The typical and atypical reading brain:

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

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www.gaablab.com
www.babymri.org
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?
- Developing a dyslexia screening App
- Educational and Clinical Implications
- The role of Neuroscience in Education and how to navigate the brain training maze
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Timeline of typical reading development:

- **Learning to read**
  - Sound and Language Processing
  - Visual Processing
  - Phonological Processing
  - Letter Recognition

- **Reading to learn**
  - 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
- Receptive/expressive vocabulary
- Rapid automatized naming abilities
- Letter name knowledge
- Verbal short-term memory

(e.g., Catts et al. 2015; Schatschneider et al., 2004; Georgiou et al., 2008; de Jong & van der Leij, 1999; Scarborough, 1998; Pennington & Lefly, 2001; Hamilton et al., 2013).
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
- …
“Children are wired for sound, but print is an optional accessory that must be painstakingly bolted on.” Steven Pinker

[in McGuinness D: Why Our Children Can't Read, and what We Can Do about it: A Scientific Revolution in Reading: Simon and Schuster; 1997 p. ix-x].
BRAIN LESIONS

Paul Broca, 1862

- patient who would not say anything but `tonton`
- → Broca aphasia

Carl Wernicke, 1874

- lesion in `Wernicke area`: the fluent aphasia
ANIMAL STUDIES
Do you know what MRI/fMRI measures?

**MRI** studies brain **anatomy**.

**Functional MRI** (fMRI) studies brain **function**.

Source: www.fmri4newbies.com/
Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging uses radio waves and a strong magnetic field rather than x-rays to provide remarkably clear and detailed pictures of internal organs and tissues.
MRI vs. fMRI

MRI
- shows difference between different types of tissues
  (“difference in space”, e.g. white vs. gray matter)

fMRI
- shows difference between stimulated and non-stimulated tissue
  (“difference in time course”)
Diffusion Weighted Imaging data

Diffusion weighted imaging (DWI) is a form of MR imaging based upon measuring the random Brownian motion of water molecules within a voxel of tissue.

Color-FA map

Red
transverse axis (x-axis)

Blue
superior-inferior (z-axis)

Green
anterior-posterior axis (y-axis)

Demonstrates the direction of fibres

Whole-Brain Tractography
Electroencephalography (EEG)

EEG is used to record electrical activity in the brain.

How EEG Works

- Electrical activity is generated by the flow of ionic currents when neurons in the brain are active.

- Signal from several neurons firing in synchrony, known as a ‘brain wave’, is picked up by several small electrodes on the scalp.

- Clinically, EEG is important for diagnosing epilepsy and sleep disorders, as well as patient management for coma patients.
Magnetoencephalography (MEG)

MEG is used to measure magnetic fields produced by brain activity.

How MEG Works

- Since the ionic currents generated by brain activity (what we measure directly with EEG) are moving through the neurons, they generate small magnetic fields.

- MEG uses extremely sensitive devices called ‘superconducting quantum interference devices’, or SQUIDs, to measure the magnetic fields.

Images provided by Christos Papadelis, PhD
Fetal-Neonatal Neuroimaging and Developmental Science Center
BCH
Reading words…

(Dale et al., 2000)
Is there any learning without the brain?
The typical reading network with its key components

[Dehaene, 2009]
Arcuate Faciculus, a neural pathway connecting the posterior part of the temporoparietal junction with the frontal cortex.

- Patients with lesions in the left AF exhibit profound deficits in phonological processing, reading fluency, speech production, language comprehension, and speech repetition (e.g., Fridrikson et al., 2013; Rauschecker et al., 2009).

- Acquisition of literacy in previously illiterate adults is accompanied by increased integrity of the left AF (Thiebaut de Schotten et al., 2014), and microstructural properties of the left arcuate predict artificial word-learning ability (Wong et al., 2011).

- Integrity of the left AF (as e.g. measured by fractional anisotropy) in children correlates positively with phonological awareness (Yeatman et al., 2011) and predicts later reading outcome in beginning readers (Myers et al., 2014).
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, Elizabeth S. Norton, David E. Osher, Sara D. Beach, Abigail B. Cyr, Ola Ozernov-Palachik, Anastasia Yendiki, Bruce Fischl, Nadine Gaab, and John D.E. Gabrieli

a.

