University of Cincinnati

Date: 3/10/2015

I, John S Hutton, hereby submit this original work as part of the requirements for the degree of Master of Science in Clinical and Translational Research.

It is entitled:

Home Reading Environment and Brain Activation in Preschool Children Listening to Stories

Student's name: John S Hutton

This work and its defense approved by:

Committee chair: Erin Nicole Haynes, Dr.P.H.

Committee member: Mekibib Altaye, Ph.D.

Committee member: Scott Holland, Ph.D.



14068

Home Reading Environment and Brain Activation in Preschool Children Listening to Stories

A thesis submitted to the

Graduate School

of the University of Cincinnati

in partial fulfillment of the

requirements for the degree of

Master of Science

in Clinical & Translational Research

In the Department of Environmental Health

Division of Epidemiology & Biostatistics

of the College of Medicine

April, 2015

by

John S. Hutton, MS, MD

Bachelor of Science, Mathematics, Davidson College, 1991 Master of Science, Operations Research, University of North Carolina at Chapel Hill, 1994

Doctor of Medicine, University of Cincinnati, 1998

Committee Chair: Erin N. Haynes, DrPH

Abstract:

Background and Objectives

Parent-child reading is widely advocated to promote cognitive development, including in recommendations from the American Academy of Pediatrics to begin this practice at birth. While parent-child reading has been shown in behavioral studies to improve oral language and print concepts, quantifiable effects on the brain have not been previously studied. Our study utilized blood oxygen level dependent functional magnetic resonance imaging (BOLD fMRI) to examine the relationship between home reading environment and brain activation during a narrative comprehension task in a sample of preschool-age children. We hypothesized that while listening to stories, children with greater home reading exposure would exhibit higher activation of left-sided brain regions involved with semantic processing (extraction of meaning from language).

Methods

A total of twenty-three, 3-5 year-old children enrolled in a longitudinal study of normal brain development (C-MIND) were eligible for this study. All had completed BOLD fMRI using an age-appropriate story listening task, where narrative alternated with tones. Nineteen families were able to be contacted for survey administration and agreed to participate, with four excluded despite multiple attempts. We performed a series of whole-brain regression analyses applying composite, subscale, and individual reading-related items from the validated STIMQ-P measure of home cognitive environment as explanatory variables for BOLD activation, controlling for household income (low or not low, according to 2015 federal poverty guidelines).

Results

Higher reading exposure (STIMQ-P Reading subscale score) was positively correlated (p<0.05, corrected) with BOLD activation in the left-sided parietal-temporal-occipital association cortex supporting mental imagery and semantic processing, adjusting for household income category. These brain areas are critical for oral language, and later integrated into the mature reading network.

Conclusions

Our study findings suggest that children from more stimulating home reading environments show more robust activity in brain regions supporting mental imagery and narrative processing, key emergent literacy skills. These neural biomarkers may help inform eco-bio-developmental models of emergent literacy and its promotion, and guide further research into the foundations of reading readiness.

Copyright Notice:

This manuscript is currently under consideration for publication in the journal, *Pediatrics*.

Table of Contents:

Title and Author Information

Contributor's Statement

Structured Abstract

Introduction

Methods

Participants
Behavioral Measures
Functional MRI Acquisition Specifications and Preliminary Analyses
Narrative Comprehension Task
Regression with STIMQ-P

Results

Demographic Characteristics STIMQ-P and Other Behavioral Predictors Group Mean Activation for the Narrative Comprehension Task Regression of Neural Activation with STIMQ-P Scores and Other Predictors

Discussion

Conclusion

Acknowledgments

References

Tables and Figures

List of Tables and Figures:

- **Table 1.** Demographic characteristics of C-MIND sample subjects.
- **Table 2**. STIMQ-P scores and responses to reading-related items.
- **Figure 1.** Group mean activation map for the narrative comprehension task.
- **Figure 2.** Regression map (stories>tones activation) with STIMQ-P Reading subscale score as explanatory variable.
- **Figure 3.** Regression map (stories>tones activation) with STIMQ-P Reading subscale score as explanatory variable, controlling for household income.
- **Figure 4**: Detail slice (z=12) from regression map in Figure 3 (stories>tones activation) with STIMQ-P Reading subscale score as explanatory variable, controlling for household income.

Introduction

Emergent literacy is defined as the skills, knowledge, and attitudes supporting reading and writing, which accrue from infancy.¹ Whereas organic reading disability (dyslexia) affects an estimated 5-12% of US children,² the majority of illiteracy is preventable, attributable to inadequate resources, motivation, and/or stimulation required to learn to read.³ As parents are "a child's first and most important teachers," the quality of cognitive stimulation in the home, especially prior to school entry, strongly influences achievement and health outcomes.⁵⁻⁸ Children's books are catalysts for parent-child engagement during sensitive developmental stages when brain growth and plasticity are maximal.^{9,10} They provide broader, more grammatically correct vocabulary and range of subject matter than everyday conversation, especially in low-socioeconomic status (SES) households.^{11,12} Given these factors, the American Academy of Pediatrics (AAP) recommends shared reading beginning at birth, citing direct, lasting benefits for the developing brain, ¹³ a claim echoed by many advocacy groups.¹⁴

While behavioral evidence affirms moderate to large benefits of shared reading on a subset of emergent literacy skills (oral language and print concepts) through kindergarten, 5,15 quantifiable effects on the brain have not been previously studied. Similarly, interventions improving home literacy environment – a variably defined measure of reading behaviors and access to books – have been shown to improve oral language and school readiness, 16-20 though neurobiological mechanisms have yet to be described. Neuroimaging offers a means to address these knowledge gaps, informing an eco-bio-developmental model of emergent literacy incorporating genetic, environmental, and neurobiological factors. 21-25 Such models have been advocated by the AAP and National Institutes of Health, 25 and are especially valuable for young

children, where behavioral measures can be difficult to interpret and underestimate the effects of learning and experience on brain networks. ^{10,26} Neuroimaging has been extensively applied in dyslexia research (albeit in older children and adults), identifying activation patterns associated with disability and response to intervention, ^{2,27-29} as well as helping define the mature reading network. ^{30,31} Only recently has high-resolution neuroimaging been applied in younger, preliterate children, ³² most often in the context of normal language development. ^{33,34} How language networks become "ready" for reading, and to what extent they are influenced by home literacy environment or interventions during the critical pre-kindergarten period, however, are unclear.

