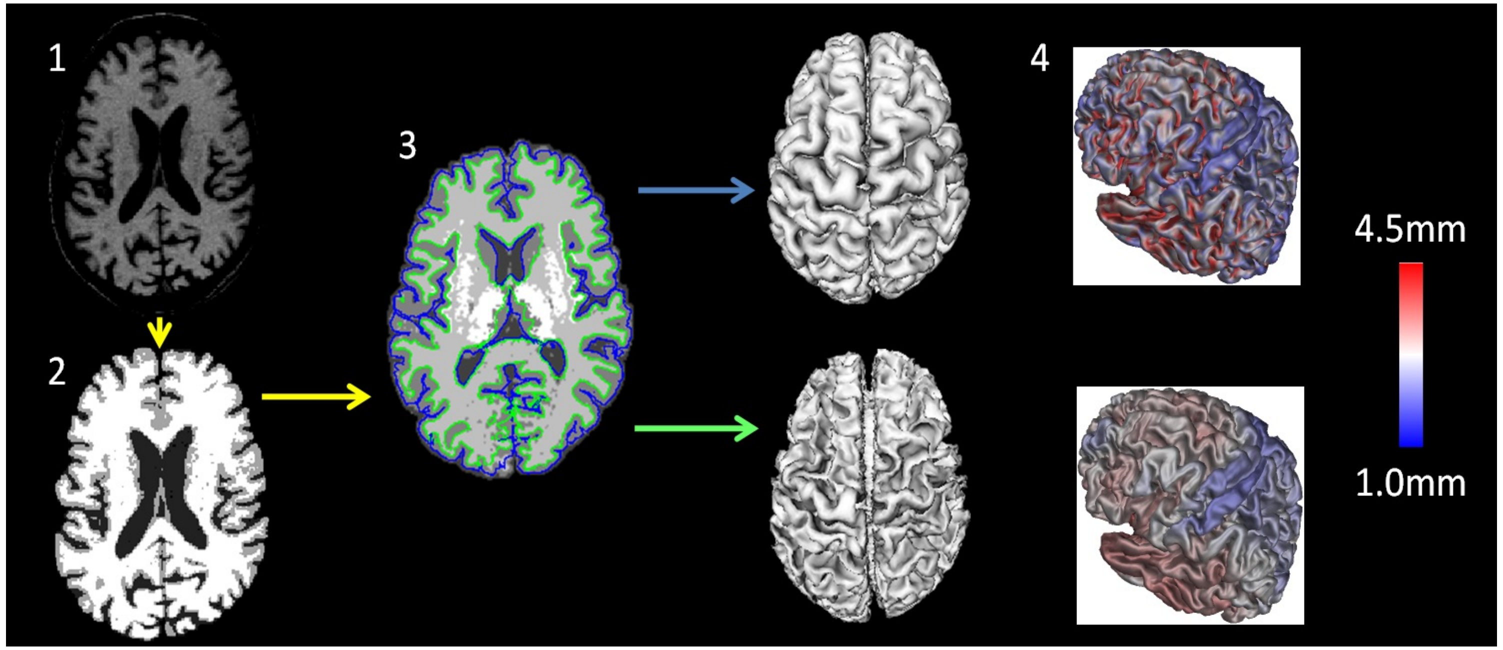
- 3) Do appropriate remediation content / practices modify these neurodevelopmental differences?

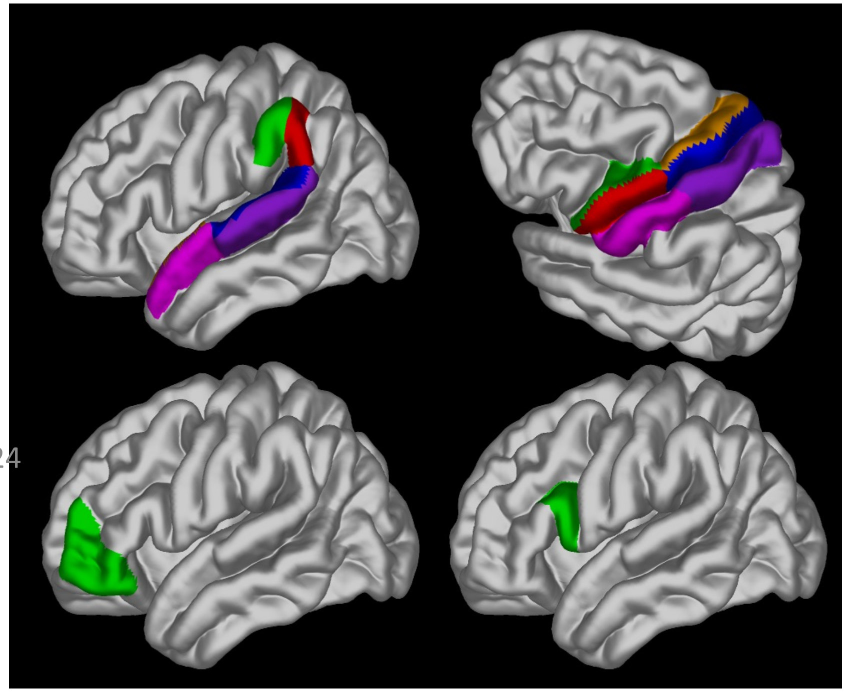
Acquisition techniques

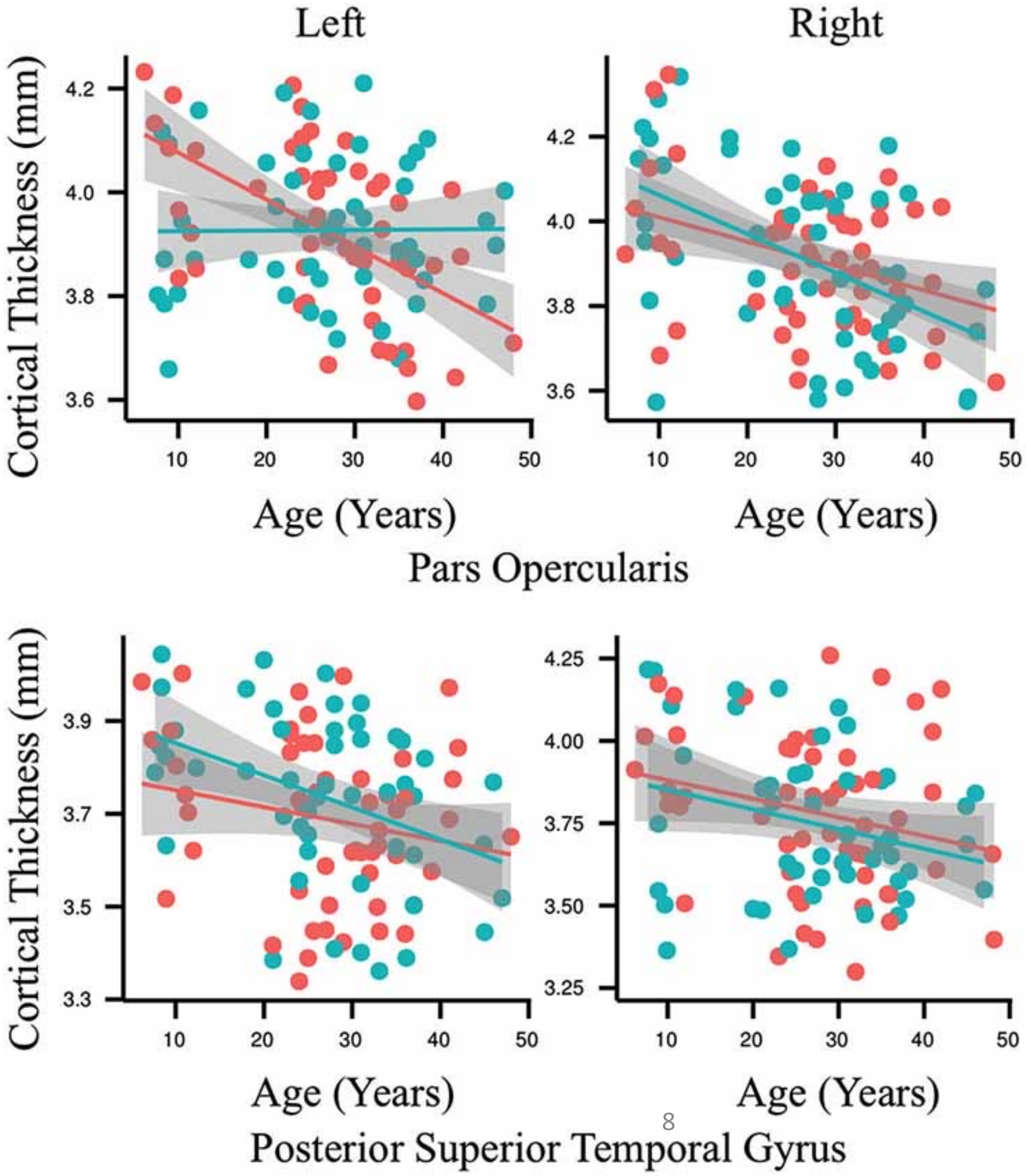




Cortical thickness

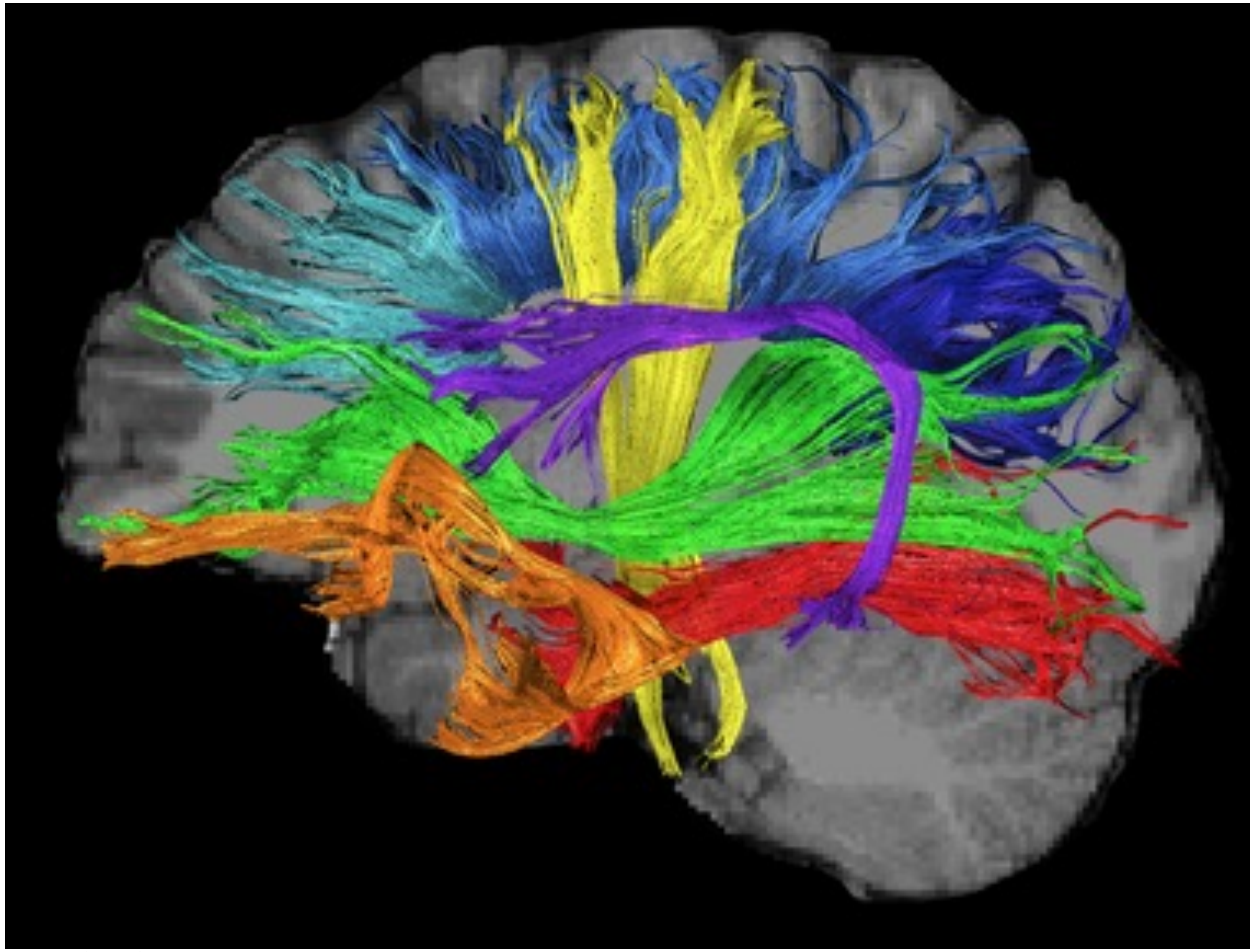


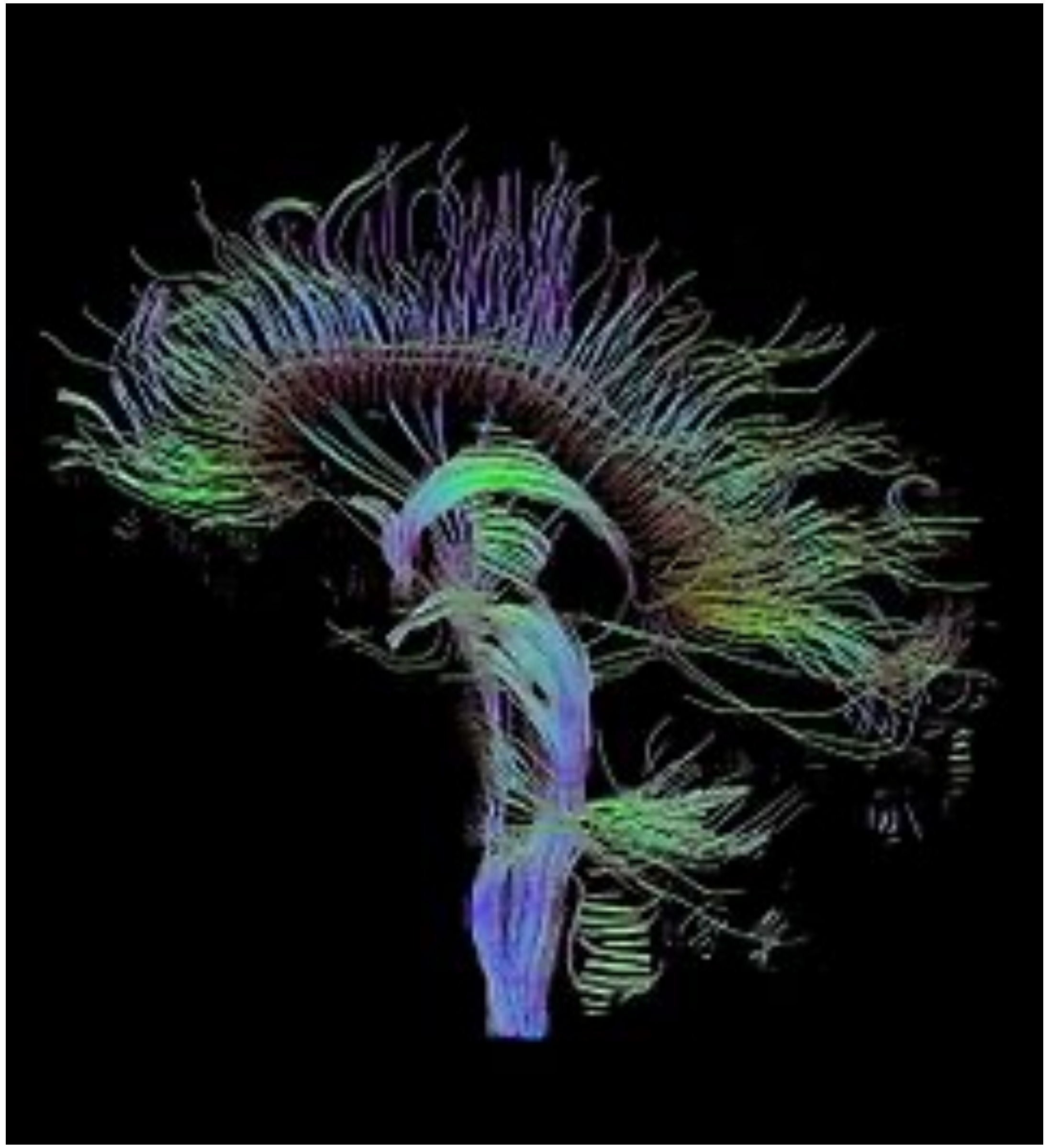




Beal et al., (2015). Frontiers in Human Neuroscience. The trajectory of gray matter development in Broca's area is abnormal in people who stutter

Diffusion tensor imaging

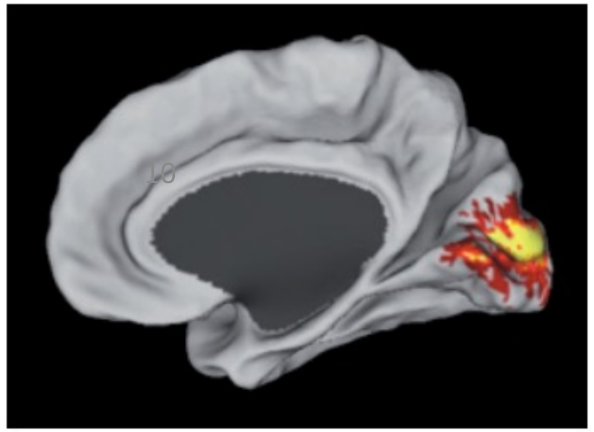




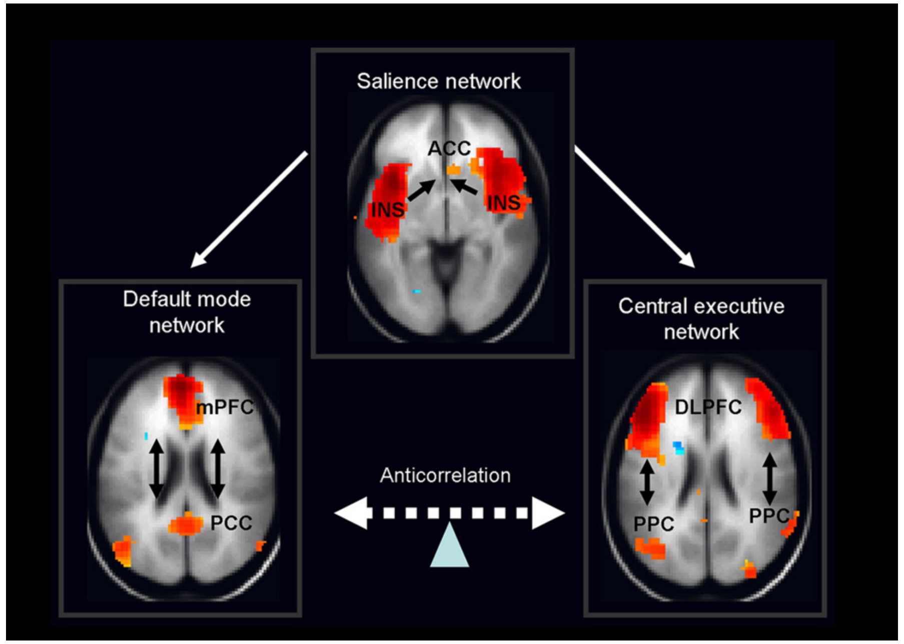
fMRI: Mapping the functional organization of the brain

