In How Children Learn To Read: Current Issues And New Directions In The Integration Of Cognition, Neurobiology And Genetics Of Reading And Dyslexia R Edited by K.R. Pugh and P. McCardle

Conclusion: Integration of Methodologies in Cognitive Neuroscience—Research, Planning, and Policy

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As noted at the outset of this book, in recent years, research on assessment and treatment of specific reading disability (dyslexia) has become a magnet for the application of new techniques and technologies from genetics, neuroscience, cognitive psychology, and cognitive neuroscience. This interdisciplinary trend has yielded numerous and diverse findings regarding the brain and cognitive bases of this syndrome, but work aimed at integrating these findings from very different levels of analysis is just beginning (and was a key motivating factor in the choices we made regarding themes and participants at the symposium from which this book arose). At the level of genetics, a number of candidate genes have been proposed, but this work is just beginning. At the level of brain systems, neurobiological anomalies at key left hemisphere (LH) posterior regions have been observed with surprising consistency in different languages and across different developmental stages, and links between individual differences in brain circuits and behavioral profiles of strengths and weaknesses have been reported. Moreover, several recent studies have demonstrated that intensive remediation/intervention can be associated with increased response of these LH posterior systems, suggesting some degree, at least, of latent functionality in these circuits. These seminal findings on brain plasticity in dyslexia are highly promising but need to be expanded to include a deeper focus on individual differences, differential profiles in distinct written languages, and greater integration across levels of analysis.

This symposium brought together leading researchers from a range of disciplines and several countries to address crucial, cutting-edge, and interrelated topics on the cognitive, neurobiological, and genetic bases of reading disability. We chose to focus on a wide range of topics rather than a singular theme to identify gaps in current knowledge, methodology, and theoretical frameworks that will merit higher research priority in the coming years. We asked the participants to begin with a presentation on the state of the science in their particular field of study, with presentations ranging from genetics through remediation. After the

presentations, we engaged in a 2-day session to identify next steps and implications for research design, policy, and planning across the various disciplines and scientific areas. The presentations and discussions (and thus the chapters in this volume) were stimulating and challenging. There were many points of agreement among participants regarding next steps, along with important disagreements. In broad terms we discussed (a) new research directions and priorities and (b) the methodological developments necessary to support them; (c) how best to extend research to new and diverse languages, populations, and ages; (d) ways to strengthen links between research and practice (the presence of several school directors at the meeting triggered important discussions on translational research and curriculum development); and (e) implications for policy and funding priorities. We begin our conclusion for this volume with a summary of the major themes raised across the chapters, and follow this with a set of key recommendations reflecting the full input of the symposium participants on necessary next steps in dyslexia research.

SUMMARY OF MAJOR THEMES RAISED BY PRESENTATIONS

One focus of this volume is to examine recent findings at multiple levels of analysis: genetics, brain structure and function, and cognitive phenotype. Progress in the field depends, in part, on developing the means to allow these distinct levels of analysis to inform and constrain one another in moving toward a neurobiologically grounded account of dyslexia.

Three chapters focus on genetic investigations. Rosen, Wang, Fiondella, and LoTurco (Chapter 2) discuss three candidate genes in dyslexia (*Dcdc2*, *Kiaa0319*, and *Dyx1c1*) and new techniques aimed at determining the role these genes play in typical or atypical brain development (including contributions from animal models). Early findings from this group have revealed a preponderance of mild cortical malformations known as ectopias (reflecting anomalous neuronal migration) in postmortem analyses of dyslexic brains. Thus Rosen's group targets genes that might be associated with atypical neurogenesis; their ongoing work with gene-disruption models in rats aims to make this crucial link. Although some of the work is in early stages, the integrated use of genetic analysis, animal models, and human phenotype studies promises to fill in important gaps in the extant knowledge. Grigorenko and Naples (Chapter 7) provide a critical review of the state of candidate genes for dyslexia, and their review suggests notable limitations on replicability (across studies) at present for key candidate genes. Striking a cautionary note, they make the case for both larger scale epidemiological studies in the next phase and a more cognitive view of reading and its component processes, which might encourage increased focus on complex genetic interactions in dyslexia research. Olson, Byrne, and Sameulsson (Chapter 11) provide us with an update on cross-linguistic longitudinal twin studies, which suggest a high degree of heritability for reading readiness and early formal literacy skills that appear to be similar in different languages and cultures. They raise a challenge from some of their data suggesting quite limited effects of instruction relative to heritability