For our study, a sample of 3-5 year-old children underwent blood oxygen level dependent functional magnetic resonance imaging (BOLD fMRI) using a narrative comprehension (story listening) task, ^{35,36} with a validated measure of home cognitive environment applied as a predictor of neural activation. This task requires the application of early emergent literacy skills, including vocabulary and listening comprehension. ³⁷⁻⁴⁰ Given behavioral evidence, ^{1,5} we hypothesized that children with more stimulating home environments, particularly shared reading exposure, would show more robust activation in brain areas supporting semantic processing (extraction of meaning). The semantic network includes left-sided inferior frontal, middle temporal, inferior parietal, and lateral occipital lobes, ^{35,39,41} which we selected as regions of interest for our analysis. We predicted that differential activation would remain significant after controlling for household income, a common confounder in studies of cognitive ability. ⁴²⁻⁴⁴

Methods

Participants

All participants in this analysis were enrolled in a longitudinal study of normal brain development at our institution (C-MIND). ⁴⁵ Inclusion criteria for C-MIND are: full-term gestation, healthy, right-handed, native English speakers, and no standard contraindications to MRI. By design, the C-MIND cohort is demographically diverse (38% non-white, 55% female, median household income \$42,500), intended to reflect the US population. At the time of our study, 23 children between 3-5 years of age had completed BOLD fMRI while performing a narrative comprehension task, in accordance with the C-MIND protocol. Of these, we were able to contact 19 (82.6%) for enrollment and survey administration. Despite multiple attempts, we were unable to contact the other 4 families, who were excluded. Informed consent was obtained from each child's custodial parent, families were compensated for time and travel, and our study was approved by the Cincinnati Children's Hospital Medical Center Institutional Review Board.

Behavioral Measures

Cognitive stimulation in the home was assessed using the preschool version of the STIMQ (STIMQ-P), ⁴⁶ which was administered to a custodial parent via telephone or during C-MIND follow-up visits by a trained clinical research coordinator. Time elapsed between fMRI scan and STIMQ administration ranged from 0 to 20 months (10±8.8). The STIMQ-P is validated for ages 36 to 72 months, and involves mostly "yes/no" questions. Three subscales were utilized: 1) Reading, reflecting access to books, frequency of shared reading, and variety of books read, 2) Parental Involvement in Developmental Advance (PIDA) reflecting the teaching of specific concepts such as letters, and 3) Parental Verbal Responsivity (PVR), reflecting verbal interaction. Parents were also asked to report the age of initiation of reading to their child, which is not included in the STIMQ-P.

Functional MRI Acquisition Specifications and Preliminary Analyses

Details of techniques used to acclimatize children to the MRI acquisition process are described by Vannest, et al.³² Details of BOLD MRI acquisition specifications utilized in the C-MIND study are described in Schmithorst, et al.^{35,47} Details of individual- and group-level analyses for the C-MIND study preceding our analysis are described in Sroka, et al.⁴⁸ All children were awake and non-sedated during MRI scans. Voxel size utilized for acquisition and analysis was 3x3x4 mm.

Narrative Comprehension Task

The narrative comprehension (story listening) task consists of 10 alternating blocks of active and control conditions (5 each), of 64 seconds duration. During the "active" condition, a series of 5 recorded stories of 9-10 sentences each read in a female voice was presented via headphones. The stories were designed by a speech pathologist with vocabulary and syntax appropriate for young children (download: https://www.irc.cchmc.org/software/pedaudio.php). The control condition consisted of non-speech tones in a range of frequencies simulating human speech, to control for baseline acoustic processing. Subjects closed their eyes or saw a blank screen during acquisition.

Regression with STIMO-P

We performed a series of regression analyses using the FEAT (fMRI Expert Analysis Tool) modality of FSL (fMRI-Brain Software Library, Oxford, United Kingdom). ⁴⁹ Utilizing BOLD fMRI datasets for our 19 subjects, a whole-brain, group mean activation map was first obtained, representing mean neural activation across subjects while listening to stories, minus activation listening to tones (i.e. activation attributable to the story task, excluding general

acoustic processing). Mean neural activation (stories > tones) was then used as the dependent variable in a series of regression analyses, individually applying STIMQ-P scores (Reading, PIDA, PVR, Composite) and age of initiation of reading as the explanatory variable. Income category (low/not low) was applied as a binary covariate when significant neural activation was found. Household income under 200% of the 2015 Federal Poverty Guidelines, adjusted for household size, was defined as low-income (see **Table 1**). Subject age and gender were considered as covariates but excluded, as no significant correlation was found between neural activation and either variable. To control for multiple comparisons across the brain, a False Discovery Rate (FDR) correction was applied in all analyses. Regression maps of neural activation, along with summary statistics for size, intensity, and location of activation clusters are reported for all significant results. The FSLView package was used to identify brain areas corresponding to active clusters in normalized, 3-dimensional, Montreal Neurological Institute (MNI) coordinate space. Utilizing the Harvard-Oxford Cortical Structural Atlas (2mm scale).

Results

Demographic characteristics for our sample are described in **Table 1**.

---Insert Table 1 about here---

STIMO-P and Other Behavioral Predictors

A summary of STIMQ-P subscale and composite scores, and reported age of initiation of shared reading are described in **Table 2**.