![Graph showing correlation between Blending Words Raw Score and volume (mm³).](image)

BW score=0
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

Factors contributing to atypical reading development

- Genetics
- Brain
- Perception & Cognition
- Environment

Atypical Reading Development
What is Developmental Dyslexia?

- Affects 10-12% of children.

- Specific learning disability with a neurobiological origin characterized by
  - difficulties with accurate and/or fluent word recognition
  - poor spelling and decoding abilities

- Secondary consequences may further include
  - problems in reading comprehension
  - Reduced reading experience that can impede vocabulary and background knowledge

- Cannot be explained by poor vision or hearing, lack of motivation or educational opportunities.

International Dyslexia Association, 2002
Psychological and Clinical Implications of DD

- Children with DD are often perceived by others as being ‘lazy’ or as those who ‘do not try enough.

- Teachers, parents and peers often misinterpret the ‘dyslexic’ child’s struggle to learn as negative attitude or poor behavior and decreased self-esteem is often a result [Saracoglu et al., 1989; Riddick et al., 1999].

- These negative experiences leave children with DD vulnerable to feelings of shame, failure, inadequacy, helplessness, depression and loneliness [e.g.; Valas et al., 1999].

- Possible anti-social behavior with long-standing consequences [Baker et al., 2007].

- Less likely that these children will complete high school [Marder et al., 1992] or join programs of higher education [Quinn et al., 2001], and increased probability that they will enter the juvenile justice system [Wagner et al., 1993].
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
Impaired reading

Deficient phonological representations

Grapheme-phoneme mapping

Poor phonological skills

Left hemisphere peri-sylvian dysfunction

[ after Ramus, 2003]
Structural and functional brain alterations in DD

(A) Gray matter (volumetric analyses)

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

(B) Gray matter (functional analyses)

[Dys < Control]

[<e.g. see Meta-analyses: Richlan et al., 2011; Temple et al., 2002>]
White matter alterations in DD

(C) White matter

- Left Superior Longitudinal Fasciculus
- Left Arcuate Fasciculus
- Left Inferior Frontal-Occipital Fasciculus
- Left Inferior Longitudinal Fasciculus
- Corpus Callosum
  (forceps minor - genu and major - splenium)
Variant function in any number of **Generalist genes**, such as COMT, VAL/MEL, FOXP2, and/or **Dyslexia susceptibility genes**, such as ROBO1, DCDC2, DYSXI, KIAA0319

**Brain Level**
- Atypical neuronal migration and/or synaptic/cell development
  - Atypical axonal growth, atypical glutamatergic transmission, subtle focal cortical malformations, atypical sulcal pattern, atypical focal neural response characteristics, and/or atypical levels of neurometabolites Cho and Glu
- Atypical development of cortical thickness, myelination, functional activity pattern, and/or functional connectivity
- Atypical development of structural and functional connectivity of the reading circuitry

**Perceptual/Cognitive Level**
- Atypical sensorimotor (vision and hearing) and/or perceptual functions
- Atypical development of language and/or attention functions
- Atypical phonological awareness, verbal working memory, rapid automatized naming, letter knowledge, vocabulary, and/or executive functions

**Environmental Factor**
- Low home literacy, low parental educational background and socioeconomic status, adverse neighborhood characteristics, and/or cultural influences
- Ineffective schooling, limited instructional resources, and/or insufficient involvement of parents

**Prenatal** — **Birth** — **Postnatal**
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Brain Changes After Remediation

Midway through the exam, Allen pulls out a bigger brain.
Neural deficits in children with dyslexia ameliorated by behavioral remediation: Evidence from functional MRI

Elise Temple†, Gayle K. Deutsch§, Russell A. Poldrack§, Steven L. Miller, Paula Tallal††, Michael M. Merzenich‡‡, and John D. E. Gabrieli††

Control

Frontal AND Temporo-parietal

Example:
- B D = Rhyme
- B K = Do Not Rhyme

Dyslexia

Frontal but NOT Temporo-parietal

n= 45
8 weeks intervention

[Temple et al. (2003) PNAS, 100]
Neural effect of intervention

Pre-Intervention

Frontal but NOT Temporo-parietal

After training, metabolic brain activity in dyslexics more closely resembles that of typical readers.