weighting. This notion raises to the forefront ongoing questions regarding the relative weight of nature versus nurture and poses a challenge to the discussion on optimal instruction and remediation. We suspect that this dynamic will motivate new research questions and will figure prominently in next-phase remediation educational investigations.

All three of these chapters encourage gene–brain–behavior linkage research, but also reinforce the need for crucial developments in cognitive neuroscience to understand the phenotype more precisely. Clearly the next phase of research will need to attend to how we can make use of integrated brain–behavior measures to mediate the link between genetic variability and atypical reading behavior.

On the brain–behavior front, several chapters deal with current findings in cognitive neuroscience (with particular emphasis on powerful tools for structural and function brain imaging in humans). S. Frost et al. (Chapter 1) presented an update of recent functional magnetic resonance imaging (fMRI) findings: converging evidence from functional neuroimaging studies indicates that a key neurobiological marker of dyslexia is reduced activation of LH posterior regions relative to activation levels for nonimpaired readers during tasks that make demands on language and printed-word processing. However, it is interesting that recent evidence from intervention studies suggests that compromised LH systems appear to be responsive to intensive training in young reading disabled (RD) populations (Meyler, Keller, Cherkassy, Gabrieli, & Just, 2008; Meyler et al., 2007; Shaywitz et al. 2004; Simos et al., 2002; Temple et al. 2003). That is, many LH regions that are critically involved in reading and are not activated during reading tasks in young RD readers prior to an intervention period show increased activation after intervention. This reinforces the notion that these LH systems are poorly tuned but not fundamentally disrupted, opening the "for which children" question for the next-phase research—that is, which approaches to treatment will work for a given neurocognitive profile. Although some fairly consistent group differences are found in neurocircuits for reading and these are evident in different languages and with different imaging modalities (see Cornelissen, Chapter 9, for magnetoencephalography findings), functional mapping data largely describe a neurophenotype but do not provide information on the neurodevelopmental mechanisms responsible for the altered circuits. Frost et al. discuss these limits of functional neuroimaging and the need to broaden the investigation of neurobiological underpinnings in dyslexia. This broadening, they argue, should include increased focus on structural brain development and the neurochemistry of brain learning and plasticity, which they illustrate with preliminary findings from a longitudinal study that tracks at-risk children from 7 to 9 years of age with genetics, structural imaging, magnet resonance spectroscopy focused on measuring important neurochemicals and neurotransmitters, functional imaging, and cognitive testing. Ultimately, the aim of their work is to develop a multilevel, brain-based phenotype for genetic candidate analyses.

With a clear agreement across chapters on the need to use multimodal brain imaging techniques to gain a fuller account of both typical and atypical development, Mencl, Frost, and Pugh (Chapter 5) focus on the difficult but critical task

of using integrated neuroimaging designs (e.g., combined fMRI, event-related potential [ERP] measures to more fully reveal spatiotemporal patterns in reading) in developmental research. Clearly, the development of integrated imaging techniques and a new generation of multivariate analyses for these complex data will be a crucial target in the next phase of research.

Much of the symposium discussion focused on powerful tools for handling the sorts of data likely to emerge in next-steps research. Rueckl and Seidenberg (Chapter 6) provide a systematic account of computational models (with special focus on parallel distributed processing architectures) in reading and language. They propose that neural network classes of models could be employed to (a) develop a better understanding of complex neural dynamics in reading and language processing observed with functional neuroimaging studies, and (b) provide a means of capturing important differences from one language to another and across the developmental span associated with reading acquisition. They assert that computational models must provide a means of capturing learning, not just static performance levels.