---Insert Table 2 about here---

Group Mean Activation for the Narrative Comprehension Task

Group mean activation for the narrative condition compared to baseline tones (all voxels p<0.05, FDR correction) involved bilateral, left-lateralized cortical and subcortical regions involved with acoustic, phonological, and semantic language processing (see **Figure 1**), as described by Karunanayaka, et al.⁵³

---Insert Figure 1 about here---

Regression of Neural Activation with STIMQ-P Scores and Other Predictors

Applying linear regression, STIMQ-P Reading subscale scores were positively associated with higher activation in a confluent region of left-sided, posterior cortex involving the occipital fusiform, lateral occipital, posterior inferior temporal, posterior middle temporal, posterior cingulate, and angular gyri, and left precuneus, as illustrated in **Figure 2** (all voxels p<0.05, FDR correction). Collectively, these areas reside within the parietal-temporal-occipital (PTO) association cortex, which supports multi-modal semantic processing, especially for language. An exception is the posterior cingulate gyrus, which plays a role in semantic processing and other functions, including memory encoding and visual attention.

---Insert Figure 2 about here---

The association of neural activation within the left PTO cortex remained consistent and highly significant even expanding the statistical model to control for household income as a binary covariate (low/not low). Activation clusters were of similar intensity, with slight to moderate decreases in size, as shown in **Figure 3** (all voxels p<0.05, FDR correction). The largest decreases were in posterior cingulate, inferior temporal, occipital fusiform, and the most superior lateral occipital areas. **Figure 4** displays a single axial slice (z=12) of the image series from **Figure 3** to better illustrate the anatomical regions encompassed in the cluster.

No significant correlation was found between brain activation during the narrative comprehension task and other STIMQ-P subscales, STIMQ-P composite, age of initiation of reading, or months of reading exposure (initiation to scan).

---Insert Figures 3 and 4 about here---

Discussion

"Biological embedding," describes the long-term impact on brain development resulting from the quality of cognitive stimulation and nurturing during early childhood. 6,56 Learning to read involves the integration of a formidable array of skills sequentially and efficiently, supported by language, visual, and association brain networks whose growth and plasticity peak in the first few years of life. During this critical pre-kindergarten period, children are highly vulnerable to disparities in cognitive stimulation, especially spoken language, as well as toys and books promoting constructive parent-child engagement. Among Many children arrive at school at a significant disadvantage in reading readiness, and it is clear that those who are poor readers in first grade are unlikely to catch up with peers, at great societal cost. This underscores the need for effective interventions applied as early as possible, when brain networks are most amenable to change. 10,57,61

Our findings support our hypothesis that while listening to stories, young children from more stimulating home reading environments more robustly engage neural circuitry supporting narrative comprehension, a foundational component of emergent literacy. Specifically, children in our study with higher STIMQ-P Reading scores showed greater activation in the left parietal-temporal-occipital (PTO) association cortex, a "hub" region facilitating semantic processing. 41,63

Outbound PTO connections include limbic areas involved with long-term memory (e.g. hippocampus) and assigning emotional value to experiences, and prefrontal executive function areas, each integral for learning. ⁶⁴ "Recycling" their role in oral language, areas within the PTO are recruited for reading, facilitating efficient assignment of meaning to letters and words. ^{41,65,66} The angular gyrus (located in the inferior parietal lobe) at the core of the PTO is particularly noteworthy, and plays an integral role in this process. ^{23,41,67} Though not observed in our subjects, hypo-activation of the angular gyrus during reading tasks has been cited as a biomarker for dyslexia, with potential application for early identification and remediation. ^{27,68}

Importantly, PTO activation in our subjects associated with home reading environment reflects recruitment of oral language skills supporting context and comprehension (semantics), not word-level decoding. This is consistent with behavioral evidence for the influence of parent-child reading exclusively on "outside-in" oral language skills (understanding outside of the word itself) described by Whitehurst, et al.^{1,5} Vocabulary is among the most important of these skills,⁶⁹ shown to be influenced by home reading environment,¹⁷ and recently found to be positively associated with left angular gyrus activation during our story listening task in young children.⁴⁸ Thus, PTO activation may offer potential as a biomarker of oral language ability (the outside-in domain of emergent literacy), though further studies are needed to clarify how the PTO is integrated into the reading network. That home reading environment was not associated with activation of brain areas supporting phonological processing ("inside-out" decoding skills) in our study reinforces behavioral evidence⁵ that these skills seem largely dependent on explicit instruction.¹⁵ Additional research in this area is also needed.

Higher Reading scores were associated with particularly robust activation in occipital areas within the PTO cortex, notably lateral occipital gyrus and precuneus. Schmithorst, et al.,

attributed activation in these areas during the narrative comprehension task (when no visual stimulus is presented) to mental imagery. The ability to "see" what is being heard is a potent, durable comprehension tool, as evidenced by Horowitz-Kraus, et al., who found that 5-7 year-old children showing greater activation of lateral occipital cortex during the narrative comprehension task manifest higher reading scores at age 11. Recruitment of left-sided PTO areas during high-imagery tasks has also been described in adults. Thus, our results provide a neurobiological correlate to the enchantment often seen at preschool story time, especially in children with greater practice at home: activation of PTO circuits to visualize and understand what is happening. It is intriguing to infer that children better able to recruit these circuits and apply mental imagery may better manage the transition from picture- to text-based books as they advance in school. Conversely, those with less practice seeing and understanding, with consequently under-developed visual-semantic neural infrastructure, may be more likely to struggle.

Surprisingly, we did not find significant association between neural activation and PIDA, PVR, or Composite STIMQ-P scores. We view this as likely a byproduct of subscale themes. The STIMQ-P Reading subscale measures reading-specific practices, assessing frequency, access to books, and variety of subject matter. As these opportunities and experiences are directly related to story listening, small variations, even with scores skewed towards the maximum, may be adequate to differentiate subjects performing this task. By contrast, PIDA measures the teaching of specific cognitive skills and PVR assesses parent-child conversation, each possibly more applicable to abilities other than narrative comprehension. Any composite effect was likely diluted by PIDA and PVR scores.