Haskins Global Literacy Hub

Open – Closed =



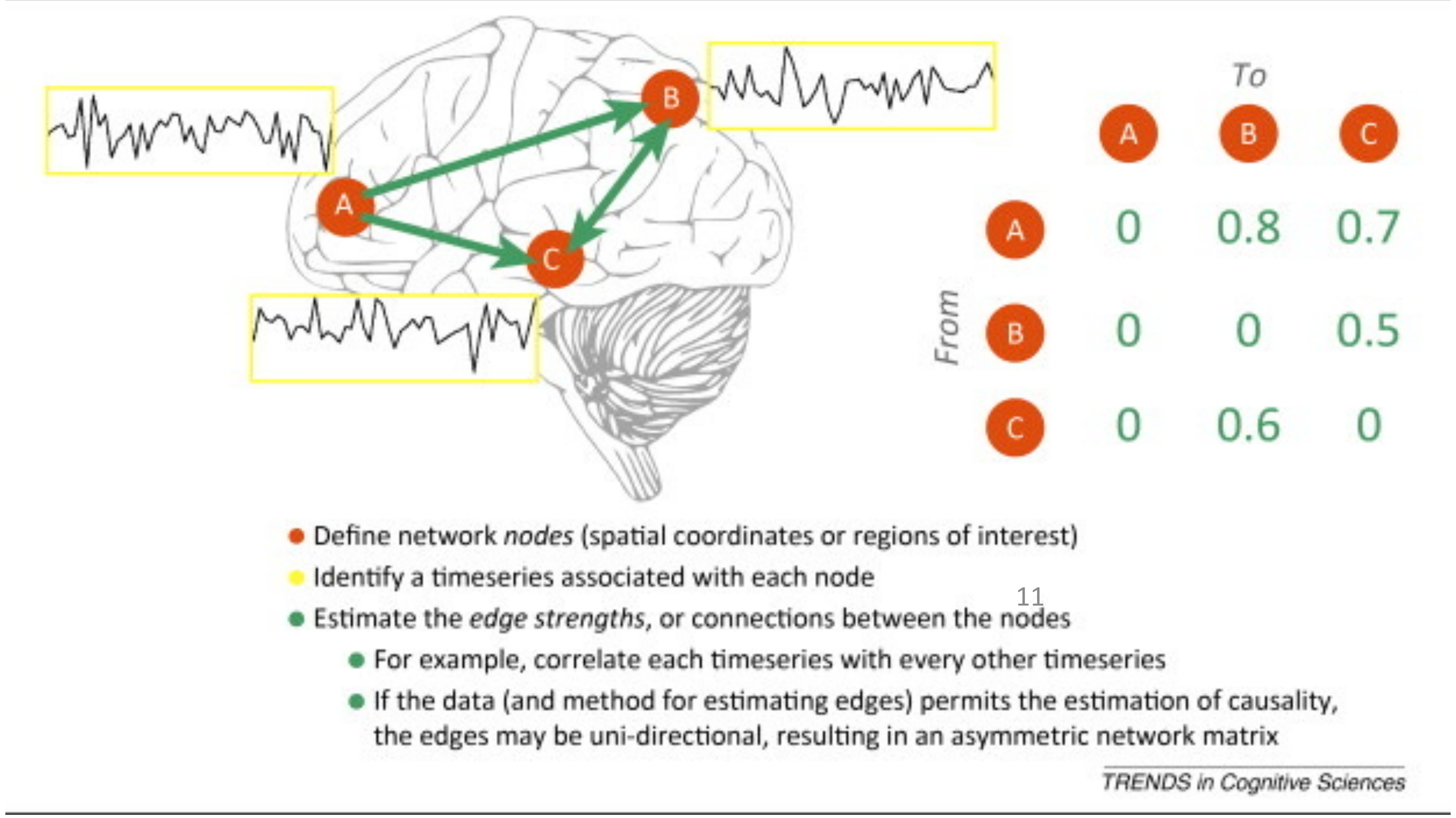
Functional Connectivity

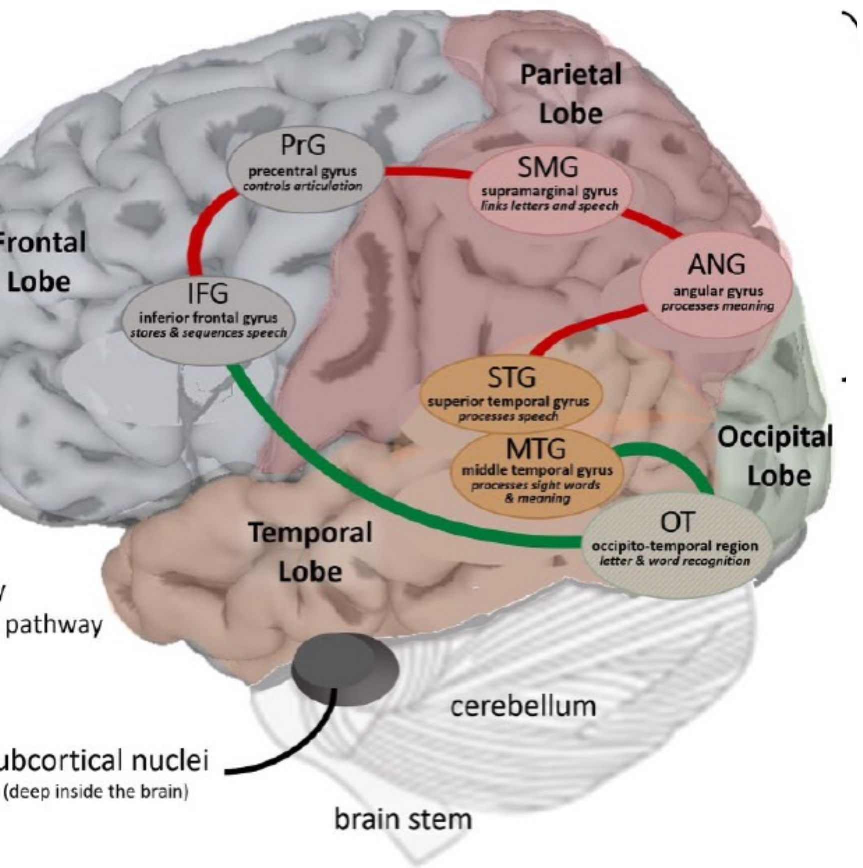


Architecture

Functional Integration

Networks of interactions among specialized regions





Language, Reading, and the Brain

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Cognitive Neuroscience: Neuroplasticity and the challenge of learning to read

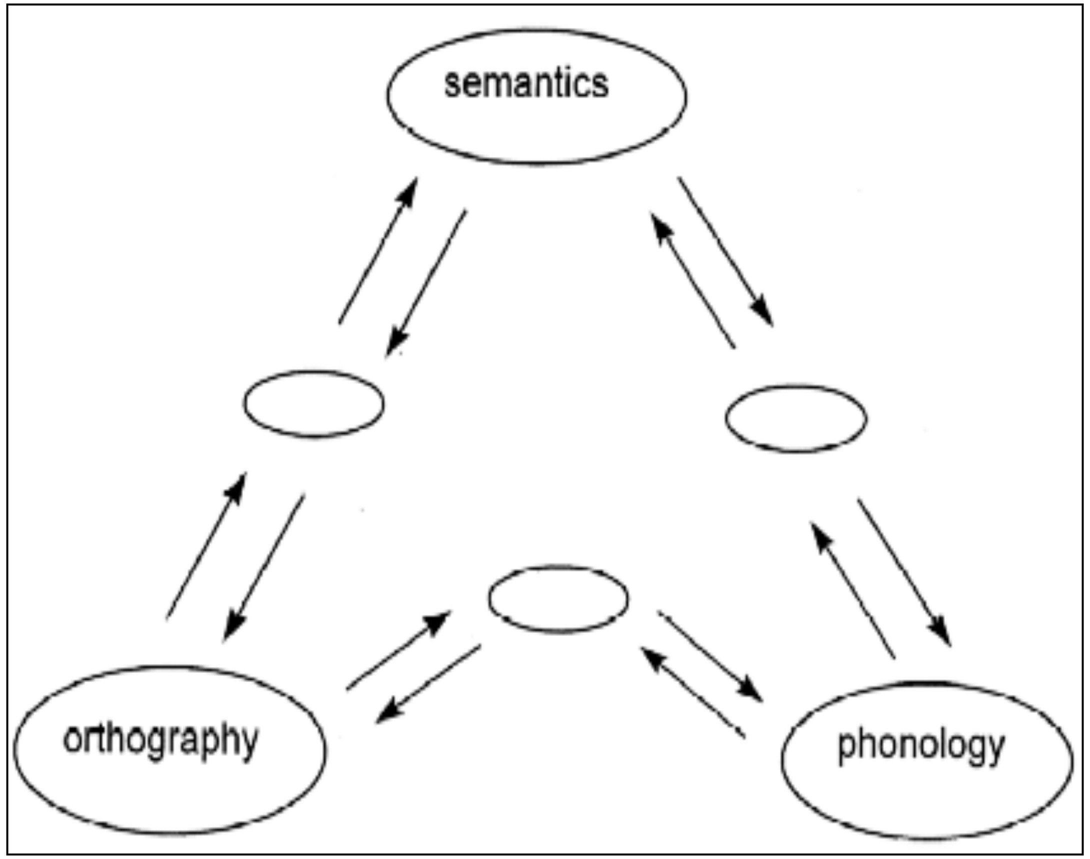
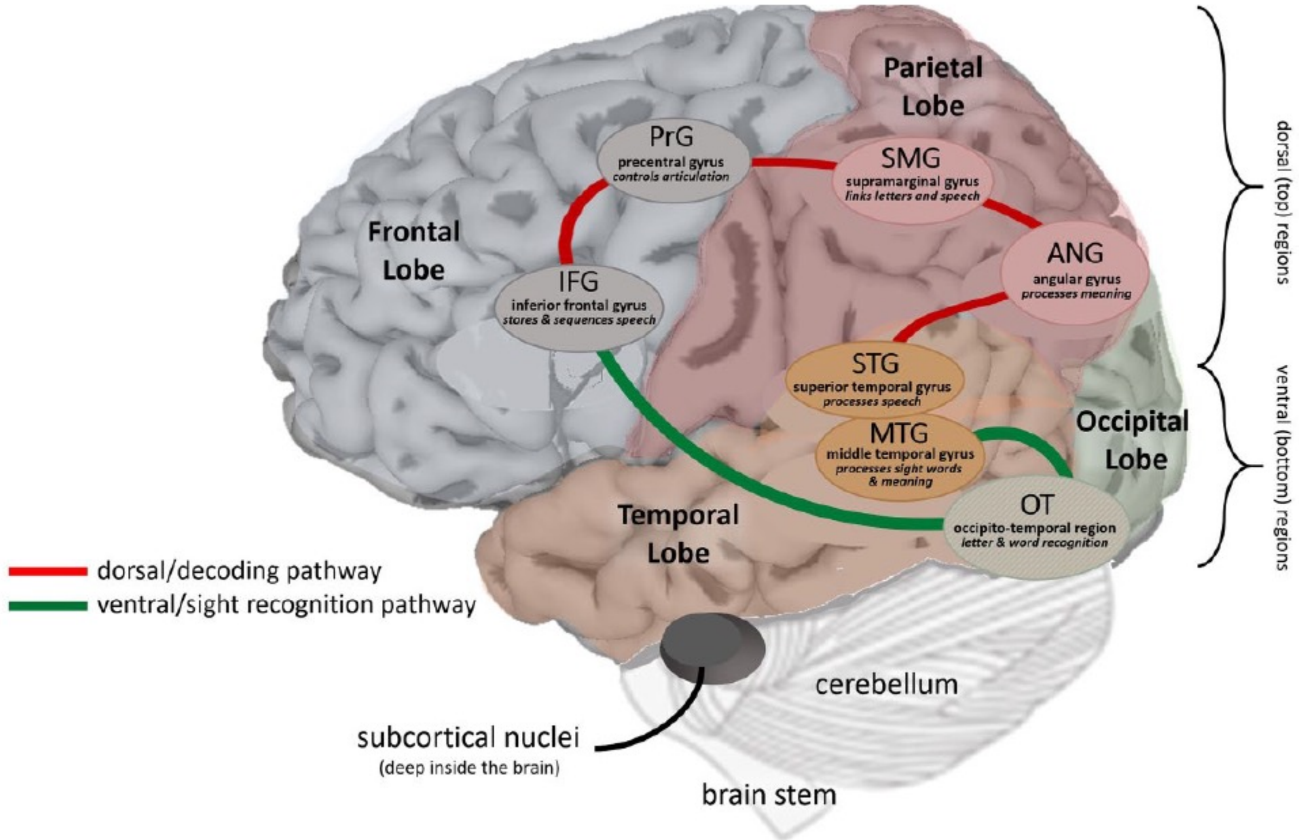


Figure 2. Regions of the reading brain



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The relationship between phonological and auditory processing and brain organization in beginning readers

Kenneth R. Pugh [a,b,e], Nicole Landi [a,c], Jonathan L. Preston [a,d], W. Einar Mencl [a], Alison C. Austin [a], Daragh Sibley [a], Robert K. Fulbright [a,b], Mark S. Seidenberg [a,f], Elena L. Grigorenko [a,c], R. Todd Constable [a,b], Peter Molfese [a], Stephen J. Frost [a,*]

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[b] *Yale University, School of Medicine, Department of Diagnostic Radiology, United States*
[c] *Yale University, Child Study Center, United States*
[d] *Southern Connecticut State University, Department of Communication Disorders, United States*
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[f] *University of Wisconsin, Madison, Department of Psychology, United States*

A R T I C L E I N F O

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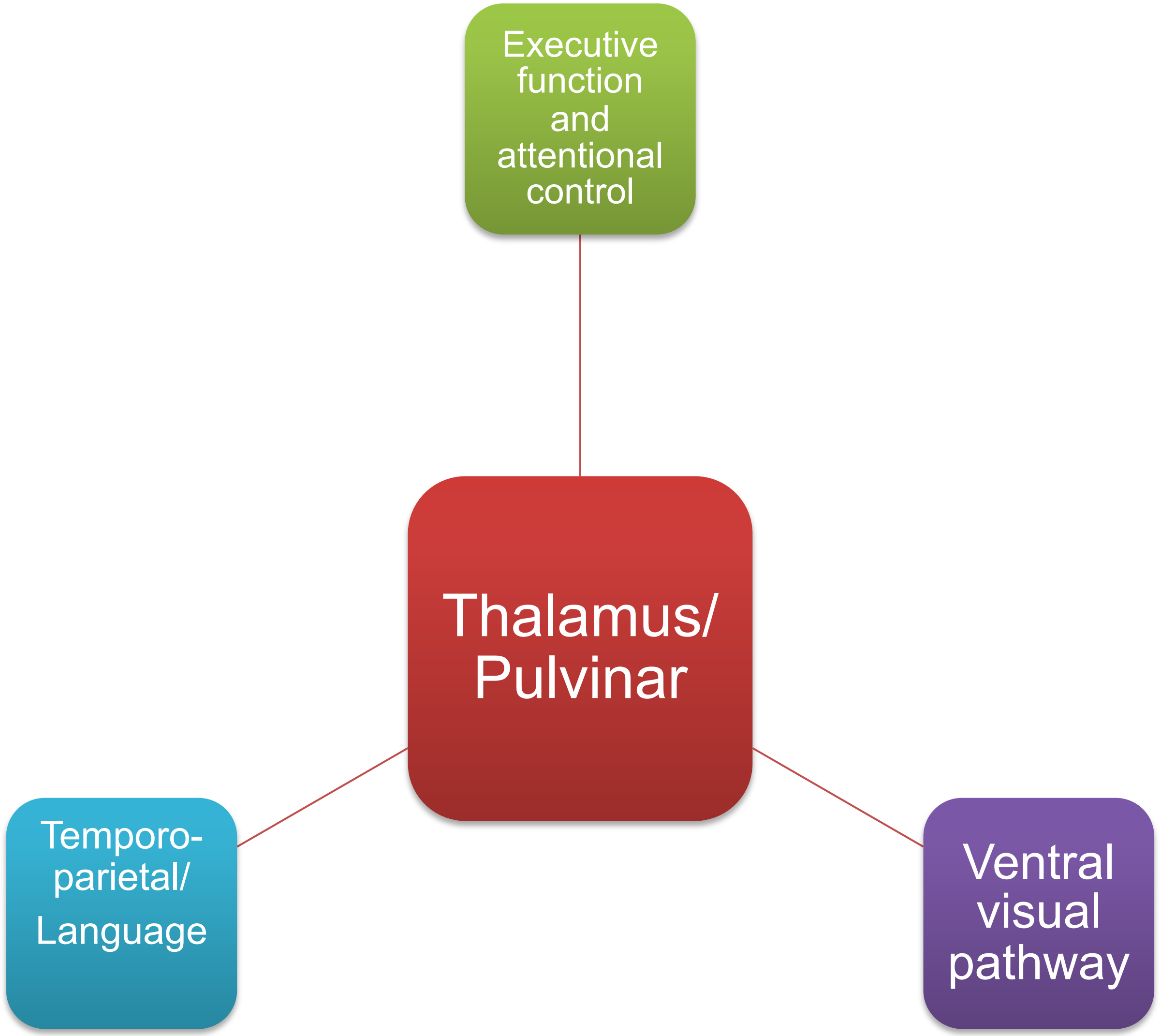
Rapid auditory processing
Thalamus

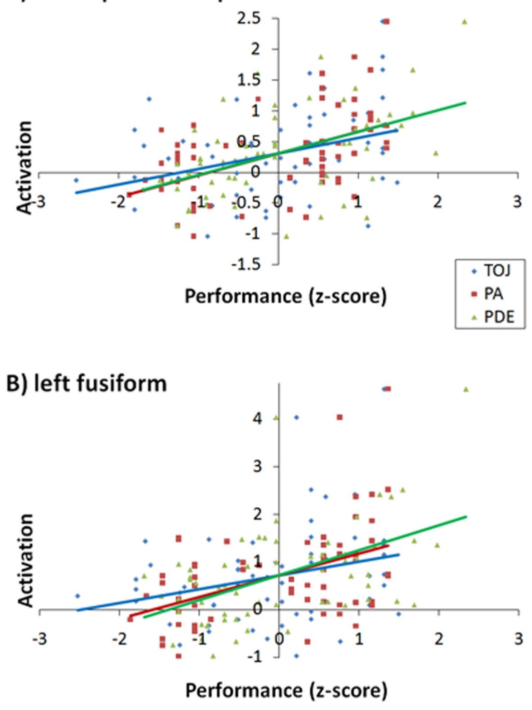
A B S T R A C T

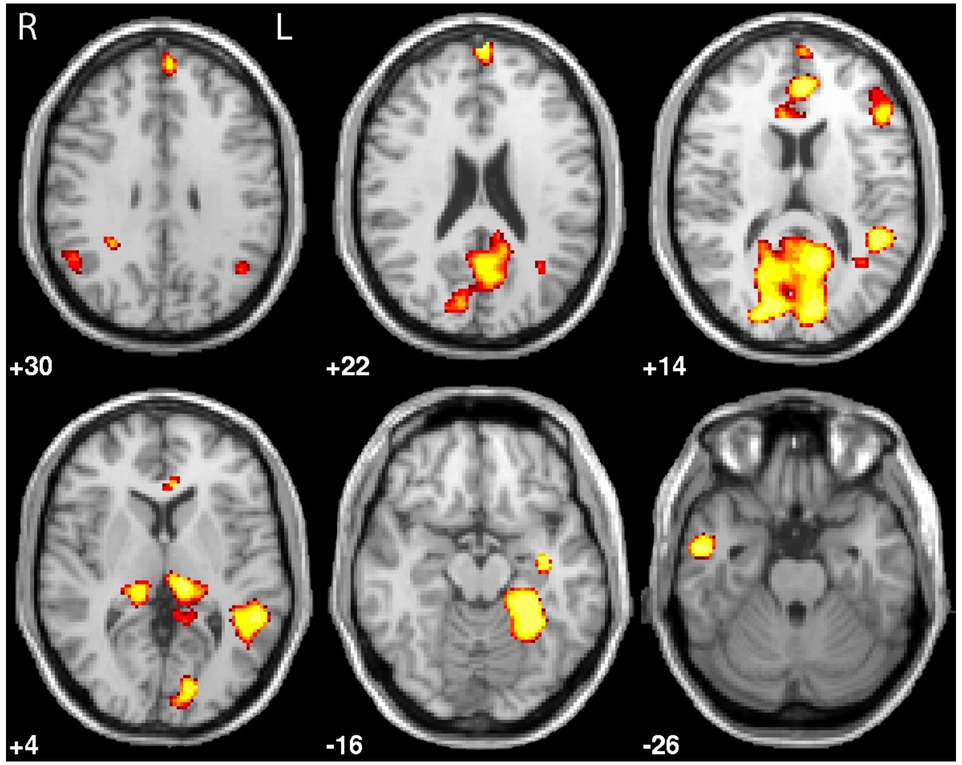
We employed brain–behavior analyses to explore the relationship between performance on tasks measuring phonological awareness, pseudoword decoding, and rapid auditory processing (all predictors of reading (dis)ability) and brain organization for print and speech in beginning readers. For print-related activation, we observed a shared set of skill-correlated regions, including left hemisphere temporoparietal and occipitotemporal sites, as well as inferior frontal, visual, visual attention, and subcortical components. For speech-related activation, shared variance among reading skill measures was most prominently correlated with activation in left hemisphere inferior frontal gyrus and precuneus. Implications for brain-based models of literacy acquisition are discussed.