With regard to new analytic tools, Francis (Chapter 4) provides an overview of powerful multivariate statistical methods that are relevant to the goal of multimodal data integration in cognitive neuroscience and to different definitional accounts of dyslexia. Francis particularly addresses whether dyslexia is best viewed as a continuous or discrete syndrome, and whether there may be legitimate subgroups in this population with distinct brain–behavior etiology. This emphasis on statistical methods for dealing with complex data sets will be crucial for meeting the research goals that call for larger scale, next-generation studies discussed later in this chapter.

Cognitive-behavioral profiles have a relatively longer history of empirical research than do genetics and neurobiology in the investigation of reading and reading disability. Therefore, there is sometimes a tendency to assume greater consensus on the phenotype than might be warranted by the state of current theory. Indeed, while most discussions on this topic reinforced the importance of phonological deficits that are uncontroversially implicated in dyslexia, a few major gaps in current cognitive accounts were discussed at the symposium.

Several symposium participants noted that the phenotypes present in variable forms across development, from preschool risk profiles where phonologically analytic processing deficits are pronounced to adolescence where comprehension difficulties play an increasing role. For instance, in Chapter 8, Ramus and Szenkovits acknowledge phonological deficits but report on a line of studies that did not indicate basic spoken-language processing difficulties in young adult dyslexics, although such difficulties would be anticipated by several prominent theories. Cutting, Eason, Young, and Alberstadt (Chapter 10) identify an important but understudied issue: whether deficits in comprehension might emerge as stumbling blocks in older struggling readers, even where phonologically analytic skills and basic word decoding that depends on these skills are within normal limits. Wolf, Gottwald, Galante, Norton, and Miller (Chapter 15) taking up these gaps, argue that reading is a highly integrated set of cognitive operations and that deficits

in any part or parts will retard development of fluency and comprehension. R. Frost (Chapter 12), presenting studies contrasting reading in Hebrew and English, argues that cognitive accounts may need to be adjusted to account for linguistic differences in different languages.

Much lively debate arose in the symposium sessions where these ideas were discussed, and these issues are touched upon in the preceding chapters. The key take-home message for next steps in dyslexia/reading disability research is simply that we cannot become too comfortable with general notions of phonological deficits; rather, we must continue to probe cognitive mechanisms with new research tools and we must do so considering developmental trajectories. Indeed, several symposium participants called for renewed focus on whether dyslexia in its behavioral manifestation is better viewed as continuous (the lower end of a normal distribution of language-related cognitive skills) or discrete. This is an old question, and given that it can still be legitimately debated suggests that phenotypic research needs are still acute.

We also have tried to bring renewed focus on language differences: to the degree that developmental dyslexia is gene based, we anticipate its presence in vastly different written languages. The cross-linguistic discussions at the symposium fueled enthusiasm for new research that will include systematic cross-language comparisons, as well as studies of individuals learning to speak and read more than one language. Such studies will allow us to identify both language invariant and idiosyncratic profiles in dyslexia and will promote better theory in the estimation of these participants.

Siegel (Chapter 14), Sherman and Cowen (Chapter 3), and Foorman and Al Otaiba (Chapter 13) provide stirring updates on intervention and instructional research that in broad terms are asking how we can best shape the learning environment to maximize outcomes for children with these distinctive brain–behavior profiles. Siegel notes that systematic remediation along the lines promoted in response-to-intervention (RTI) approaches can dramatically reduce the numbers of high-risk children (identified in first grade) by sixth grade. Moreover, this benefit was seen in her studies equivalently for bilingual and monolingual children. Foorman and Al Otaiba discuss current views on best practice in remediation and curriculum development, with a focus on the importance of monitoring student progress adequately and structuring remediation to the complex classroom environment. Wolf et al. (Chapter 15) explicitly discuss the need for treatments that can flexibly address component skills that are poorly realized in an individual and focus on strengthening complex brain circuits for reading. Sherman and Cowen discuss the need to understand strengths and talents in dyslexia and utilize this in differentiating instruction. They also raise the important issue of how literacy might be changing in this digital age, calling for this to be considered by educators in working with struggling readers.

