The Dyslexia Debate

Dyslexia Today: Lessons from the Past and Hopes for the Future

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I am facing an impossible task...

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Goal & Structure

• Goal
  - Summary of the field
    • Neurobiological and genetic correlates of ...
      - Developmental dyslexia
      - Specific reading disability (disabilities)
      - Reading difficulties
      - Reading

• Structure
  - Eight statements
    • Numbered
Context

Reading (as is the case with any acquired academic skill) is a complex skill that evolves from a solid foundation of componential cognitive skills.
Points of the eight statements

• Bad teaching & reading
• Biological bases of reading
• Correlation & causation
• Reading & the brain
  – In SRD/DD
  – In reading acquisition
  – In remediation

• Reading & the genome
  – Where
  – What
  – How
• Heritable ≠ unmodifiable
• Environmental influences on the genome
• SRD/DD assessment and the relevance of RTI to studies of the brain and the genes
SRD/DD does not arise from bad teaching (1)
SRD/DD does not arise from bad teaching

- SRD/DD has a specific etiology & genesis
- 15-20% school-aged children have difficulties reading, but only 85% of them have SRD/DD
  - http://www.interdys.org, Fact Sheet #62-05/00
- Bad teaching makes SRD/DD worse
  - But bad teaching does not cause SRD/DD
- Reading problems generated by bad teaching/bad schooling are preventable and remediable
“True” SRD/DD is biologically grounded (2)
“True” SRD/DD is biologically grounded

- SRD/DD has its own biological signature
  - Where?
    - In the eyes
    - In the blood
    - In the belly
    - In the brain
    - In the genes

- SRD/DD is a disorder of genetic origin with a basis in the brain
We know a lot about the correlates of SRD/DD in the brain and in the genes (3)
SRD/DD in the brain & in the genes

• We know a lot about the correlates
• We know little about the causes
• What we know is
  – Who the “players” are
  – Where things are happening
• What we do not know
  – How things are happening
  – Why they are happening
The brain does not have “the part(s)” for reading (4)
The brain does not have “the part(s)” for reading

• Reading in the brain unfolds via a complex chain of activation of various structures, which is distributed in space and in time
  - There is no brain “locus” for reading, but there is a “reading brain”
  - The “reading brain” is a developmental stage of the brain
  - We are born with an “illiterate brain” that has the capacity to become a “reading/literate brain”

• This chain is malleable
  - Developmentally
  - As a result of interventions
Reading brain (1)

• A number of areas appear to be engaged in reading
• Robust multivariate differences between people with and without difficulties
• Developmental differences (before and after the onset of reading)
• Differences between remediated and nonremediated readers
Reading brain (3)

Elliott & Grigorenko, 2014
Reading brain (4)

Elliott & Grigorenko, 2014
Illustration One: Pathway(s) for reading

Elliott & Grigorenko, 2014
Abnormal activity:
Phonological processing (rhymes, segmentation)
Word reading

Attenuated activity:
Single words
Pseudowords
Rapid naming

Enhanced activity:
Articulatory recoding
Word reading
Pseudoword reading

Abnormal activity:
Phonological processing (rhymes, segmentation)
Word reading

Illustration One:
Pathway(s) for reading

Schulte-Körne et al., 2007
Illustration Two: Reading acquisition

Schlagger & McCandliss, 2007
Illustration Three:
Reading intervention (1)
Illustration Three:
Reading intervention (2)

Elliott & Grigorenko, 2014
The reading brain

- Is a dynamic system that
  - Is characterized by temporal and spatial distribution of activity
  - Is sensitive to the nature of stimuli
  - Changes developmentally
  - Is malleable in response to intervention
Both typical and atypical (DD) reading are familial and heritable (5)
Reading is familial and heritable

• Family studies
  – High risk for relatives of probands with DD
  – High relative risk

• Twin studies
  – Reading itself and all its components (e.g., phonemic awareness, decoding, single-word reading) are heritable
Illustration One: Family Studies

• First observations on the familiality of DD
  – Thomas, 1905; Orton, 1937; Norrie, 1939; Kagen, 1943

• Multiple prospective, retrospective, and concurrent family studies
  – Familiality is very high
  – Estimates (Ziegler et al., 2005):
    • Spelling (cutoff at 10%): GRR S = 3.813 (CI: 3.217–4.437)
    • Reading (cutoff at 10%): GRR S = 3.516 (CI: 2.825–4.257)
Illustration Two: Twin studies