The Learning Circuitry

(Pugh et al., 2013)

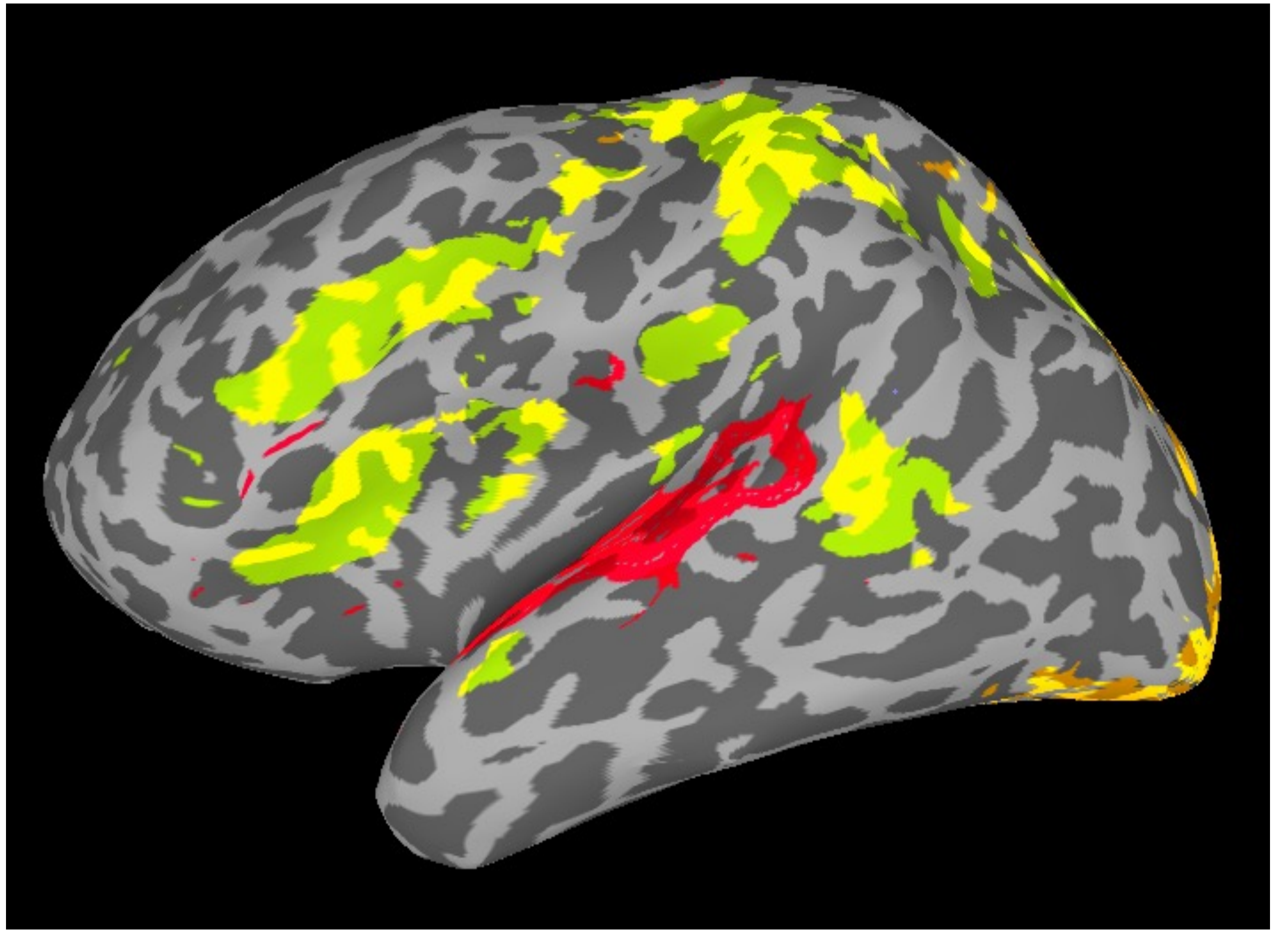






The development of fluent reading depends on print and speech integration

(Frost…Pugh, 2009; Preston…Pugh 2015)



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Research Article

Psychological Science
1–10

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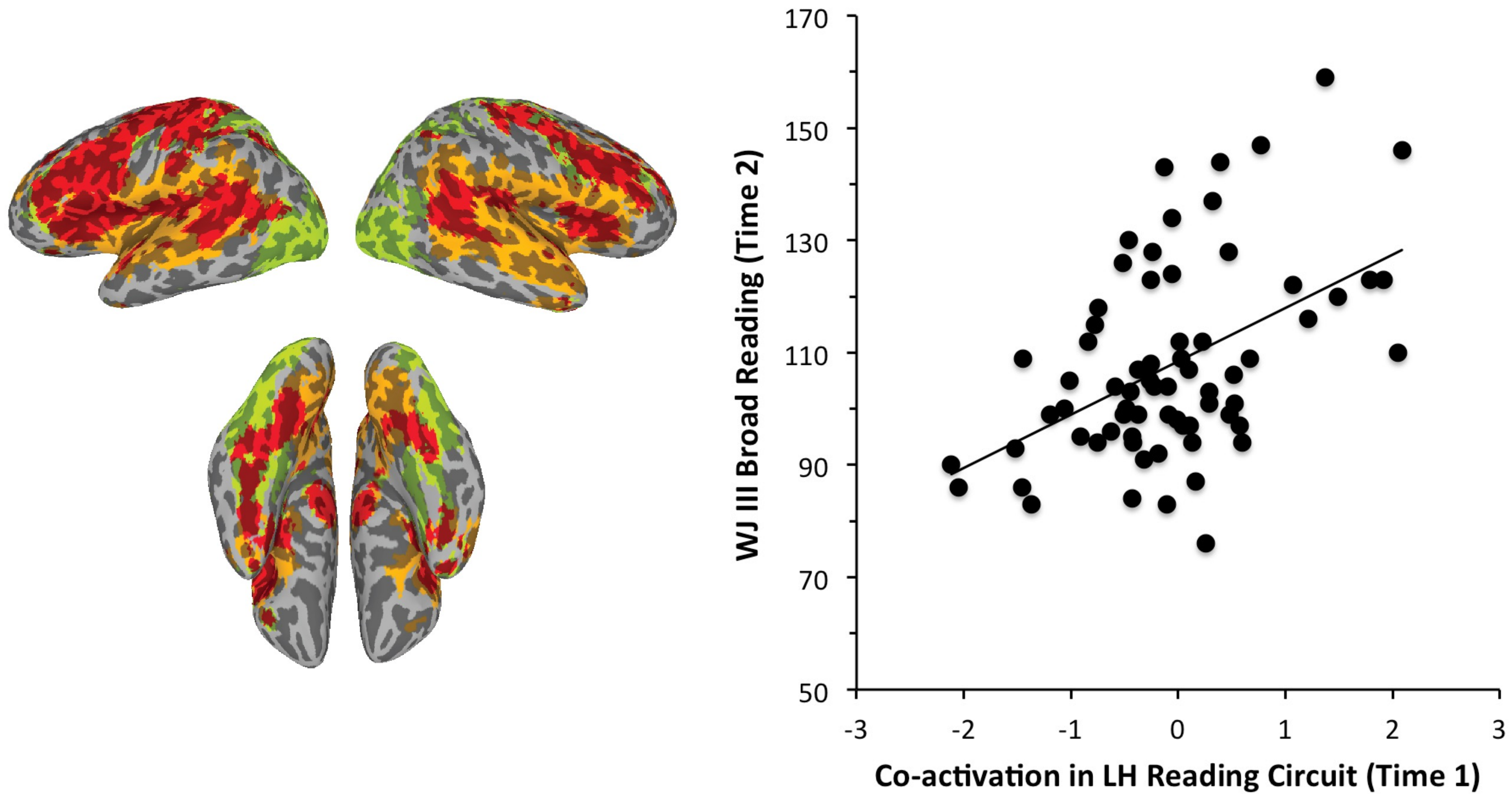
Print-Speech Convergence Predicts Future Reading Outcomes in Early Readers

Jonathan L. Preston[1,2], Peter J. Molfese[2,3], Stephen J. Frost[2], W. Einar Mencl[2], Robert K. Fulbright[4], Fumiko Hoeft[2,5], Nicole Landi[2,3], Donald Shankweiler[2,3], and Kenneth R. Pugh[2,3]

[1]Department of Communication Sciences & Disorders, Syracuse University; [2]Haskins Laboratories, Yale University; [3]Department of Psychology, University of Connecticut; [4]Diagnostic Radiology, Yale University School of Medicine; and [5]Department of Psychiatry, University of California, San Francisco

Abstract

Becoming a skilled reader requires building a functional neurocircuitry for printed-language processing that integrates with spoken-language-processing networks. In this longitudinal study, functional MRI (fMRI) was used to examine convergent activation for printed and spoken language (print-speech coactivation) in selected regions implicated in printed-language processing (the reading network). We found that print-speech coactivation across the left-hemisphere reading network in beginning readers predicted reading achievement 2 years later beyond the effects of brain activity for either modality alone; moreover, coactivation effects accounted for variance in later reading after controlling for initial reading performance. Within the reading network, effects of coactivation were significant in bilateral inferior frontal gyrus (IFG) and left inferior parietal cortex and fusiform gyrus. The contribution of left and right IFG differed,


WJ III Broad Reading (Time 2)
Co-activation in LH Reading Circuit (Time 1)
170
150
130
110
90
70
50
-3
-2
-1
0
1
2
3

PNAS

Universal brain signature of proficient reading: Evidence from four contrasting languages

Jay G. Rueckl[a,b], Pedro M. Paz-Alonso[c], Peter J. Molfese[a,b], Wen-Jui Kuo[d], Atira Bick[e], Stephen J. Frost[a,1], Roeland Hancock[f], Denise H. Wu[g], William Einar Mencl[a], Jon Andoni Duñabeitia[c], Jun-Ren Lee[h], Myriam Oliver[c], Jason D. Zevin[a,i,j], Fumiko Hoeft[a,f], Manuel Carreiras[c,k], Ovid J. L. Tzeng[l,m,n], Kenneth R. Pugh[a,b,o], and Ram Frost[a,c,e]

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Edited by Michael I. Posner, University of Oregon, Eugene, OR, and approved November 2, 2015 (received for review May 12, 2015)

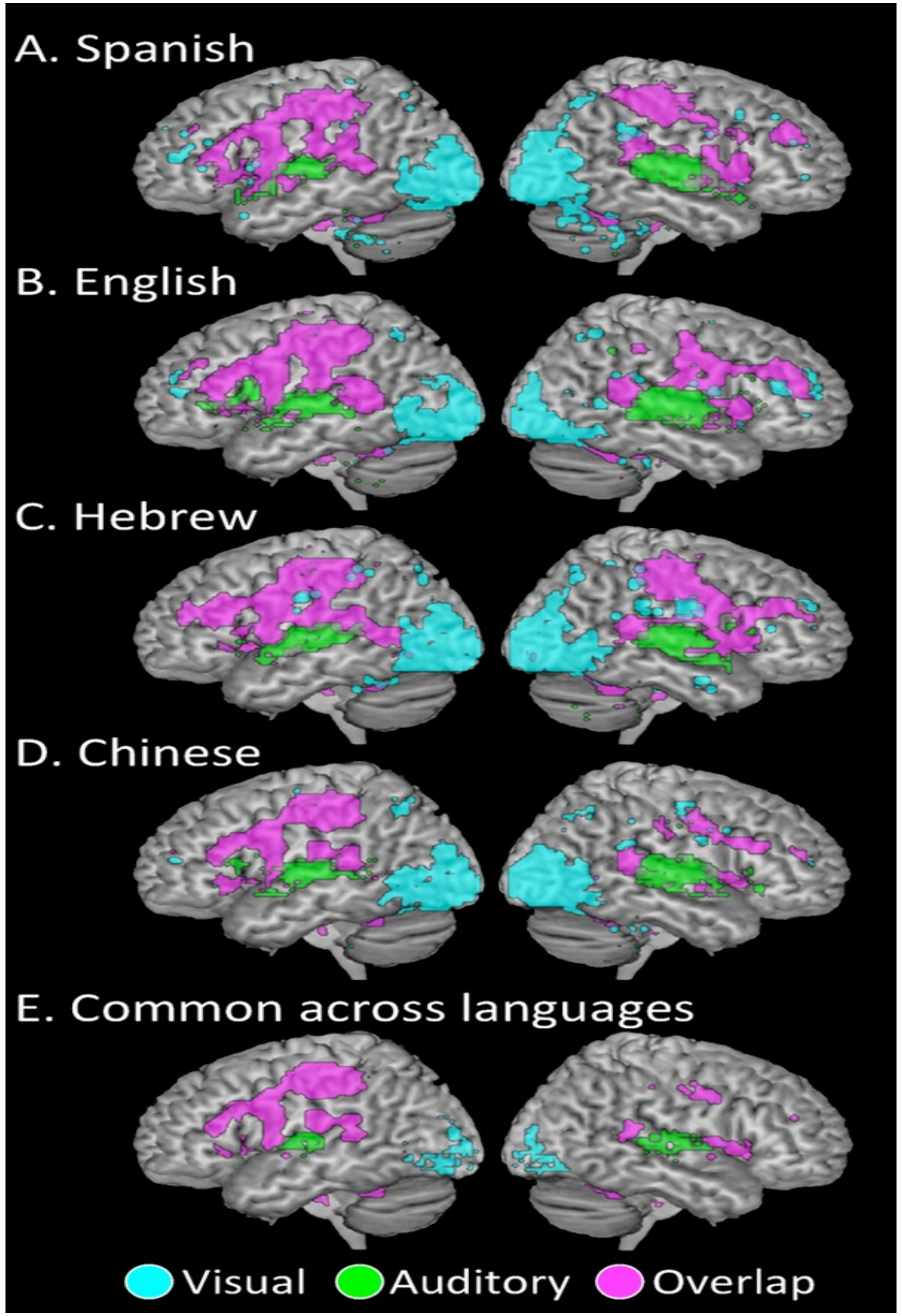
We propose and test a theoretical perspective in which a universal hallmark of successful literacy acquisition is the convergence of the speech and orthographic processing systems onto a common network of neural structures, regardless of how spoken words are represented orthographically in a writing system. During functional MRI, skilled adult readers of four distinct and highly contrasting languages, Spanish, English, Hebrew, and Chinese, performed an identical semantic categorization task to spoken and written words. Results from three complementary analytic approaches demonstrate limited language variation, with speech–print convergence emerging as a common brain signature of reading proficiency across the wide spectrum of selected languages, whether their writing system is alphabetic or logographic, whether it is opaque or transparent, and regardless of the phonological and morphological structure it represents.

cross-language invariance | word recognition | functional MRI

reading would not only recruit the neural circuits best suited for processing its orthographic symbols (which could show some front-end variation due to visuospatial differences) but would fundamentally depend on access to existing neurocircuits implicated in processing meaningful spoken words (16). By this view, a universal hallmark of successful literacy acquisition would be the emergence of a reading network that is strongly constrained by the brain network underlying the processing of spoken words (a network itself likely to be largely universal across languages), regardless of how these words are represented orthographically (17, 18).

We examined the extent of convergence of neural networks involved in spoken and written word recognition in 84 right-handed, healthy, and skilled adult readers in Spanish, English, Hebrew, and Chinese (n = 21 per language; see Table S1 for details on group matching). These languages were selected because they provide contrasts of transparent vs. opaque orthographies with alphabetic vs. logographic writing systems, which map into monomorphemic and monosyllabic words vs. morphologically

PSYCHOLOGICAL AND COGNITIVE SCIENCES

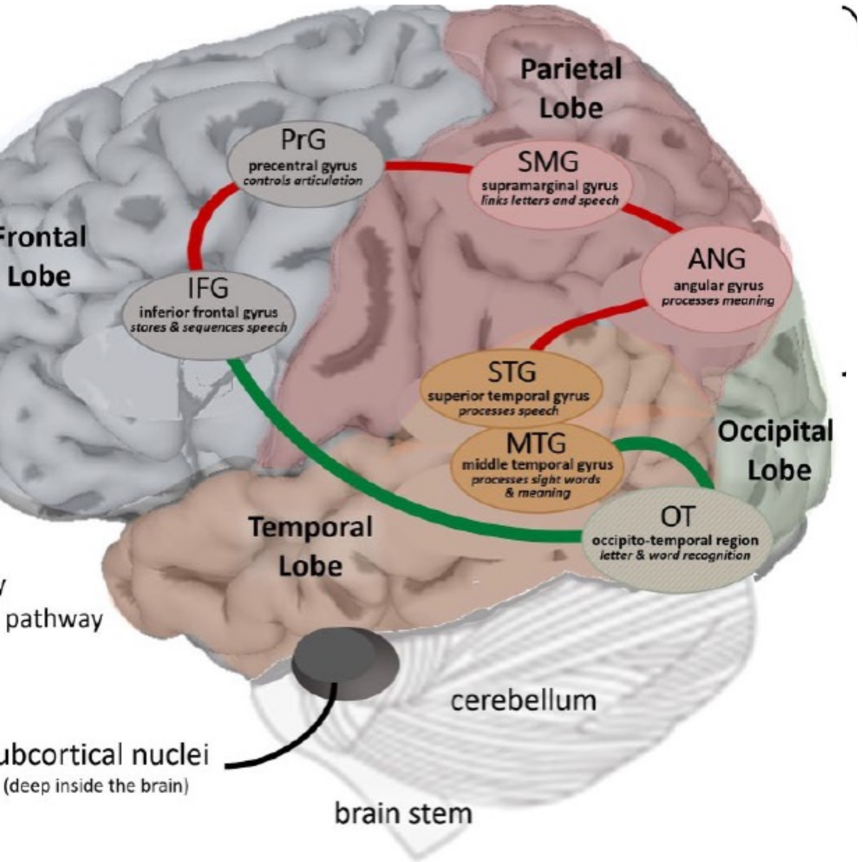


Summary: Cross modal integration and reading skill

- Our studies indicate that a critical factor discriminating skilled from less skilled readers **is the degree of print/speech integration in key LH circuits (IFG/STG/SMG).**

- **This has clear implications for instruction and remediation**

- **And given our cross-language brain imaging findings we strongly hypothesize that this would also be true for early instruction in non-alphabetic writing systems like Chinese**



Language, Reading, and the Brain

- Three major questions for this presentation:

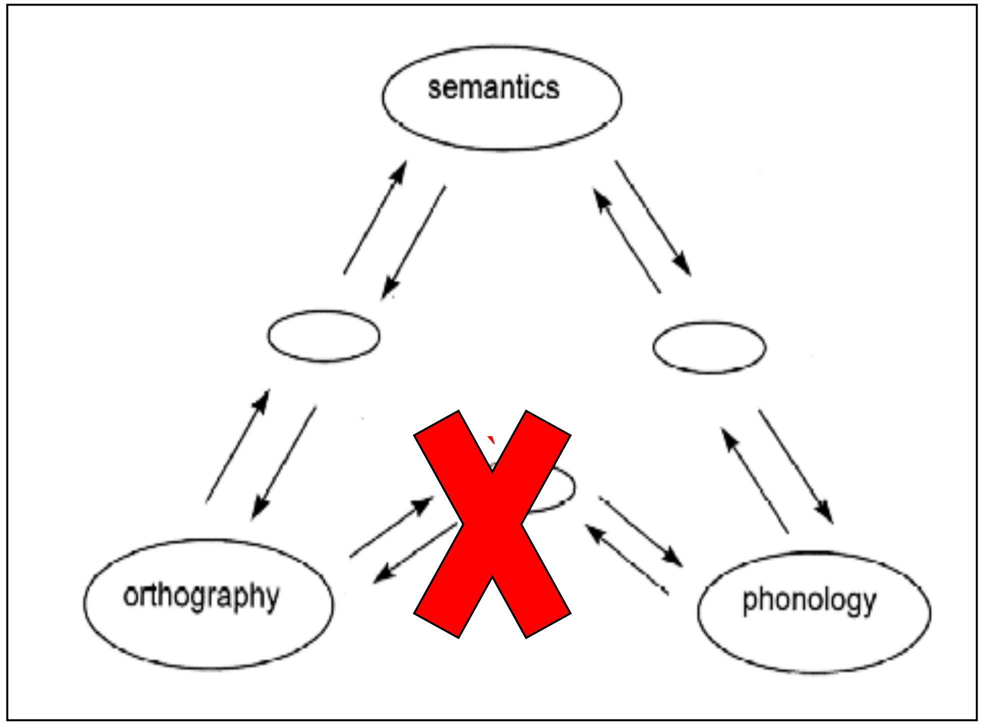
- 1) How do typically developing learners build a neurocircuitry for reading?

- 2) How (and why) does this neurodevelopmental trajectory differ in atypically developing learners?

- 3) Do appropriate remediation content / practices modify these neurodevelopmental differences?

Reading Disability (Developmental Dyslexia)

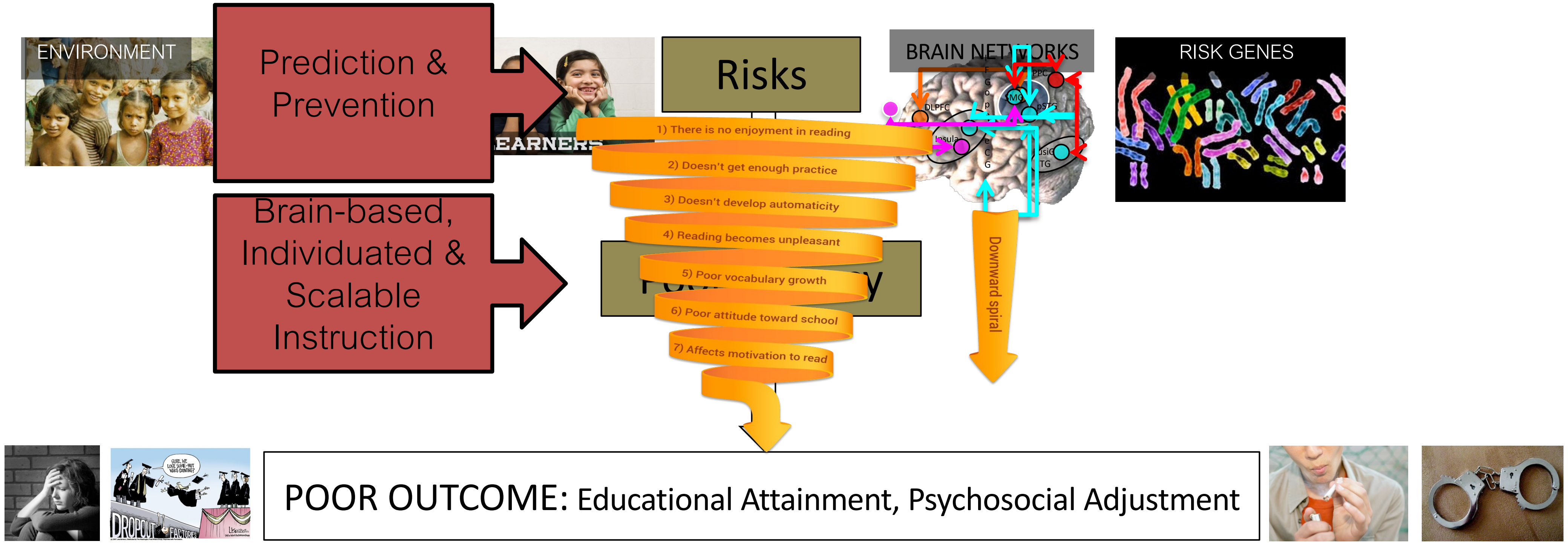
- Dyslexia primarily affects the skills involved in accurate and fluent word reading and spelling.
- Characteristic features of dyslexia are difficulties in phonological awareness, verbal memory and verbal processing speed.
- **Dyslexia occurs across the range of intellectual abilities.**
- It is best characterized as a **dimensional, rather than a discrete, disorder.**