Symposium participants agreed that treatment must be tailored to the individual. Even the best evidence-based practices will not impact some children. New advances in brain–behavior phenotype research hold promise of providing a more sensitive account of individual differences. As this phenotype is developed, we

will be better able to assess "what works for whom." Participants also acknowledge within this the need for preschool (school readiness) instruction as a crucial need in the field, to not only prevent reading difficulties for many children but also to enable us to better understand early brain–behavior risk markers. This should be a high priority in next-phase studies.

NEXT STEPS: A SUMMARY

With the symposium's discussions and debates as well as the updated presentations that have become the chapters of this volume in mind, we offer the resulting recommendations for next steps in research, policy, and practice. Symposium discussions were wide ranging and participants were initially encouraged to generate their wish lists for next steps. Some themes came through with high frequency:

- There is a need for a new generation of epidemiological studies with integrated genetics–brain–behavior designs, and with age ranges from pre-readers through older adolescent samples to assess age-appropriate skill sets.
- New and better tools are needed, particularly computational approaches for multimodal neuroimaging and cross-language comparative studies.
- There should be a renewed focus on definitions (e.g., continuous vs. discrete, subtypes, comorbidities, RTI, and what constitutes nonresponse).
- Work in the classroom and laboratory must be better integrated to improve delivery of reading instruction (e.g., cognitively informed, optimal-learning research; large-scale, school-based research projects; and a deeper focus on brain-based, individually tailored treatment research).

Each of these general targets will demand genuinely interdisciplinary teamwork and the development of a common language, multisite cooperation, and appropriate commitments from funding agencies and foundations. We discuss some of these in greater detail next.

New Generation of Epidemiological Studies With Integrated Genetics–Brain–Behavior Designs Across Age Ranges

The many intriguing findings from genetics through brain circuitry discussed at the symposium, and in this volume, are at present still largely descriptive (e.g., good readers and poor readers differ on some biologic index but we have limited information on cause versus consequence) and findings are still somewhat unconnected across levels of analysis and across age ranges. To generate a more integrated brain-based phenotype for dyslexia, the group unanimously called for a new generation of epidemiological studies using integrated neuroscience measures in conjunction with state-of-the-art behavioral testing to address key gaps in

knowledge with sufficient power and a clear developmental focus. Indeed, studies of this sort will demand large and representative samples of at-risk children and would perhaps be feasible only via a multisite collaboration.

Neuroscience measures would include state-of-the-art genetics with continued exploration of candidate genes, measures of the neurochemistry of learning and plasticity (with techniques like spectroscopy this can be done in vivo), structural neuroimaging (including morphometry and diffusion weighted tensor imaging), integrated multimodal functional neuroimaging (yoked electrophysiological and hemodynamic measures will allow more precise specification of the spatiotemporal organization for language and reading at different stages), and a renewed consideration of postmortem histological data to explicate links to animal models of dyslexia. The previous generation of large-scale epidemiological studies have been of great importance in establishing, longitudinally, the behavioral phenotype and developmental trajectories in high-risk populations, but given the explosion of findings in neuroscience, it seems rather clear that a next generation of large-scale longitudinal studies will need to examine the potential causal roles played by individual differences in these neurobiological factors in long-term reading outcomes.

At the behavioral level, renewed attention to the cognitive primitives underlying phonological processing deficits demands cognitively sophisticated paradigms that have not been the focus of previous large-scale studies using primarily standardized assessments. In addition, a new emphasis on reading comprehension and other postcode learning skills in older cohorts will be important in establishing age-appropriate expectations and in determining how higher level skills relate to basic phonological and language issues. Indeed, given the long-term limitations of conventional interventions, a deeper understanding of how decoding feeds into higher level comprehension mechanisms is clearly needed. By targeting toddlers and preschoolers, we can examine early speech perception/production trajectories in relation to later preliteracy skills and enable the targeting of genetic and neurobiological markers of risk. In short, by proposing a new generation of longitudinal studies with many of the tools discussed in this volume, a more integrated understanding of the brain–behavior bases of dyslexia is hoped for.