Post-Intervention

Increased activity in Frontal AND Temporo-parietal

[Temple et al. (2003) PNAS, 100]
Neural Changes following Remediation in Adult Developmental Dyslexia

Guinevere F. Eden,1,* Karen M. Jones,1 Katherine Cappell,1 Lynn Gareau,1 Frank B. Wood,2 Thomas A. Zeffiro,1 Nicole A.E. Dietz,1 John A. Agnew,1 and D. Lynn Flowers1,2

n = 38
Intervention: Lindamood-Bell (8 weeks)

Sound deletion > word repetition

Post remediation > Pre-remediation
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The dyslexia paradox

Window for most effective intervention

Typical window for a ‘Diagnosis’

‘FAILURE-MODEL’
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; Wanzek et al., 2013).

- 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 (Catts, et al., 2015; 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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Early behavioral predictors of dyslexia

Key childhood predictors of reading problems (e.g. Scarborough, 1998, Catts et al., 2015):

- phonological awareness
- short-term memory
- rapid naming
- expressive vocabulary
- pseudoword repetition
- letter naming

Puolakanaho et al., 2007 showed that familial risk, letter knowledge, phonological awareness and rapid automatized naming at 3.5 years predicted later DD. Additionally, those children who later developed DD, exhibited auditory and speech processing deficits at a very early age.
Diagnosis
Dyslexia/Reading difficulty

Functional MRI
Structural MRI
Behavioral tests
Psychophysics
Questionnaires
DNA

With/without family history

Kindergarten
3rd grade
Middle School

Early Identification
children at-risk

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

The Boston Longitudinal Dyslexia Study (BOLD)
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

Questionnaires:
- 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
<table>
<thead>
<tr>
<th>YEAR 1 (prereading status)</th>
<th>YEAR 2 (beginning readers)</th>
<th>YEAR 3/4 (readers)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Significant differences in:</strong></td>
<td><strong>Significant differences in:</strong></td>
<td><strong>Significant differences in:</strong></td>
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<tr>
<td>Expressive and receptive language/content</td>
<td>Expressive language/language content</td>
<td>Core and receptive Language</td>
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<tr>
<td>Phonological processing</td>
<td>Phonological processing</td>
<td>Rapid automatized naming</td>
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<td>Rapid automatized naming</td>
<td>Rapid automatized naming</td>
<td>Single word reading (timed/untimed)</td>
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<td>Letter knowledge</td>
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<td>Passage comprehension</td>
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<td>Spelling</td>
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<tr>
<td></td>
<td>Reading Fluency</td>
<td></td>
</tr>
</tbody>
</table>

*No differences in* IQ, age, Home Literacy, SES

*all p<0.05*
Functional characteristics of developmental dyslexia in left-hemispheric posterior brain regions predate reading onset

Nora Maria Raschle, Jennifer Zuk, and Nadine Gaab

[Raschle et al., PNAS 2012]
Structural brain alterations associated with dyslexia predate reading onset

Nora Maria Raschle, Maria Chang, Nadine Gaab*

[Figures a, b, c, d, e showing brain scans and scatter plots]

[Raschle et al., Neuroimage 2010]
Brain changes in response to three months of reading instruction in typical developing children and children at-risk for dyslexia.

(Yamada et al., 2012)
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
Cross-sectional results (n = 78): Arcuate Fasciculus

[Image of graphs showing fractional anisotropy for Pre-readers, Beginning readers, and Fluent readers.]

[Wang et al., 2016]
Longitudinal Analysis: Development rate of the AF (n=45)

Wang et al., 2016
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).
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.
The READ Study
(Researching Early Attributes of Dyslexia)


- 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., 2016

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].

READ KG Battery:
- Battery cost: $1,800
- Training: 4 hours
- Testing time: 30 min
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. Gabrieli1

a.