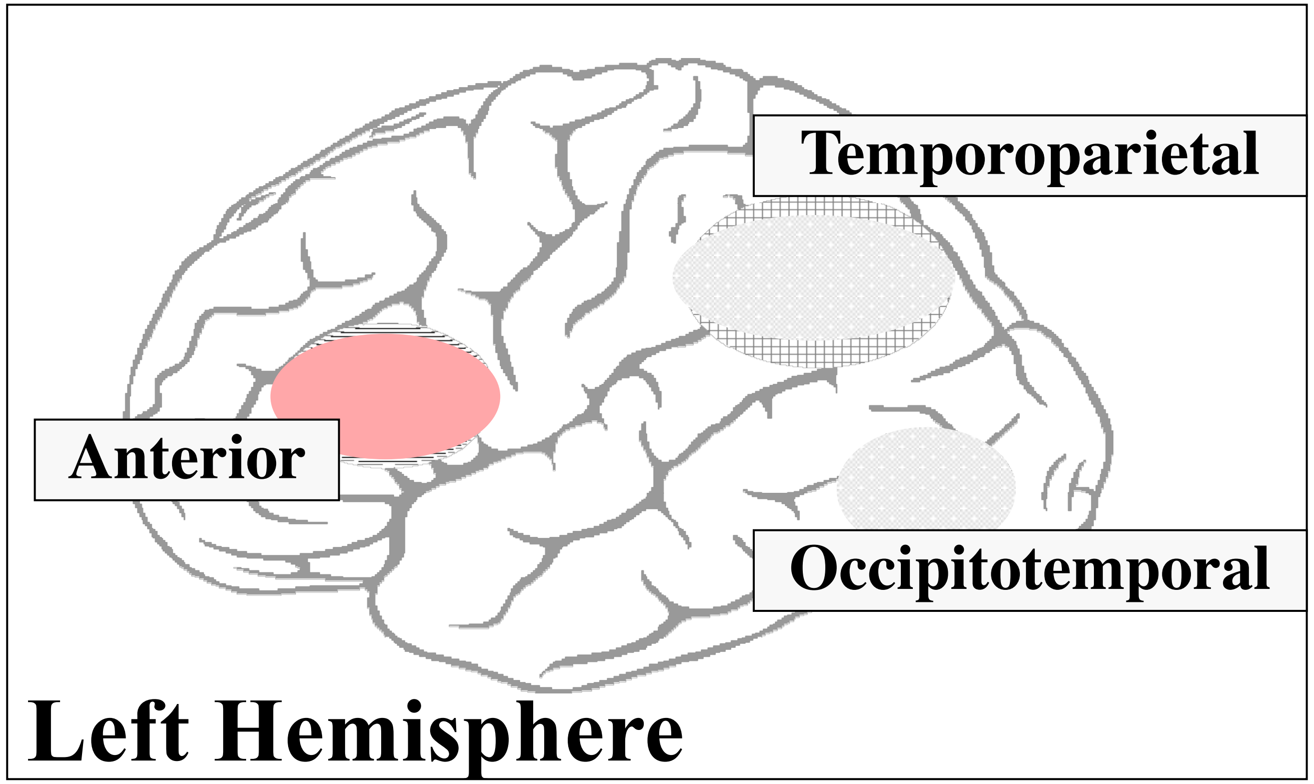
Reading disabilities are grounded in early language development

and risk **reflect complex contributions of both genes and environment**

A key focus of the Haskins Global Literacy Hub is on neurodevelopment



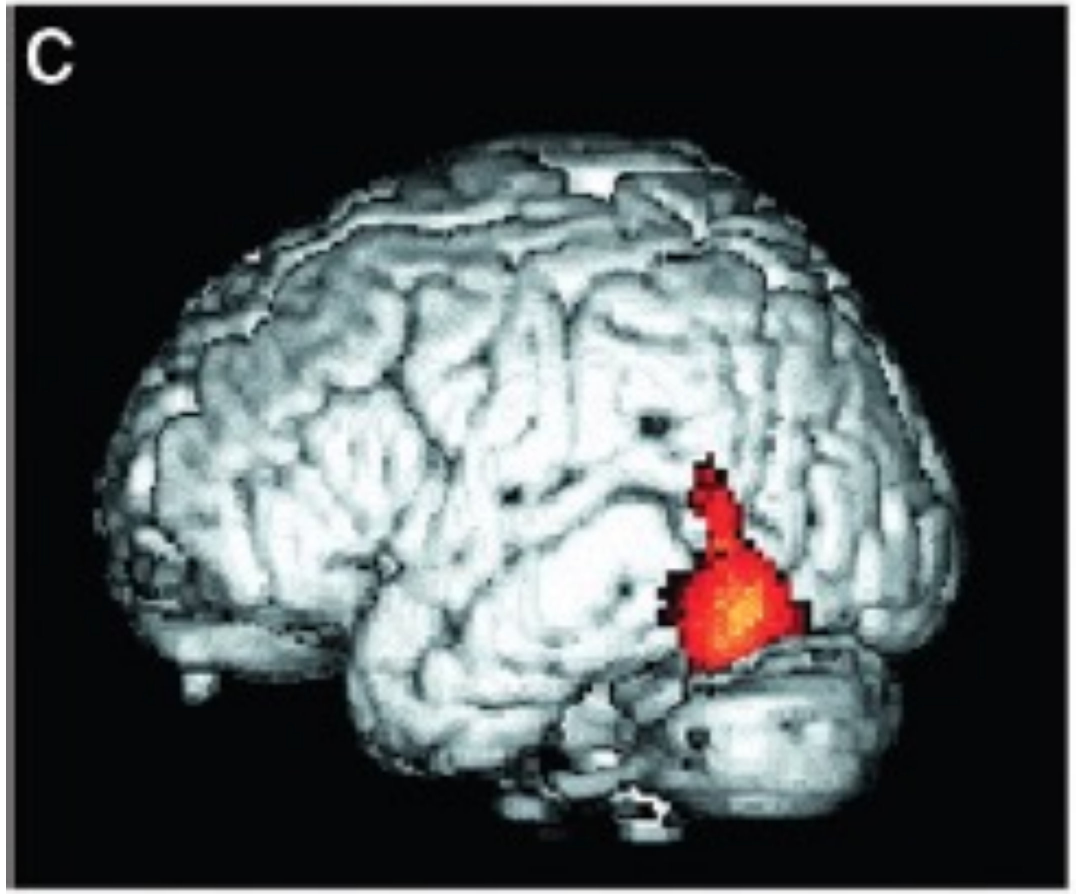
Brain circuits and reading difficulties

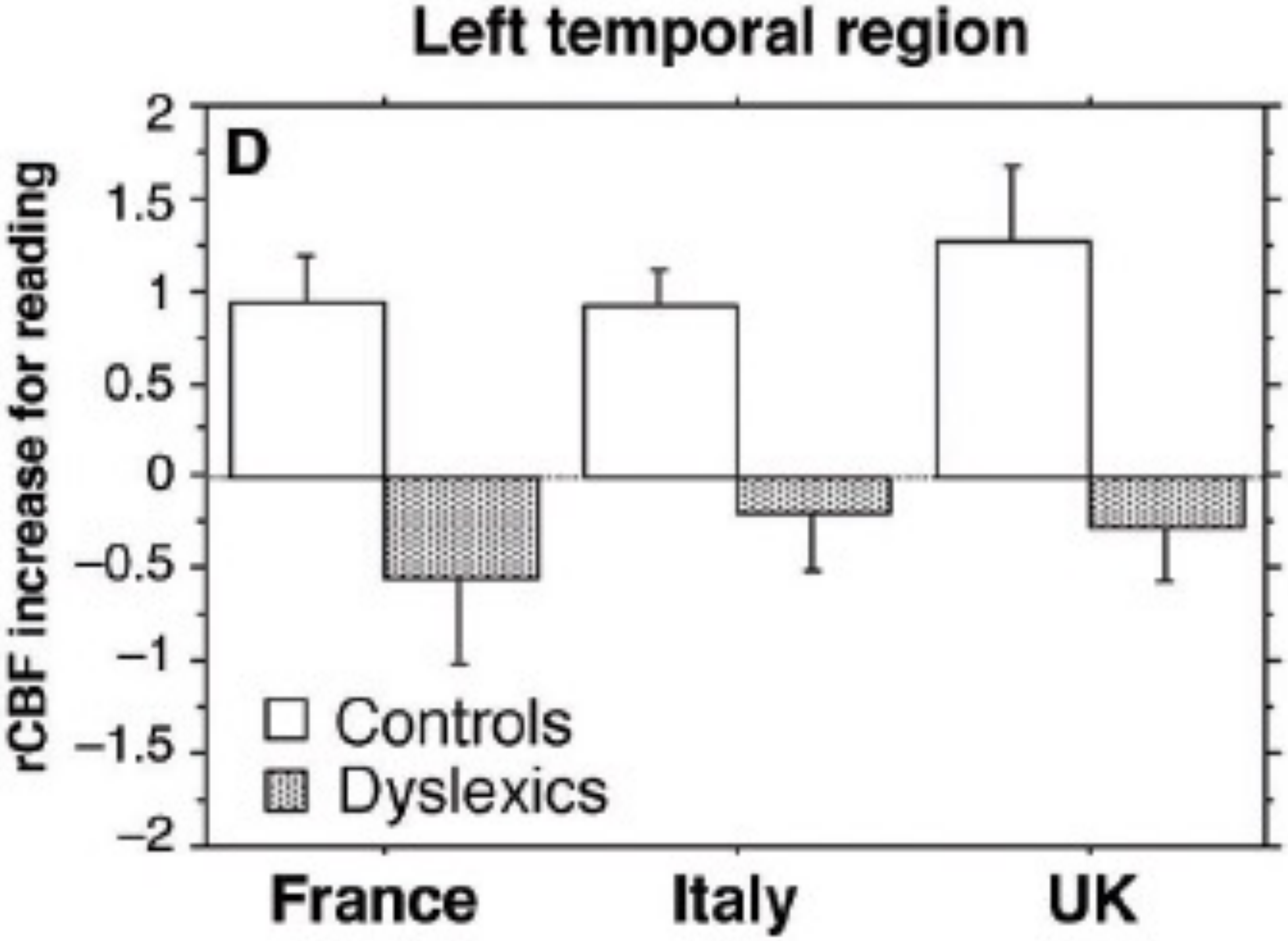


- Frequent finding: A large number of studies indicate that RD readers show anomalous patterns in **LH temporoparietal and LH ventral (occipitotemporal)** regions.
- **RH and frontal "compensatory" shift in RD often reported**

Dyslexia: Cultural Diversity and Biological Unity

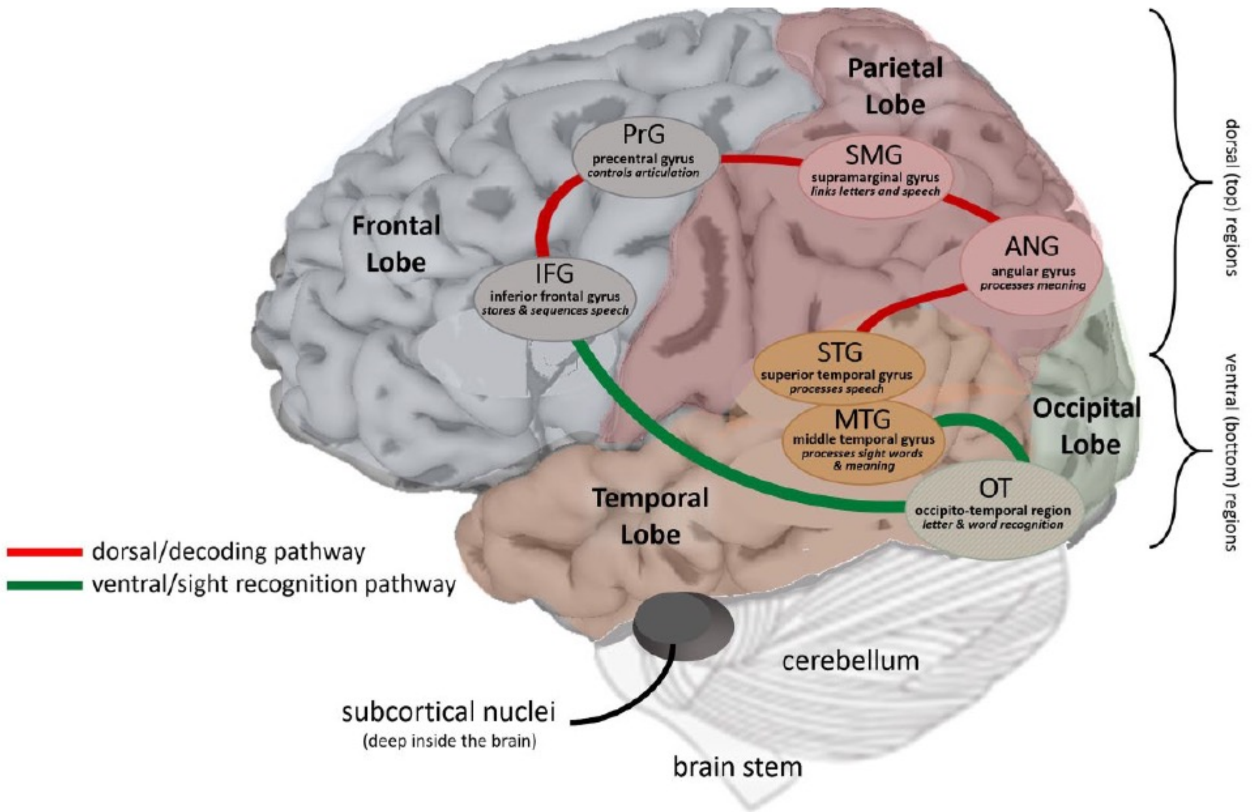
E. Paulesu,[1,2]* J.-F. Démonet,[3] F. Fazio,[2,4] E. McCrory,[5]
V. Chanoine,[3] N. Brunswick,[6] S. F. Cappa,[7] G. Cossu,[8] M. Habib,[9]
C. D. Frith,[6] U. Frith[5]



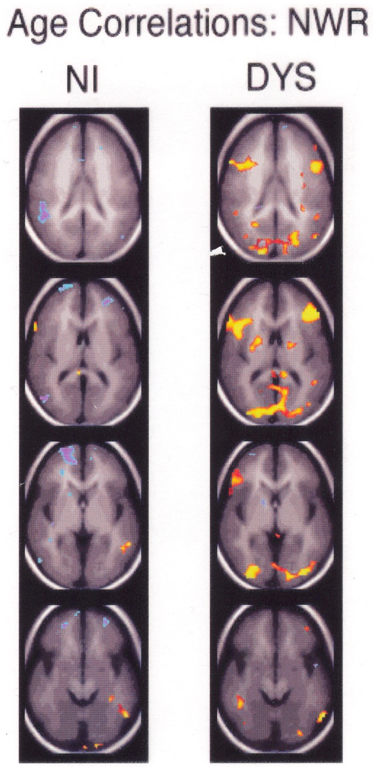


Atypical reading development: Insights from developmental neuroimaging

Figure 2. Regions of the reading brain



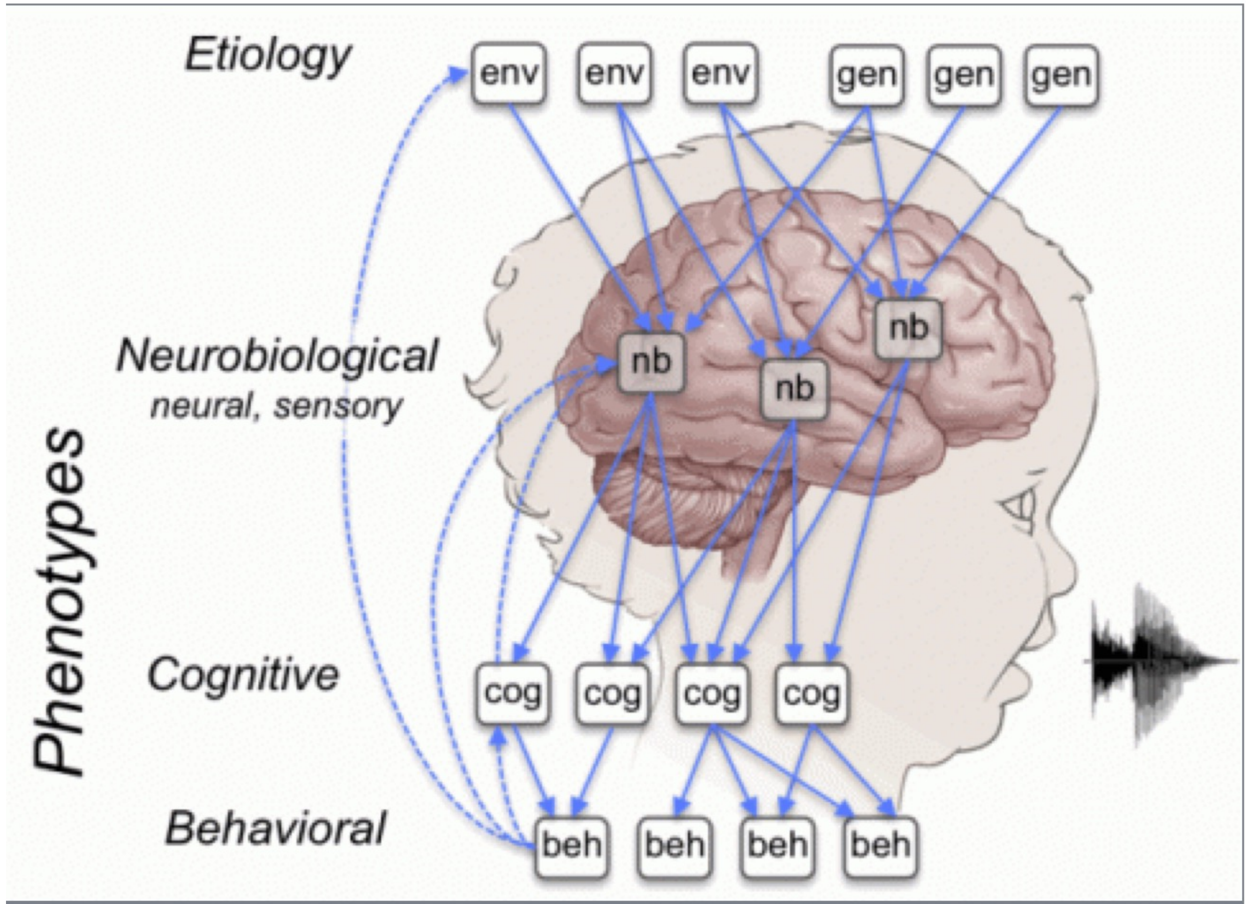
Developmental trajectory is abnormal in dyslexia (Shaywitz Pugh et al. BP 2002)



Atypical readers:
Insights from functional/ structural neuroimaging to date

Functional/structural neuroimaging reveals:

- **Atypical brain activation** (Pugh et al., 2013; Preston et al., 2015)
- **Reduced functional connectivity** (Pugh et al., 2000; Siegelman at al., 2021)
- **Problems in learning, and consolidation of new learning**
- (Pugh et al., 2008; Malins et al., 2021)
- **Reduced grey and white matter volume** (Richlan, 2014)
- **Abnormal neurochemistry** (Pugh et al., 2014; Bruno et al., 2013)



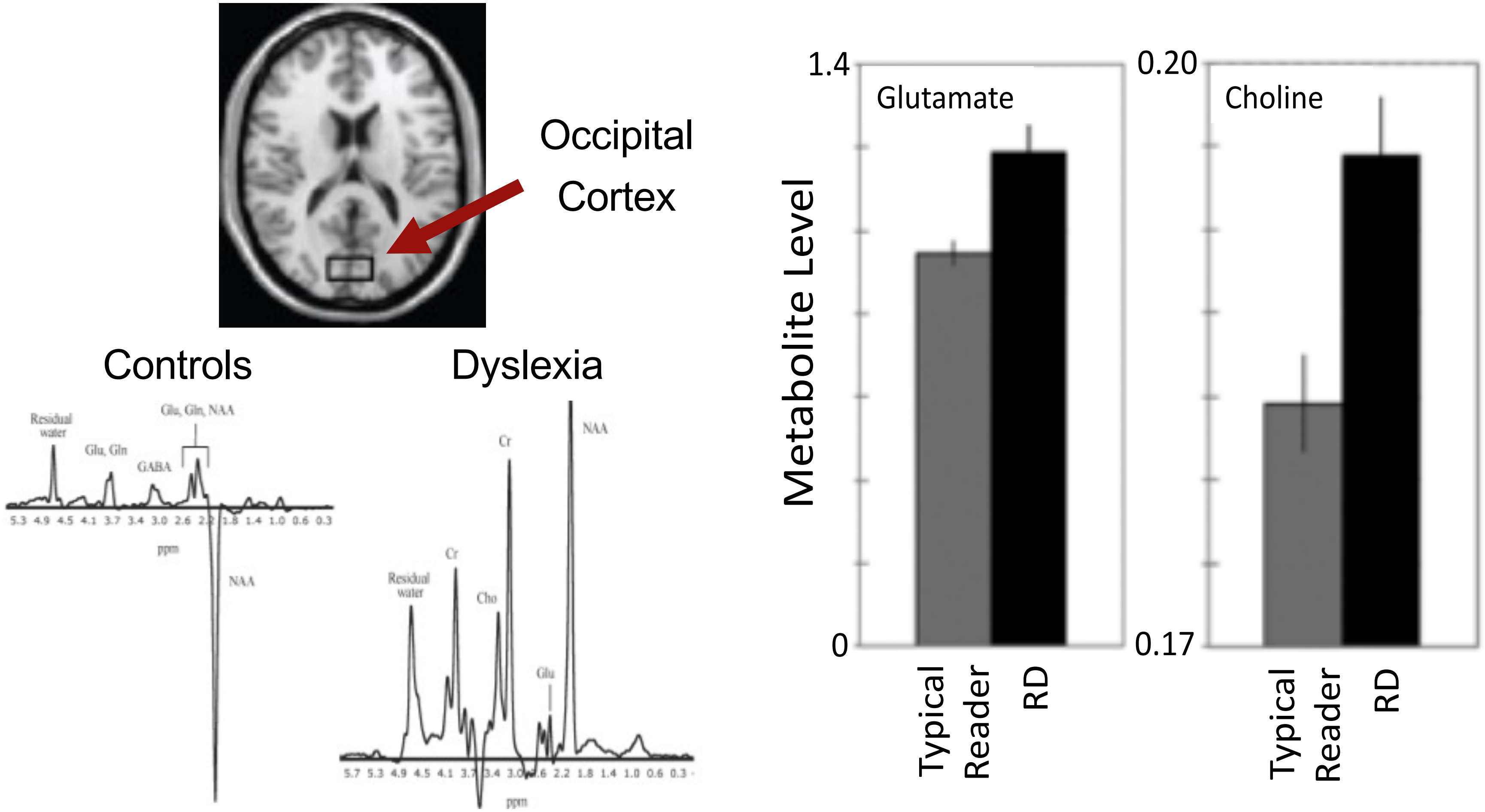
The same etiological context can result in disparate phenotypes, and a single trait can result from

A deeper dive into mechanisms…

- It is critical that we move beyond mere identification of structural and functional biomarkers

toward **brain-based causal models** focused on how and why these structural and functional differences impede the development of LH specialization for print.