Contrary to our hypothesis, age of initiation of shared reading and months of reading exposure were not associated with neural activation, though behavioral studies have associated these with home literacy orientation. 9,71 This may be attributable to responses skewed by social desirability and/or recall bias, or more likely, greater predictive power of the validated STIMQ-P measure. The Reading subscale captures three aspects of home reading environment: frequency (4 points, including for days/week), access to books (5 points, including for number of books in the home), and variety of content (10 points, for different types of books, e.g. concepts, beliefs, relationships). The relative influence of each of these factors on neural activation supporting narrative processing is complex, likely involving behaviors and proclivities that are more difficult to capture, and merits further study. For example, greater variety may reflect differences in *how* books are shared, in addition to how many and how often. This qualitative aspect of reading aloud (notably dialogic reading, where the child actively participates) has been shown to provide a disproportionate share of its benefits, behaviorally 72,73 and possibly in terms of neurobiological effect.

Our study has several important strengths. Our sample of 3-5 year-old children is considerably younger than most neuroimaging-based studies of emergent literacy,²⁷ with ample sample size⁷⁴ drawn from a diverse cohort, applying an established fMRI paradigm and validated measure of home cognitive environment. Our findings are consistent with current models of language and reading brain networks,²³ complimentary with behavioral models of emergent literacy,¹⁵ and robust controlling for household income, a common confounder in studies of cognitive development.⁷⁵ Utilizing an innovative approach, our results also inform clinical practice during a foundational stage of development, where "preventative medicine" may offer maximal benefit. For example, as there is evidence that the Reach Out and Read (ROR)

intervention advocated in AAP recommendations¹³ improves home reading environment,^{13,18} and we have found that home reading environment is positively associated with activation of brain circuits supporting semantic processing, logical inference leads us to speculate that early home literacy intervention such as ROR, consistently applied, has the potential to enhance the development of these brain circuits.

Our study also has several limitations. Though it utilized existing imaging and behavioral data, the STIMQ-P was retrospectively administered, with a variable time from fMRI acquisition. Thus, recall and social desirability bias are possible, with parents over-reporting reading practices. That said, household reading behaviors have been shown to be stable during the preschool period, tempering such recall effects. ⁷⁶ Families agreeing to participate in our study may be more likely to constructively engage in their child's development (participation bias), though C-MIND is not advertised in the context of reading, its demographic mix is diverse by design, and all subjects who were able to be contacted agreed to participate, minimizing the prospect of self-selection. The exclusion of 4 low-SES families was a consequence of unreliable contact information (i.e. phone out of service), shifting our demographic profile towards higher SES, though 37% of our sample were low-income. Our high reported STIMQ-P subscale scores suggest potential ceiling effects, though the Reading subscale provided sensitivity ideal for our task. Finally, whereas our results show robust association between home reading environment and neural activation, our cross-sectional design cannot establish causation. Longitudinal studies are needed to discern the influence of parent-child reading and interventions on emergent literacy skills beginning in infancy, especially in low-SES populations. Thus, we might optimize resources and anticipatory guidance via improved access to books, dialogic reading training, and

early identification and remediation of reading disabilities, to ensure the best possible story for all children.

Conclusions:

Our study utilized functional MRI to for the first time demonstrate an association between home reading environment and activation of specific brain regions supporting emergent literacy during the pre-kindergarten period. Children exposed to higher levels of parent-child reading showed significantly greater activation during a story listening task, in brain areas within a left-sided, multi-modal association cortex facilitating mental imagery and semantic processing (extraction of meaning), controlling for household income. Critical for language, this region is recruited during reading acquisition, with hypo-activation a biomarker of reading disability. This study provides a novel, neurobiological correlate to oral language skills fostered by parent-child reading in early childhood, offering insight into how this practice may shape the developing brain, and informing an eco-bio-developmental model of emergent literacy and its promotion.

Acknowledgments:

The author would like to thank Claire Sroka and Sarah Finucane for their invaluable help conducting the STIMQ surveys and organizing behavioral data. He would also like to thank Molly Grainger for her assistance with the FSL fMRI analysis package.

The C-MIND database utilized for this study can be accessed free of charge at https://research.cchmc.org/c-mind/. The authors would like to thank the ⁶C-MIND Authorship Consortium:

Scott K. Holland, Ph.D. ^{1,6,9,10}
Jennifer Vannest, Ph.D. ^{1,5}
Vincent J. Schmithorst, Ph.D. ^{1,2}
Mekibib Altaye, Ph.D. ^{1,7}
Gregory Lee, Ph.D. ^{1,6}
Luis Hernandez-Garcia, Ph.D. ³
Michael Wagner, Ph.D. ^{1,8}
Arthur Toga, Ph.D. ^{12,13}

Jennifer Levitt, MD¹⁴

Anna W. Byars, Ph.D^{1,5}
Andrew Dimitrijevic, Ph.D.^{9,10}
Nicolas Felicelli⁸
Darren Kadis, Ph.D.^{1,5}
James Leach, MD^{1,6}
Katrina Peariso, MD, Ph.D.⁵
Elena Plante, Ph.D.⁴
Akila Rajagopal, M.S.¹
Andrew Rupert, M.S.⁸
Mark Schapiro, MD^{1,5}

Karen Crawford ¹² Ronald Ly¹⁴ Katherine Narr, Ph.D.¹¹ Petros Petrosyan¹² JJ Wang, Ph.D.¹¹

Lisa Freund, Ph.D.¹⁵

Cincinnati Children's Hospital Medical Center University of Cincinnati 3333 Burnet Ave. Cincinnati, OH 45229

²Pediatric Imaging Research Center, Dept. of Radiology Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA

³Functional MRI Laboratory Department of Biomedical Engineering University of Michigan, Ann Arbor, MI