Of course, it is unsurprising that a group of researchers such as those participating in this symposium would call for new and larger scaled epidemiological longitudinal studies, given the intriguing findings at multiple levels of analysis available that nonetheless make evident such large gaps. However, this group suggested something more. It noted a need for integration across laboratories and research teams and projects, resulting in the use of common core sets of measures, analyses, and sampling decisions; in this way data acquired at different sites, and with different cohorts, might be cumulative in some very substantial manner. This suggestion begins to make sense when considering the value of extremely large samples for gene/phenotype studies. Without common standards, it would be difficult to aggregate data across labs.

Renewed Focus on Definitions

Definitional criteria for diagnosis of dyslexia are still subject to debate, confusion, and disagreement. This lack of consensus on defining characteristics can result in different researchers obtaining samples that are not comparable to one another, which muddies the waters when trying to assess why some findings fail to replicate across samples. This becomes even more acute when trying to examine dyslexia across different languages and orthographies, where again criteria are variable. As an example, in English, disabled readers are both error prone and dysfluent in word decoding, but in a very regular orthography like Finnish (where each grapheme maps to only one phoneme and vice versa), dysfluency is similarly seen but errors do not appear to be phenotypic in that language; however, diagnostic criteria are nonuniform across languages. This reinforces the need for ongoing research aimed at classification. It was generally agreed that brain–behavior methodologies have real promise in sharpening our classification and further research on biomarkers is recommended.

At present some researchers continue to employ a discrepancy criterion, where the discrepancy between IQ and some achievement measure is considered diagnostic of a learning disability, at least in terms of legally qualifying that student for special education services. Others simply use low achievement in reading as the inclusion or selection criterion for studies of reading difficulty/disability. However, recent work noting problems with the discrepancy criterion suggests that RTI is a potentially more useful approach (Department of Education Office of Special Education and Rehabilitation Services, 2002). In fact, based on the large body of research cited by the President's Commission on Special Education, the 2004 reauthorization of the Individuals with Disabilities Education Improvement Act (IDEIA, 2004) now allows states an alternative for identifying students with learning disabilities for special services. That alternative is RTI (Fletcher, Lyon, Fuchs, & Barnes, 2006; Haager, Klingner, & Vaughn, 2007): If a child fails to respond to increasingly intensive instructional interventions, then he or she is targeted for special, individualized educational services. RTI has great intuitive appeal, but validation studies will be crucial in order to set standards that will allow age, language, and cross-cultural comparative studies to be on a common footing. Thus, classification research for reading disability should be a continuing priority.

Even with fairly neutral criteria, such as achievement-based statistical diagnosis or promising uses of RTI, our ability to disentangle congenital from environmental factors is difficult because of the heterogeneity seen both in behavioral profiles and brain activation patterns within any cohort with reading difficulties. Fundamental questions like whether dyslexia represents the lower end of a normal distribution or a discrete typology await further research with some of the new statistical and neuroscience tools discussed earlier. However, it remains that there are large individual differences in any cohort of struggling or impaired readers, and even with similar reading deficits, it is hard to predict which children will be treatment responders or resistors to standard interventions. It was suggested by several participants at this symposium that additional gene–brain–behavioral

research be focused on parsing this heterogeneity by examining with neurocognitive tools whether there are legitimate subtype dimensions in those with reading problems, particularly in those with comorbidities (e.g., attention deficit/hyperactivity disorder [ADHD], math disability, general cognitive deficits). Although previous behavioral studies have been hard pressed, with conventional testing, to identify robust differences across these potential subtypes, it may be that conventional accuracy or latency measures lack the sensitivity needed. This matters because if dyslexia does not represent a uniform syndrome but rather a condition with many distinct neurobiological pathways with a common end-state (poor phonological and reading skills), this will have profound implications for theory, genetic mapping, and tailoring treatment. Many of the necessary tools are in place, so the potential for real momentum in classification and subtyping work is high.