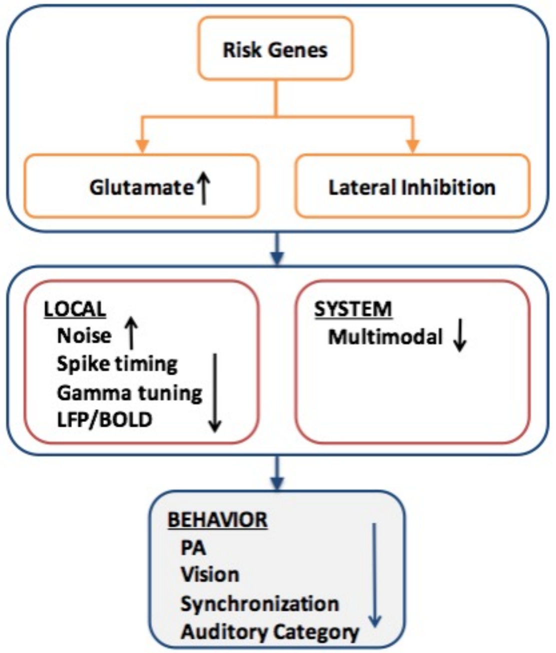
Reading disability: glutamate & choline links (Pugh et al., J Neuroscience 2014)

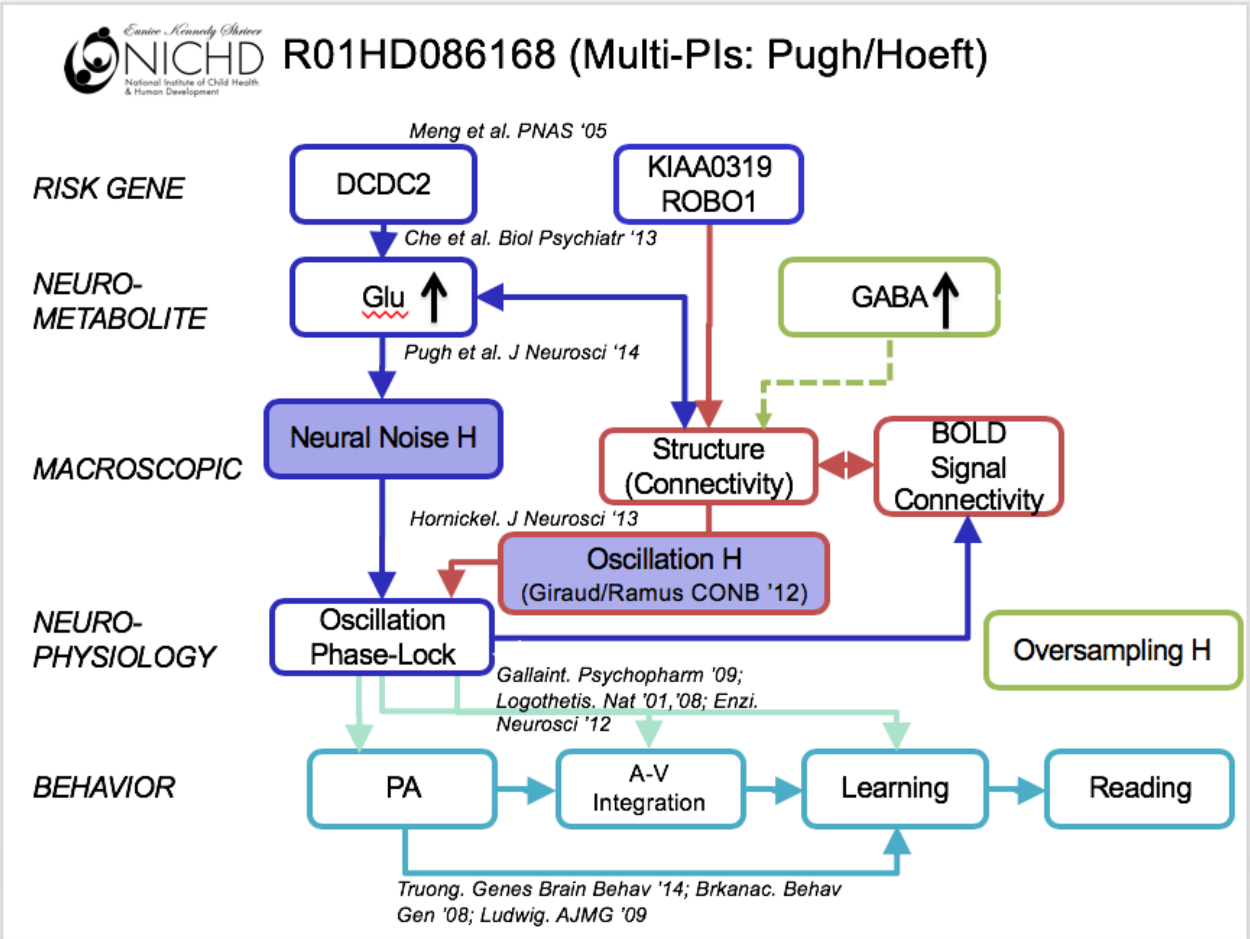


Neural Noise Hypothesis

Hancock, Pugh, Hoeft, TICS 2017

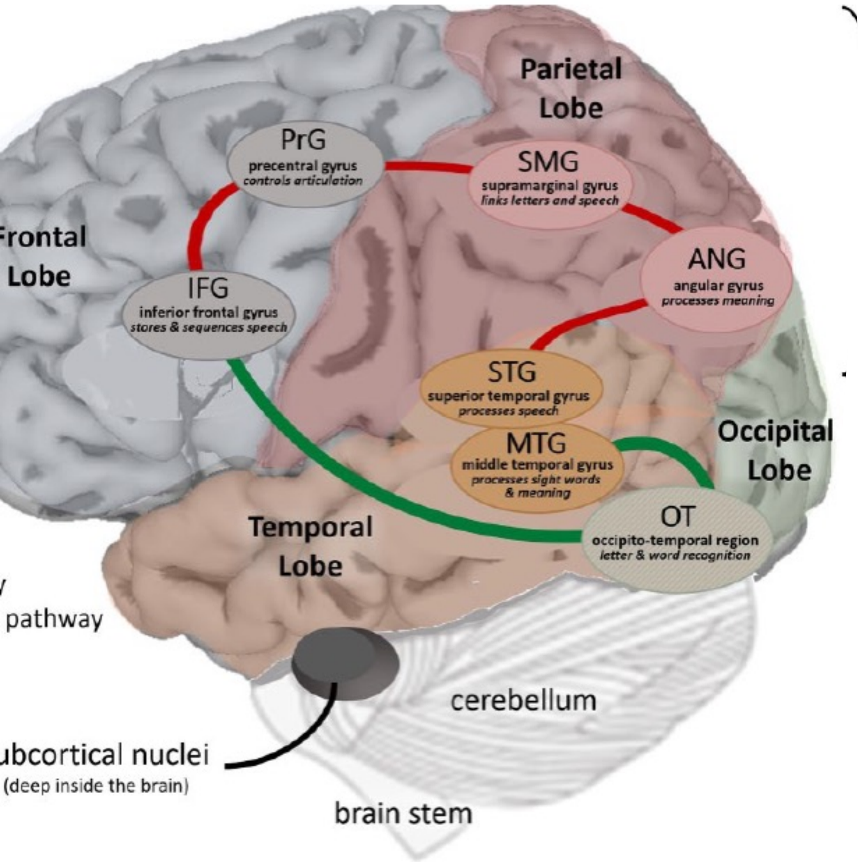
- Excess neural noise disrupts precise spike timing needed for
  - auditory processing and temporal integration
  - multi-sensory integration
- Possibly due to hyper excitability in critical reading-related neocortical regions
- Empirical framework for integrating animal, human and intervention studies





Value-added by neuroimaging thus far…

- Limited causal models to date (work ongoing)
- But
- the current state of the literature on neurophenotypes in reading disability does provide clear neurobiological targets for intervention….



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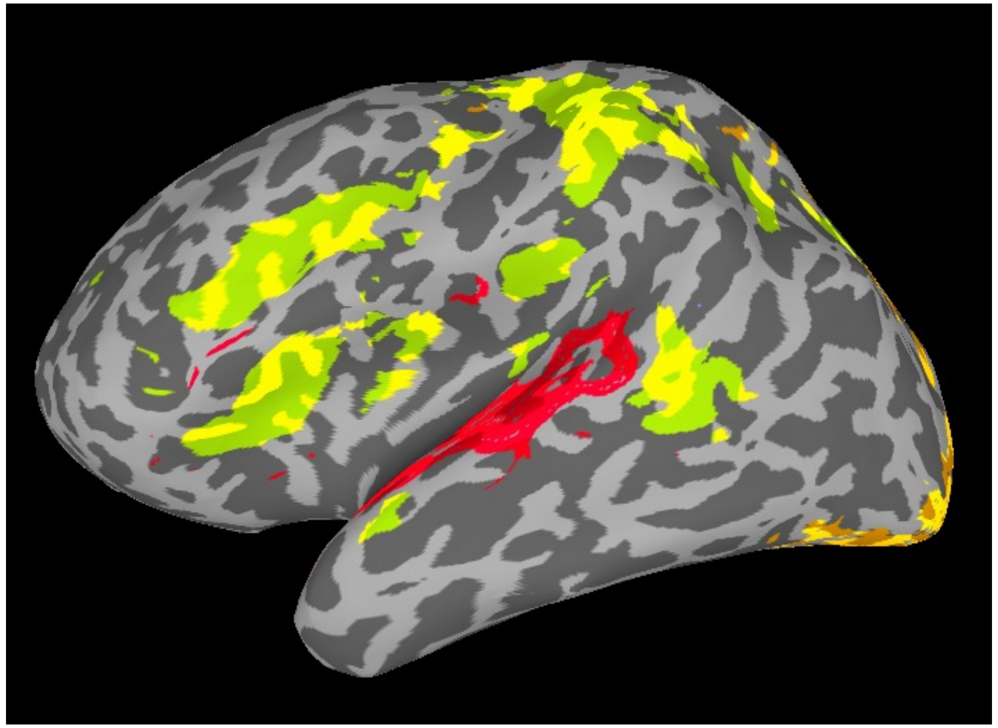
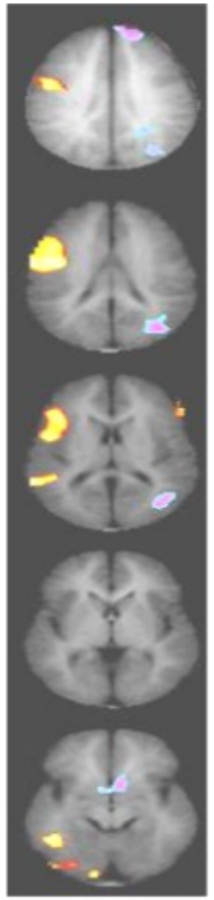
Treatment Studies: Strengthening print/speech connections



A consistent story on treatment effects is emerging…

- A growing number of treatment studies have shown modulation of LH reading circuits with effective treatment (see Richlan 2021 for review)

- **However, we must better understand why some children do not respond to conventional treatment and what to do for this kids!**



Treatment can modify trajectory
(Shaywitz Pugh et al. BP 2004)

Individual differences in intervention gains

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A large body of evidence regarding the types of interventions that are effective at remediating reading disabilities (RD) *on average.*

A significant proportion of children with RD fail to respond even to the best available interventions.

- ~30% low responders (Torgesen, 2000)

The challenge: Limited predictive value
(see meta-analysis: Stuebing et al., 2015)

Can the sensitivity of cognitive neuroscience methodologies to individual differences improve this situation?

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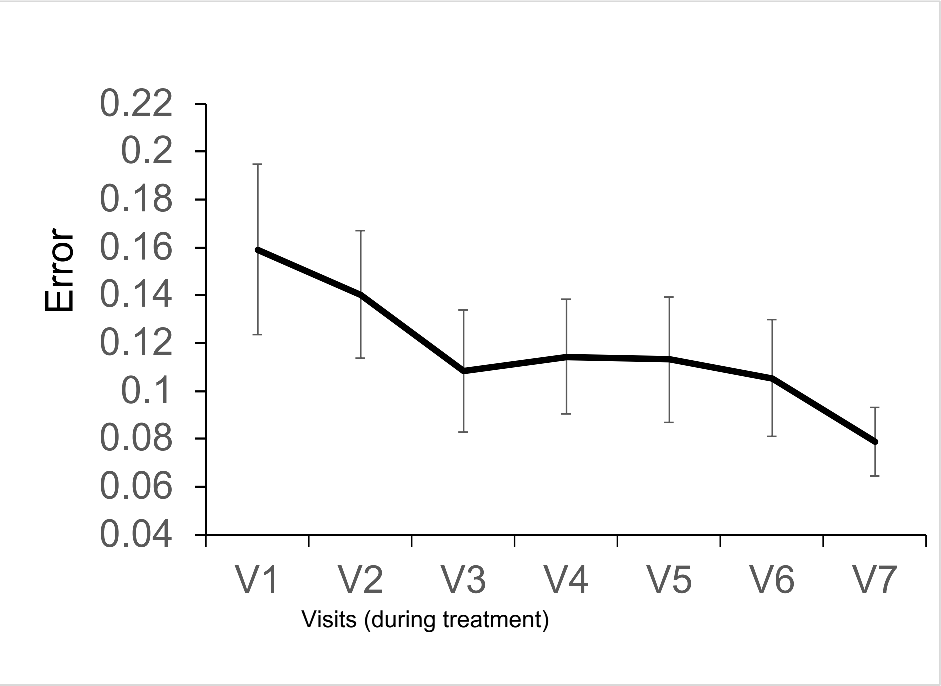
Neurocognitive bases of treatment resistance in developmental dyslexia

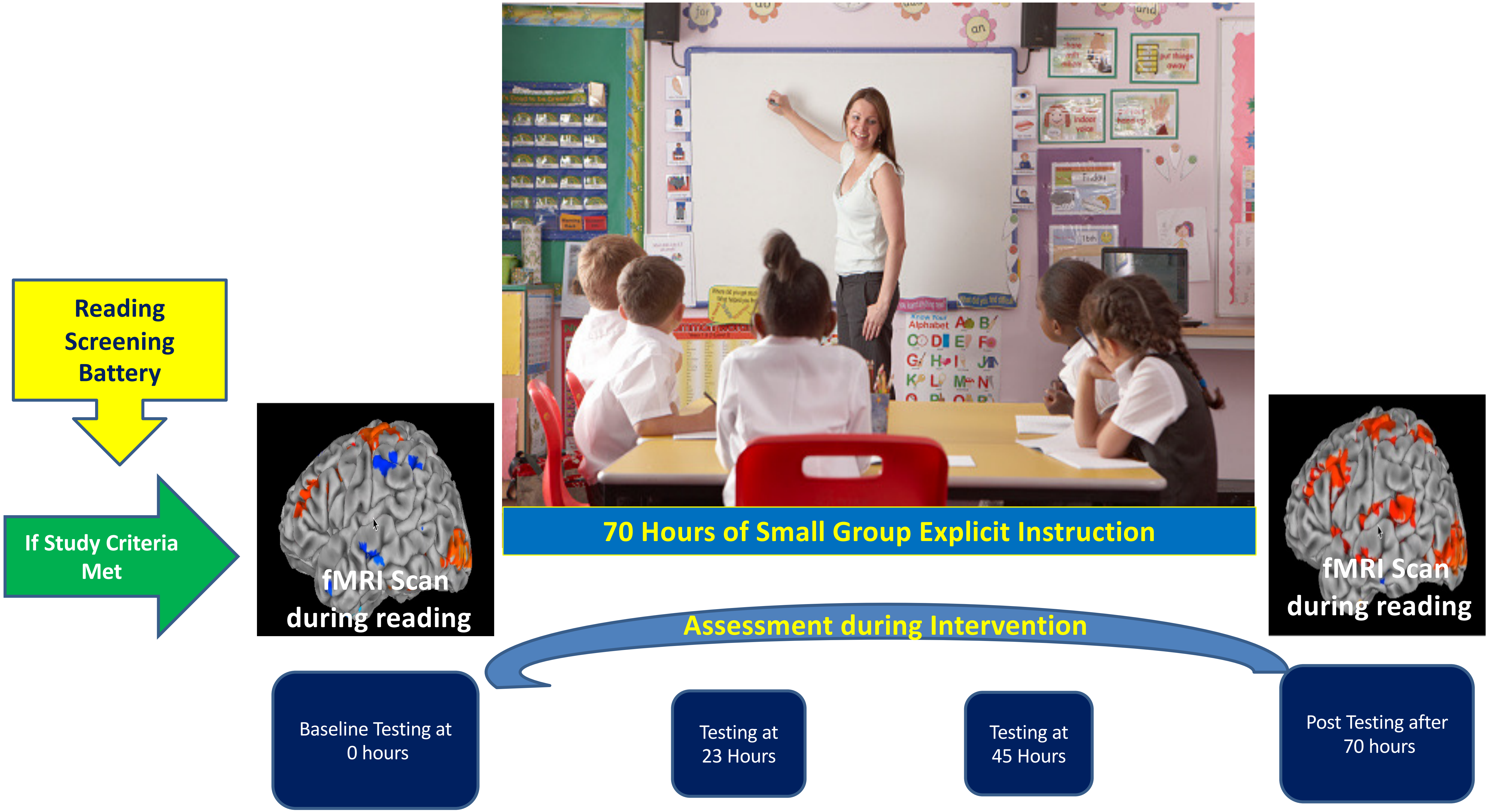
University of Toronto · SickKids · Haskins Laboratories · Brock University 50 1964-2014 · UCONN · USC · Wisconsin University of Wisconsin–Madison · Georgia State University

NIH R37 MERIT Award (Pugh): In a collaboration with Devin Kearns we conducted a a treatment study, and we used frequent multimodal brain imaging sessions during treatment to gain insight into HOW treatment works.

The C.A.R.I.N.G. Project

Reading together
with UConn, Yale,
and Haskins Laboratories.