¹Pediatric Neuroimaging Research Consortium

⁵Div. of Neurology, Dept. of Pediatrics

⁶Dept. of Radiology

⁷Div. of Biostatistics and Epidemiology, Dept. of Pediatrics

⁸Div. of Biomedical Informatics, Dept. of Pediatrics

⁹Dept. of Otolaryngology

¹⁰Communication Sciences Research Center

References:

- 1. Whitehurst GJ, Lonigan CJ. Child development and emergent literacy. *Child Dev.* Jun 1998;69(3):848-872.
- 2. Norton ES, Beach SD, Gabrieli JD. Neurobiology of dyslexia. *Curr Opin Neurobiol.* Oct 4 2014;30c:73-78.
- 3. Cree A. *The Economic and Social Cost of Illiteracy: A Snapshot of Illiteracy in a Global Context.*World Literacy Foundation; April 2012 2012.
- 4. Ramey CT, Ramey SL. Early intervention and early experience. *The American psychologist*. Feb 1998;53(2):109-120.
- 5. Panel NEL. *Developing early literacy: Report of the National Early Literacy Panel.* Washington, DC: National Institute for Literacy;2008.
- 6. Bradley RH, Corwyn RF. Socioeconomic status and child development. *Annual review of psychology*. 2002;53:371-399.
- 7. Cates CB, Dreyer BP, Berkule SB, White LJ, Arevalo JA, Mendelsohn AL. Infant communication and subsequent language development in children from low-income families: the role of early cognitive stimulation. *J Dev Behav Pediatr*. Sep 2012;33(7):577-585.
- 8. Sanders LM, Federico S, Klass P, Abrams MA, Dreyer B. Literacy and child health: a systematic review. *Arch Pediatr Adolesc Med.* Feb 2009;163(2):131-140.
- 9. Zuckerman B, Augustyn M. Books and reading: evidence-based standard of care whose time has come. *Acad Pediatr.* Jan-Feb 2011;11(1):11-17.
- 10. Knudsen El. Sensitive periods in the development of the brain and behavior. *Journal of cognitive neuroscience*. Oct 2004;16(8):1412-1425.
- 11. Duursma E, Augustyn M, Zuckerman B. Reading aloud to children: the evidence. *Arch Dis Child.* Jul 2008;93(7):554-557.
- 12. Hart B, Risley T. *Meaningful Differences in the Everyday Experience of Young American Children.*Baltimore (MD): Paul Brookes Publishing Company; 1995.
- 13. High PC, Klass P. Literacy promotion: an essential component of primary care pediatric practice. *Pediatrics*. Aug 2014;134(2):404-409.

⁴Dept. of Speech, Language, and Hearing Sciences University of Arizona, Tucson, AZ

¹¹Dept. of Neurology, UCLA, Los Angeles, CA

¹²Laboratory of Neuroimaging, Keck School of Medicine of USC, Los Angeles, CA
¹³ Departments of Ophthalmology, Neurology, Psychiatry, and the Behavioral Sciences,
Radiology and Engineering, Keck School of Medicine of USC, Los Angeles, CA

¹⁴ Psychiatry and Biobehavioral Sciences, UCLA, Los Angeles, CA

¹⁵ Eunice Kennedy Shriver National Institute of Child Health and Human Development Bethesda, MD

- 14. Fail TST. Hillary Rodham Clinton to Unveil Early Literacy Toolkit for Pediatricians and Parents at American Academy of Pediatrics National Conference. 2014; http://toosmall.org/news/press-releases.
- 15. Storch SA, Whitehurst GJ. Oral language and code-related precursors to reading: evidence from a longitudinal structural model. *Developmental psychology*. Nov 2002;38(6):934-947.
- 16. Golova N, Alario AJ, Vivier PM, Rodriguez M, High PC. Literacy promotion for Hispanic families in a primary care setting: a randomized, controlled trial. *Pediatrics*. May 1999;103(5 Pt 1):993-997.
- 17. Mendelsohn AL, Mogilner LN, Dreyer BP, et al. The impact of a clinic-based literacy intervention on language development in inner-city preschool children. *Pediatrics*. Jan 2001;107(1):130-134.
- 18. Needlman R, Toker KH, Dreyer BP, Klass P, Mendelsohn AL. Effectiveness of a primary care intervention to support reading aloud: a multicenter evaluation. *Ambul Pediatr*. Jul-Aug 2005;5(4):209-215.
- 19. Sharif I, Rieber S, Ozuah PO. Exposure to Reach Out and Read and vocabulary outcomes in inner city preschoolers. *J Natl Med Assoc.* Mar 2002;94(3):171-177.
- 20. Whaley SE, Jiang L, Gomez J, Jenks E. Literacy promotion for families participating in the women, infants and children program. *Pediatrics*. Mar 2011;127(3):454-461.
- 21. Child NSCotD. *Working Paper #5: The Timing and Quality of Early Experiences Combine to Shape Brain Architecture.* Cambridge, MA: Harvard University Center on the Developing Child;2008.
- 22. Carreiras M, Seghier ML, Baquero S, et al. An anatomical signature for literacy. *Nature*. Oct 15 2009;461(7266):983-986.
- 23. Dehaene S. Reading in the Brain: The New Science of How We Read. USA: Penguin Books; 2010.
- 24. Shonkoff JP. Building a new biodevelopmental framework to guide the future of early childhood policy. *Child Dev.* Jan-Feb 2010;81(1):357-367.
- 25. Development AAoPCoEBaC. Eco-Bio-Developmental Model of Human Health and Disease. 2014; http://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/EBCD/Pages/Eco-Bio-Developmental.aspx, 2014.
- 26. Hoeft F, Ueno T, Reiss AL, et al. Prediction of children's reading skills using behavioral, functional, and structural neuroimaging measures. *Behav Neurosci.* Jun 2007;121(3):602-613.
- 27. Shaywitz SE, Shaywitz BA. Paying attention to reading: the neurobiology of reading and dyslexia. *Dev Psychopathol.* Fall 2008;20(4):1329-1349.
- 28. Blau V, Reithler J, van Atteveldt N, et al. Deviant processing of letters and speech sounds as proximate cause of reading failure: a functional magnetic resonance imaging study of dyslexic children. *Brain.* Mar 2010;133(Pt 3):868-879.
- 29. Maisog JM, Einbinder ER, Flowers DL, Turkeltaub PE, Eden GF. A meta-analysis of functional neuroimaging studies of dyslexia. *Ann N Y Acad Sci.* Dec 2008;1145:237-259.
- 30. Dehaene S, Pegado F, Braga LW, et al. How learning to read changes the cortical networks for vision and language. *Science (New York, N.Y.)*. Dec 3 2010;330(6009):1359-1364.
- 31. Brem S, Bach S, Kucian K, et al. Brain sensitivity to print emerges when children learn letter-speech sound correspondences. *Proc Natl Acad Sci U S A*. Apr 27 2010;107(17):7939-7944.
- 32. Vannest J, Rajagopal A, Cicchino ND, et al. Factors Determining Success of Awake and Asleep Magnetic Resonance Imaging Scans in Nonsedated Children. *Neuropediatrics*. Aug 21 2014.
- 33. Szaflarski JP, Schmithorst VJ, Altaye M, et al. A longitudinal functional magnetic resonance imaging study of language development in children 5 to 11 years old. *Ann Neurol.* May 2006;59(5):796-807.
- 34. Kuhl PK. Early Language Learning and Literacy: Neuroscience Implications for Education. *Mind, brain and education: the official journal of the International Mind, Brain, and Education Society.* Sep 2011;5(3):128-142.