Cross-linguistic research will benefit from classification work. With comparable neurocognitive measures, and agreed upon sampling criteria, we can begin to examine whether there are core language-invariant features of reading difficulty. There has been some speculation that the sets of deficits needed to produce reading failure in distinct languages and orthographies, varying in orthographic to phonologic regularity, might be partially nonoverlapping. At present, dyslexia research on brain bases or candidate genes is often done in different languages, but this is rarely considered as a potential complication by those researchers. Much more work on language-invariant markers versus language dependencies will be needed to bring this growing body of international research into alignment. Integrated cross-language collaborations are needed to generate a more nuanced understanding of reading difficulties.

Integration of Laboratory Research and Classroom Instruction

A good deal of emphasis was placed on learning, plasticity, and optimal treatment at this meeting. Moreover, the dialogue between researchers and school directors at the meeting brought the questions of what works for whom into central focus. Again, given the early findings that brain imaging can be sensitive to treatment responses, there was a good consensus on the potential value of further neurocognitive plasticity studies. Brain–behavior profiles can reveal important individual differences not always evident in performance on standardized assessments. A next generation of studies looking at pretreatment subtypes by treatment interactions may be able to begin to deliver on the promise of brain-based learning. Again, such work would benefit from multisite collaborations. One tangible outcome from this discussion was a plan to bring research into schools more fully. Independent dyslexia school directors have organized a consortium of educational leaders and researchers to identify designs and plans for school-based research, potentially facilitating the use of schools as research laboratories in a mutually beneficial partnership. For multisite collaborations, it will be crucial to ensure common outcome measures across sites, carefully gathered demographic and cognitive data, state-of-the-art measures (both brain and behavior), and data quality control.

An important question to be addressed through such large-scale networks is which treatments work for whom. However, a high level of enthusiasm was seen in the discussion for a next generation of studies that will systematically vary learning protocols based on cognitive principles. For instance, if a treatment must include A, B, and C, is there a theory-driven "best way" to sequence and weigh these necessary elements (and does this optimal approach vary in different ages, subtypes, languages, or brain phenotypes)? Indeed, Pugh and colleagues reported on a new study reinforcing latent plasticity in older poor readers at the level of brain circuitry, but suggested that learning may not become well consolidated in many dyslexics. Can the treatment be tailored to reflect principles of learning and memory that are well established in humans and animals so as to enhance gains? Of course, the question is whether a more developmentally broad focus will lead us to think somewhat differentially about optimal learning strategies in older and younger cohorts, and how instruction in decoding can be built upon to include higher level language operations relevant to comprehension.

Finally, with respect to optimal instruction, several participants from both the research and school communities pointed to an acute need to better understand talents and strengths in dyslexia to optimize learning environment (see Sherman & Cowen, Chapter 3, this volume). School-based research, while challenging, has already shown great promise to allow a richer and larger scale approach to optimal instruction. Access to concentrated groups of students with reading difficulties may enable even more rapid progress in some areas of investigation. Thus, strengthening partnerships with schools to promote innovative instructional research, development of better gene–brain–behavior models, statistical methods to assess heterogeneity and subgrouping, cognitively motivated work with optimal instruction, and cross-linguistic comparative studies were all topics of high interest in our discussion of next steps in remediation and optimal instruction.

In conclusion, as we consider the wealth of new information presented by the authors in this volume, and as a group their recommendations for how to go about improving our current understanding with new epidemiological studies that are gene–brain–behavior based, renewed focus on definitions with these new tools, and more integrated and cognitively grounded treatment research (supported by strong school–researcher partnerships), we are enthusiastic about these next steps. We hope that the development of new measures, the launching of new neurobiological longitudinal studies, and school–research cooperation will facilitate putting ideas raised in the chapters in this book into action.

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