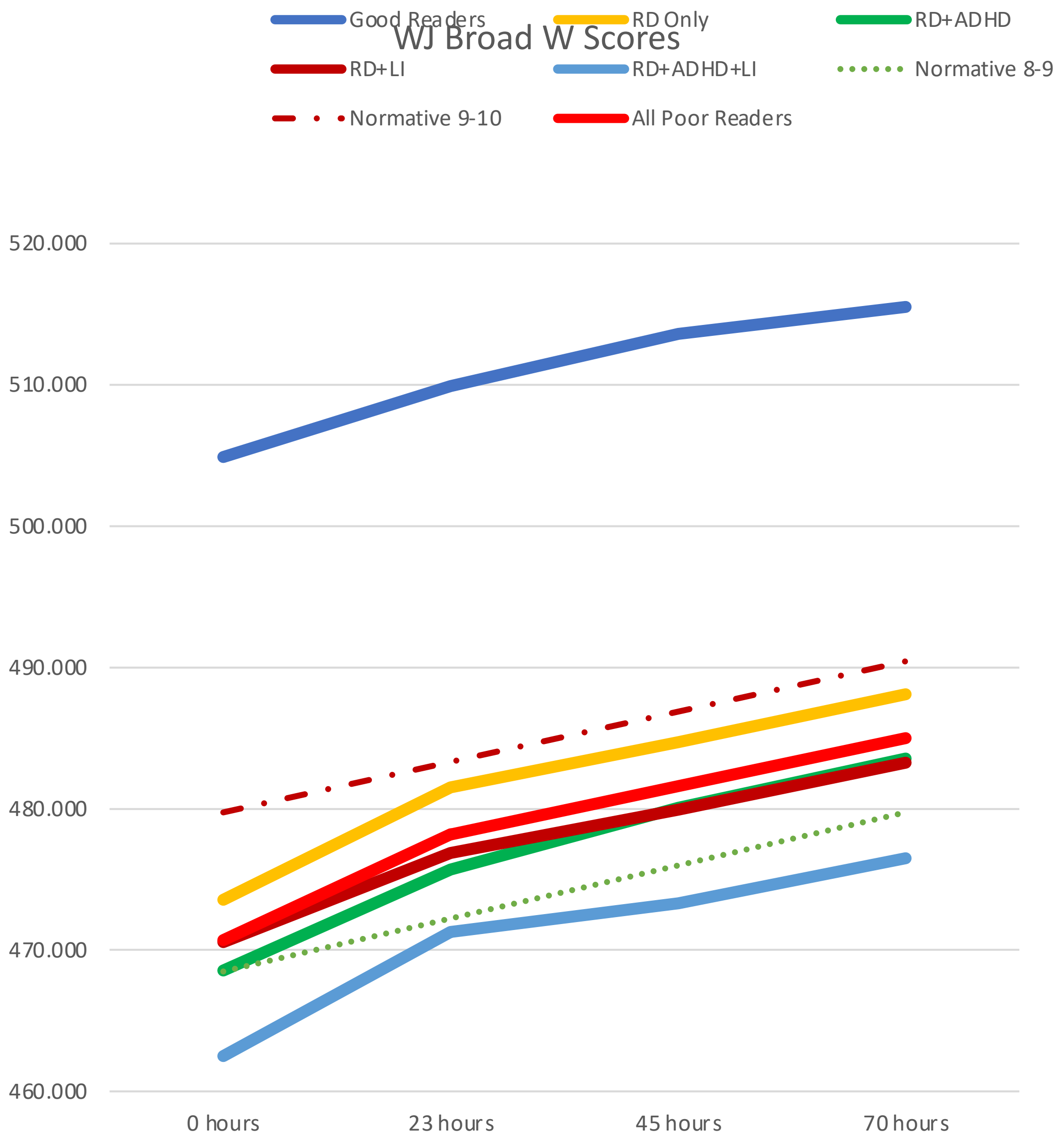
Reading Screening Battery
If Study Criteria Met
fMRI Scan during reading
70 Hours of Small Group Explicit Instruction
fMRI Scan during reading
Assessment during Intervention
Baseline Testing at 0 hours
Testing at 23 Hours
Testing at 45 Hours
Post Testing after 70 hours

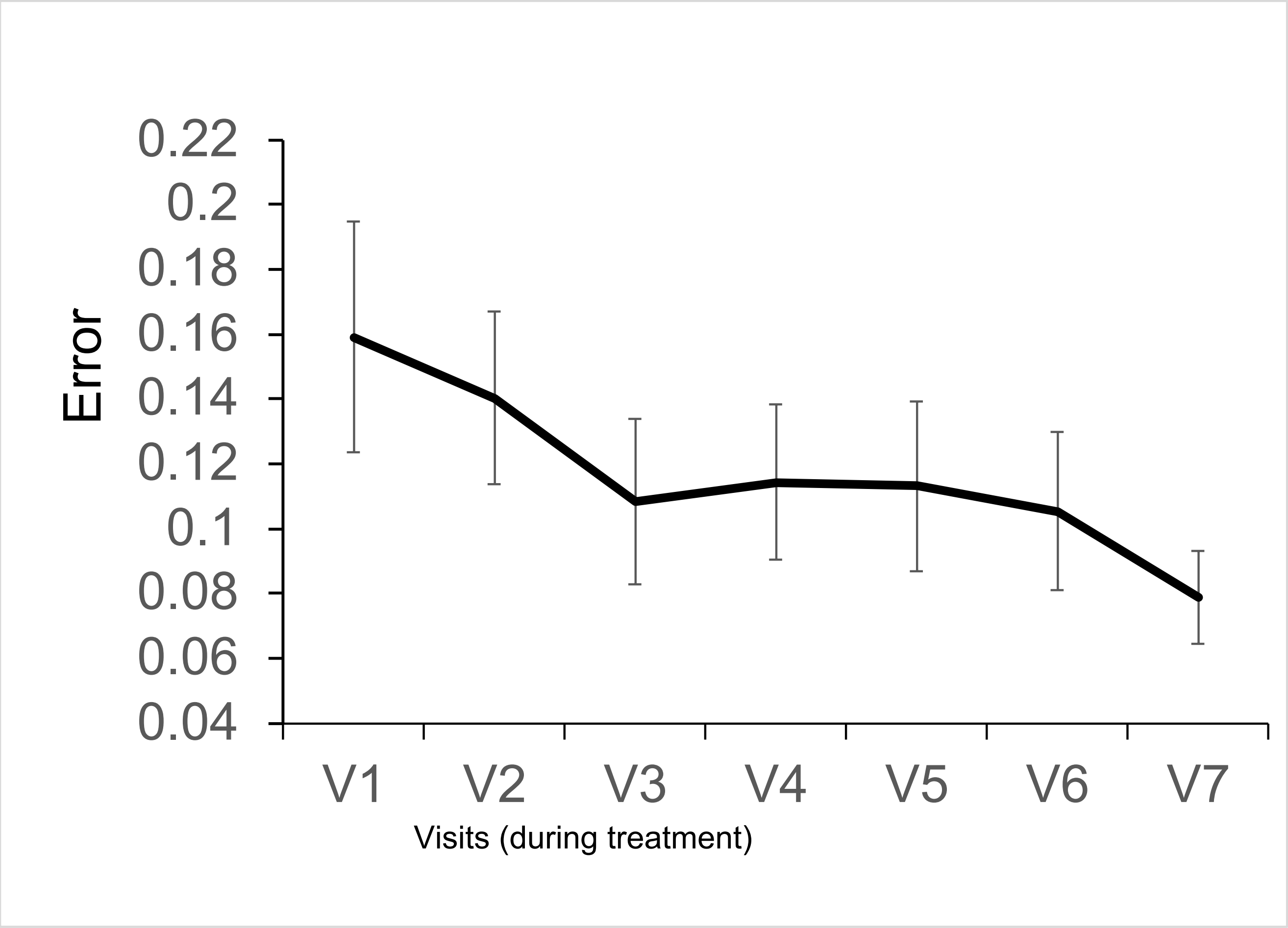
Neuroimaging - fMRI and fNIRS

- **fMRI: Functional Magnetic Resonance Imaging**

- **fNIRS: Functional Near-Infrared Spectroscopy**

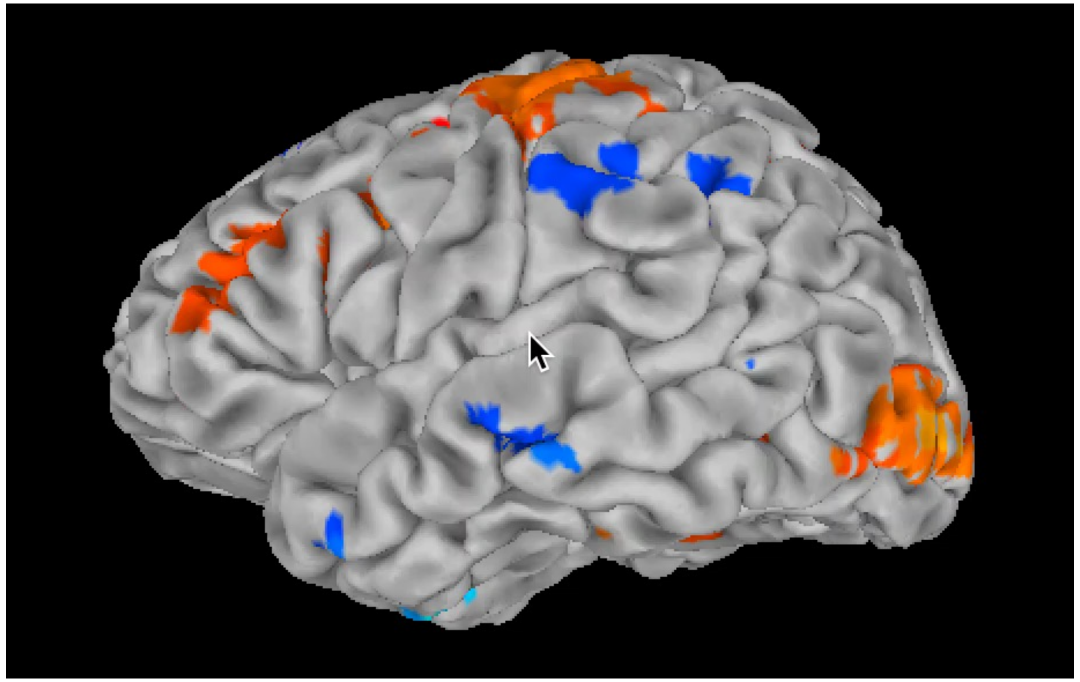
Behavioral data: Changes in reading “on average” over the course of treatment



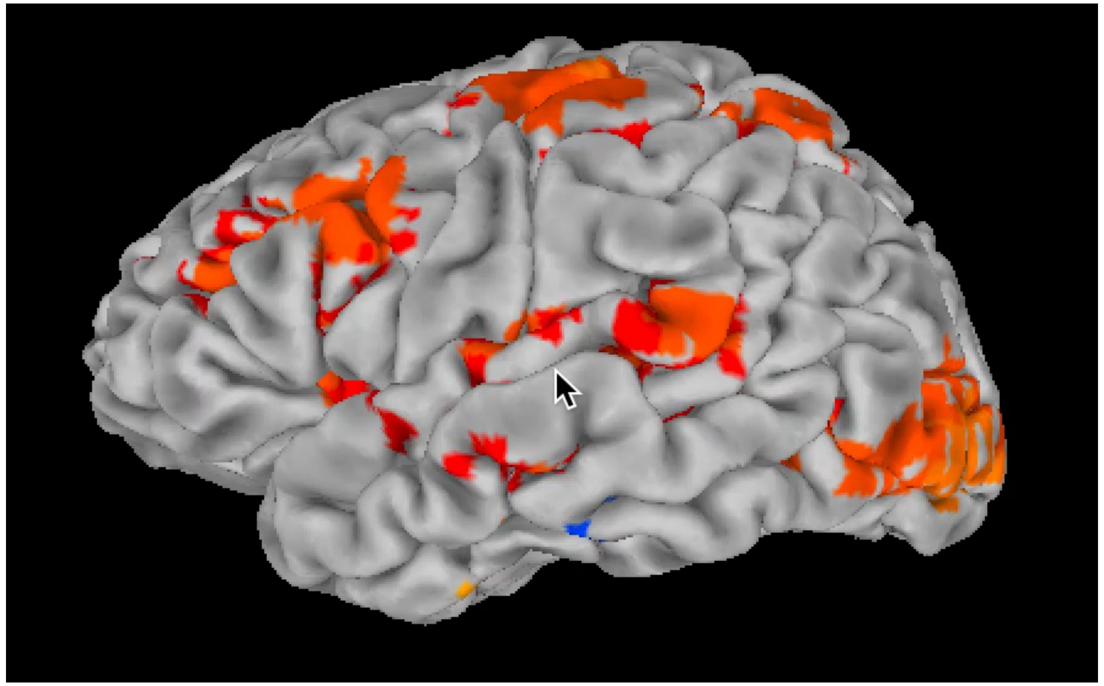


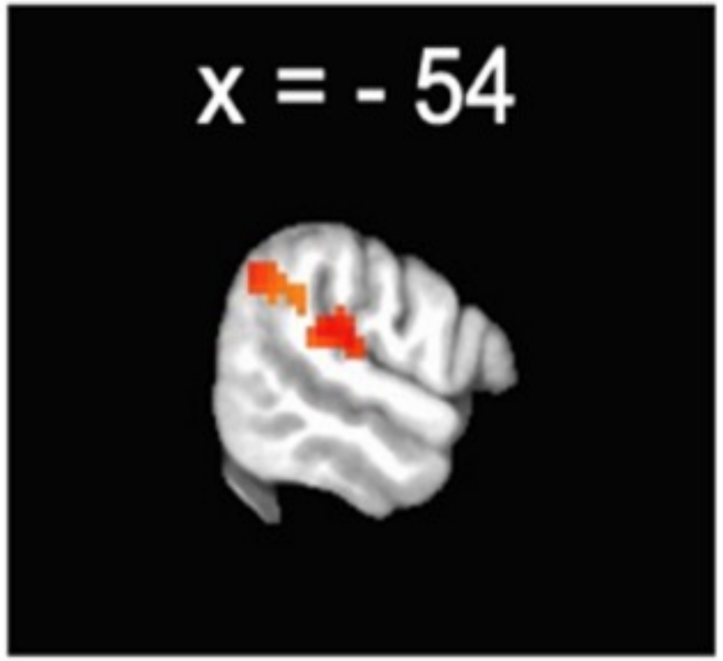
The neurobiological bases of treatment effects

Pre
Intervention



Post
Intervention



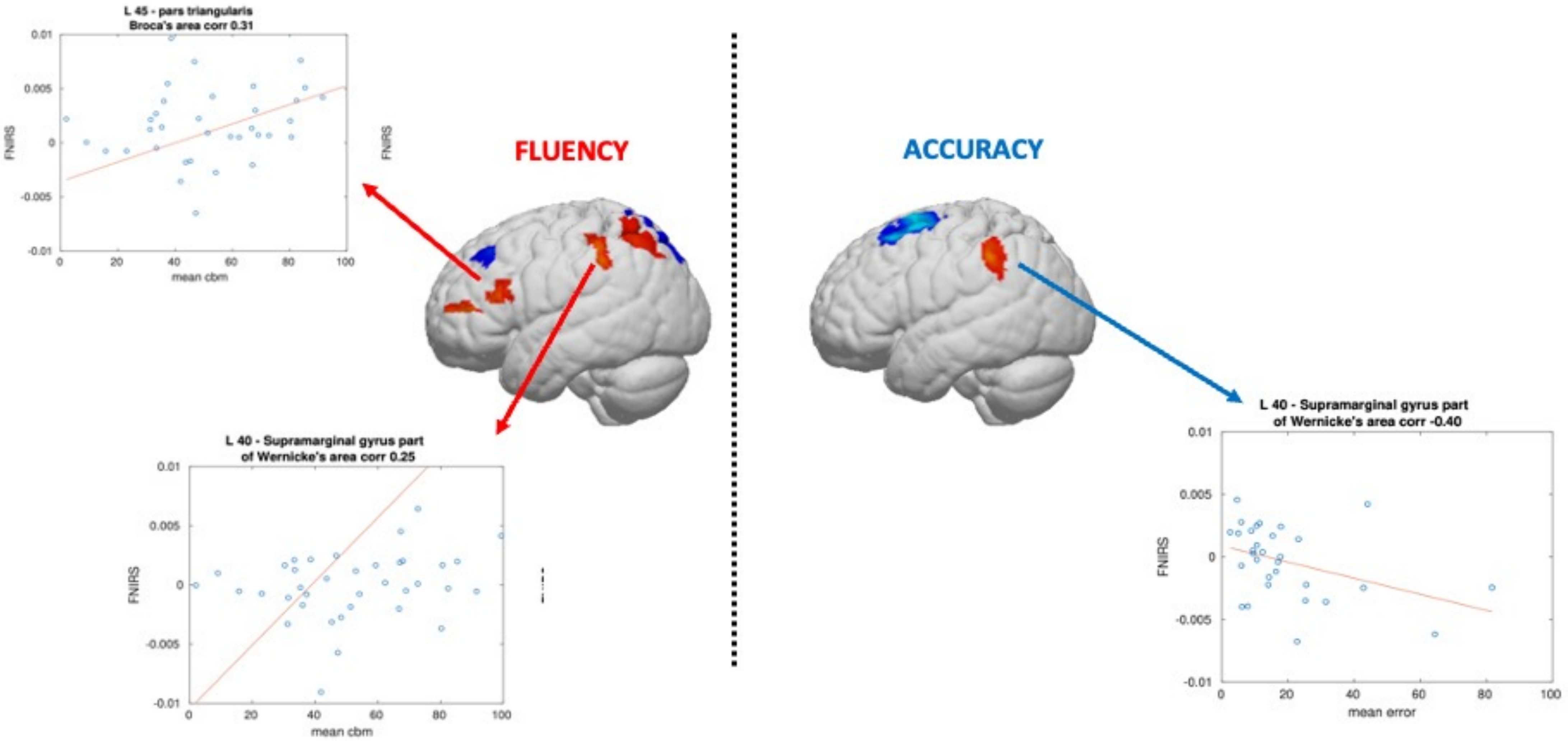


$p < .005$ voxelwise (uncorrected)

Figure 3. Predictors of response to intervention in pre-treatment neural activation.

fNIRS: brain/behavior relations for gains in word reading fluency and accuracy

Brain-behavior relationship for improvements in reading fluency and word reading accuracy.



fNIRS: Better responsiveness is associated with degree of RH to LH shift during learning

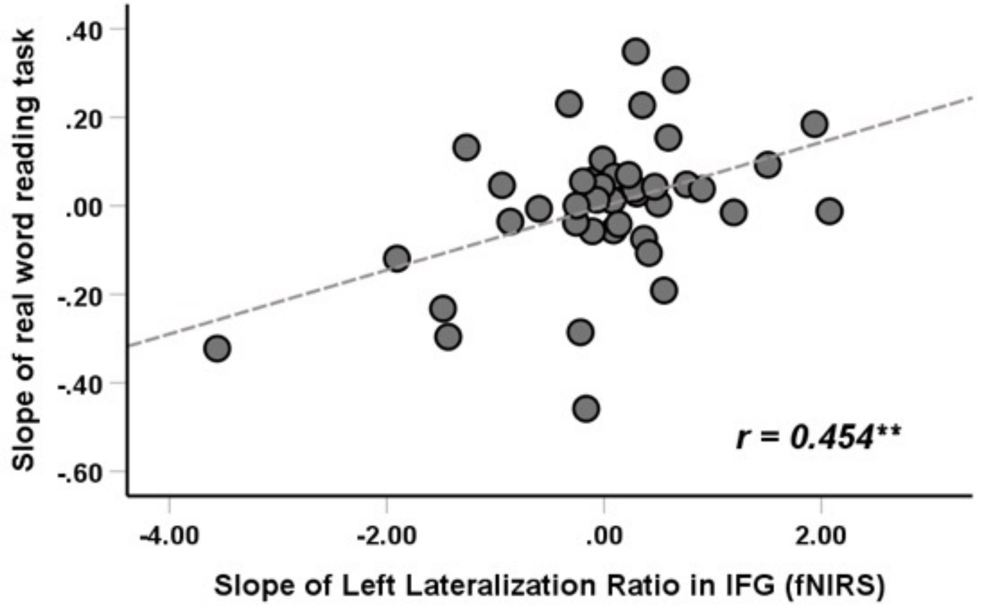
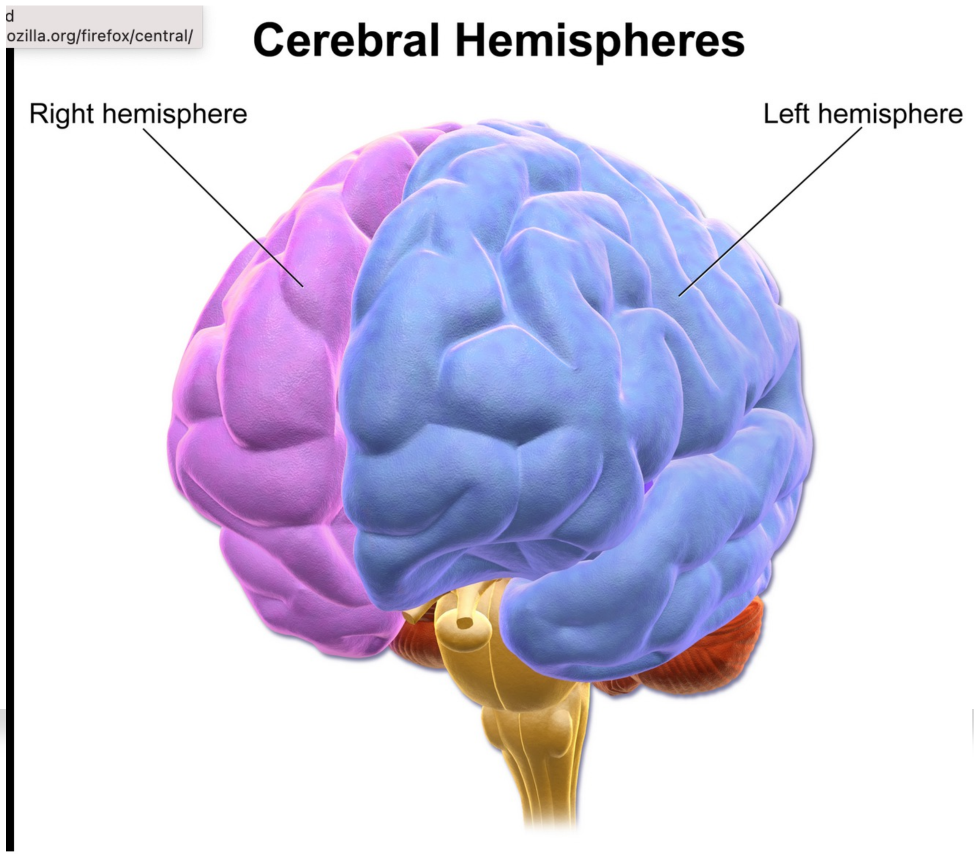


Figure 9. Correlation plot for the neural changes in laterization and behavioral reading performance (intercept controlled).



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Cognitive predictors: Can *the way* in which a child reads predict their response to intervention?