- 35. Schmithorst VJ, Holland SK, Plante E. Cognitive modules utilized for narrative comprehension in children: a functional magnetic resonance imaging study. *Neuroimage*. Jan 1 2006;29(1):254-266.
- 36. Vannest JJ, Karunanayaka PR, Altaye M, et al. Comparison of fMRI data from passive listening and active-response story processing tasks in children. *J Magn Reson Imaging*. Apr 2009;29(4):971-976.
- 37. Holland SK, Vannest J, Mecoli M, et al. Functional MRI of language lateralization during development in children. *Int J Audiol*. Sep 2007;46(9):533-551.
- 38. Pugh KR, Landi N, Preston JL, et al. The relationship between phonological and auditory processing and brain organization in beginning readers. *Brain Lang.* May 2013;125(2):173-183.
- 39. Berl MM, Duke ES, Mayo J, et al. Functional anatomy of listening and reading comprehension during development. *Brain Lang.* Aug 2010;114(2):115-125.
- 40. Horowitz-Kraus T, Vannest JJ, Holland SK. Overlapping neural circuitry for narrative comprehension and proficient reading in children and adolescents. *Neuropsychologia*. Nov 2013;51(13):2651-2662.
- 41. Binder JR, Desai RH, Graves WW, Conant LL. Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. *Cereb Cortex*. Dec 2009;19(12):2767-2796.
- 42. Noble KG, Tottenham N, Casey BJ. Neuroscience perspectives on disparities in school readiness and cognitive achievement. *The Future of children / Center for the Future of Children, the David and Lucile Packard Foundation*. Spring 2005;15(1):71-89.
- 43. Noble KG, McCandliss BD, Farah MJ. Socioeconomic gradients predict individual differences in neurocognitive abilities. *Dev Sci.* Jul 2007;10(4):464-480.
- 44. Noble KG, McCandliss BD. Reading development and impairment: behavioral, social, and neurobiological factors. *J Dev Behav Pediatr*. Oct 2005;26(5):370-378.
- Holland SK VJ, Schmithorst VJ, Wagner M. Overview of the Pediatric Functional Neuroimaging Research Network Project, Methods, Tools and Database: a.k.a CMIND. Paper presented at: New Horizons in Human Brain Imaging: A Focus on the Neuroimaging of Brain Development; May 5-7, 2014, 2014; Turtle Bay, HI.
- 46. STIMQ. STIMQ Cognitive Home Environment.

 http://pediatrics.med.nyu.edu/developmental/research/the-belle-project/stimq-cognitive-home-environment, 2014.
- 47. Schmithorst VJ, Vannest J, Lee G, et al. Evidence that neurovascular coupling underlying the BOLD effect increases with age during childhood. *Hum Brain Mapp.* Jan 2015;36(1):1-15.
- 48. Sroka MC, Vannest, J., Maloney, T.C., Horowitz-Kraus, T., Byars, A.W., Holland, S.K., and the CMIND Authorship Consortium. Relationship between receptive vocabulary and the neural substrates for story processing in preschoolers. *Brain Imaging and Behavior*. 2015;In Press.
- 49. S.M. Smith MJ, M.W. Woolrich, C.F. Beckmann, T.E.J. Behrens, H. Johansen-Berg, P.R. Bannister, M. De Luca, I. Drobnjak, D.E. Flitney, R. Niazy, J. Saunders, J. Vickers, Y. Zhang, N. De Stefano, J.M. Brady, and P.M. Matthews. Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage*. 2004;23(S1):208-219.
- 50. Secretary Oot. Annual Update of the HHS Poverty Guidelines In: Services DoHaH, ed. Vol 80. Washington, DC: Federal Register; 2015.
- 51. Foundation THJKF. State Health Facts. 2015.
- 52. Brett M CK, Cusack R, Lancaster J. . Using the Talairach atlas with the MNI template. *Neuroimage*. 2001;13(6):85.
- 53. Karunanayaka PR, Holland SK, Schmithorst VJ, et al. Age-related connectivity changes in fMRI data from children listening to stories. *Neuroimage*. Jan 1 2007;34(1):349-360.