The Colorado Learning Disabilities Research Center
Davis et al., 2001
Gayán & Olson, 2001, 2003

The London Twin Studies
Stevenson et al., 1987
Hohnen & Stevenson, 1999

Twins Early Developmental Study (TEDS)
Harlaar, Spinath, Dale, & Plomin, 2004
Grigorenko, 2004
There is no “gene for reading”
Reading the genome for “reading” genes

• There is no single “gene” for reading

• There are many genes that contribute to the formation of the biological bases of both typical and atypical (SRD/DD) reading acquisition

• These genes exert small effects

• These genes are multi-task genes
Illustration One:
Where in the genome (1)

Schulte-Körne et al., 2007
Illustration One:
Where in the genome (2)

Elliott & Grigorenko, 2014
Illustration Two: Candidate genes

- **DYX1C1** (also known as EKNI)  
  - Dyslexia Candidate Region 1, Candidate 1
- **KIAA0319**  
  - Human Unidentified Gene-Encoded (HUGE) protein, cDNAs identified in the Kazusa cDNA sequencing project
- **DCDC2**  
  - Doublecortin domain containing 2
- **SEMA6D**  
  - Sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6D
- **ROBO1**  
  - Roundabout 1
Candidate gene expression patterns in the brain

Paracchini et al., 2007
Disrupted migration in the developing rat neocortex

Joe LoTurco et al., 2006-2007
Protein-protein interaction (1)
Protein-protein interaction (2)
Illustration Three: Types of genes

• The “migration” genes can, indeed, contribute to the initial anatomical differences characteristic of the brains of individuals with SRD/DD; they cannot explain the whole story.

• There are many types of genes and genetic mechanisms that could potentially be involved in the manifestation of SRD/DD:
  - Brain development
  - Brain connectivity
  - Signal transduction
Key indicators (1)

- Congenital
- Genetic
- Familial
- Molecular
- Heritable
- Oligogenic
  - Substantial relative risk
- CDCV
- CDRV

Differentiated by...
(age, ethnicity/language, severity, IQ, environment – SES, instruction,...)
Key indicators (2)

- Exome
- Genome
- Methylome
- Transcriptome

In vivo

- Control
- Disease model

In vitro

iPSC
Discovery cycle

Prime Structure (Genome)

Epi (derived) Structure (Epigenome)

Acquisition Development Change

Expressed Structure (Transcriptome)

In vitro models

In vivo models

Behavior
Heritable ≠ Unmodifiable (6)
Heritable ≠ Unmodifiable

- Mean effects
- Structured environment (controlling the variance)
Environmental influences on genes (7)
Environmental influences on genes

• Nonlinear G-by-E effects
  - Gene-environment correlations refer to genetic effects on individual differences in liability to exposure to particular environmental circumstances.
    • Evidence suggests that environmental risk exposure is NOT randomly distributed
  - Gene-environment interactions concern genetically influenced individual differences in sensitivity to specific environmental factors.
    • Remarkable individual differences in vulnerability to a variety of types of environmental hazards

• Regulatory effects

• Epigenetic effects
SRD/DD assessment and the relevance of RTI to studies of the brain and the genes (8)
Further Tasks

• Inclusion of/transfer to other learning disabilities (e.g., dyscalculia, SMD) within the same framework of “pedagogical neuroscience”*;

• Development of ‘tools’ of pedagogical neuroscience [general and specific assessments (i.e., educational, neuropsychological, genetic, and neuronal)];

• Development of a meta-theory of pedagogical neuroscience for multiple domains of achievement.

*Fawcett & Nicolson, 2007
Conclusions

- There is an overwhelming amount of evidence suggesting that reading difficulties are heterogeneous and that many are due to bad schooling/teaching.
- Yet, there is a group of children in whom those difficulties cannot be explained only by bad/unfortunate schooling experiences.
- Such kids are typically characterized by a family history of learning/reading problems (as compared to the “generic” category of bad readers).
- The skills of such children are typically harder to remediate.
- Accurate and theory-informed assessment/phenotyping of children with SRD/DD is crucial for establishing biological (including genetic) correlates and causes of SRD/DD.
- The concept/approach of RTI might be informative in differentiating “true” from teaching-based reading problems. Independent schools, where the ideology/pedagogy of RTI unfolds in reality as everyday practices are especially important for making ground-breaking contributions to the search for the biological foundations of SRD/DD.