(Siegelman et al., 2020; 2021)

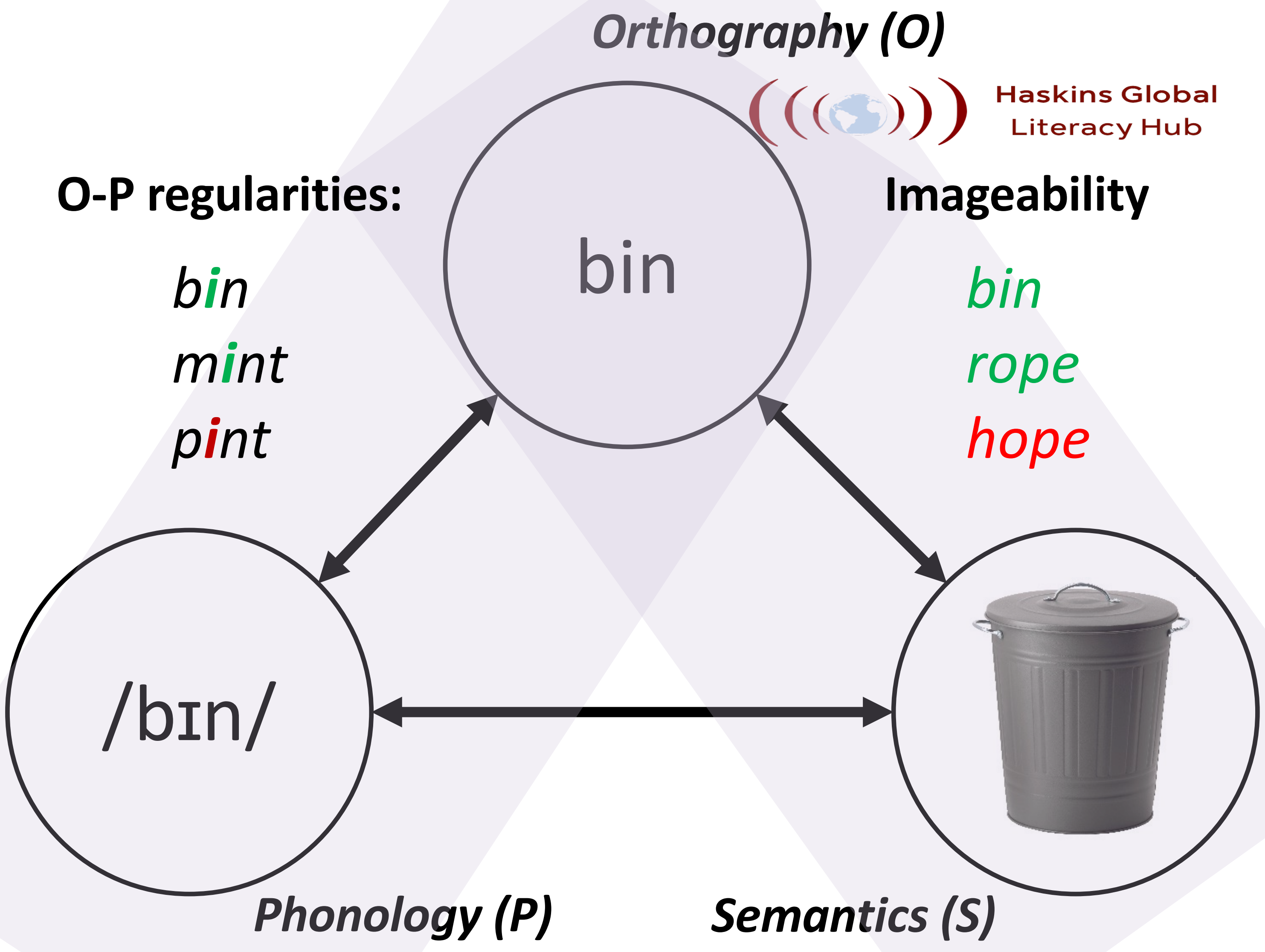
The functional organization of reading system

The Triangle Model of Reading (Seidenberg & McClelland, 1989; Harm & Seidenberg, 2004)

Operationally: Manipulating word properties in a reading task to tap into the reading system's components.

Group-level findings:

- ❑ Readers are impacted by both types of information.
- ❑ Adults show an efficient division of labor between O-P and O-S (Strain et al., 1995)



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Individual differences in reliance on O-P and O-S associations

N=399 2nd-5th graders, a word reading aloud task with 160 trials (modeled after Strain et al., 1995).

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Items vary along the two critical dimensions:

- ❖ O-P regularities (e.g., bin ----- child):
  - Surprisal of the vowel grapheme-phoneme (Siegelman, Kearns, & Rueckl, 2020)
  - e.g., bin, -log(p(i → \ɪ\)) < child, -log(p(i → \aɪ\))
- ❖ Imageability (e.g., dog ----- verb):
  - Standard ratings (Paivio et al. 1968)

For each child, we examine to what extent they **rely on each source of information**:

Slope scores quantifying the relation between a child's accuracy in each trial and item properties.

If a child reads correctly words with increasingly more regular O-P associations

→ evidence for reliance on O-P regularities

If a child reads correctly words that are increasingly more imageable

→ evidence for reliance on O-S processes.

Siegelman et al., 2020, Journal of Memory & Language

Individual differences in reliance on O-P and O-S associations

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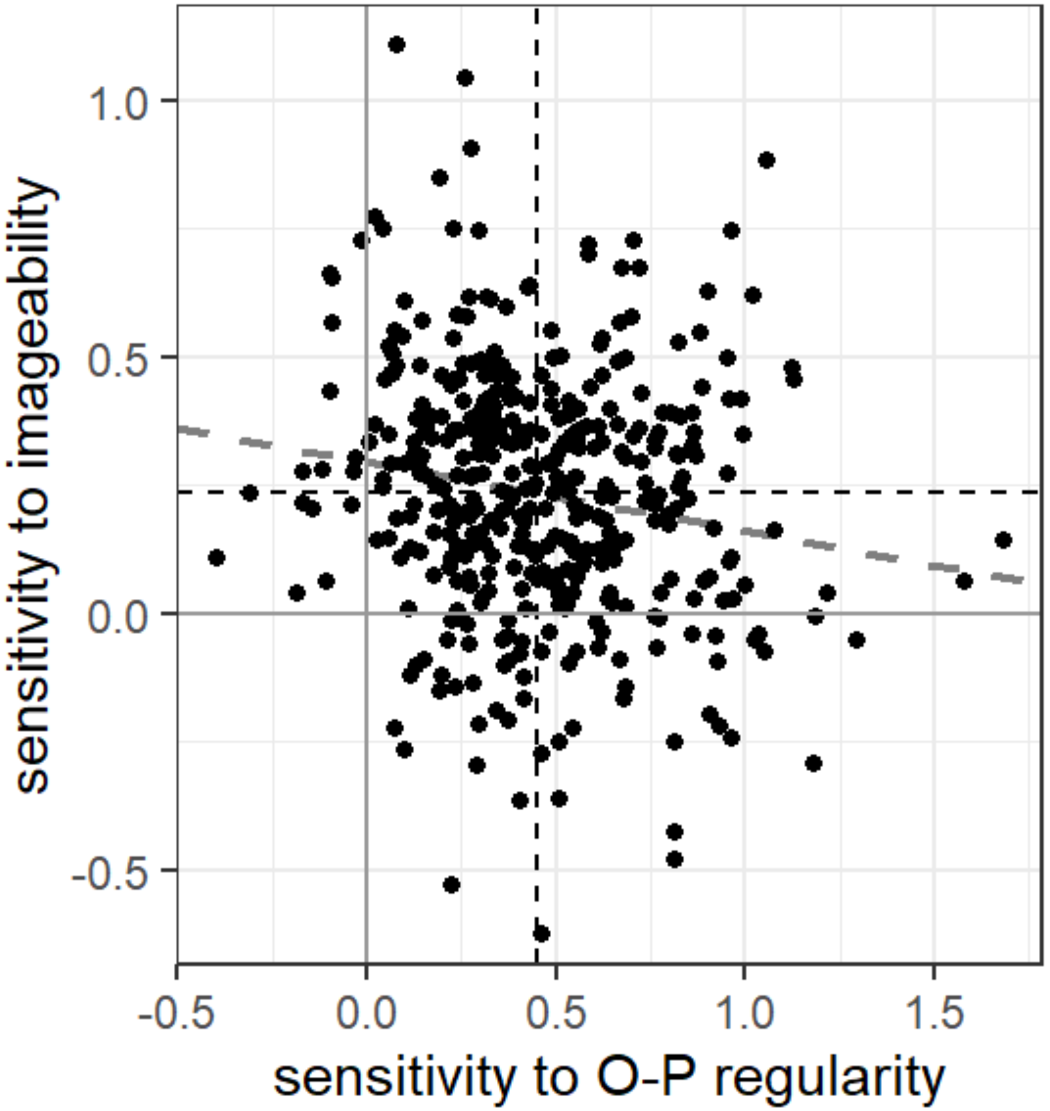

Substantial variability in reliance on O-P and imageability.

Siegelman et al., 2020, Journal of Memory & Language

Individual differences in reliance on O-P and O-S associations

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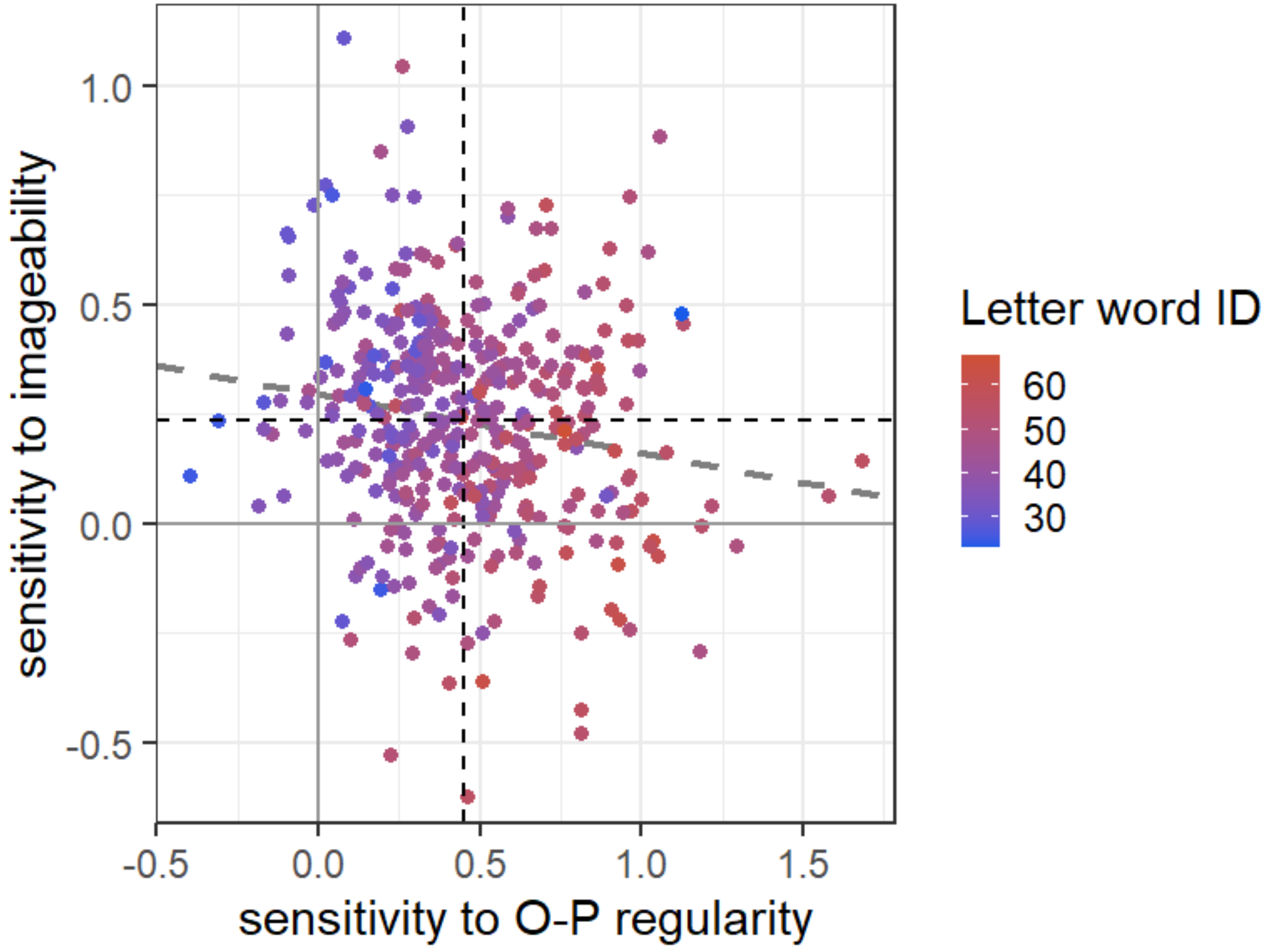

Substantial variability in reliance on O-P and imageability.

These two factors are strong predictors of (concurrent) reading skill (R^2=32-45%):

- ❑ ***Higher*** reliance on ***O-P*** → better reading skill
- ❑ ***Less*** reliance on ***imageability*** → better reading skill

Siegelman et al., 2020, Journal of Memory & Language

Reading Treatment study (Siegelman et al., 2021): Predicting intervention gains

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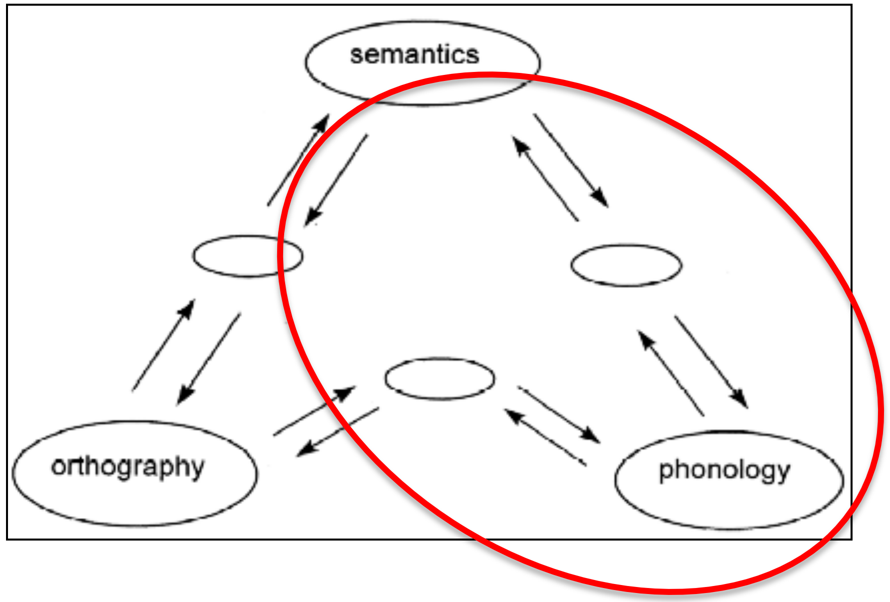
Can a child's pre-intervention reliance on consistency (O-P) or imageability (O-S) predict intervention gains?

The sample: **N=118 RD children** (3rd-4th grade) who go through a **phonologically-weighted intervention program** (PHAST program, Lovett et al., 2000).

Key findings
(Siegelman et al., 2021)



- **At pre-test,** individual-differences in reliance on O-P consistency and O-S imageability are strongly predictive of reading skills.

- Both are very strong predictors of treatment outcomes but in opposite direction:

- **More pre-intervention sensitivity to consistency** (greater reliance on O-P) **and less pre-intervention sensitivity to imageability** (less initial reliance on O-S) predict **better response to treatment** across reading sub-tests.

- This has rather profound implications for how we should teach reading and/or remediate reading difficulties!

Results: Controlling for 'typical' predictors of gains

Pre-intervention scores in: vocabulary, phonological awareness, auditory attention, IQ, and RAN.

Limited unique R^2 associated with 'typical' predictors

In measures of word and pseudoword gains: All ΔR^2: 1.4-6.6%.

Reliance on O-P and imageability still predict gains:

Significant predictors remain significant; Non-significant remain non-significant.

Added predictive value: ΔR^2: 7.8-21.3%.

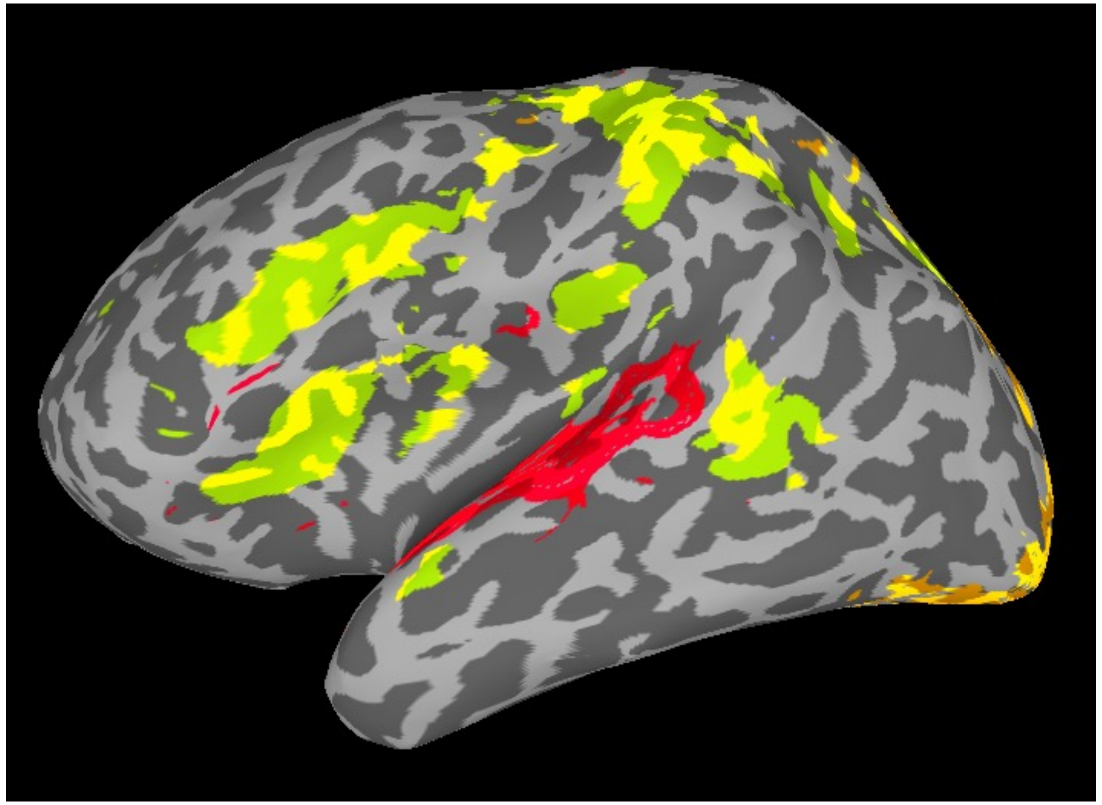
Siegelman et al., 2021, Journal of Educational Psychology

fMRI: Print-speech convergence and how individuals read (i)

Measures of reliance on consistency and imageability associated with print speech overlap in STG, IFG, IPC and FG (both left and right) in ~90 struggling readers (9 years old)

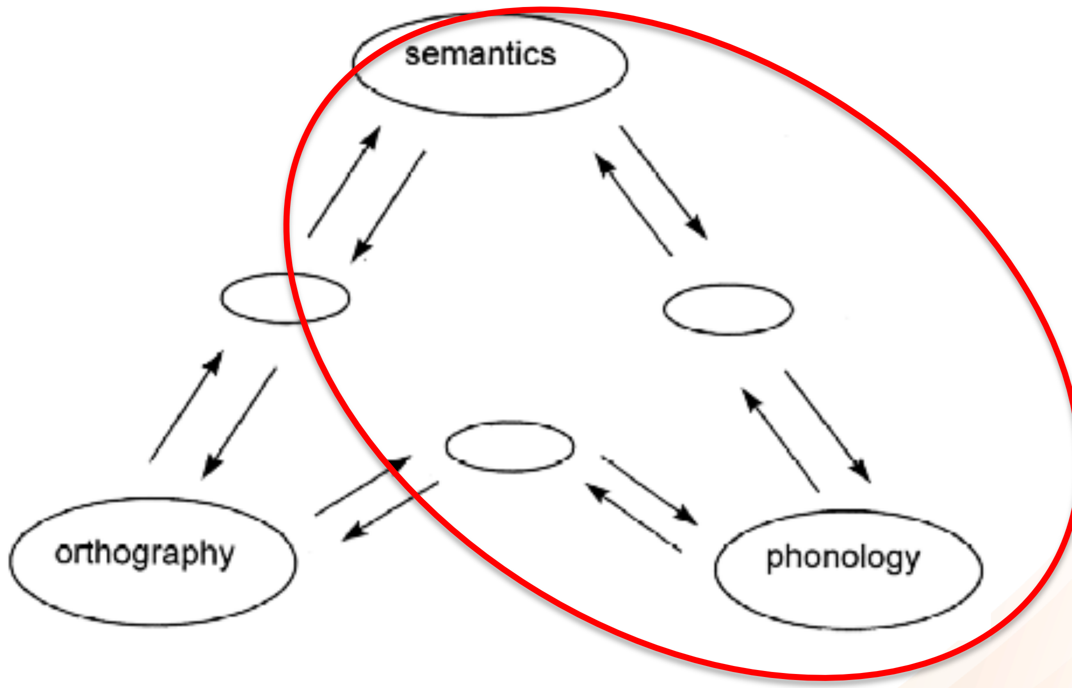
Correlations when controlled for total print & speech activation + Age

	Consistency	Imageability	Word reading
Left ROIs	**.42**	**-.22**	**.32**
Right ROIs	.12	-.04	.05



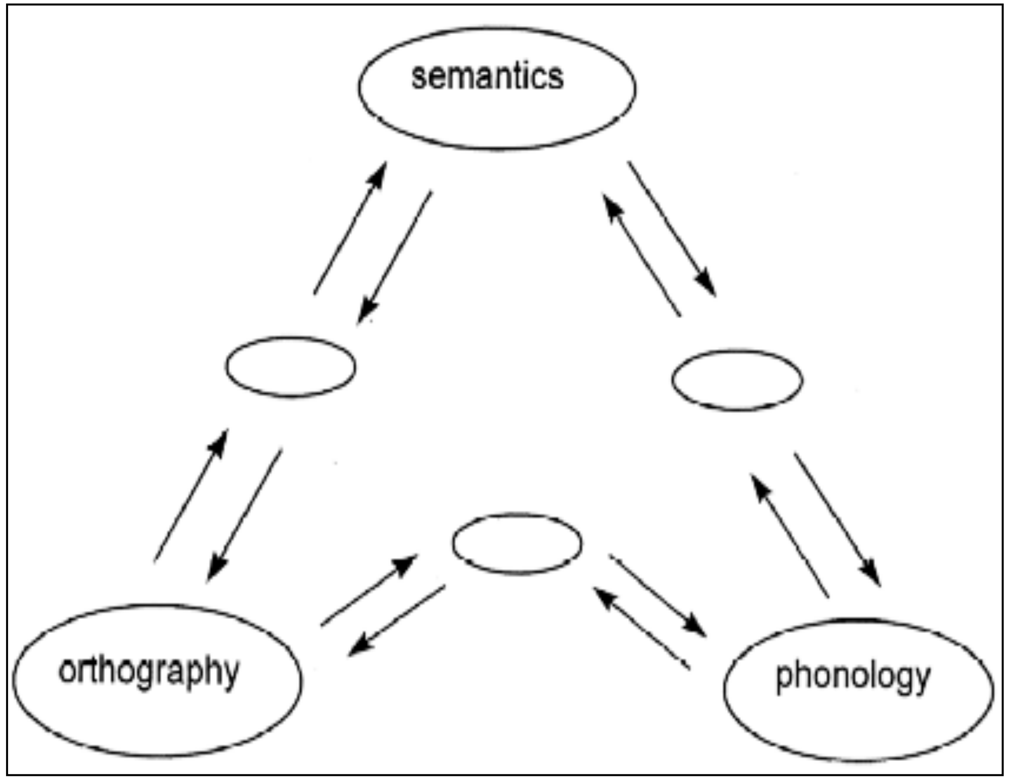
Next steps: Questions being addressed in the Year 6-10 continuation of the NIH R37 MERIT grant project

- **What causes** these individual differences in relative reliance on O-P or O-S in reading?
- **Can we move** at-risk kids stuck in this suboptimal "state-space" to a more efficient code emphasis?
- Should we use more intense programs of the same type or ones with a greater emphasis on additional reading and language components?
- Do we need additional focus on EF problems, anxiety mitigation, and the like in low responders?
- Can we tailor the content to the brain (brain-guided learning) using BCI and neurofeedback?