- 54. Sabsevitz DS, Medler DA, Seidenberg M, Binder JR. Modulation of the semantic system by word imageability. *Neuroimage*. Aug 1 2005;27(1):188-200.
- 55. Leech R, Sharp DJ. The role of the posterior cingulate cortex in cognition and disease. *Brain.* Jan 2014;137(Pt 1):12-32.
- 56. Hertzman C. The biological embedding of early experience and its effects on health in adulthood. *Ann N Y Acad Sci.* 1999;896:85-95.
- 57. Development NRCaloMColtSoEC. From Neurons to Neighborhoods: The Science of Early Childhood Development. Washington, DC: National Academy Press; 2000.
- 58. Redcay E, Haist F, Courchesne E. Functional neuroimaging of speech perception during a pivotal period in language acquisition. *Dev Sci.* Mar 2008;11(2):237-252.
- 59. Tomopoulos S, Dreyer BP, Tamis-LeMonda C, et al. Books, toys, parent-child interaction, and development in young Latino children. *Ambul Pediatr.* Mar-Apr 2006;6(2):72-78.
- 60. Gabrieli JD. Dyslexia: a new synergy between education and cognitive neuroscience. *Science* (New York, N.Y.). Jul 17 2009;325(5938):280-283.
- 61. Foundation. TAEC. *Double Jeopardy: How Third Grade Reading Skills and Poverty Influence High School Graduation.* Baltimore, MD: The Annie E. Casey Foundation;2012.
- 62. Cornelissen PH, Peter; Kringelbach, Morten; Pugh Ken. *The Neural Basis of Reading.* 1st ed: Oxford University Press; 2010.
- 63. Ganis G, Thompson WL, Kosslyn SM. Brain areas underlying visual mental imagery and visual perception: an fMRI study. *Brain research. Cognitive brain research.* Jul 2004;20(2):226-241.
- 64. Wright A. Higher Cortical Functions: Association and Executive Processing. *Neuroscience Online:*An Electronic Textbook for the Neurosciences. Houston, TX: Department of Neurobiology and Anatomy at University of Texas Medical School at Houston; 2014.
- 65. Dehaene S. Inside the letterbox: how literacy transforms the human brain. *Cerebrum.* May 2013;2013:7.
- 66. Shankweiler D, Mencl WE, Braze D, Tabor W, Pugh KR, Fulbright RK. Reading differences and brain: cortical integration of speech and print in sentence processing varies with reader skill. *Developmental neuropsychology.* 2008;33(6):745-775.
- 67. Pugh KR, Mencl WE, Shaywitz BA, et al. The angular gyrus in developmental dyslexia: task-specific differences in functional connectivity within posterior cortex. *Psychol Sci.* Jan 2000;11(1):51-56.
- 68. Hoeft F, Meyler A, Hernandez A, et al. Functional and morphometric brain dissociation between dyslexia and reading ability. *Proc Natl Acad Sci U S A*. Mar 6 2007;104(10):4234-4239.
- 69. Duff FJ, Reen G, Plunkett K, Nation K. Do infant vocabulary skills predict school-age language and literacy outcomes? *Journal of child psychology and psychiatry, and allied disciplines.* Jan 4 2015.
- 70. Just MA, Newman SD, Keller TA, McEleney A, Carpenter PA. Imagery in sentence comprehension: an fMRI study. *Neuroimage*. Jan 2004;21(1):112-124.
- 71. Needlman R, Silverstein M. Pediatric interventions to support reading aloud: how good is the evidence? *J Dev Behav Pediatr*. Oct 2004;25(5):352-363.
- 72. Whitehurst GJ. Dialogic Reading: An Effective Way to Read to Preschoolers. 2013; http://www.readingrockets.org/article/400/.
- 73. Swanson E, Wanzek J, Petscher Y, et al. A synthesis of read-aloud interventions on early reading outcomes among preschool through third graders at risk for reading difficulties. *Journal of learning disabilities*. May-Jun 2011;44(3):258-275.
- 74. Desmond JE, Glover GH. Estimating sample size in functional MRI (fMRI) neuroimaging studies: statistical power analyses. *J Neurosci Methods*. Aug 30 2002;118(2):115-128.

- 75. Raizada RD, Kishiyama MM. Effects of socioeconomic status on brain development, and how cognitive neuroscience may contribute to levelling the playing field. *Frontiers in human neuroscience*. 2010;4:3.
- 76. NHES. Children's School Readiness Skills: 1993 and 2007. Washington, DC: US Census Bureau Statistical Abstract of the United States; 2012.

Table 1. Demographic characteristics of C-MIND sample subjects.

%

Sample	19	100
Age (years)		
3+	10	52
4+	6	32
5+	3	16
Sex		
Male	8	42
Female	11	58
Annual household income (\$)		
Under 5,000	0	0
5,000-10,000	1	5
10-15,000	1	5
15,000-25,000	2	11
25,000-35,000	1	5
35,000-50,000	2	11
50,000-75,000	4	21
75,000-100,000	4	21
100,000-150,000	2	11
Above 150,000	2	11

Household income level

Above 200% poverty Children in the household

1

2-3 4-5

6

Below 200% poverty (low)

Characteristic

 Table 2. STIMQ-P scores and responses to reading-related items.

Item	possible	mean	std	min	max
STIMQ-P					
Reading	19	18	2.0	13	19
PIDA	15	12	2.2	8	15
PVR	7	6	1.2	3	7

37

16

16

5

12 63

7 12 63

3

3

1

Composite	41	35	3.7	27	41
Specific Items					
Age (mos) initiation of reading	**	5	5.5	0	24
Months of reading exposure	**	43	9.5	30	63
Children's books in the home	**	162	113	10	400
Reading nights/week	7	6	1.9	2	7

Table 2. Summary of STIMQ-P subscale and composite scores, and reading-related items. Minimum, maximum, mean, standard deviation (std) and total possible (where applicable) scores are presented. Individual questions other than age of initiation of reading are part of the STIMQ-P Reading subscale.