Blending Words Raw Score

volume (mm³)

FA

0

0.5

1

BW score=0
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Compensatory mechanisms, resiliency and protective factors

- Despite the genetic and cognitive risk factors, only approximately half of FHD+ children subsequently develop DD (e.g., Leppänen et al., 2011; Regtvoort et al., 2006; Schulte-Körne, 2001)

- Protective factors, such as enhanced oral language skills and executive function as well as high IQ and high home literacy may facilitate typical reading development in FHD+ children (e.g., Carroll et al., 2014; Hulme et al., 2015; Snowling et al., 2013; Torppa et al., 2010; Thompson et al., 2015; Eklund et al., 2013)

→ WHO compensates and HOW?

→ What is the brain basis of compensation or resilience?
Can an instructional approach change brain circuitry?

**Yoncheva et al., 2015**

Fig. 5. Training focus modulates N170 lateralization during subsequent reading. Reading words trained under GP focus elicits a significantly more left-lateralized N170 topography relative to words trained under WW focus as evident over the 197 – 222 ms N170 interval in the grand-average voltage maps for each training condition.
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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 ($p = 0.001$)
FA values correlate with ‘expressive language Scores’

\[ R = 0.481 \]

\[ p = 0.037 \]

Langer et al., 2015
Atypical development of AF from infancy to late elementary school

Infants
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Ozernov-Palchik et al., 2016

Genetic Factor

- Generalist genes, such as COMT, VAL/MEL, FOXP2
- Dyslexia susceptibility genes, such as ROBO1, DCDC2, DYX1C1, KIAA0319

Brain Level

- Atypical neuronal migration, and/or synaptic/cell development
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- Atypical development of cortical thickness, myelination, functional activity pattern, and/or functional connectivity of the reading circuitry

Perceptual/Cognitive Level

- Atypical sensorimotor (vision and hearing) and/or attention functions
- Atypical development of language and/or attention functions
- Atypical phonological awareness, verbal working memory, rapid automatized naming, letter knowledge, vocabulary, and/or executive functions

Environmental Factor

- Low home literacy, low parental educational background and socioeconomic status, adverse neighborhood characteristics, and/or cultural influences
- Ineffective schooling, limited instructional resources, and/or insufficient involvement of parents

Atypical reading performance

Complex interactions among different levels

Genetics

Perceptual/Cognitive level

Brain level

Protective factors and compensatory mechanisms in typical readers with familial risks

- Protective environmental variables (e.g., home literacy, teaching efficiency etc.)
- Protective cognitive abilities (e.g., high IQ, high vocabulary etc.)

Compensatory neural mechanisms (e.g., increased involvement of the right hemisphere)
(A) Gray matter (volumetric analyses)
- Left Inferior Frontal Gyrus
- Left Precuneus
- Left Parieto-Temporal Area
- Left Occipito-Temporal Area
- Left Planum Temporale
- Left/Right Fusiform Gyrus

(B) Gray matter (functional analyses)
- Left Inferior Frontal Gyrus
- Left Parieto-Temporal Area
- Left Occipito-Temporal Area

(C) White matter
- Green: Left Superior Longitudinal Fasciculus
- Red: Left Arcuate Fasciculus
- Yellow: Left Inferior Frontal-Occipital Fasciculus
- Blue: Left Inferior Longitudinal Fasciculus
- Cyan: Corpus Callosum
  (forceps minor - genu and major - splenium)

(D) Sulcal pattern
- Left Parieto-Temporal and Occipito-Temporal Areas

Ozernov-Palchik et al; 2016
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).
Collaborators:
John Gabrieli, MIT
Ellen Grant, CHB
Charles Nelson, BCH
Sandra/Joseph Jacobson, Wayne State
Maryanne Wolf, Tufts University
Georgio Sideridis, BCH
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Nora Raschle (former Postdoc)
Nicolas Langer (former Postdoc)
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Michael Figuccio (former Graduate student)
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Clarissa Carruthers (RA BabyBOLD)
Bryce Becker (former Project Coordinator)
Meaghan Maurer (former 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 (former RA, READ)
Zeynep Saygin (former postdoc READ)
MRI Team, Children’s Hospital Boston & MIT

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- 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