Years 6-10 extension studies for R37:

Integrated fNIRS/EEG during learning experiments that vary code emphasis in order to examine the neurocognitive bases of individual differences in optimal code learning and to move toward brain-informed content



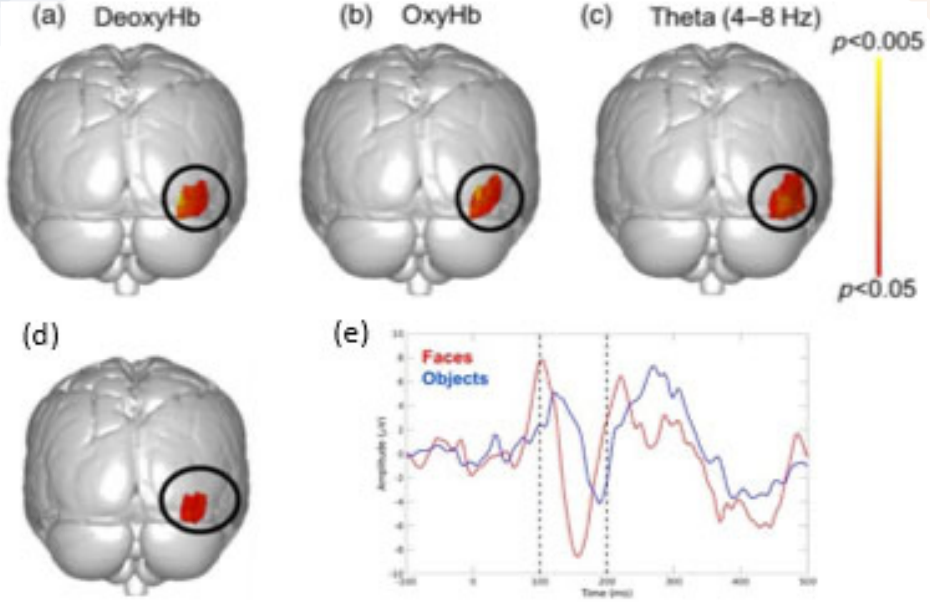


Figure 1. Comparison of fNIRS (A and B) and EEG responses (C, D, and E) for contrast face > object. These are responses to conventional static stimuli. Hemodynamic responses are shown in ventral occipital face area (indicated by black circle) for deOxyHb and OxyHb signals (A, B). Co-localization of EEG responses during face vs object task for theta power spectra (C). ERP comparison of n170 responses for face versus object responses (E). Source localized n170 response (D). (Dravida et al 2019).

fNIRS- Koirala et al., in prep

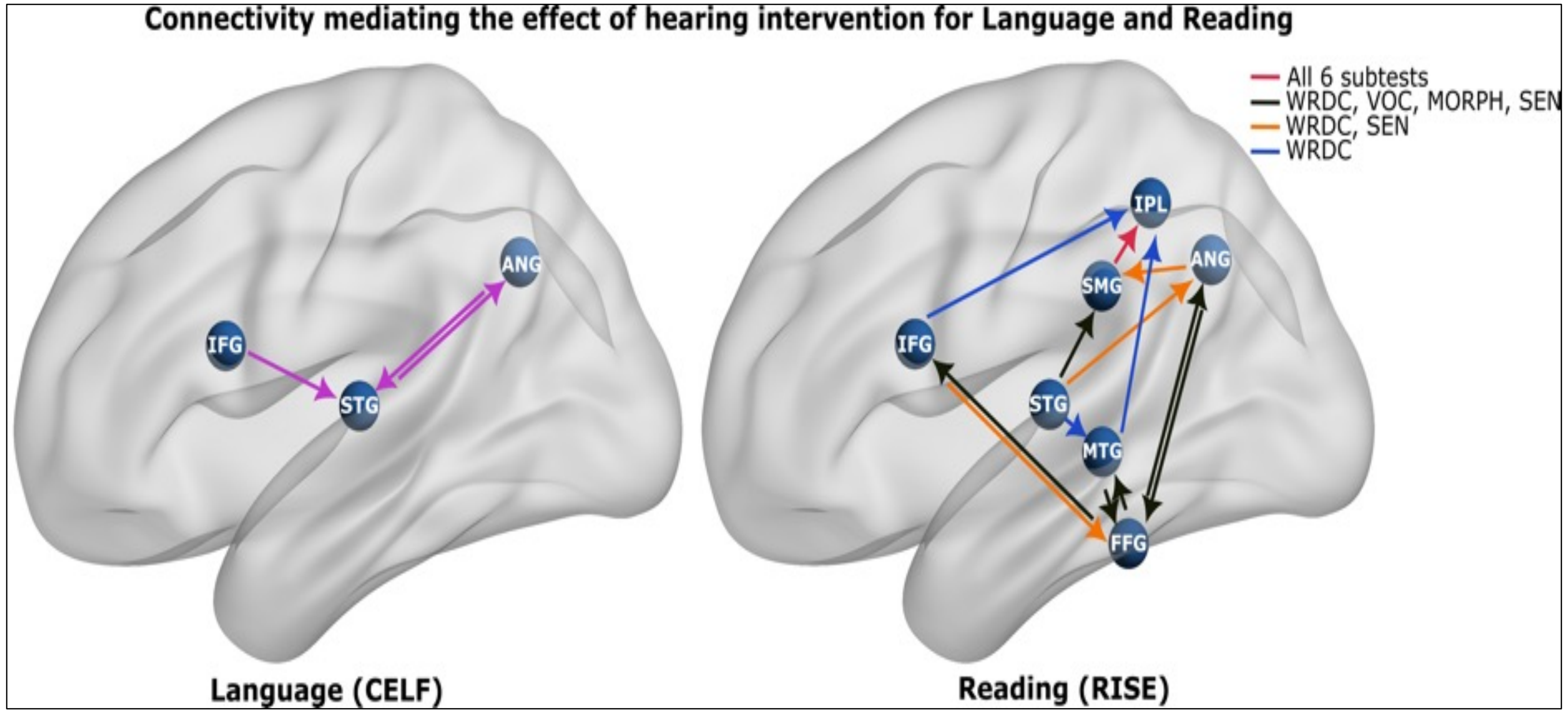


Figure 10: Significant connections mediating the effect of intervention factor (age of initial hearing intervention) to the language and reading outcome for CI children. Direction of the arrow indicates the direction of causality.

EEG—Koirala et al., 2023

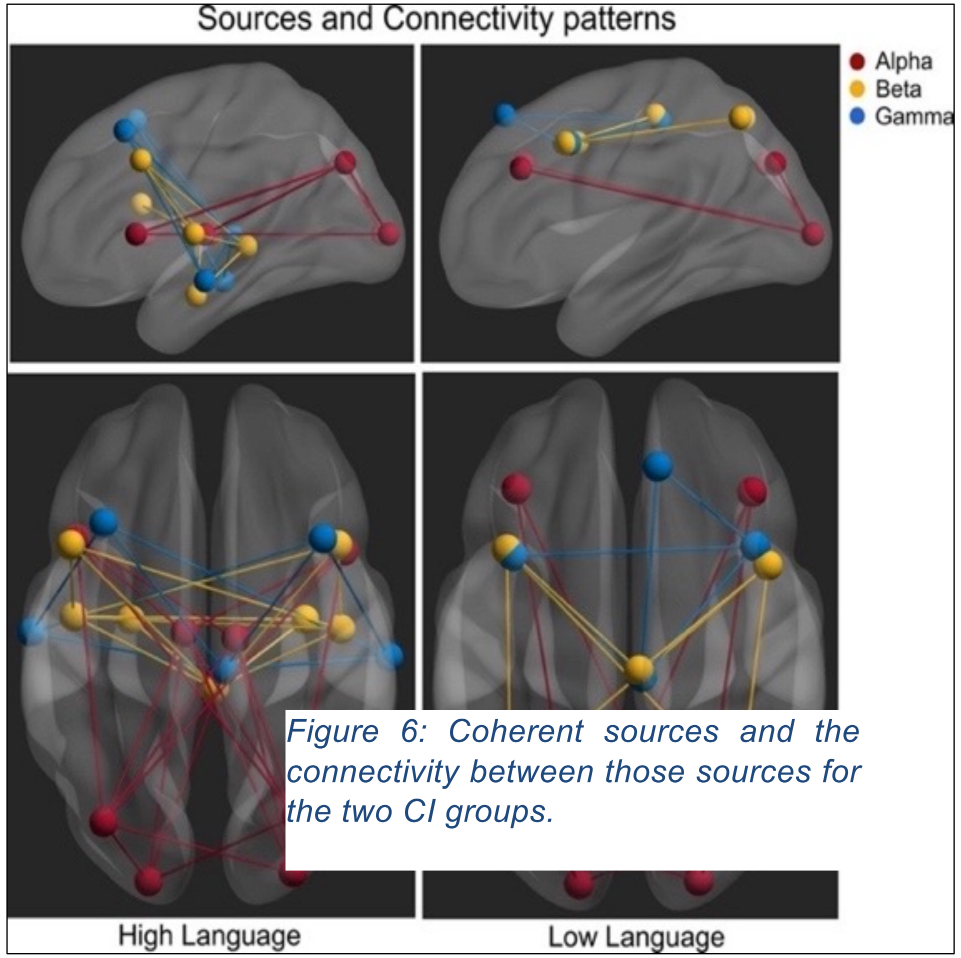


Figure 6: Coherent sources and the connectivity between those sources for the two CI groups.

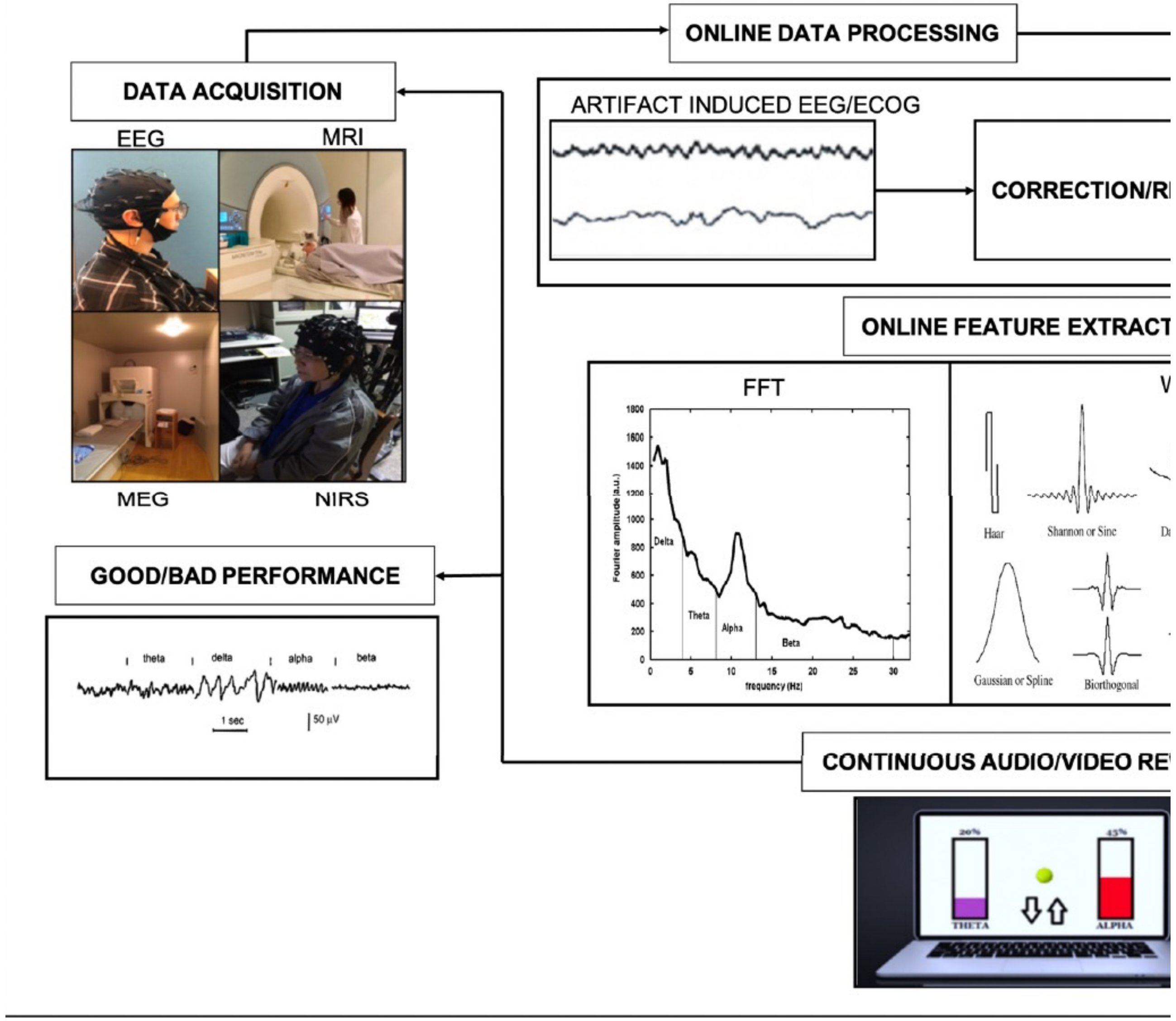
https://doi.org/10.3389/fnins.2023.1141886

- **New Directions for this project in Years 7-*10*:**

- Brain Computer Interface (BCI)

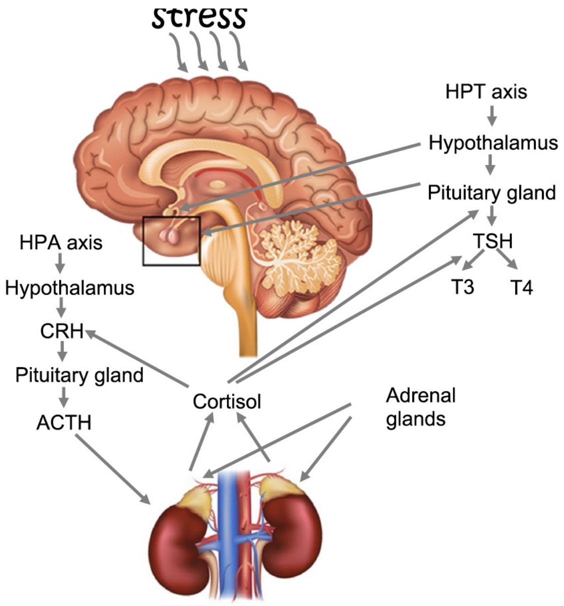
- and

- Neurofeedback training



****A brief final word about anxiety and learning difficulties and the potential of mindfulness programs to address this problem****

Buddhist monk Matthieu Ricard in preparation for conducting an electroencephalography (EEG) test at the EEG facility in the Waisman Center at the



Trends in Endocrinology & Metabolism

Figure 1. The Role of the Endocrine System in Mediating Stress. Abbreviations: ACTH, Adrenocorticotropin hormone; CRH, corticotropin-releasing hormone; HPA, hypothalamic–pituitary–adrenal; HPT, hypothalamic–pituitary–thyroid; T3, triiodothyronine; T4, thyroxine; TSH, thyroid-stimulating hormone.

Trends in Endocrinology & Metabolism, July 2020, Vol. 31, No. 7 47

Clinical Research and Biomedical Implications

Psychoneuroendocrinology 68 (2016) 117–125

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

Reduced stress and inflammatory responsiveness in experienced meditators compared to a matched healthy control group

Melissa A. Rosenkranz[a,*], Antoine Lutz[a,b,c], David M. Perlman[a,d], David R.W. Bachhuber[a], Brianna S. Schuyler[a], Donal G. MacCoon, Richard J. Davidson[a,d,e]

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Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Brief, daily meditation enhances attention, memory, mood, and emotional regulation in non-experienced meditators

Julia C. Basso[a,b,*], Alexandra McHale[a], Victoria Ende[a], Douglas J. Oberlin[a], Wendy A. Suzuki[a,*]

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GRAPHICAL ABSTRACT

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Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Differential DNA methylation in experienced meditators after an intensive day of mindfulness-based practice: Implications for immune-related pathways

R. Chaix[a,*], M. Fagny[b], M. Cosin-Tomás[c], M. Alvarez-López[d], L. Lemee[e,f], B. Regnault[e,g], R.J. Davidson[h], A. Lutz[i], P. Kaliman[h,j,*]

Social Cognitive and Affective Neuroscience, 2019, 777–787

doi: 10.1093/scan/nsz050
Advance Access Publication Date: 3 July 2019
Original article

Mindfulness-Based Stress Reduction-related changes in posterior cingulate resting brain connectivity

Tammi R.A. Kral,[1,2,3] Ted Imhoff-Smith,[1] Douglas C. Dean, III[1,3] Dan Grupe,[1,3] Nagesh Adluru,[1,3] Elena Patsenko,[1] Jeanette A. Mumford,[1,3] Robin Goldman,[1,3] Melissa A. Rosenkranz,[1,3] and Richard J. Davidson[1,2,3,4,]

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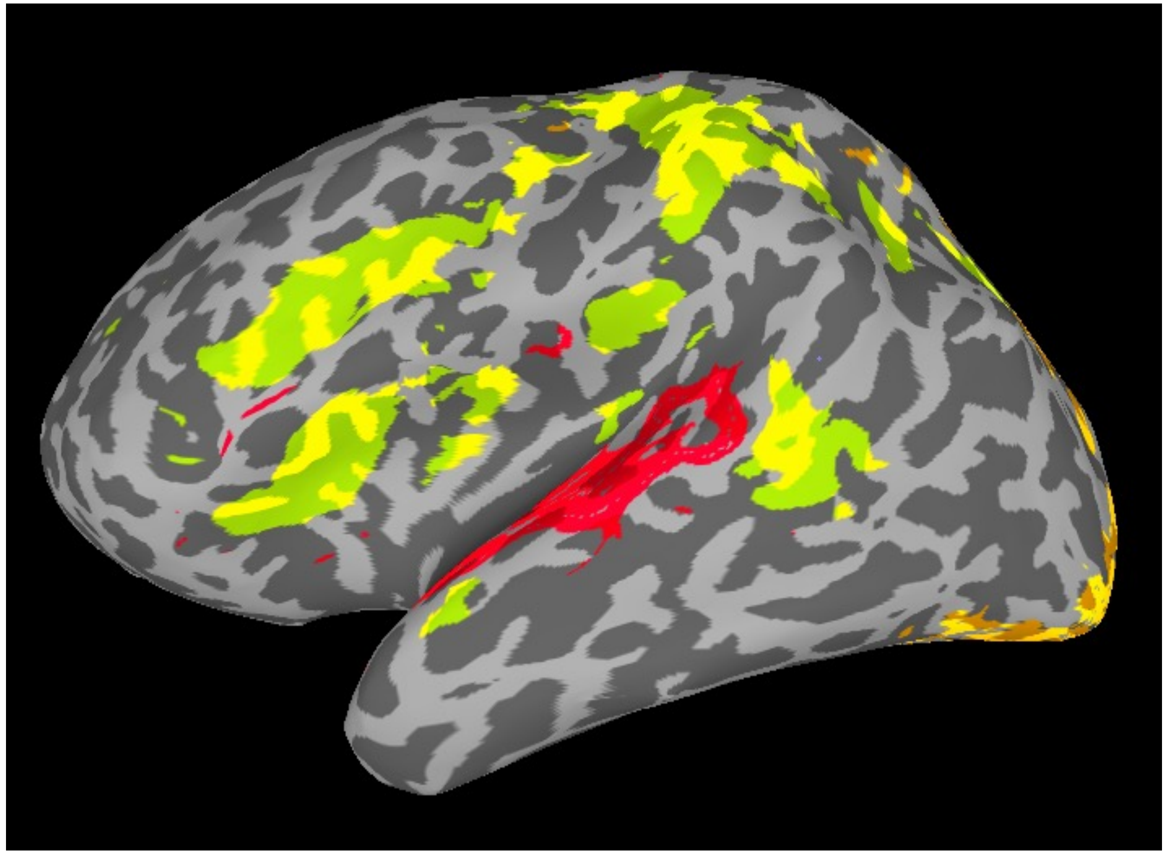
Thanks for your attention!



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