Figure 1. Group mean activation map for the narrative comprehension task.

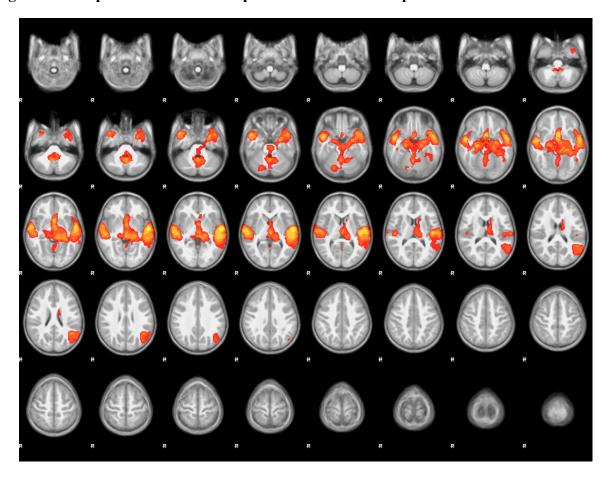


Figure 1: Group mean BOLD fMRI activation map (stories>tones) in 3-5 year-old children (N=19). All voxels significant at p<0.05 (corrected), slice thickness 5 mm for contiguous slices. Slices range from z=-28 to z=74 in the Talairach⁵² frame. Color scale ranges from t=1.25 (cooler) to 4 (hotter). Radiological orientation, left=right, right=left.

Figure 2. Regression map (stories>tones activation) with STIMQ-P Reading subscale score as explanatory variable.

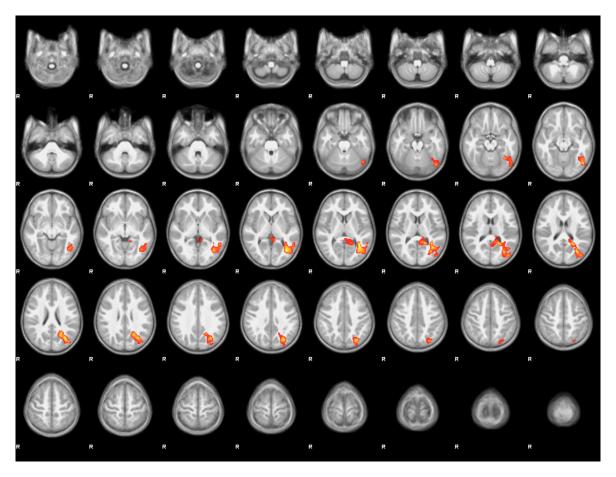


Figure 2: Regression map for the narrative comprehension task (stories>tones) in 3-5 year-old children (N=19), with STIMQ-P Reading score as explanatory variable. Cluster size 4087 voxels all significant at p<0.05 (FDR corrected), z-score local maxima 3.25-3.44. 5mm slices from z=-28 to z=74 in the Talairach⁵² frame. Color scale from t=1.25 (cooler) to 4 (hotter). Radiological orientation, left=right, right=left.

Figure 3. Regression map (stories>tones activation) with STIMQ-P Reading subscale score as explanatory variable, controlling for household income.

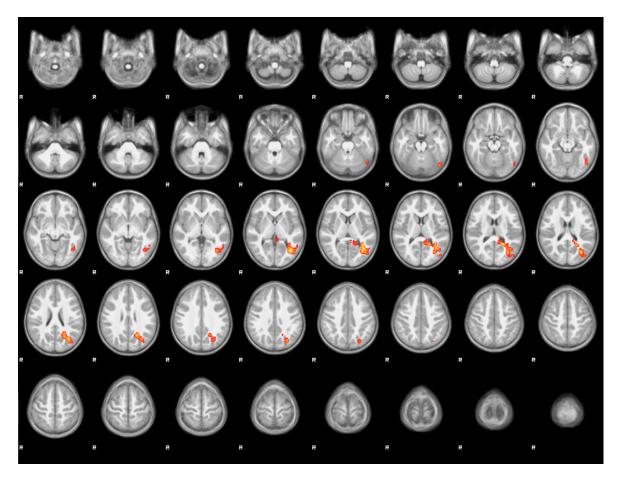


Figure 3: Regression map for the narrative comprehension task (stories>tones) in 3-5 year-old children (N=19), with STIMQ-P Reading score as explanatory variable, controlling for household income. Cluster size 2467 voxels all significant at p<0.05 (FDR corrected), z-score local maxima 3.15-3.38. 5mm slices from z=-28 to z=74 in the Talairach⁵² frame. Color scale from t=1.25 (cooler) to 4 (hotter). Radiological orientation, left=right, right=left.

Figure 4: Detail slice (z=12) from regression map in Figure 3 (stories>tones activation) with STIMQ-P Reading subscale score as explanatory variable, controlling for household income.

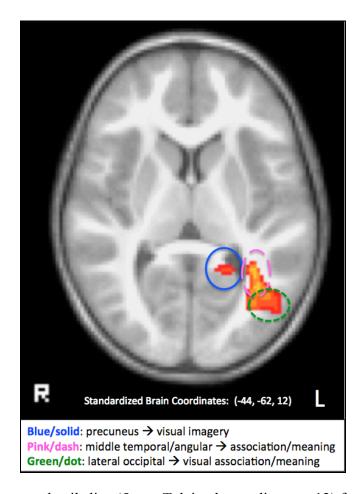


Figure 4: Regression map detail slice (5mm, Talairach coordinate z=12) for the narrative comprehension task (narrative>tones), with STIMQ-P Reading score as explanatory variable, controlling for household income. Regions involved with semantic processing and mental imagery are circled. Color scale ranges from t=1.25 (cooler) to 4 (hotter). Radiological orientation, left=right, right=left.